SEVENTH FRAMEWORK PROGRAMME
THEME 3
Information and Communication Technologies

Challenge 5. Towards Sustainable and personalised healthcare
Objective ICT-2009.5.1: Personal Health Systems

Collaborative Project – Large scale collaborative Project

REACTION

Annex I - "Description of Work"

Project acronym: *REACTION*
Project full title: Remote Accessibility to Diabetes Management and Therapy in Operational healthcare Regimes.
Grant agreement no.: *FP7 248590*

Date of preparation of Annex I (latest version): v5.2, 09/12/2009
Date of approval of Annex I by Commission: *(to be completed by Commission)*

Table of Content

PART A

A1. Project summary and budget breakdown

A.1 Project summary

A1:
Our project

Project Number [1]	248590	Project Acronym [2]	REACTION

One form per project			
General information			
Project title [3]	Remote Accessibility to Diabetes Management and Therapy in Operational healthcare Networks		
Starting date [4]	01/01/2010		
Duration in months [5]	48		
Call (part) identifier [6]	FP7-ICT-2009-4		
Activity code(s) most relevant to your topic [7]	ICT-2009.5.1: Personal Health Systems		
Free keywords [8]		Diabetes care management, remote monitoring, SOA, interoperability, GCM, Continous Glucose Monitoring, closed-loop feedback	

Abstract [9]
The REACTION project will develop an integrated approach to improved long term management of diabetes; continuous blood glucose monitoring, clinical monitoring and intervention strategies, monitoring and predicting related disease indicators, complemented by education on life style factors such as obesity and exercise and, ultimately, automated closed-loop delivery of insulin.   The REACTION platform will feature an interoperable peer-to-peer communication platform based on a (SoA) service oriented architecture – all functionalities, including devices, are represented as services and applications consisting of a series of services orchestrated to perform a desired workflow. The REACTION platform also features a Model Drive Application Development environment based on extensive use of dynamic ontologies and advanced Data Management capabilities with algorithms for clinical assessment and rule-based data processing. The intelligent, interoperable platform developed by REACTION will provide integrated, professional, management and therapy services to diabetes patients in different healthcare regimes across Europe, including 1) professional decision support for in-hospital environments, 2) safety monitoring for dosage and compliance, 3) long term management of outpatients in clinical schemes, 4) care of acute diabetic conditions and 5) support for self management and life-style changes for diabetic patients.   A range of REACTION services will be developed targeted to insulin-dependent type 1 diabetic patients. The services aim to improve continuous blood glucose monitoring (CGM) and insulin therapy, by both basal dose adjustment and contextualised glycaemic control based on patient activity, nutrition, stress level, etc. Decision support will assist healthcare professionals, patients and informal carers to better manage diabetes therapy and make correct choices about e.g. good blood glucose control, nutrition and exercise.

A.2 List of beneficiaries

A2:
List of Beneficiaries

Project Number [1]	248590	Project Acronym [2]	REACTION

List of Beneficiaries					
No	Name	Short name	Country	Project entry month[10]	Project exit month
1	ATOS ORIGIN SOCIEDAD ANONIMA ESPANOLA	ATOS	Spain	1	48
2	CNet Svenska AB	CNET	Sweden	1	48
3	DELTA DANSK ELEKTRONIK, LYS & AKUSTIK	DELTA	Denmark	1	48
4	INSTITUT FUER MIKROTECHNIK MAINZ GMBH	IMM	Germany	1	48
5	FOUNDATION FOR RESEARCH AND TECHNOLOGY HELLAS	FORTH-ICS	Greece	1	48
6	FRAUNHOFER-GESELLSCHAFT ZUR FOERDERUNG DER ANGEWANDTEN FORSCHUNG E.V	FHG-SIT	Germany	1	48
7	Hellenic Telecommunications & Telematics Applications Company	Forthnet	Greece	1	48
8	IN-JET APS	IN-JET	Denmark	1	48
9	ALKALMAZOTT LOGIKAI LABORATORIUM KUTATO FEJLESZTO SZOVETKEZET (Applied Logic Laboratory)	ALL	Hungary	1	48
10	Medizinische Universitaet Graz	MUG	Austria	1	48
11	JOANNEUM RESEARCH FORSCHUNGSGESELLSCHAFT MBH	MSG	Austria	1	48
12	Chorleywood Health Centre	CHC	United Kingdom	1	48
13	BRUNEL UNIVERSITY	UBRUN	United Kingdom	1	48
14	VRIJE UNIVERSITEIT BRUSSEL	VUB	Belgium	1	48
15	BAYER TECHNOLOGY SERVICES GMBH	BTS	Germany	1	48
16	SOLIANIS MONITORING AG	SOLIANIS	Switzerland	1	48

A.3 Overall budget breakdown for the project

A3:
Budget Breakdown

| Project Number [1] | 248590 | | | Project Acronym [2] | REACTION | | | |

One Form per Project

Participant number in this project [11]	Participant short name	Fund. % [12]	Ind. costs [13]	Estimated eligible costs (whole duration of the project)					Total receipts	Requested EC contribution
				RTD / Innovation (A)	Demonstration (B)	Management (C)	Other (D)	Total A+B+C+D		
1	ATOS	50	A	349,316.00	26,624.00	463,452.00	13,312.00	852,704.00	0.00	664,734.00
2	CNET	75	A	1,414,916.00	108,772.00	211,873.00	24,172.00	1,759,733.00	0.00	1,351,618.00
3	DELTA	75	A	1,390,140.00	158,240.00	6,000.00	31,648.00	1,586,028.00	0.00	1,159,373.00
4	IMM	75	A	1,838,171.00	0.00	6,000.00	90,514.00	1,934,685.00	0.00	1,475,142.00
5	FORTH-ICS	75	A	1,030,450.00	0.00	4,750.00	8,793.00	1,043,993.00	0.00	786,380.00
6	FHG-SIT	75	A	1,083,010.00	24,360.00	4,000.00	48,720.00	1,160,090.00	0.00	877,157.00
7	Forthnet	50	A	647,900.00	24,300.00	6,000.00	16,200.00	694,400.00	0.00	358,300.00
8	IN-JET	75	F	466,600.00	20,400.00	12,000.00	267,607.00	766,607.00	0.00	639,757.00
9	ALL	75	T	513,600.00	0.00	3,000.00	14,720.00	531,320.00	0.00	402,920.00
10	MUG	75	T	728,280.00	0.00	21,280.00	37,120.00	786,680.00	0.00	604,610.00
11	MSG	75	A	884,207.00	0.00	6,000.00	10,679.00	900,886.00	0.00	679,834.00
12	CHC	75	T	430,120.00	0.00	3,000.00	34,560.00	467,680.00	0.00	360,150.00
13	UBRUN	75	T	896,160.00	0.00	26,480.00	69,120.00	991,760.00	0.00	767,720.00
14	VUB	75	T	391,800.00	0.00	3,000.00	8,800.00	403,600.00	0.00	305,650.00
15	BTS	50	A	1,724,909.00	0.00	6,000.00	16,781.00	1,747,690.00	0.00	885,235.00
16	SOLIANIS	75	T	622,960.00	0.00	3,000.00	11,200.00	637,160.00	0.00	481,420.00
Total				14,412,539.00	362,696.00	785,835.00	703,946.00	16,265,016.00	0.00	11,800,000.00

PART B

B1. Concept and objectives, progress beyond state-of-the-art, S/T methodology and work plan

B.1.1 Concept and project objective(s)

Overview

The REACTION project aims to research and develop an intelligent service platform that can provide professional, remote monitoring and therapy management to diabetes patients in different healthcare regimes across Europe.

The REACTION platform will feature an interoperable peer-to-peer communication platform based on a service oriented architecture – all functionalities, including devices, are represented as services and applications consist of a series of services orchestrated to perform a desired workflow.

The REACTION platform can execute various clinical applications for monitoring of vital signs, context awareness, feed-back to the point of care, integrative risk assessment, event and alarm handling as well as integration with clinical and organisational workflows and external Health Information System. The REACTION platform features a Model Drive Application Development environment based on extensive use of dynamic ontologies and advanced Data Management capabilities with algorithms for clinical assessment and rule-based data processing.

A range of REACTION applications will be developed mainly targeting insulin-dependent type 1 patients. The applications aim to improve continuous blood glucose monitoring (CGM) and tight glycaemic control for improved insulin therapy management and bolus dose adjustments.

The developed applications will assist healthcare professional, patients and informal carers, to better manage diabetes insulin therapy in a variety of settings, help patients understand their disease, support self-management and provide a safe environment by monitoring adverse and potentially life-threatening situations with appropriate crisis management.

In the REACTION environment, type 1 diabetes patients will be continuously monitored with wearable non-invasive and minimally invasive Continuous Glucose Monitoring (CGM) sensors based on novel technologies such as Impedance and IR spectroscopy. The CGM sensors are micro machined and embedded in electronic plasters (ePatch) for wearability and comfort. They connect through a wireless Body Area Network to any available network infrastructure in the patients surroundings. Other body and room sensors provide contextualisation. Data are transmitted in a secure way to healthcare professionals and medical knowledge systems and legacy Health Information Systems and results are fed back to the point of care.

The project will focus on and validate the REACTION platform in two operational healthcare domains 1) professional decision support in hospital environments for diabetic patients admitted to the general wards, and 2) control and management of outpatients in clinically diabetes schemes, including therapy compliance and support for self management. All applications will include closed-loop feedback mechanisms in a variety of forms.

In the first application domain, the REACTION platform will connect to healthcare professional, medical expert knowledge systems and legacy healthcare systems and offer closed-loop feedback in hospital environments to carers at the point of care. In the second application domain, the REACTION environment will target the outpatient regime and facilitate personalised feedback to clinicians and patients, including medium term risk assessment for patient education and life-style change support. In a third application, the project aims to demonstrate and

evaluate closed-loop glycaemic control schemes with autonomous regulation of insulin dose through a closed-loop approach, which will include some predictive insulin assumptions.

REACTION will be based on the concept of trust as a multilateral relation between stakeholders in a community of patients, informal carers and professional healthcare providers. Hence, the platform will include mapping and brokering between security models, and user and device profiling management. The REACTION privacy model will also have support for virtualisation of devices and users for secure connectivity and delegation of services, as well as user empowered authentication and authorisation.

Security and safety of the proposed services will be studied and necessary solutions to minimise risks and preserve privacy will be implemented. Particularly in relation to automatic glycaemic control, the safety aspects are extremely important. A legal framework for patient safety and liability as well as privacy and ethical concerns will be analysed and an outline of a policy framework will be defined.

The REACTION environment will be complemented by sociological research aimed at understanding ethical and social aspects of monitoring. The research will provide insight into regional cultures and ethical localism focusing on issues such as autonomy, privacy, fear of surveillance. Further, usability aspects, inclusion and techno-animism will be studied and fed back into the REACTION environment to improve the design.

Finally, aspects of health economics and organisational implementation will be studied in the context of implementation of REACTION platforms in real life healthcare domains. The work will provide a suitable framework for analysis of value creation and business modelling, which will allow accurate and viable metrics for cost-effectiveness and organisational adaptability.

Background

Diabetes mellitus is a metabolic disorder characterised by hyperglycaemia (high blood sugar) resulting from defects in the production of or in the body's response to insulin. The disease has two main forms: type 1 and type 2. Type 1 disease is characterised by diminished insulin production resulting from the loss of beta cells in the pancreatic islets of Langerhans, in most cases caused by immune-mediated cell destruction. Disease management entails administration of insulin in combination with careful blood glucose monitoring. Type 2 diabetes sufferers in contrast exhibit both reduced insulin production and resistance or reduced sensitivity to insulin.

Type 2 diabetics are typically over 50 years old with additional health problems, especially cardiovascular disease (CVD). Management principally involves the adjustment of diet and exercise level and the use of oral anti-diabetic drugs (OADs) and insulin to control blood sugar.

Diabetes mellitus has reached epidemic proportions in western countries (Zimmet2001). Diabetes type 2 is one of the fasted growing chronic conditions in the developed world. In Britain, a total of about 3% (1.3 million) of the population have diagnosed diabetes. It is estimated that an additional 2% of the population have undiagnosed diabetes. Type 2 diabetes is very closely linked to the emerging epidemic of obesity and life style, which is now a major cause of preventable health problems.

The associated morbidity and mortality of diabetes represents a major healthcare burden. Diabetes can cause many complications if the disease itself and associated risk factors (e.g. blood pressure and hyperlipidemia) are not adequately controlled. These complications include CVD, chronic renal failure, eye disease leading to blindness and neuropathy. Thus, diabetes increases CVD risk 2-3 fold, which is the most common cause of renal failure and blindness, and increases the risk of amputation by 20-30%.

There is abundant evidence that shows tight control of the blood glucose level to be vital for good diabetes management and insulin therapy. Good glucose control requires frequent measurement of blood glucose levels and complicated algorithms for assessing the insulin dose needed to adjust for short term variations in activity, diet and stress.

On the other hand, good control of diabetes, as well as increased emphasis on blood pressure control and lifestyle factors, may improve the risk profile of most complications and attain future good health. Hence, self-management of diabetes is an area that offers exceptionally good prospects, both in clinical terms and in economical terms. The overall health status of type 2 diabetics can be improved by adequate treatment of diabetes and of the associated risk factors. Self-management of diabetes in which the patient measures blood glucose several times a day and uses the resultant data to gauge the required insulin dosage is a promising modality.

Blood glucose is typically measured in a drop of capillary blood using a disposable dry chemical strip and reader device, an uncomfortable and slow process. Tight Glucose control (TGC) requires almost continuous measurements and different sensors for continuous blood glucose measurement have been under development for the last two decades.

Minimally invasive sensors able to measure glucose in interstitial fluid, and thus more suitable for self-monitoring, have also been developed. To date, however, none of these has delivered a level of performance sufficient for use in routine glucose monitoring. Robust, clinically acceptable devices are however widely expected to become available in the near term. The REACTION platform will be developed with a view to integrating the most promising transcutaneous and minimally invasive continuous glucose sensor into an ePatch technology platform.

Vision and aims

The vision of the REACTION project is:

> *that the REACTION platform will assist healthcare professionals in hospital wards to improve glycaemic control of admitted patients with diabetes type 1 and type 2 using continuous blood glucose monitoring (CGM) and therapy feed-back.*

> *that the REACTION platform will help insulin-dependent type 1 diabetic outpatients to better control their disease with closed-loop feedback from their physician and provide appropriate risk assessment services that can help them to better understand their disease and how they can manage it.*

> *that the REACTION platform will implement enhanced strategies to support pro-active long term management of type 1 and type 2 diabetes to reduce risk of developing long term complications.*

> *that the REACTION platform will better support diabetes patients in the case of adverse and potentially life-threatening episodes and experiencing short term acute exacerbations.*

> *that the REACTION platform will demonstrate automatic closed loop glycaemic control using autonomous regulation of the devices' own operation.*

> *that the REACTION platform will be able to successfully demonstrate Automatic Glycaemic Control (AGC) using autonomous regulation of the devices' own operation and automatic insulin dose pumps.*

The REACTION platform thus has the potential to become a Europe-wide eHealth service platform for improved glycaemic control of diabetes patients whether admitted to hospital, in an outpatient programme or just coping with their disease in their daily lives.

The REACTION concept and technological objectives

The REACTION platform consists of subsets of production servers for data management, security, application execution and communication. All servers interoperate on the basis of web services and are thus completely platform agnostic and scalable.

A software development toolkit allows for rapid development of REACTION applications. The REACTION platform connects to sensors and devices in the Patients' Sphere and to healthcare professionals and informal carers as well as emergency and crisis management teams in the Carers' Sphere. It also connects to Health Information Systems (HIS) and external medical knowledge repositories (e.g. biomedical models) and security providers as visualised in Figure 1.
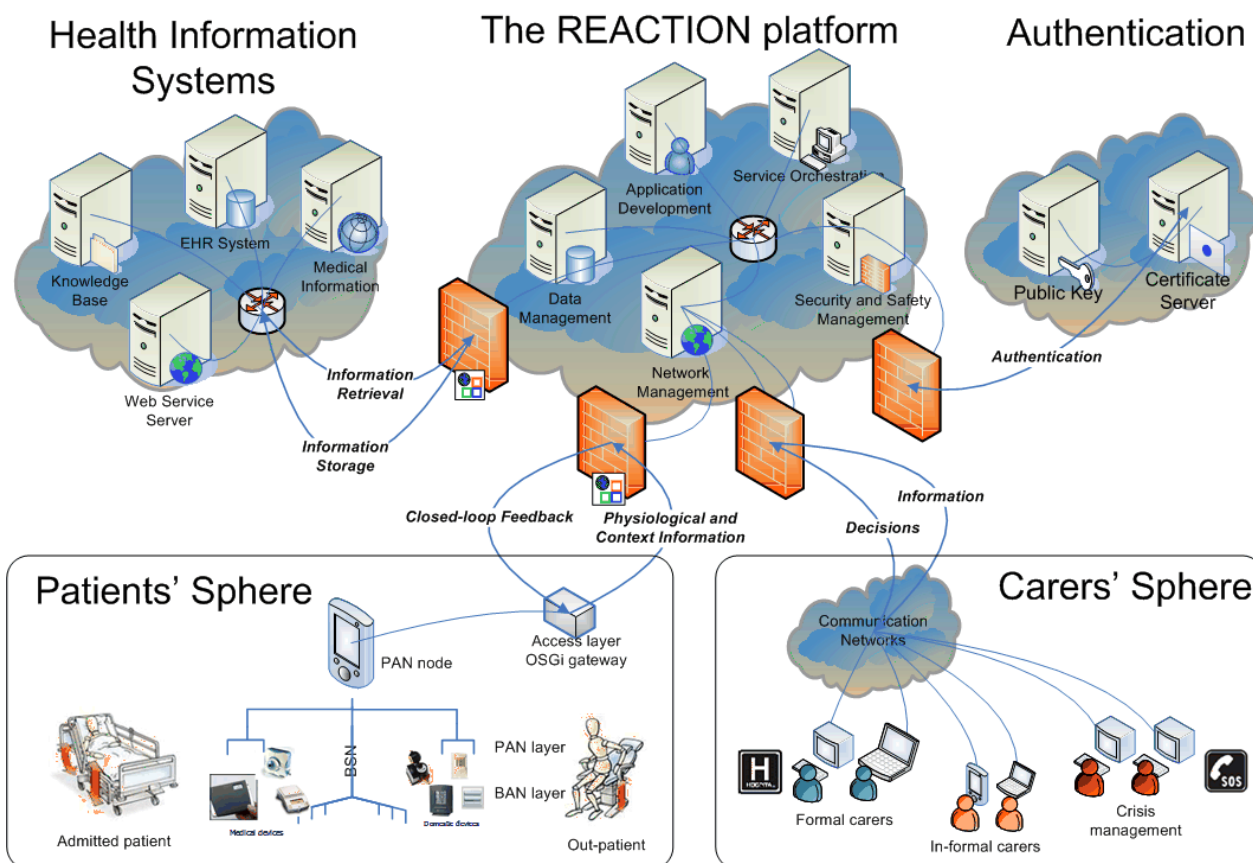
Figure 1 The REACTION platform concept

The Patients' Sphere

Wearable medical sensors are connected in a Body Area Network (BAN) for multi-parametric recording of vital physiological parameters. The BAN interconnects with other sensors in the environment that can record contextual information about the other vital parameters and the patients' activities (Personal Area Network – PAN). Data are pre-processed and formatted in the access layer active nodes/ gateways, which operates personalised software bundles in an OSGi (Open Service Gateway initiative) framework. The gateway can also handle simple episode monitoring and alarm handling and other services, which are needed during periods of non-connectivity.

The gateway also manages personalised feedback from health professionals adapted to the available user terminals, as well as self-monitoring and autonomous regulation of the connected devices in the BAN. For devices not capable to operate web services (due to resource constraints or proprietary concerns), the gateway also dubs as a platform for virtualisation of devices.

Data are transmitted securely to and from the REACTION platform through fixed or mobile public or proprietary networks.

The REACTION platform

The REACTION platform is the central production environment for the deployment of REACTION applications. It consist of five subsets each responsible for their part of the overall functionality.

1. The Data Management subset is central to the high level functioning of applications and services deployed on the platform. It implements the model-driven architecture for application development and deployment, the service oriented architecture for core service functionalities, data manipulation, data fusion and event handling. It also manages data transfer to and from nodes and stakeholders in a REACTION environment.

2. A Service Orchestration subset will orchestrate the different services available in a pre-described sequence for execution. This component introduces higher abstraction mechanisms and makes the application developer independent of using a specific programming environment to orchestrate REACTION applications.

3. The Network Management subset is responsible for the physical communication between devices, persons and external repositories. Each PAN node will have its own Network Manager and each Network Manager will have an external Web Service based interface where it can exchange data with remote Network Managers.

4. The Security Management subset will perform mapping and brokering between security models, user and client devices profiling management, mapping and usability between trust domains, and semantic standards and generalisation ontologies development.

5. The Application Development subset is an open SDK toolkit for model-driven development of applications that use the REACTION platform.

Applications are developed and deployed to execute comprehensive tasks. Each application serves specific goals and is constructed from a series of standardised workflows and business rules. An example of this could be monitoring of a patient's correct insulin intake. One workflow consists of reading blood glucoses levels and dietary intake at determined intervals. Another workflow will determine recommended bolus dose (fast acting) insulin from these readings and feed it back to the patient. A third workflow will read the actual insulin intake whereas a fourth workflow will compare the two and fuse the information to various stakeholders. Applications are developed and stored in the form of conceptual domain models (ontologies). The domain model describes the functionality, the objects involved (devices, users, rule sets, repositories, etc), the security model to be used and the run-time environment. Applications are easy to build, modify and deploy and features very effective application development and roll-out to various locations. The various levels of abstraction handled in the REACTION platform are explained in Figure 2.
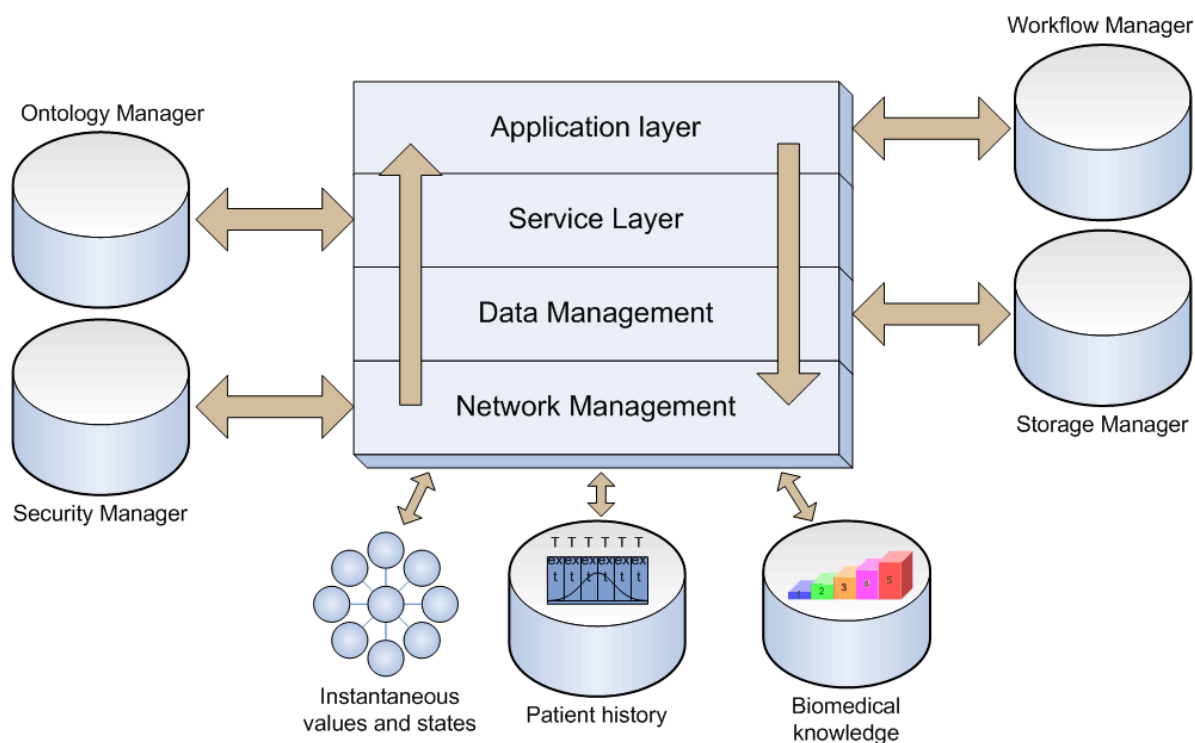
Figure 2 REACTION abstraction levels

At the very top we find the Application Layer. Applications are developed and deployed to execute complex tasks. Each application serves specific goals and is constructed from a series of standardised workflows. Applications are developed and stored in the form of conceptual domain models. The domain model describes the service, the objects involved (devices, users, rule sets, repositories, etc). An adapted subset of the HL7 standard will be used to describe the domain taxonomy. The common domain model will be mapped to an operative data model, which is implemented in the Service Layer.

At the second layer, the Service Layer, applications are translated into service components. Each workflow in the application consists of a series of services. The services are structured in an operative data model, which is implemented by XML schemas and a set of Web Service interfaces. The service ontology presents high level concepts describing service related information, which will be used in both development and run-time processes. Since each device, person and repository is basically accessible as a service, the service device ontology enables a developer to create new instances for any device type, which are filled with real data at run time. A set of services will be developed for monitoring, feedback, alarm handling, user interaction, etc.

The Data Management subset is basically a runtime environment that transforms data into information. It performs data manipulation and conditioning, translation between state domain and real time domain, simple data analysis, queries, contextualisation of data, and fusion of data to the next node, either upwards to the Service Layer or downwards to external devices or repositories.

Data manipulation may take the form of linearization, extrapolation, interpolation, extraction or contraction, reformatting etc. Translation between state domain and time domain is also performed here. The simple data analysis can consist of basic Boolean operations comparing real time data with thresholds or observing state changes. Data Management may also invoke extended services for special tasks such as prediction of short term insulin needs, e.g. changes in bolus dose insulin according to pre-programmed algorithms.

It can invoke extended services that query healthcare professionals for intervention and decisions. One service could present historic data on insulin therapy and query for at decision on changes in basal (long term) insulin dose. The Data Management subset also provides more advanced querying functionality hardcoded in specific Web-Service methods.

Context awareness is achieved through semantic annotation of patients' device data, data coming from the environment, and data from the patients' historical information in EPR repositories. Finally, the server is responsible for providing transparent storage for the various services.

A series of Data Management services will be developed. Some are common services across the platform and some are specific services encompassing special algorithms to be used in the developed prototypes.

The Data Management subset also implements the security model. Security will be implemented either centrally or locally; the pros and cons depending on the actual applications. For strongly centralised applications, i.e. in hospital wards, where the objects are relatively tightly coupled, a centralised security model is a possibility. For achieving the protection goals, the Security Manager has to be contacted before every call to the Network Manager for decryption, verification of signatures, logging, etc.

For applications using very loosely coupled devices that come and leave the platform, a decentralised structure is preferable and functionalities for communication protection have to be included in every single component. In these cases, the Security Manager can be used as a stand-alone security component key management and general cryptographic purposes.

Health Information Systems (HIS)

The information flows and interaction between the health information systems (HIS) and the REACTION platform provide the Knowledge Management capabilities of REACTION applications. The data are promoted to information by context awareness in the Data Management subset. And information can be promoted to knowledge by querying Health Information Systems. Information about the patient's actual health parameters needs to be place in the context of the patient's medical history, which is obtained from the HIS Electronic Patient Record. Evidence Based case management requires access to knowledge bases where carers can correlate medical knowledge to the case in question. Knowledge bases can be automatically updated with randomised case information for improved case management. Also health information from outside the REACTION platform is accessible. Comprehensive physiological models can be access via web interfaces and the result fed back to the physician responsible for the case. General medical and clinical information in the open internet can be semantically queried and the results put together in a comprehensive report on risk assessment, which will be personalised and presented to the patient in the self-management scheme.

Also information to assist in crisis management is available via web services, such as route planning, resource planning, i.e. where is the nearest qualified nurse and how long time will it take to get to the patient?

Health Information Systems will be integrated in REACTION applications in form of services. Services can be simple query services or data storage services. Or they can be more complex interactive services. In all cases, these services can subsequently be orchestrated in workflows by the Service Orchestration subset.

The Carers' Sphere

The REACTION platform connects to a broad range of stakeholders and provides multiple ways of feedback to the patient or to any object in the Patient's Sphere, including actuators. Data, information and knowledge are transmitted in personalised form from the Data Manager to various stakeholders.

Medical information and clinical pathway assessment and adjustment, medication adjustments or general medical information is available to healthcare professionals in hospital wards, outpatient clinics, general practice, therapy and rehabilitation centres, etc. Health status, risk assessments, self-management incitements, and other data about the patients are transmitted to patients and other informal carers such as family members, friends, neighbours etc. Finally, contextualised health information is transmitted to crisis management centres and emergency response teams.

Time lags

Applications using feedback loops, which are deployed on the REACTION platform, are subject to various forms of loop delays. The delays originate from various sources: Physiological delays in the patient, delays in the sensor body itself (measuring times, averaging, relaxation) and delays embedded in the communication network and the REACTION platform.
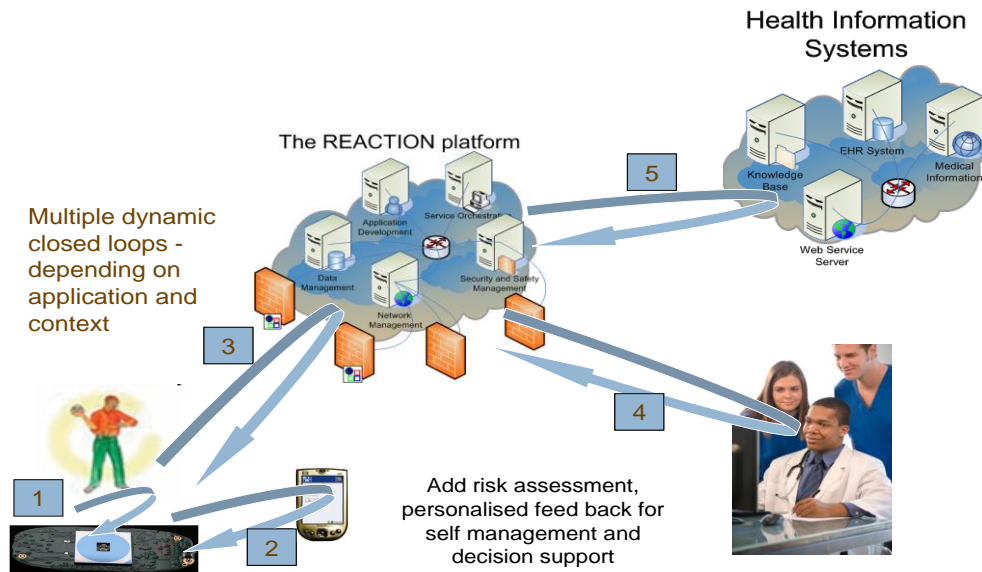
Figure 3 Five types of closed-loop applications in REACTION

It is important that these delays are considered during the design of the application. Some delays may have severe medical impact on the performance of the application and its services.

Delays in sensors and the immediate BAN and PAN networks are coursed mainly be physiological and sensor delays (loop 1). The physiological delays are functions of blood flow whereas the sensor delays depend on the computation time of the sensor logic. If the BAN and PAN network are involved (loop 2), further delays are caused by protocol handling and data transmission in the BAN and PAN networks. A special type of delays that must be taken into account is black-out or uptime on these networks. When designing applications, it must be carefully studied what delays and black-outs are acceptable. Some applications cannot accept this and should be designed to run as close to the sensor as possible, if not on the sensor itself. However, this may severely restrict the functionality of the application and some compromise will have to be done. Some BAN and PAN networks may have data storage which may alleviate the problem of black-out, but introduce severe security issues in return.

Applications that involve the REACTION platform (loop 3) and the HIS backend (loop 4) are subject to even further network delays and black-outs. The added functionality and the access to extreme data repositories comes with a price. The designer should keep in mind that the use of SoA and web services throughout the REACTION platform is not without cost. Real time or near-real time applications should be kept as close to the patient and the sensor as possible.

Finally, when applications involve humans in the loop in the form of healthcare professionals or informal cares, delays become very large and may even be unpredictable.

In the table below the most important sources of delay are listed as well as some pointers to the cause of the delay.

Loop Typical time lag	BAN <1 sec	PAN <1 sec	Platform <30 sec	HIS < 10 m	Carers 1 m - 3 h
Physiological	Blood flow rate and tissue perfusion, etc. Small, comp. by app.	Same Small, comp. by app.	Same Small, comp. by app.	Anthropometrics, Disease progression	Physical activity, diet, insulin secretion Human intervention
Sensor	Computational power Simple rules	Communication. Used for storage requirements	n/a	n/a	n/a
Network	n/a	Protocols Used with more complex rules	Significant and stochastic, SOA Rules processing	Search methodology Data mining Knowledge	n/a

**Table 1 Comparison of target outcome and REACTION feature**

Clinical focus

The application focus for the REACTION project is three-fold and will be developed through the entire length of the project.

In-hospital hyperglycaemia has been found to be an important marker of poor clinical outcome and mortality among diabetic patients. The first application domain of the REACTION platform will feature a suite of services aiming at Tight Glycaemic Control (TGC) of diabetics in the general hospital ward using multi-parametric monitoring and closed-loop feedback to the healthcare professionals at the point of care.

Figure 4 Clinical domain focus
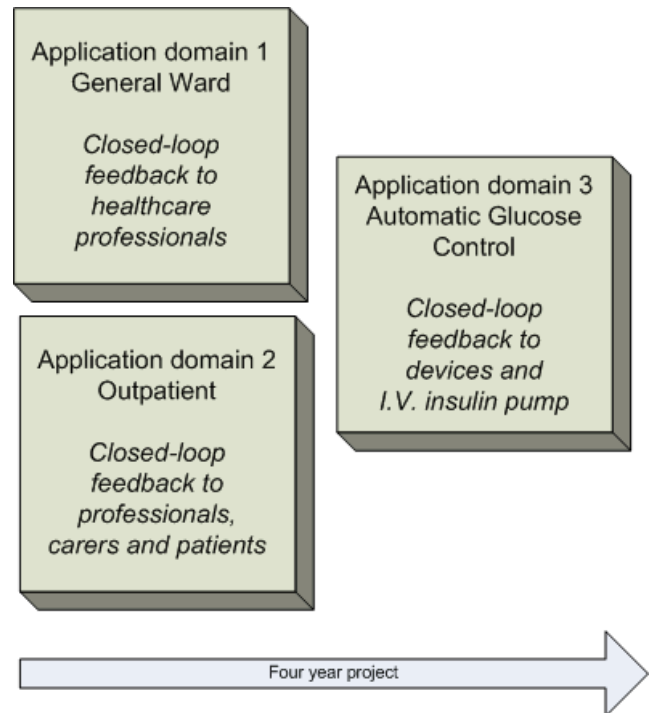
The other focus area is an integrated approach to long term management of diabetes control; improved blood glucose monitoring, monitoring related disease indicators, clinical monitoring and intervention strategies, as well as education on life style factors such as obesity and exercise.

Application domain 1
General Ward

Closed-loop feedback to healthcare professionals

Application domain 2
Outpatient

Closed-loop feedback to professionals, carers and patients

Application domain 3
Automatic Glucose Control

Closed-loop feedback to devices and I.V. insulin pump

Four year project

REACTION applications will be developed for this domain that will monitor medication compliance, multi-parametric monitoring of related disease indicators as well as episode monitoring and emergency alarm handling.

All applications will be developed and validated in field trials using clinical infrastructures provided by the partners (a hospital and an outpatient clinic).

After the successful implementation of applications in these two domains, the project will further explore an Automatic Glucoses Control system, in which control parameters from CGM sensors are analysed in the REACTION Data Management subset and results are fed directly to I.V. insulin infusion pumps.

General ward domain

Although several guidelines for treatment regimen for outpatient management of type 2 diabetes have been defined (Sakharova2005); (Das2005); (Charles2005), no clear definitions of treatment regimen have been found for the establishment of glycaemic control of hospitalised patients (Clement2004);(Gautier1996).

Diabetes mellitus has been associated with a two- to four-fold increase in hospitalization rates and in-hospital hyperglycaemia has found to be an important marker of poor clinical outcome and mortality especially in patients with type 2 diabetes. Hyperglycaemia and insulin resistance are common

"Diabetes is the fourth most common co-morbid condition complicating all hospital discharges."

"In 1997, diabetes was present in 9.5 percent of all patients discharged from hospitals and in 29 percent of patients undergoing cardiac surgery."

"Diabetes is associated with a two- to four-fold increase in hospitalization rates; its presence increases the length of hospital stays by one to three days, depending on the admission diagnosis."

"In-hospital hyperglycemia is an important marker of poor clinical outcomes and mortality in patients with or without diabetes."

"Although several organizations have issued guidelines for outpatient management of diabetes, no guidelines have been formulated for inpatient management."

"Metabolic regulation of hyperglycemia translates into improved outcomes in patients with diabetes and in those who develop hyperglycemia in the hospital."

"The next great challenge will be implementation of these standards. Hospital systems will have to change to achieve the goals defined above. Hospital- and ward-wide protocols for administration and monitoring of blood glucose levels and insulin infusions will be needed, as will protocols for risk management for hypoglycemia. Furthermore, a broad base of medical and surgical specialists must participate if we are to be successful in reducing diabetic inpatient mortality and morbidity rates; greater integration of care across units and the support of nursing and pharmacy staff will be needed."

ALAN J. GARBER, M.D., Ph.D., is professor in the Departments of Medicine, Molecular and Cellular Biology, and Biochemistry and Molecular Biology at Baylor College of Medicine, Houston, Texas.

in severe illness and are often associated with physical and mental stress. Stress-induced hyperglycaemia can lead to significant deterioration in glycaemic control in individuals with

diabetes and can cause stress-induced diabetes mellitus in non-diabetic patients. Studies have shown that frequency of hypoglycaemia in surgical ICU's (Intensive Care Units) can amount to 15 - 17 % of all admitted patients (Ellmerer2008) and there are increasing efforts world-wide to establish tight glycaemic control in critically ill and hospitalised patients.

Hyperglycaemia and use of aggressive insulin therapy in surgical ICU's is relatively well known. Not so for the much more widespread cases of stress-induced hyperglycaemia in the 90 % of patients not admitted to an ICU but to a general ward. Especially for the app. 40 % of the patients with diabetes (diagnosed or unrecognized), stress induced hyperglycaemia can have very adverse consequences.

The first application area of the REACTION platform will thus be a suite of services aiming at Tight Glycaemic Control (TGC) using multi-parametric monitoring of admitted patients in hospitals.

One of the major differences between inpatient and outpatient control of glycaemic levels is the fact that tight glycaemic control in hospitalised patients has to be provided by healthcare physicians and/or nurses. Achieving the goal of tight glycaemic targets requires extensive nursing efforts, including frequent bedside glucose monitoring, training to handle control algorithms or guidelines with intuitive decision taking and most importantly additional responsibility to prevent hypoglycaemic episodes.

A REACTION field trial application will be set up in a hospital setting to continuously monitor blood glucoses level and a range of vital parameters. The data will be contextualised in the Data Management component and mathematical algorithms will be used to predict insulin doses. Results will be fed to dedicated diabetes specialists (usually placed in a diabetes specialist centre) for verification and evaluation. Their results and recommendations will then be fed back to the physicians or nurses at the point of care i.e. in the ward.

Outpatient domain

Careful monitoring of multiple parameters may represent a useful integrated basis for achievement of strict and sustained glucose control that will provide a better opportunity to reduce diabetic complications and improve patients' quality of life.

The results may implement the daily patients' management of diabetes, and reduce diabetic acute and chronic complications and their costs. Moreover, the simplification of the model may extend the multi-parametric monitoring to a bigger number of diabetic patients and the integrated analysis of multiple risk factors may significantly reduce the impact of chronic diabetes complications. This approach is, obviously, of great importance for insulin-dependent type 1 diabetic patients. Nonetheless, the technology is likely to introduce better opportunity for type 2 diabetes as well. While in type 2 diabetes, punctual blood glucose readings may not necessary trigger therapeutic changes, analysis of blood glucose profiles over the time may allow early detection of trends thus allowing timely treatment adjustments.

The proper use and integration into the REACTION platform of existing methods for metabolic monitoring and control, together with the systematic deployment of such platform in real-life healthcare systems, is expected to greatly help reducing the risk of developing complications in general, and the rate of hospital admissions. Devices for glucose and physical activity monitoring will be simultaneously used to determine whether multi-parametric monitoring provide a reliable measurements as compared to classical mono-parametric monitoring.

While new monitoring schemes will allow better management of diabetes to reduce the burden of chronic diabetic complications, technological aids are needed to improve prevention of diabetes itself. Although pharmacologic prevention cannot be excluded in the next future, lifestyle modification will remain a necessary (and powerful) tool. The use of movement sensors, calorie balance and media tools supported by the REACTION platform will serve to implement applications to monitor lifestyle modifications. These procedures can become cost effective if implemented in high risk individuals. Hence, the effects of medication compliance and on self-management schemes and life-style changes will also be addressed in the field trials.

Automatic glycaemic control

The final application of the REACTION project will develop and demonstrate the feasibility for automatic diabetic control in which continuous glucose monitoring measurements are used to control directly the insulin delivery of the infusion pump. This would provide optimum management and could provide diabetes patients with insulin profiles close to that of the normal patient, although problems remain to develop long term accurate continuous monitoring systems, delivery systems, control algorithms and ensuring safety of the system (Steil2002).

Today's commercial CGM may well show errors up to 20%, in some situations even more, and they still provide useful support for insulin therapy. Current closed-loop control approaches – while applying various control algorithms (Youssef2009) – all rely on abstract, empirical compartmental models with only implicit representations of patient, sensor and insulin properties (e.g. Hovorka2004). The additional use of optimised algorithms for glucose control can help alleviate the problem, since trends in blood glucose level are continuously monitored and preventive action taken earlier. Even without high absolute accuracy continuous glucose measurement with discontinuous calibration combined with biomedical modelling may offer a revolution in disease management where the focus is on stabilisation of glucose levels, i.e. primarily the prevention of excursions of any type, instead of comparing current glucose levels with lower and upper thresholds.

The REACTION project will integrate its work on developing improved and reliable accurate continuous monitoring sensors, predictive mechanistic glucose-insulin models, and control algorithms to develop a closed loop delivery system for testing in initial clinical feasibility trials. Safety considerations remain paramount, and will restrict trials to laboratories and well controlled environment such as I.C.U. (Hovorka2005).

Detailed scientific and technological objectives

Research and development will be performed in a number of work areas. The main clinical, technological, socio-economic research challenges will be in the following work areas:

ID	Objectives	Date of achievement	Work Package	Milestones
O1	Research and development of non-invasive or minimally invasive sensors for Continuous Glucoses Monitoring (CGM) and Automatic Glucose Control (AGC) and Closed Loop Control (CLC).	M30 for CGM, M36 for AGC and M48 for CLC.	WP3	MS1, MS5 and MS6
O2	Research and development of continuous, context aware, multi-parametric monitoring with resource constrained wearable sensor networks in Body and Personal Area Networks.	M24	WP4	MS3
O3	Integration of devices and interoperability using loosely coupled devices with reflective properties.	M24 and M36	WP5	MS3 and MS7
O4	Research and development of data management, analysis and correlation of multi-parametric data using semantic annotation, context awareness, and distributed decision support.	M24 and M36	WP4 & WP6	MS3 and MS7
O5	Research and implementation of system for integrative risk assessment to predict likelihood of developing disease (or complications) given their present and historic health status using, among others, physiology-based models suited for personalization.	M22	WP6	n/a
O6	Research and development of service orchestration with workflow management, alarm and crisis management.	M36	WP4	MS7
O7	Research and implementation of network architecture for seamless semantic interoperability of applications and services	M24 and M36	WP5	MS3 and MS7
O8	Research and development of secure and trusted data fusion with patient empowerment and full respect for privacy	M18 and M30	WP7	n/a
O9	Research on socio-economic foundation for ethical and social consideration in Remote Patient Monitoring and a framework for cost-effectiveness metrics and viable business models.	M30 and M40	WP9	n/a

An overview of the scientific and technological objectives related to the work areas is presented below. A detailed outline of the implementation will be given in the workpackage descriptions.

Glucose monitoring

Tight Glycaemic Control (TGC) is important in order to reduce micro-vascular complications and recent guidelines emphasise the importance of TGC. The glycaemic control may be influenced by a number of factors e.g. type of medication and patient self-management. A part of the self-management is adherence to the treatment regimen and adherence has been shown to vary significantly in patients with chronic diseases.

So far, management of diabetes has been approached by home blood glucose monitoring requiring, at best, 8 time points a day. The procedure is, however, unlikely to be sustained over the time because of repeated finger sticks and episodic blood glucose measurements. An improvement has been introduced with continuous subcutaneous glucose monitoring (CSGM) allowing careful blood glucose profiling under normal life conditions. However, monitoring time span remains limited to maximum 3-4 days. Therefore, technologies for dynamic blood glucose monitoring do exist, but they are not easily accessible to patients and, when available, results are not easy to be analyzed. Furthermore, the often long waiting time and queues for medical consultation may create additional difficulties to the patient with diabetes as interpretation of glycaemic profile should result in appropriate therapeutic modifications allowing prompt achievement of glycaemic control and proactive management of deviations from glycaemic goals.

Continuous blood glucose monitoring (CGM) is essential for good diabetes management and a very important project objective is thus to evaluate several sensor principles with respect to their suitability for a wearable continuous glucose monitoring device in closed loop operation. The aim is to develop and integrate prototypes of two different, non-invasive and minimally invasive principles based on 1) impedance spectroscopy and 2) infrared spectroscopy.

In particular, one objective of the first clinical trials is to investigate what measurement accuracy is needed for the continuous monitoring, when healthcare professionals are part of the closed-loop system. The focus will be on clinical and endocrinological requirements. Later work will be evaluating the same requirements for accuracy in Automatic Glucose Control systems.

Wearable devices and interoperability

The REACTION platform is based on seamless integration of wearable ePatch sensors and off-the-shelf medical devices, environmental sensors and actuators.

A key objective in the REACTION project is to demonstrate the use of non-invasive and minimally invasive monitoring devices. Despite technological developments in sensing and monitoring devices, issues related to system integration, sensor miniaturization, low-power sensor interface circuitry design, wireless telemetric links and signal processing still have to be investigated. Moreover, issues related to quality of service, security, multi-sensor data fusion, and decision support are active research topics.

The REACTION project will develop wireless body networks with wearable and non-invasive or minimally invasive sensors based on the electronic patch (or ePatch) concept. Body Area Networks will be used for multi-parametric monitoring of physiologic health data.

Figure 5 ePatch sensor

An electronic patch is a small body sensor, which senses physiological signals and is embedded in a skin-friendly adhesive. An ePatch looks like a normal plaster but contains various kinds of miniaturised body sensors for measuring physiological parameters, microelectronics for data

analysis, a wireless radio module for communication and a battery power source. ePatch sensors have been developed for applications such as myographic recordings, skin temperature, and skin impedance. The monitoring can encompass multiple ePatches around the body for multi-parametric sensing.

Wearable sensors will be connected through a patient centric Body Area Network (BAN). Decentralised decision support at the point-of-delivery (the patient) will be achieved with active nodes/gateways (PDA, Smart Phone operating personalised software bundles in an OSGi framework or Apples iPhone OS 3.0). Communication will be based on standards where possible. For optimum patient comfort and usability, ePatches and BAN need to have the following properties:
- They are wearable for up to one week in the course of normal human activity
- They are easy to wear and mount without being visible or attracting undue attention
- They do not disturb normal daily activities or cause discomfort
- They consume very little power and can run on a small battery for a week
- They can cope with transmission black-outs and different communication networks
- They may be disposable and may be manufactured in mass production processes at low costs and with environmental materials and substances

A Personal Area Network (PAN) will connect the patient to loosely coupled ambient sensors. Communication protocols with built-in reflective properties (such as BlueTooth and ZigBee) will be preferred, but other communication protocols will be supported. The PAN node will be used for data fusion and inference. Data will be combined with descriptive context data such as GPS data, ambient temperature, human activity indicators, etc. and fused to Data Management.

Seamless integration will be achieved using a middleware developed in the FP6 project Hydra which will turn each device into a Web Service that proxy the functionality of the device. The Hydra middleware employs semantic technologies and automatically detects physical devices irrespective of their underlying communication protocol (it supports Bluetooth, ZigBee, RFID, RF, WiFi, Serial port and many more). Through the use of device ontologies the middleware resolves the type of device that has been detected and automatically creates a web service interface that allows other devices and applications to use and control the device.

Data manipulation may take the form of linearization, extrapolation, interpolation, extraction or contraction, reformatting etc. Translation between state domain and time domain is also performed here. The challenge is to identify, develop, and implement the computer algorithms needed to support the clinical workflows.

Data management and analysis

Data Management in the REACTION platform is central to the high level functioning of applications and services deployed on the platform. It implements the model-driven architecture for application development and deployment, the service oriented architecture, for core service functionalities, the data manipulation, and data fusion and event handling. It also manages all data transfer to and from the various nodes and stakeholders in the REACTION environment.

Data Management may also invoke extended services for special tasks and services that query healthcare professionals for intervention and decisions. It also provides more advanced querying functionality hard coded in specific Web-Service methods. The queries are implemented in the SPARQL language.

Context awareness is achieved through semantic annotation of patients' device data, data coming from the environment, and data from the patients' historical information in EPR repositories. The backend knowledge discovery processes will be implemented using Semantic Web Services to prove an automated environment for executing services and applications.

The REACTION platform can support both distributed and centralised services for decision support. Distributed monitoring and decision support is typically used for monitoring of the patient health status at the point of care. Distributed decision support is essential in critical

services such as event handling, when connectivity is not guaranteed. It is anchored in the Personal Area Network and can support decision making among patients and informal carers.

Centralised decision support involves querying established biomedical knowledge and expertise to derive clinically relevant information and risk assessment based on the contextualized medical data and patient history. The centralised decision support is anchored in the Data Management subset.

Semantic Retrieval

The basis for the envisioned semantic retrieval functionality will be developed mainly by workpackage 4 in cooperation with workpackage 6. To start with Reaction will make use of different ontologies. There will be one Device ontology describing various aspects of devices, sensors and actuators and the services they offer. One or several domain ontologies will describe a particular domain such as healthcare (HL7)/diabetes. All our ontologies will be expressed using OWL (Ontology Web Language) and created with one of the available tools on the market such as Protogé or Topbraid.

The services offered by various devices and sensors will be annotated using the W3C standard SA-WSDL. This means that for instance a particular data value is given an annotation which points back to the domain ontology. In this way we know that data value X from service Y is conforming to a particular HL7 class.

So once data is retrieved and/or pushed from the device/sensor the data are encoded based on the SA-WSDL annotations. Data are stored and managed by the Reaction Data Management System. Since the annotations are grounded in a common ontology, a common understanding of data from different sources is achieved and it will be possible to compare and analyse them.

For retrieval and analysis of data from the data management system an ontology query language, SPARQL, will be used and evaluated as first choice but other languages might also be considered.

Integrative risk assessment

From the information systems perspective, integrative risk assessment involves data from several sources to be combined using semantically based information retrieval tools. The formalisation of pre-existing clinical knowledge and the discovery (e.g. with semantic data mining techniques) of new elicited knowledge represent one of the main innovations in the REACTION project.

In the UK, all primary health care electronic patient databases (which cover 100% of population) must support MIQUEST as standard enquiry tool, and this supports queries at semantic level. Where necessary pre-compiler can convert from semantic to MIQUEST. This provides standard information retrieval tool that can be scaled to all UK primary care records.

Data mining methodologies and heuristic algorithms will be applied to large well defined datasets (such as held by primary care in the UK or other publicly available data) to evaluate the multi-parametric health status profiling approach. Physiology-based models suited for personalization will be used to predict additional input data for risk assessment models.

The REACTION platform will integrate the assembly of a patient's "Health Status Profile" with a series of REACTION services that integrate the different risk assessment models. The result will be personalised and easy to understand risk assessment that is directed to clinicians and patients as well as informal cares.

Service orchestration and event handling

The REACTION applications are based on numerous individual services that can be developed and deployed to perform clinical monitoring and feedback tasks, execute distributed decision support and security tasks, support work flow management, and perform event handling and crisis management.

A service-oriented architecture (SOA) is a collection of services that communicate with each other. The aim is to have interoperable and loosely coupled services distributed in the network. In this context, a service is a function that is well-defined, self-contained, and does not depend on the context or state of other services. Although the SOA term is not new, it is widely used nowadays thanks to the Web Services technology (Milagro2008).

In the REACTION platform, each device is enabled to offer Web Services that can be consumed by other devices, services or applications through an overlying mobile P2P network. Every service offered by a physical device is identified and invoked using SOAP messages that are transmitted over the P2P network to create a robust connection, and WSDL to define the interface of the services, no matter the implementation language used.

Ensembles of REACTION services are orchestrated by a specific high-level workflow e.g. based on BPEL. The workflow will be specified in the application and interpreted by the Orchestration Manager. The Orchestration Manager will make sure the different services available are executed in a pre-described sequence. This component introduces higher abstraction mechanisms and makes the application developer independent of using a specific programming environment to orchestrate REACTION applications. It will also eliminate the interdependencies of services, solve conflicts of services and provide the most flexibility environment needed to realise service-oriented applications. The Orchestration Manager will also interface with legacy back end systems such as operational workflow and resource scheduling systems (SAP, EPR systems).

Monitoring and event handling are important aspects of REACTION services. Any REACTION applications will be able to react ubiquitously to change in the patients' health state and/or environment and perform pre-defined activities or alarm handling according to pre-programmed rules or through closed loops involving formal and informal carers. In order to provide fast, complex and robust event handling, the REACTION platform will develop an event handling framework based on the well known state machine concepts[1] from the field of control theory.

Monitoring will thus be based on mapping of data into "states". In principle, all data are expressed in the time domain. Dynamic values change as function of time – also static value are function of time, although they change less often or never. However the mechanism of event handling becomes much simpler when time resolved data are mapped into states. An event occurs when a transition (change of state) take place and alarm responses can be initiated by the occurrence and detection of events corresponding to a pre-defined scheme. The alarm handling can take the form of a simple, predefined feedback to the patient: "Your blood sugar level is slightly elevated. You need to adjust your insulin dose at next injection" or more complex medical feedback to healthcare professional. It can also involve physical actions in the Patients' Sphere (ringing a bell, turning on lights) and invoking professional emergency response teams with the inclusion of a complete medical history and contact information.

An advanced alarm handling scenario involving both personal alerts and crisis management alarms could be as follows:

The patient is ASK, a 48 year patient with type-1 diabetes. She carries a wearable CGM that monitors her blood glucose levels. If the measured value exceeds a preset level set by her physician, the device sounds an alarm to alert her of the need to take an insulin injection. The dose is automatically derived from the context data and her sensitivity factor.

Her injections are kept either in her fridge or in the special cooler container for use when she is away from her home. All the injections have a small RFID tag on them. The RFID tag reader in the fridge or inside the lid of the container records when the insulin injection is removed. Provided this is done within 10 minutes of the original event, no further action is initiated. However, if it does not happen, a second alarm is triggered on her wearable device and an alarm is sent off to the emergency centre with information of where she is, as identified by the GPS component of the wearable device and that she has not responded.

---

[1] A state machine is a model of behaviour composed of a finite number of states, transitions between those states, and actions.

If the event takes place during the day, a REACTION service will automatically identify the nearest community nurse identified via GPS. If the incident occurs at night then the first alert on the wearable device will also trigger a signal to the lights in her bedroom, which will be automatically turned on as an additional feature to make sure she wakes up to take the injection. If the RFID reader in the fridge does not detect the removal of an insulin injection within 10 minutes, the lights in her bedroom will flash and the emergency centre will be contacted. The light in front of the house and on the stairway will turn on and the front door can be opened by an enabling RDIF carried by the crisis team.

Model-based application development and scalability

An architecture supporting model-driven development of services will be provided. It will allow service providers to rapidly build, maintain and update services operating on the REACTION platform.

The REACTION development platform is an open toolkit used for model-driven development of services that use the REACTION platform. It will be based on a structure of service ontologies. A conceptual domain model describes the application, the services to be deployed and the objects involved (devices, users, rule sets, repositories, etc). A domain model will be mapped to an operative data model, which is implemented by an XML schema, and a set of Web Service interfaces. Each externally accessible component provides a WSDL interface, which exposes a subset of the domain model XML schemas.

Device specific services can be integrated with external services, such as knowledge extraction, accessing an EPR or providing feedback to a carer, merged with workflow and resource scheduling services and supplied with security model and authentication services.

The deployment of applications will take the form of high-level, dynamic orchestration of individual services. The actual service will then take the form of instances of basic services requiring only personalisation and instantiation of objects and parameters.

Network architecture and semantic interoperability

Connectivity in the REACTION infrastructure must be network agnostic in order to support any monitoring and support application, regardless of time, bandwidth, and protocol constraints. Emergency, rescue and other time critical applications must offer real-time connectivity and critical monitoring applications must offer geographically dispersed, always-on features regardless of heterogeneous network structures and diverse operators across Europe.

The REACTION project will solve this challenge by incorporating Personal Area Network technologies, which allow intelligent and seamless wireless connectivity between patients' Body Area Networks and the personal environment and the REACTION Data Management subset.

The implementation will use seamless switching between available, wireless connections (WLAN, UMTS, GPRS, WiMAX etc.). Since connectivity cannot always be guaranteed, the system will have provisions for caching data locally for data persistency. The implementation will encompass components that not only keep the key device in contact with available networks, but also keep the power consumption at a minimum, since continuous connection reduces a device's standby time significantly. Data persistence poses a special challenge to the security framework.

The Network Management subset is responsible for the physical communication between devices, persons and external repositories. Each PAN node will have its own Network Manager and each Network Manager will have an external Web Service based interface where it can exchange data with remote Network Managers.

The Network Management subset also implements the security model. Security will be implemented either centrally or locally; the pros and cons depending on the actual applications. For strongly centralised applications, i.e. in hospital wards, where the objects are relatively tightly coupled, a centralised security model is a possibility. For achieving the protection goals,

the Security Manager has to be contacted before every call to the Network Manager for decryption, verification of signatures, logging, etc.

For applications using very loosely coupled devices that come and leave the platform, a decentralised structure is preferable and functionalities for communication protection have to be included in every single component. In these cases, the Security Manager can be used as a stand-alone security component key management and general cryptographic purposes.

Security, privacy and safety

The issues of security, confidentiality and liability are crucial elements of eHealth development and are some of the major challenges of eHealth. The document e-Health - making healthcare better for European citizens: An action plan for a European e-Health Area[2] defines several security issues. Because health information, products, and services have the potential both to improve health and to do harm, organisations and individuals that receive and provide health information remotely have obligations to be trustworthy, provide high quality content, protect users' privacy, and adhere to best practices for online professional services in healthcare.

Requirements for security, privacy and trust have to be determined not only in terms of the global regulatory framework and security and privacy objectives for healthcare services but also in terms of the technology enhanced context-aware security features that suit the particular security models involved in any distributed healthcare environment.

When physical boundaries are eroding, security depends on the ability to appropriately manage logical boundaries. Existing healthcare solutions, however, are mostly integrated in a traditional security framework focusing on perimeter security, e.g. intrusion protection, repudiation and authentication. The distributed nature of REACTION platform greatly increases the vulnerabilities against malicious conduct.

Virtualisation of devices is thus an important method to protect devices from attacks and balance users' security risks and ensure damage control. Both devices and users can operate with virtual identities. Two devices with respective users can thus connect based on semantic security description according to the security model.

To manage security in the REACTION platform and empower users with privacy enhancing tools, a trust concept will be defined based on a definition of "trust" as the human way of balancing risk and benefit of a transaction in a subjective way (Cahill2003). Trust requires adapting policies dynamically to changing requirements. The security and privacy chain as well as important trust concerns will therefore be identified and ranked so that secure identity management can be implemented throughout the platform. Hence the REACTION project aims to provide a visible and controllable distributed security and privacy model, which is based on the concept of trust as a multilateral relation between stakeholders in a community of patients, informal carers and healthcare professionals and providers.

Safety plays an important role in any closed-loop system, but for healthcare applications, the safety aspects become paramount. The device risk assessment will be undertaken using existing risk management methodologies and frameworks. Where possible it will include existing standards and industry best practice.

Ethical, socio-economic and legal frameworks

The scientific objective is to describe which ethical, social and legal perspectives are applied to the REACTION service platform for remote diabetes management and therapy in Europe.

The ethical and social aspects of REACTION applications will be assessed against the background on the European Union Charter of Fundamental Rights and the EU Data Protection principles. Three main questions will be asked: are there special rights for people with diabetes? Which are they? And how can we ensure that privacy and ethics are linked to technology development over

---

[2] http://europa.eu.int/information_society/doc/qualif/health/COM_2004_0356_F_EN_ACTE.pdf

time? In order to answer these questions, the project will assess the ethical and social issues emerging in relation with dignity, individual autonomy and self-development, equality and inclusion.

Effort will also be put in unravelling the relation between legal and technological solutions in the area of privacy and data protection. We will consider which checks and balances in using data should be put in place in the overall architecture, as a part of a broader shift to privacy-by-design and privacy-enhancing technologies (PETs) seem necessary.

Legal issues of patient rights, product liability and Intellectual Property Rights will also be investigated. At the EU level, the building block for patient rights can be found in article 35 of the EU Charter of Fundamental Rights, but a specific EU Charter of patients' rights does not exist. Likewise, it is not clear how product liability legislation can be applied to distributed services and it could be very difficult to determine which producer or provider to hold liable for damages caused by such services. The REACTION platform will make extensive use of available digitalised knowledge. Without adequate copyright protection and enforcement, authors may not make their knowledge available. All of these issues will be investigated and documented and solutions will be proposed for the REACTION platform for remote healthcare management.

The provisioning of long-term healthcare and home-care differs between the EU Member States and this work area aims to define the socio-economic foundation for sustainable implementation of REACTION remote monitoring services across Europe. A solid economic foundation is required for a successful integration of REACTION applications into healthcare systems in Europe. A suitable framework for analysis of value creation and business modelling will be developed, which will allow accurate and viable metrics for cost-effectiveness, organisational adaptation and sustainable business and cost-benefit models for the stakeholders.

Relevance to the call objective

The main objectives of the REACTION project are perfectly aligned with the objectives of the call:

REACTION will demonstrate a new context aware, closed-loop monitoring platform which can improve productivity of healthcare systems by **facilitating better integrated care and management of chronic diseases at the point of need**, both in hospitals and in the private sphere.

REACTION services will facilitate continuous, contextualised and personalised care solutions, **addressing the participation of patients in care and prevention processes** in order to create continuous and personalised care solutions for chronic disease management.

The REACTION project will further focus on remote management and treatment of patients with diabetes at the point of need **by developing automatic closed-loop glycaemic control systems** and use heterogeneous data to **build risk assessment models for early diagnosis of further complications** and the inclusion of hypo-and hyper-glycaemia **alarm handling for crisis management**.

REACTION will finally demonstrate **continuous, minimally or non-invasive glucose measurements**. Requirements for accuracy will be evaluated.

A direct comparison of REACTION features with the objectives of the work programme shows an excellent alignment of target outcome and project objectives:

Target outcome in objective ICT-2009.5.1	REACTION will feature…
(i) the accuracy of measurements and operation of the devices	… a target of 5-10% for the impedance and infrared a target to meet or exceed the state-of-the-art (accepted guideline POCT05-A) for the impedance and infrared spectroscopy sensors. The need for enhanced accuracy will be investigated in the Automatic Glucose Monitoring trial.

Target outcome in objective ICT-2009.5.1	REACTION will feature…
(ii) remote control of the devices by health professionals, as well as self-monitoring and autonomous regulation of the devices' own operation, to personalise and optimise care by considering changes in health status, activity levels or response to treatment	… Data Management services with two-way connectivity between health professionals in one end and sensors and patients in the other. Multi-parametric monitoring services support automatic, personalised feedback to device and patient based on health status (see WP4).
(iii) continuous, context-aware, multi-parametric monitoring of health parameters, activity, lifestyle, environment and operational parameters of the devices	… PAN network technology for integration of heterogeneous sensors in the environment that provide context awareness to the multi-parametric medical sensors (see WP3 & WP5).
iv) analysis and correlation of the multi-parametric data with established biomedical knowledge and expertise to derive clinically relevant and useful information	Data mining methodologies and heuristic algorithms will be applied to large well defined datasets to evaluate the multi-parametric health status profiling approach. Physiology-based models suited for personalization will be used to predict input data for risk assessment models.
(v) clinical workflows to support remote applications, addressing also alarms and crisis management	… a Service Orchestration mechanism that can combine clinical workflows and resource scheduling to control the monitoring process including event handling, alarm and integration with emergency teams (see WP4 and WP8).
(vi) education and feedback to patients	… Data Management services that assemble personalised, educational information packages to patients based on their actual health status.

Table 2 Comparison of target outcome and REACTION features

B.1.2 Progress beyond the state of the art

The REACTION project is leaning heavily on leading-edge methods and technologies in various research fields. A collection of state of the art background information relevant to the REACTION research strands is presented below. The expected advances are highlighted in each area.

eHealth and remote monitoring

The term eHealth has been used in the literature to refer to a variety of applications including telemedicine, electronic patient records (EPRs), consumer health websites, teletraining for health professionals, and electronic referrals and bookings that might be categorised as using information and communication technologies (Oh2005). Telemedicine may be described as the use of these technologies by healthcare professionals to practice medicine at a distance, and again numerous definitions have appeared in the literature. One that is favoured by many researchers is that by Reid (Reid1996): "Telemedicine – the use of advanced telecommunications technologies to exchange health information and provide healthcare services across geographic, time, social and cultural barriers". This definition is sufficiently broad, and emphasises the fact that telemedicine does not only overcome distances of space, but also of other, perhaps less widely acknowledged barriers. It also emphasises the potential of telemedicine to improve access to healthcare for those who do not live within the reach of high-rated or specialist hospitals and medical centres. It should be added to the definition that telemedicine relies not only on telecommunications but also on information technologies.

Remote patient monitoring (RPM) can be seen as a subcategory of telemedicine. It entails the electronic monitoring of physiological measurements in a setting other than a hospital, such as a patient's home, or a community setting such as a residential or nursing home. Physiological measurements can include blood glucoses, heart rate, blood pressure, ECG, SpO2 (oxygen saturation of the blood), temperature, respiration and weight. In the context of this project, RPM is defined as: "The electronic monitoring of physiological measurements of patients not confined to hospital, using information and communication technologies to transfer data over geographical distances" (adapted from Bratan & Clarke (Bratan2005)). RPM can lead to better clinical outcomes (Hopp2006); (Clarke2005) and be more convenient and cost-effective (Finkelstein2006); (Hersch2001) than traditional institutional care, since it enables patients to remain in their usual environment whilst being looked after professionally. However, not all reviews of cost-effectiveness have proven conclusive, which has been blamed on the poor design of projects (Whitten2002).

RPM overlaps with telecare, which is defined as the monitoring of non-medical data such as general behaviour patterns, falls and, and is referred to as "social alarms", as the response is most commonly by a non healthcare professional.

There have been research efforts for developing a generic system architecture for telemedicine or telecare (Jasemian2005); (Lamminen2002); (Schorr2002); (Williams1998), but the focus is usually on the software and hardware architecture.

Coughlan et al. (Coughlan2006) developed a new approach for evaluating telemedicine services, which focuses on clinical and organisational aspects and uses patient pathways and simulation modelling ("patient pathway simulation"). The use of the patient pathway as a tool for comparing traditional healthcare and telemedicine is promising and forms an important aspect of developing the generic architecture. Patient pathways show the patient's journey through the healthcare system and are usually represented diagrammatically.

Success and sustainability factors for telemedicine have been extensively researched (e.g. (Yellowlees1997); (Yellowlees 2005); (Doolittle2001); (Watson2001); (Saligari2002); (Whitten2003)), but so far no studies have been carried out to compare the different approaches in terms of implementation in order to identify common elements that would inform the design of a generic architecture for an RPM system. There have also been no studies that have optimised current implementations.

RPM remains to be integrated into mainstream healthcare (Barlow2006); (Yellowlees2005), despite its potential for improving health outcomes and effective use of resources, and the efforts of government, industry and academia. This can be seen in the relatively low utilisation and success rate of many projects, and the lack of routine services. A number of contributing factors have been identified:
- Lack of definitive evidence for cost-effectiveness when applied wide-scale (Whitten2002)
- Lack of definitive evidence for clinical effectiveness (Wootton2001)
- Lack of funding to establish services (Hopp2006)
- Lack of experience (Richards2005)
- Technical issues, especially with the early equipment (Hopp2006)
- Uncertainty due to the lack of standards (Loane2002), guidelines (Stanberry2003) and service models (Barlow2006)

Some authors argue that the design and implementation of system architectures (beyond technical) is often given insufficient consideration when establishing a RPM service, which not only leads to poor design and difficulties in implementation, but, more importantly, also results in the development of a service that does not fulfil technical, clinical, organisational or user requirements.

The REACTION project has very clear objectives for overcoming the deployment obstacles inherent in previous programmes by taking a holistic view and pay proper consideration to all aspects of this complex issue.

REACTION will incorporate socio-economic aspects of diabetes monitoring and its deployability in large scale health systems; investigate cost effectiveness of proposed solutions as well as viable business models for the providers thus creating the foundation for a viable and sustainable industry.

REACTION will demonstrate a stable yet technologically highly innovative platform by using the right blend of mainstream proven technologies (backend health information systems, wireless technologies), new innovative solutions based on proven research experience (PAN networking and interoperability) as well as state-of-the art technological solutions developed during the course of other projects (ePatch multi sensors, semantic web annotations, networked systems middleware).

REACTION will seek to influence important standardisation work in bodies such as ISO TC215 WG 7 (Medical devices), CEN TC251 WG IV (interoperability), IEEE PHD (personal health data) interfaces and security (WWRI) as well as Continua Health Alliance working groups on architectures through it's active partners in these bodies.

A large number of EU funded project have been active in the area of telemedicine and RPM, many of them in the Framework Programmes. Some of these projects are approaching telemedicine and home care solutions such as proposed by the REACTION project:

Projects /Concepts	Scope of the project/Concept	REACTION Innovation
METABO The main objective is to design an interoperable platform for the continuous effective monitoring of metabolic levels for the generation of predictive personalized models for diabetes patients.	Focus on implementing a pragmatic personal modelling approach for metabolic control. Develops an integrated technological platform enabling integration and interoperability of different monitoring devices. Interoperability is based on a Representational State Transfer architecture[3]	REACTION adopts a holistic, multi-parametric approach in providing closed loop feedback involving both formal and informal carers to improve insulin therapy. REACTION implements the interoperability mechanisms using Web Services in a Service oriented Architecture.

---

[3] Representational state transfer (REST) is a style of software architecture for distributed hypermedia systems such as the World Wide Web. As such, it is not strictly a method for building "web services." The term is often used in a looser sense to describe any simple interface which transmits domain-specific data over HTTP without an additional messaging layer.

Projects /Concepts	Scope of the project/Concept	REACTION Innovation
DIAdvisor™ It develops a tool for people with diabetes to better predict and thereby control their blood glucose level.	DIAdvisor focus on short term prediction of blood glucose levels.	REACTION focuses on real-time monitoring and event handling as well as long term risk assessment. As such, there is full complementarity between the two projects. One REACTION partner is close to the Novo Nordisk, the coordinator of the DIAdvisor project and collaboration, in particular in the area of medical algorithms, can be foreseen.
P-CEZANNE The main objective of P-CEZANNE[4] is to research and develop a novel implantable long-term nano-sensor for continuous BGL monitoring. The nano-sensor is linked to the wireless device platform of the ICT system and the data will be automatically collected, stored and processed.	The project focuses on sensor and pump technology, which is very relevant for the REACTION project. The processed data will also be used for automatic regulating of the glucose level by linking it to an insulin pump that accurately releases insulin into the body in response to the fluctuations of glucose concentrations.	The service oriented architecture in REACTION could be a strong supplement to the data processing infrastructure in P-CEZANNE. FORTH-ICS is a sister institute to the Institute of Molecular Biology and Biotechnology, which is a partner in P-CEZANNE and can thus maintain close link to this project.
eVITAL eTEN project investigating provision of vital signs monitoring in residential homes.	CHORLEYWOOD established effective remote monitoring services in three local residential homes to manage both acute medical conditions and patients with chronic disease. The results were published in (Bratan2005b).	
TMA – BRIDGE Support Action funded under FP6 with the aim of building a vision for provision of Telemedicine and eHealth to European citizens by 2010.	The project will assess societal (health related), scientific, technical as well as organisational questions and propose solutions, which are relevant for REACTION.	
TELEMEDICARE Aiming at development of an open telemedicine platform solution for RPM with body sensors that supply medical data to the patient's computer through wireless communication.	The computer will analyse and store the data and trigger medical supervision, treatment or care by two-way communication over the Internet with care providers. The project does not consider power constraint devices such as wearable body sensors and rely on fixed gateways and always-on connectivity.	

---

[4] http://www.pcezanneportal.co.uk/

Projects /Concepts	Scope of the project/Concept	REACTION Innovation
M2DM Aimed to provide multi-access services to residential and mobile diabetic patients and new means to information access to physicians and patients, including Web-based services	The project is focused on technological solutions based on a central server system.	
USPTO Application #: 20080263055 A US patent has been file for a taxonomy-based platform for comprehensive healthcare management. The claim is for "A Web-Native, HIPAA compliant technology provides for real-time management of incident workflow and the delivery of actionable knowledge throughout the healthcare provider organization"	Similar to the REACTION concept of ontology based application development but does not cover the method of interaction based on semantic web services and the service oriented architecture	It does not cover on-line capture of sensor data, but addresses capture of data in HIS. However, the integration with and streamlining of workflows reinforces the need for these aspect to be covered by REACTION.

Glucose control in diabetes therapy

In-hospital control

Although several guidelines for treatment regimen for outpatient management of type 2 diabetes have been defined (Sakharova2005); (Das2005); (Charles2005), no clear definitions of treatment regimen have been found for the establishment of glycaemic control of hospitalised patients (Clement2004); (Gautier1996).

Hyperglycaemia and insulin resistance are common in severe illness and are often associated with physical and mental stress. Studies have shown that frequency of hyperglycaemia in surgical ICU's (Intensive Care Units) can amount to –50-70 % of all admitted patients (Ellmerer2008).

Based on the emerging clinical evidence from several clinical studies, there are increasing efforts world-wide to establish tight glycaemic control in critically ill and hospitalised patients (VandenBerghe2001); (VandenBerghe2006); (Furnary2004); (Meijering2006).

One of the major differences between inpatient and outpatient control of glycaemic levels is the fact that tight glycaemic control in hospitalised patients has to be provided by healthcare physicians and/or nurses. Achieving the goal of tight glycaemic targets requires extensive nursing efforts, including frequent bedside glucose monitoring, training to handle control algorithms or guidelines with intuitive decision taking and most importantly additional responsibility to prevent hypoglycaemic episodes.
> *REACTION will deploy a closed loop feed back system to tight in-hospital glycaemic control (TGC) allowing diabetes experts to handle control algorithms with intuitive decision taking and fuse therapy instructions to healthcare physicians and/or nurses at the point of care.*

Aggressive treatment in ICU's (Intensive Care Units) of stress-induced hyperglycaemia has shown remarkable results in recent years. In a randomized, controlled study conducted in a surgical intensive care unit (VandenBerghe2001), strict control of blood glucose levels with insulin reduced morbidity and mortality, significantly reducing in-hospital mortality from 11 to 7 percent in the entire study population. Strict glycaemic control also decreased morbidity from bloodstream infections by 46%, acute renal failure requiring dialysis or hemofiltration and critical illness polyneuropathy.

These dramatic findings prompted numerous hospitals to institute tight glucose control protocols, which quickly became the 'standard of care'. In many cases, these protocols are also used to manage medical and surgical patients outside the ICU. The latter approach is based, in part, on observational studies that demonstrated poor clinical outcomes in nonICU in patients with hyperglycaemia. The American College of Endocrinology and the American Diabetes Association, with the participation of prominent cardiology, critical care and anesthesiology organizations, issued a consensus statement that supported intensive glycaemic control for inpatients (ACE-ADA Task Force 2006[5]). The panel concluded that hospitalised patients should have a target glycaemic fasting level of <110 mg/dL (6.1 mM) and that insulin, whether administered intravenously or subcutaneously is the primary means of effective glycaemic control in the hospital setting (Clement2004). With state of the art technologies, TGC is only possible in dedicated centres with highly motivated personnel.

Some clinical trials fail to observe benefits with tight glucose control. The multi national NICE-SUGAR trial (NICE-SUGAR Investigators2009) was designed to test the hypothesis that intensive glucose control reduces mortality at 90 days. The study population comprised more than 6000 adults admitted to medical or surgical ICUs who were randomly assigned to intensive or conventional glucose control. Unexpectedly, mortality in the intensive control group was significantly higher than that in the conventional control group. Severe hypoglycaemia (defined as a blood glucose concentration ≤2.2 mmol/l) was also higher in the intensive group than in the conventional group.. Of note, the excess deaths in the intensive treatment group were predominantly cardiovascular, which is consistent with evidence from other studies that severe hypoglycemia might be associated with adverse cardiovascular events. (Gerstein2009)

In summary, there is an urgent need for a safe method to establish tight glycaemic control without any risk of hypoglycaemia for patients in intensive care units and the general ward.
> *The REACTION platform will allow to establish safe and stable glycaemic control for patients in the general ward by continuous multi-parametric monitoring of blood glucoses, skin temperature and nutritional intake. Furthermore, the REACTION platform will facilitate to develop TGC for patients in intensive care units and during surgery.*

Outpatient control

Several studies have demonstrated that tight glycaemic control is important in order to reduce microvascular complications and recent guidelines emphasise the importance of tight glycaemic control. The glycaemic control may be influenced by a number of factors e.g. type of medication and patient self-management.

Typical areas of improvement are blood glucose reading and insulin therapy feed-back. The technology for spot measurement of blood glucose levels is available but not directly transferable to insulin dose adjustments because of open-loop system.
> *The REACTION platform will close the loop and provide direct, on-line feedback to spot measurements of glucose levels combined with multi-parametric context awareness.*

This approach is, obviously, of great importance for insulin-dependent type 1 diabetic patients. Nonetheless, technology is likely to introduce better opportunity for type 2 diabetes as well. While in Type 2 diabetes, punctual blood glucose readings may not necessary trigger therapeutic changes, analysis of blood glucose profiles over the time may allow early detection of trends thus allowing timely treatment adjustments.
> *The REACTION applications will provide advanced risk assessment, intelligent event handling and interfaces to professional crisis management teams.*

A part of the self-management is adherence to the treatment regimen and adherence has been shown to vary significantly in patients with chronic diseases and has been reported as low as 38% in patients with diabetes on OAD treatment. The first data from direct observations of

---

[5] ACE–ADA Task Force on inpatient Diabetes. American College of endocrinology and American Diabetes Association Consensus statement on inpatient diabetes and glycemic control. Diabetes Care 29, 1955–1962 (2006).NICE-SUGAR study investigators. Intensive versus conventional glucose control in critically ill patients. NEJM 360, 1283–1297 (2009). Gerstein, H. C. et al. effects of intensive glucose lowering in type 2 diabetes. NEJM 358, 2545–2559 (2008).

treatment adherence to insulin therapy were reported by Novo Nordisk (Donsmark2008). The results obtained from this 22 week long prospective study show a positive correlation between HbA1c and the number of missed insulin injections in patients with type 1 and 2 diabetes.

Studies imply that devices and technologies that can improve patient adherence are needed in clinical practice and can improve treatment efficacy, quality of life and reduce health economic cost.

> *The REACTION platform directly supports compliance schemes with its two way mobile communication infrastructure between patients and backend combined with rules based event handling and risk assessment.*

Sensor technology

Glucose sensor technology

The standard-of-care for measuring glucose levels is by "finger-stick" blood glucose meters. For these a drop of blood, usually drawn by piercing the skin of a finger, is brought in contact with a test strip. A chemical reaction, commonly mediated by glucose oxidase, glucose dehydrogenase or hexokinase enzymes, triggers an electrochemical sensor or a colour reaction that is detected in a reader. The drawback of this method is that only a few measurements can be performed in the course of a day.

The development of a control system that infuses insulin on the basis of glucose measurements could permit tighter glycaemic control and improve clinical outcome without increasing workload of the health care professionals (Plank2006).

Only a few commercially available sensors that allow continuously monitoring the blood glucose level (CGM) have been approved for the market (Medtronic Minimed Paradigm, Dexcom SEVEN, Abbott FreeStyle Naviator among others). These sensors rely on electrochemical detection of an enzymatic reaction and are minimally invasive.

Two non invasive systems, GlucoWatch and Pendra, have reached approval by the FDA or achieved a CE marking. The first relies on iontophoresis for sample collection and electrochemical sensing while the other employs impedance spectroscopy for glucose measurement. However, the availability of both systems has ceased due to financial difficulties of their manufacturers.

A range of other sensor technologies are currently being tested for their suitability for glucose monitoring. The most promising technologies for continuous glucose monitoring can broadly be classified as follows:
   - Enzymatic (electrochemical)
   - Impedance Spectroscopy / Dielectric spectroscopy
   - Optical
        o IR-/NIR-Absorption
        o mid-IR emission
        o Polarimetric (e.g. anterior chamber of the eye)
        o Refractive index (e.g. anterior chamber of the eye)
        o Raman spectroscopy (inelastic photon scattering)
   - Photoacustic (pulsed light absorption dependent on glucose concentration)

Moreover, alternatives for invasive sampling are being investigated for electrochemical detection, for example samples may also be collected by iontophoresis or suction blister extraction trough the skin. Despite significant efforts these technologies are still in a development or evaluation phase and yet have to prove their reliability and accuracy.

> *The REACTION project will develop continuous glucose monitoring device in closed loop operation and to develop and integrate prototypes of two different, non-invasive and minimally invasive principles based on 1) impedance spectroscopy and 2) Infrared spectroscopy.*

Requirements for in vitro glucose monitoring systems for self-testing by laypersons that measure glucose concentrations in capillary blood samples are specified in the ISO norm ISO 15197:2003. According to this norm acceptance criteria for the accuracy of a measurement system are:

- for reference values < 75 mg/dL: 95% of measured values are within 15 mg/dL
- for reference values ≥ 75 mg/dL: 95% of measured values are within 20% bias.

for appropriately defined populations of glucose values the sensor has been tested on. Relevant ranges for blood glucose measurement are 25–400 mg/dl.

According to Klonoff (Klonoff2005), currently available CGMs that provide real-time readings are not sufficiently accurate to allow making therapeutic decisions such as whether to dose insulin or eat. To the best of our knowledge no current glucose monitoring system achieves relative accuracy better than 15% across the normal range. The problem of accuracy takes several forms and cannot be addressed with a simple answer. It depends on the application. Moreover, the measurement of glucose performed in vivo is unpredictably influenced by various substances of the body fluids such as proteins, cholesterol and so on. Accordingly, the newly published guidelines by CLSI (Performance Metrics for Continuous Interstitial Glucose Monitoring (POCT05-A)) does not give a definite number of accuracy needed for safe and effective use of CGM. This text reflects the state-of-the-art knowledge in CGM systems, in particular relating to Automatic Glucose Control, and serves as guideline for developers as well as regulatory bodies such as the US Food and Drug Administration (FDA) for evaluating such systems. For this reason we do not attempt to set an a priori target for the accuracy to be obtained by the developed and investigated glucose sensors. Rather we set as our goal to evaluate the performance data of the investigated systems against this background and to meet or exceed the state-of-the-art.

> *The objective of the clinical trials in REACTION is to study the precise need for measurement accuracy for CGM. Based on these studies as well as on the approved guidelines (POCT05-A) the developed sensors will be evaluated for their applicability for safe use in Automatic Glucose Control systems.*

ePatch sensor technology

The need for a new wireless sensor technology for monitoring physiologic parameters and be wearable by patients at home has been discussed for a long time, but emerged strongly in the literature since 2005. The first ePatches were developed by DELTA from 2006 to 2008 based on off-the-shelf-components in a reusable sensor unit based PCB board (Haar2008).

In further developments, sEMG (surface Electric Myografic) sensors has been integrated in ePatches, and proof of principle has been made on reflective pulse oximetry sensors designed to be integrated in ePatches. In another study, 10 patients wore ePatches for 5x24 hours while the ePatches sent ECG-data from the patients' home to the EPR via a mobile phone (Nielsen2008).

> *The ePatch technology will be taken further in the REACTION project. ePatch Continuous Glucose Monitoring sensors based on Impedance Spectroscopy and IR spectroscopy will be developed and tested in field trials. Other sensors for skin temperature and pulse oximetry will be manufactured*
> *A new ePatch prototype suitable for mass manufacturing and disposable technology will be developed and tested*

Some EU funded project and patents are relevant for the CGM and ePatch sensors:

Projects/Concepts	Scope of the project /Concept	REACTION Innovation
CLINICIP Develops a low-risk monitoring and control system for metabolic control in critically ill patients. The core of the system is a computer algorithm implemented into an ICU infusion system, which calculates insulin dosage from metabolic parameters to provide decision support for tight glycaemic control.	Clinical studies provided proof of concept for glucose and metabolite sensors in combination with a vascular body interface; support for further development is in negotiation.	REACTION partner MSG is the coordinator of CLINICPIP and the possibility for using their sensors as part of WP3 will be explored.
EU Patent application #: PCT/DK2006/050006 This patent presents an invention related	The patent is applied for by	

Projects/Concepts	Scope of the project /Concept	REACTION Innovation
to a three-dimensional adhesive device to be attached to the body surface of a mammal comprising a microelectronic sensing system characterized by a three-dimensional adhesive body made of a pressure sensitive adhesive having an upper surface and a bottom surface and a microelectronic system embedded in the body of the pressure sensitive adhesive.	the REACTION partner DELTA in cooperation with Coloplast A/S. The patented technologies can be used in the REACTION project.	

The work to be done for sensor development going beyond the state of the art is reflected within the following figure. The current state of the art for sensor technology is based on the test strip method, ,making use of the glucose oxidase reaction. This method is an invasive technology, it lacks from the required accuracy and cannot be used with automated control systems, as proposed within REACTION.
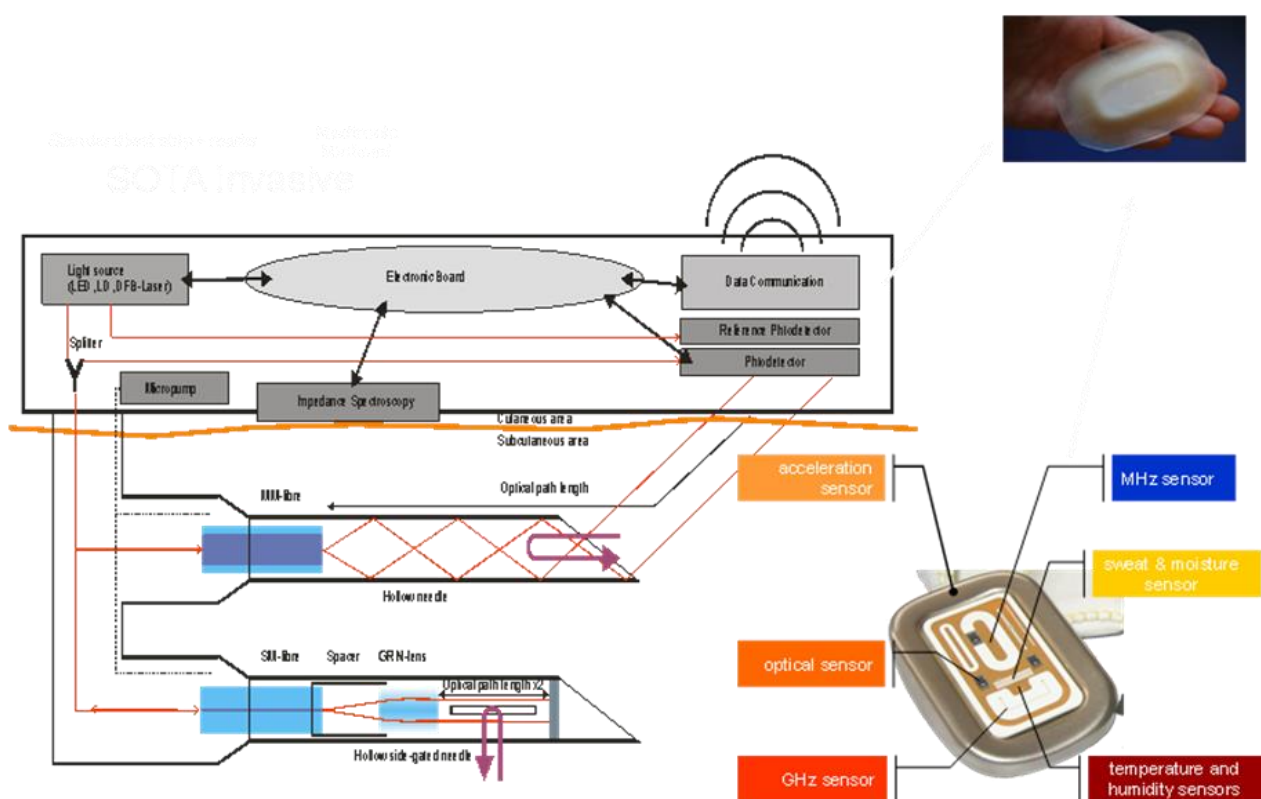
Our project will go beyond the state of the art by researching on the new approach of integrating subcutaneous minimally invasive IR-sensors, which so far have not been used for glucose online-monitoring in the patients sphere, and non-invasive impedance spectroscopy sensors into a multi-sensor ePatch technology platform. Besides the glucose monitoring also other body functions like temperature or moisture can be controlled within the same e-patch platform, allowing for a cross correlation of the corresponding data and, therefore, for an improved accuracy independent from any patient actions.

Concerning the IR-sensors at least two different concepts will be followed, both based on IR-spectroscopy in the overtone band near infrared spectral region. This method has been described in the literature already as being a suitable glucose measuring technology, but so far not been applied to stand alone glucose monitoring sensors in the patients sphere. Since in this spectral region the glucose bands are strongly interfered by water bands the technology of difference spectra will be applied which has been demonstrated already in the laboratory, giving an accuracy of about 5% (see figure below).

NIR Difference Spectra of Glucose in Water & Wate
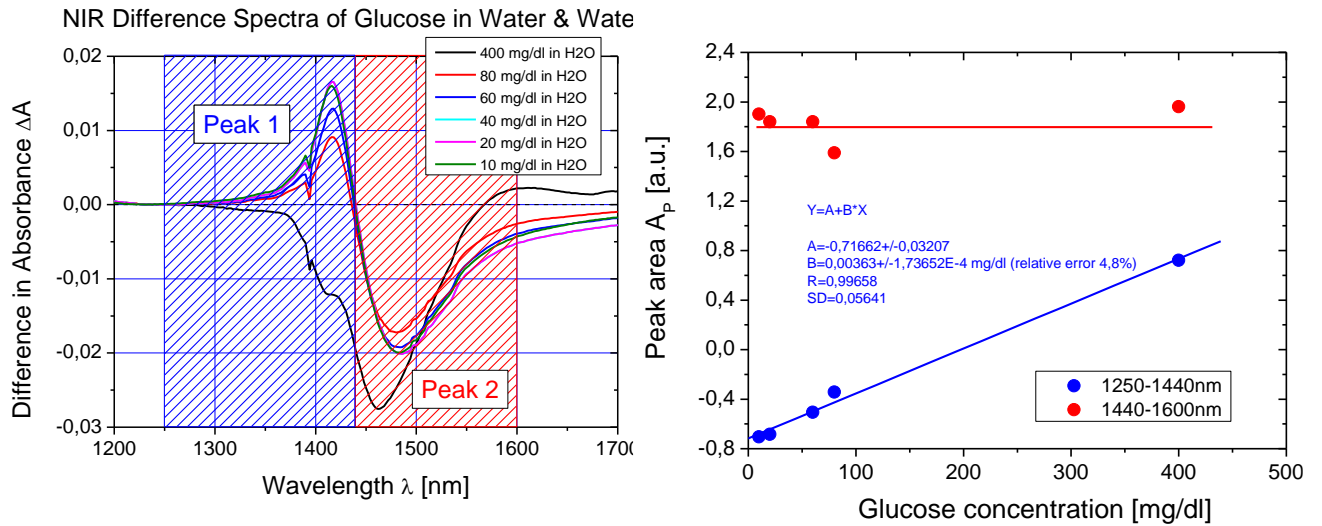
The IR-sensors consist of micro-optical cells integrated in small needles, operated without a spectrometer, applied subcutaneously and allowing the regular interchange of interstitial fluid during the monitoring period. One concept is based on a fibre coupled light source (LED or LD) connected to the needle with subsequent detection through the patients skin with a detector integrated in the e-patch platform. This concept has the disadvantage of slightly varying optical path length as well as interaction of the light with the patient's tissue but on the other hand has the higher potential for being operated as a disposable. The other concept follows a micro machined optical cell with well defined optical path length integrated into micro-needle to be applied subcutaneously. Here a higher accuracy is to be expected, since the optical path length is accurately defined. In both concepts it is planned to use a single optical source, adapted to the spectral region of interest and integrating the light intensity in that range. This avoids the usage of spectrometers within the e-patch platform, keeping them simple. In case of higher accuracy required, also a tunable light source is applicable, allowing for a spectral screening of the relevant bands, however, making the e-patch platform more expensive.

In relation to the progress beyond the state of the art and as part of REACTION objectives, the following research paradigm would be used to reach the objective of 5% accuracy in the glucose measures. It is based on three different levels of accuracy improvement, the technical level, the physiological level and the medical level.
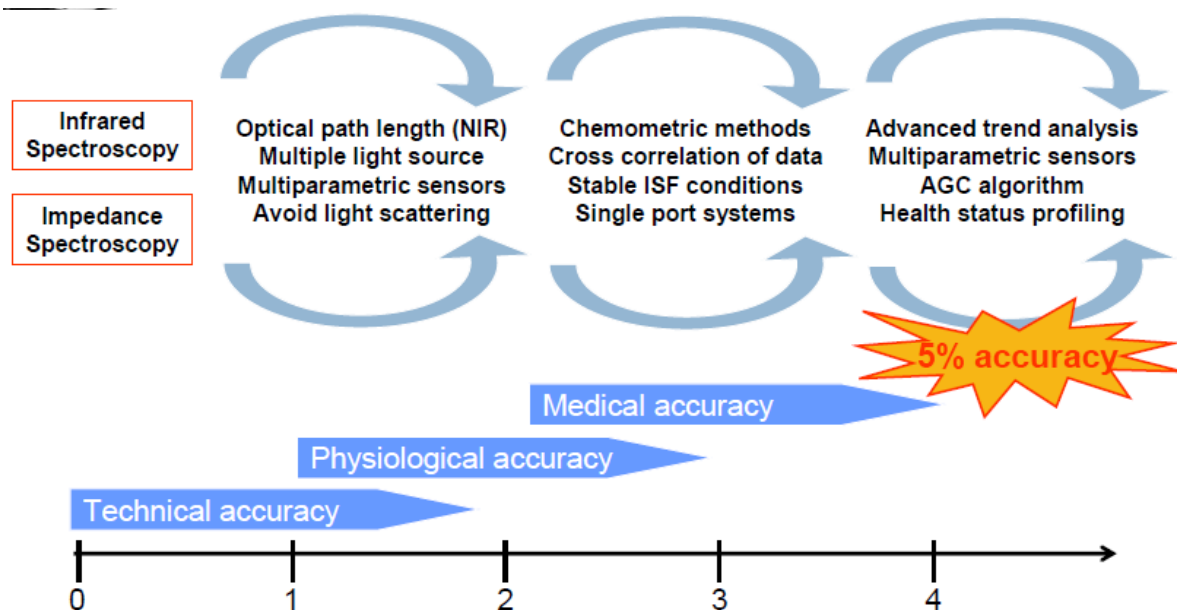
First on the technological level the sensor hardware is optimised, by taking action on the following items:
- micro-precision manufacturing to achieve a precise optical path length
- implementation of tunable or multiple light sources to increase the supporting points for the data
- implementation of a reference cell to avoid interference with water bands (difference spectra)

Secondly the accuracy is improved further by taking into account the physiological aspects:
- temperature stabilisation on body temperature
- operation close to the skin surface to avoid light scattering by lymph
- application of multiple sensors (IR and Impedance spectroscopy) for cross correlation of the data
- application of calibration models make to account for individual biological profile
- calibration of the sensor platform to account for the individual biological profile of the patient

Third, advanced data analysis is applied to ensure a high level of predictability:
- application of chemometric methods for spectroscopy
- cross correlation of the individual sensor data within the AGC algorithm

By combining these three levels of accuracy improvement it is expected to achieve the goal of 5% accuracy within the REACTION project, allowing for an advanced trend analysis and health status profiling in the patients and clinical sphere.

Continuous Glucose Monitoring

Over the last 5 years Solianis has passed through a several developed steps to reach a functional model (FM) of a Multisensor system that features 8 different sensors on a single substrate. These include sensors that allowed biophysical skin and underlying tissue characterization over a wide frequency range. Namely, 3 dielectric sensors, one optical module with 3 wavelengths, a galvanic skin response sensor as well as a temperature sensor were combined.

Within this development program the FM system was developed accompanied by experimental studies that have allowed to verify the various development steps taken. One particular experimental study was carried out to investigate the first integration of sensors on one substrate and the effect of transferring a calibration set from one study day to a second study day (e.g. Caduff et al, Biosens Bioelec 2009). This experiment showed that the first set of integrated sensors allows to track glucose variations per se. The step to be carried out now is the full integration of all the sensors onto the same substrate, add battery power and Bluetooth functionality in the same housing in order to experimentally test the resulting concept again. This system will then be a step further and will be considered a technical model (TM). If this concept is demonstrating to be feasible it will be taken into the prototyping phase next year.

Software architectures and security

Semantic interoperability

Possibly the most important European strategic objective in eHealth is to provide interoperability among healthcare information systems. The CEN/ISSS eHealth Standardisation Focus Group has identified five prominent strategic aims of healthcare informatics in Europe to be (CEN/ISSS 2004):
– Improving access to clinical records
– Enabling patient mobility and cross border access to healthcare
– Reducing clinical errors and improving safety
– Improving access to quality information on health for patients and professionals
– Improving efficiency of healthcare processes

The interoperability of healthcare information systems is the key component in meeting addressing these challenges and a number of standardization efforts are addressing the issue such as EHRcom[6], openEHR[7], HL7 Version 3[8] and HISA[9]. The Continua Alliance[10] is creating profiles for interoperability that stretch from the patient through to final report to the health care professional.

One of the most promising routes is based on semantic interoperability to support exchange of meaningful clinical information among healthcare systems. Since it is not realistic to expect all the healthcare institutes to conform to a single standard, there is a need to address the interoperability at the semantic level.

Semantic interoperability is the ability for information shared by systems to be understood at the level of formally defined domain concepts so that the information is computer processable by the receiving system (ISO2007).

The backend knowledge discovery processes in REACTION will be implemented using Semantic Web Services to prove an automated environment for delivering eHealth services and application.
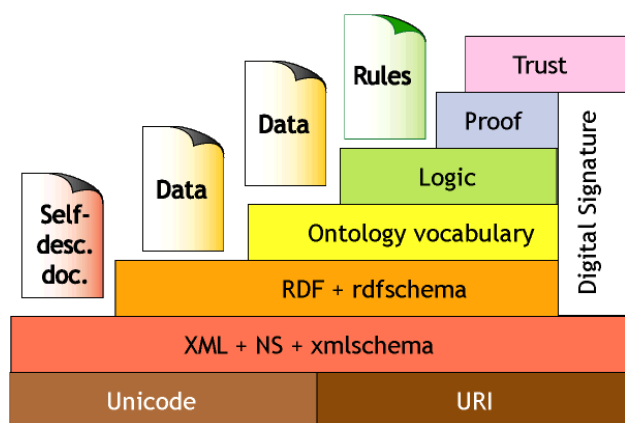
The Semantic Web principles are implemented in the layers of web technologies and standards.

The Unicode and URI layers provide means for identifying medical knowledge objects on the Semantic Web. The XML layer with namespace and schema definitions make sure that applications can integrate the Semantic Web definitions with other XML based standards in medical databases and knowledge repositories such as the "Cross Enterprise Document Sharing (XDS)" profile, which stores healthcare documents in an ebXML registry/repository architecture.[11]

With RDF and RDFSchema[12] it is possible to make statements about objects with URI's and define vocabularies that can be referred to by URI's. This is the layer where we can give types to resources and links.

The Ontology layer supports the evolution of vocabularies as it can define relations between the different concepts. An ontology based vocabulary of commonly used data exchange standards in healthcare such as Health Level 7 (HL7), which has categorized events in the healthcare domain by considering service functionality which also reflects the business logic, GEHR or CEN's ENV 13606 needs to be developed or adapted from projects. In the project eu-DOMAIN, HL7 was used to provide a domain model, which facilitated integration with legacy health systems.

The OWL Web Ontology Language is designed for use by applications that need to process the content of information instead of just presenting information to humans. OWL facilitates greater machine interpretability of web content than that supported by XML, RDF, and RDF Schema

---

[6] ENV 13606:2000 "Electronic Healthcare Record Communication", www.centc251.org/TCMeet/doclist/TCdoc00/N00-048.pdf

[7] OpenEHR Foundation, http://www.openehr.org/

[8] Health Level Seven (HL7), is an all-volunteer, not-for-profit organization involved in development of international healthcare standards HL7 Version 3 Specification, www.hl7.org/library/standards_non1.htm#HL7 Version 3

[9] The CEN Standard Architecture for Healthcare Information Systems (ENV 12967), Health Informatics Service Architecture

[10] Continua Alliance, www.continuaalliance.org

[11] The "Integrating the Healthcare Enterprise" initiative, www.ihe.net/

[12] Resource Description Framework Schema, www.w3.org/TR/rdf-schema/

(RDF-S) by providing additional vocabulary along with formal semantics. In most healthcare domains, the exchanged message instances are EDI or XML, not messages conforming to an ontology.

Several EU funded project are relevant for the work on Semantic Web Services:

Projects/Concepts	Scope of the project /Concept	REACTION Innovation
HYDRA[13] Develops middleware for networked embedded systems which allows developers to rapidly create intelligent applications	Semantic self-configuration tools for devices, semantic resolution, knowledge discovery modules and basic security models will be integrated into the REACTION platform through the use of Hydra middleware. Partners CNET, FHG-SIT and IN-JET are members of the Hydra project and can freely transfer their knowledge to the REACTION project.	
SmartHEALTH The aim of this 4-year IP[14] is to address the development and delivery of the next generation of smart diagnostic devices, with a starting point in applications for cancer diagnostics. The objectives include introducing sensor systems into future healthcare services to improve existing services, illustrating the role of Ambient Intelligent (AmI) medical devices and services for pervasive healthcare provision, as well as the development of new manufacturing technologies for realisation of unique sensor solutions	The project's Semantic Medical Device Space infrastructure is intended to enrich medical devices with ambient intelligence capabilities. This implies the provision of semantic device interoperability, secure data transfers and support for context awareness and context management. This project is in its final year and is in a phase of validation/exploitation of some of these technologies. Several aspects of this project are of interest to the REACTION project, among them, the context management and the approach to semantic medical devices.	
ARTEMIS[15] Has developed a semantic Web Service-based infrastructure for the interoperability of Medical Information Systems (MIS). The aim of the project is to provide exchange of meaningful clinical information among healthcare institutes.	Existing applications are wrapped as Web services and by use of an OWL ontology mapping tool, called OWLmt, the messages are semantically mediated to provide interoperability. This approach is generic enough to provide interoperability between any information systems but the prototype developed in Artemis currently mediates between only HL7 Version 2 and Version 3 messages.	
SEKT The EU IP project "Semantic Knowledge Technologies"[16] developed and exploited semantic knowledge technologies.	The three core technologies in the project are: ontology and metadata technology, knowledge discovery and human language technology.	The work in REACTION will extend the Semantic Knowledge technologies to the detection of useful complex features that can help in decision making process.

---

[13] http://www.hydramiddleware.eu

[14] http://www.smarthealthip.com

[15] Artemis – A Semantic Web Service-based P2P Infrastructure for the Interoperability of Medical Information Systems, www.srdc.metu.edu.tr/webpage/projects/artemis/

[16] SEKT – Semantic Knowledge Technologies, http://www.sekt-project.com

DIP		The work of DIP is relevant to
The objective of the FP6 project "Data, Information, and Process Integration with Semantic Web Services" [17] is to develop and extend Semantic Web and Web Service technologies in order to produce a new technology infrastructure for Semantic Web Services (SWS).		the further development of Semantic Web Services for healthcare in REACTION.

Web service technology

Web Service technologies provide standard, simple and lightweight mechanisms for exchanging structured and typed information between services in a decentralised and distributed environment. Traditional Service Oriented Architectures (SOAs) are based on the client/server architecture where a server application, hosted by an always-on end system, provides services to many other client applications hosted by sometimes-on end systems. The server has a fixed, well-known IP address.

However, it is a usual phenomenon in a client/server application, a single server host to be incapable of keeping up with all the requests from its clients. For this reason, clusters of hosts, sometimes referred as server farm, are often used to create a powerful virtual server in client/server architectures. In this context, providers typically publish service interfaces on index services which provide white/yellow pages functionalities.

> *REACTION applies a novel approach to large-scale SOA and envisions arbitrary pairs of peer application entities communicating and providing services directly to and with each other. In a peer-to-peer SOA, none of the participant hosts is required to be always on; moreover, a participating host may change its IP address each time it comes on. The design and implementation of the SOAP API is being carried out with the purpose to enable peer-to-peer sharing of XML-based Web Services that are programming language independent and can be developed in C# or Java.*

Distributed security architecture

Privacy is one of the key enablers for various scenarios in the eHealth domain. Concerns regarding privacy legislation, standardisation and implementation are upcoming at the same time as the introduction of Electronic Health Records or the digital patient[18]. Establishing trust in this area could be the enabler for various applications as healthcare as itself is a multidisciplinary scientific challenge.

Trust can be defined as the human way of balancing risk and benefit of a transaction in a subjective way (Cahill2003), which can be based on different foundations and can take different (discrete) values. Gambetta (Gambetta2000) provides another, often used, definition of trust: "Trust (or, symmetrically, distrust) is a particular level of the subjective probability with which an agent will perform a particular action, both before [we] can monitor such action (or independently of his capacity of ever to be able to monitor it) and in a context in which it affects [our] own action". The essence of this definition is that trust is very subjective, can have various (discrete) values and is used before an action has been performed.

Trust has different and orthogonal definitions in the context of applications for healthcare. The first definition is the dependability of the system state to ensure that a specific device is operating in its boundaries and produces the results that are expected. As this trustworthy system state can not be enforced by specific measures a reporting infrastructure for detecting altered systems could face this challenge. Privacy as the second definition aims to conceal and protect the individual records of the people. Surveys[19] show that users want to get access to

---

[17] DIP - Data, Information, and Process Integration with Semantic Web Services, http://dip.semanticweb.org/

[18] http://www.ercim.org/

[19] http://www.govtech.net/

their medical records but are very concerned about the security as well. Standards like HL7 help to spur the interaction between the involved parties but are also subject to privacy research[20]. A third dimension of trust is non-repudiation of the gathered information and transactions which means that they can be traced down to certain entities which are originating them. These entities can be the measurement devices like sensors or people issuing them. A last dimension is the long time security of the medical records in terms of eavesdropping and changes.

The first aspect is directly related to privacy requirements; the second addresses the reliability of stored data. New technologies can provide hardware security anchors for a low price addressing different dimensions of trust. For example Trusted Computing offers secure handling and usage of cryptographic means like asymmetric keys but also provides approaches for pseudonymity and system state measurement (Kuntze2006); (Kuntze2007). This hardware based security paradigm opens new ways for a holistic way securing data through the whole lifecycle beginning at their creation.

> REACTION will define "trust" and develop concepts and hardware anchors for trust to be used in application security models.

Mobility in healthcare is a more and more important topic which results also on a European level to working groups like the newly formed ERCIM eMobility[21]. Challenges in the mobile domain are mobile applications and services, middleware for mobile communications, security mechanisms, network architectures, technologies, and protocols for wireless and mobile communications which clearly can not be solved in short term. Therefore it is important to address aspects of long term evolution and security aspects in the design and specification by establishing a high flexibility with respect to used methods and algorithms.

Another important trust issue in healthcare applications is to ensure authenticity and integrity of sensitive health data, such as sensor data.

> REACTION aims to provide a visible and controllable distributed security and privacy model, which is based on the concept of trust as a multilateral relation between stakeholders in a community of patients, informal carers and formal healthcare professionals and providers.

At least one EU funded project is relevant for trust concepts in REACTION, although this project addresses more general issues in ambient intelligence:

Projects/Concepts	Scope of the project /Concept
SWAMI Aims to identify and analyse the social, economic, legal, technological and ethical issues related to identity, privacy and security in Ambient Intelligence (AmI) and will define and study various research and policy options, which could serve as safeguards and privacy-enhancing mechanisms	The aim will be to identify mechanisms, which will ensure user control, user acceptance and enforceability of policy in an accessible manner.

Security implementation

With the increase of cross-boundary services that span over several organizations or web sites and involve multiple agents, the need for a distributed way to manage the user identity becomes an increasingly concerning issue. The right identity management solution should allow people to have control over their own data and enable users to keep one or more identities over time that stay fixed, regardless of what services are still in existence.

OpenID is a distributed identity management design that works with the existing web infrastructure. An OpenID-enabled site can ensure that for a given identity URL, only the person owning that URL can authenticate, and nobody else can fake that identity. Also other emerging specifications, like the recent Web Single Sign-On Metadata Exchange (Web SSO MEX) Protocol

---

[20] http://www.ehealthnews.eu/

[21] http://www.emobility.unibe.ch

and Web Single Sign-On Interoperability Profile (Web SSO Interop Profile), jointly crafted by Sun and Microsoft, will surely have a great impact in the industry and is of relevance for REACTION.

SAML, (Security Assertions Markup Language) may contribute to provide a solution for distributed identity management in an open environment. SAML is designed to deliver interoperability between compliant Web access management and security protocols, so it should be easily integrated with the rest of the platform. It is NOT a security solution, though and does not address privacy policies.

> REACTION aims to integrate OpenID with SAML. Using SAML will enable implementation of single-sign on and enable distributed transactions by making the client application retrieve its security assertions from a trusted authority and sending it to the other end of the transaction or making the other end of the transaction look for the required assertions before the completion of the transaction.

OpenID allows linking the identity of the user with an URL. In order perform a transaction in a server, the user sends his request along with the identity URL, DSA signature, and assertion timestamp, and the server can then verify the signature using either its cached version of the ID server's public key, or get it directly from the ID server URL. Alas, currently OpenID does not work with WS security and SAML, but efforts on their integration are under research.

In REACTION we distinguish between various types of identities such as virtual identities, federated identities with respect to different domains. REACTION will combine identity virtualisation with infrastructure-based accountability negotiations, which are very efficient but also complex. REACTION will assess the feasibility of an approach, which incorporates a context server, which will take care of next generation session initiation. This can be combined with a client device layer that will take care of device and identity virtualisation and security adaptation to context.

At least one EU funded project is relevant for the security work in REACTION:

Projects/Concepts	Scope of the project /Concept
UBISEC Aims to address new technologies originating from the integration of public wide area networks and home/SOHO local area networks	UBISEC is aiming at an infrastructure for large-scale mobility and security based on SmartCard technologies for context-aware and personalised authorisation and authentication services in heterogeneous networks

Summary of expected advances with respect to state-of-the-art

Baseline (starting point, what is available)	Further developments in REACTION
Algorithms: several algorithms for closed loop control of glucose levels reported in literature. All these algorithms rely on empirical (sometimes semi-mechanistic) model kernels without an explicit representation of anatomical and physiological patient parameters. Proportional-Integral-Derivative (PID), Model Predictive Control (MPC), and Fading Memory Proportional Derivative algorithms	AGC algorithm with input from physiological condition monitoring. Based on individualized mechanistic physiologicall-based models for glucose uptake, insulin delivery and insulin-glucose interaction. A pre-parametrization of model kernels by anamnesis and diagnosis parameters will be possible and shall enhance the accuracy of control. Anatomical and physiological patient parameters are explicitly represented and can directly be used for changes in the model kernel of the control algorithm. REACTION will combine several known control theorectical concepts such as Proportional-Integral-Derivative (PID), Model Predictive Control (MPC), and Fading Memory Proportional Derivative algorithms with mechanistic physiologically models of glucose-uptake, insulin-delivery and glucose-insulin interaction.
Sensors: wireless sensor technology for monitoring physiologic parameters IR measuring principle of glucose detection Glucose sensor (impedance spectroscopy)	The ePatch technology will be taken further in the REACTION project. ePatch Continuous Glucose Monitoring sensors based on Impedance Spectroscopy and IR spectroscopy will be developed and tested in field trials. Other sensors for skin

Baseline (starting point, what is available)	Further developments in REACTION
ePatch sensor	temperature and pulse oximetry will be manufactured A new ePatch prototype suitable for mass manufacturing and disposable technology will be developed and tested New minimal invasive IR-sensors for glucose monitoring Improved impedance spectroscopy glucose sensors Integration of several sensor principles into a single e-patch platform Increased accuracy of glucose monitoring
Service Oriented Architecture: The software architecture starts from the middleware Hydra which provides a Service-Oriented approach to networks of heterogeneous embedded devices.	The service oriented architecture will be adapted to include body area and personal area networks.
Semantic Model Driven Architecture based on Hydra Device Ontology	The Hydra middleware will be extended with domain ontologies from the health care field and device ontologies for the sensors and device used in Reaction.
P2P Architecture for interconnecting subnetworks of devices	The P2P architecture of Hydra will be extended to include BAN and PAN. REACTION applies a novel approach to large-scale SOA and envisions arbitrary pairs of peer application entities communicating and providing services directly to and with each other. In a peer-to-peer SOA, none of the participant hosts is required to be always on; moreover, a participating host may change its IP address each time it comes on. The design and implementation of the SOAP API is being carried out with the purpose to enable peer-to-peer sharing of XML-based Web Services that are programming language independent and can be developed in C# or Java.
Service Orchestration and composition based on semantic technologies	The Hydra middleware will be extended with an Orchestration Manager and a rule engine for creation of e-health workflows.
Semantic interoperability between applications, devices and sensor based on semantic web technologies	The backend knowledge discovery processes in REACTION will be implemented using Semantic Web Services to provide an automated environment for delivering eHealth services and application.
Security: Trust and Privacy	REACTION will define "trust" and develop concepts and hardware anchors for trust to be used in application security models. REACTION aims to provide a visible and controllable distributed security and privacy model, which is based on the concept of trust as a multilateral relation between stakeholders in a community of patients, informal carers and formal healthcare professionals and providers.
Security: Distributed Identity Management based on OpenID	REACTION aims to integrate OpenID with SAML. Using SAML will enable implementation of single-sign on and enable distributed transactions by making the client application retrieve its security assertions from a trusted authority and sending it to the other end of the transaction or making the other end of the transaction look for the required assertions before the completion of the transaction.
Security:Virtualisation	In REACTION we distinguish between various types of identities such as virtual identities, federated identities with respect to different domains. REACTION will combine identity virtualisation with infrastructure-based accountability negotiations, which are very efficient but also complex.

Baseline (starting point, what is available)	Further developments in REACTION
	REACTION will assess the feasibility of an approach, which incorporates a context server, which will take care of next generation session initiation. This can be combined with a client device layer that will take care of device and identity virtualisation and security adaptation to context.

Key Performance Indicators

Research Indicators, Activities Performance Criteria		Way of measure	Threshold value
	User needs compilation	Quantitative, Documentation	Number of Users interviewed Specifications including requirements on: - Functionalites (number) - security and safety - Ethics and legal aspects Validation of platform
	Sensors development	Unit testing of hardware and software modules. Peer reviewing of specifications.	Quality assured code and hardware Prototype exist. Specifications approved by Technical Board
	Data Mgt and Service Orchestration	Unit testing of software modules. Peer reviewing of architecture.	Quality assured code Prototype exist Architecture approved by Technical Board
	Network Mgt and Service Execution	Unit and performance testing of software modules. Peer reviewing of architecture.	Quality assured code Prototype exist Architecture approved by Technical Board
	Risk Assessment and Feedback	Unit and performance testing of software modules. Peer reviewing of architecture, models and strategies. Usability testing of tools.	Quality assured code Prototype exist Architecture approved by Technical Board. Models and strategies peer reviewed and accepted. Tools approved by users.
	Security, Privacy and Safety	Unit, performance and security testing of software modules. Peer reviewing of architecture, framework and concepts	Quality assured code Prototype exist Architecture approved by Technical Board. Framework and concepts peer reviewed and accepted.
	Clinical Practice and field trials	Peer reviewing of setup and evaluation plans. Peer reviewing of test results	Evaluation plans approved by Medical Manager Evaluation report approved by project board and Medical Manager. Approval from the Ethics Committee before study related activities
	Platform integration	System testing. Interoperability and WS conformance testing.	Quality assured code Prototype exist Platform approved by technical board Web services conforms to WS-Basic Profile

Research Indicators, Activities Performance Criteria		Way of measure	Threshold value
	Coverage of ethical issues	Peer reviewing Clinical work will be performed according to Good Clinical Practice (GCP), ICH – Guidelines and the Declaration of Helsinki	Ethical analysis approved by project board and the local Ethical Committees before study related activities
	Legal Framework	Peer reviewing of business modelling framework. Peer reviewing of legal and regulatory framework.	Number of existing legal framework studied Business modelling framework approved by project board. Legal and regulatory framework approved by project board.
	Transfer of REACTION results in universities educational activities (e.g. theses, course materials, etc.)	Quantitative, Report	Greater than three (3)
	Technical results submitted to the standardization bodies	Qualitative, Documentation	Active participation in the WGs (attend at least 4 events).
	Scientific papers produced	Quantitative, Documentation	At least eight (8) to be revised at the beginning and all along the project in the Dissemination Plan.
	Press echoes (articles, references, etc.)	Quantitative & Qualitative	At least fifteen (15)
	Numbers of International and national papers published, conferences, expositions and joint events.	Quantitative & Qualitative	At least fifteen (15)
	Co-operation with other projects (European and world-wide)	Quantitative, Report	At least one (1)
	Dimension of REACTION community (number of subscribers)	Quantitative	At least two hundred (200)
	Web site impact (Numbers of access, feedbacks, downloads, etc.)	Quantitative, report	At least ten thousand hits (10000)

B.1.3 S/T methodology and associated work plan

B.1.3.1 Overall strategy and general description

The technological research and development will be performed in packages (WP3-6) and security, privacy and safety (WP7) as indicated in Figure 6. These activities will be supported and integrated with multidisciplinary research in clinical practice in diabetes management (WP8) and socio-economic frameworks (WP9). The work will follow an evolutionary requirement and usability engineering methodology managed from WP2 and implement and validate a total of four prototypes in three field trials.
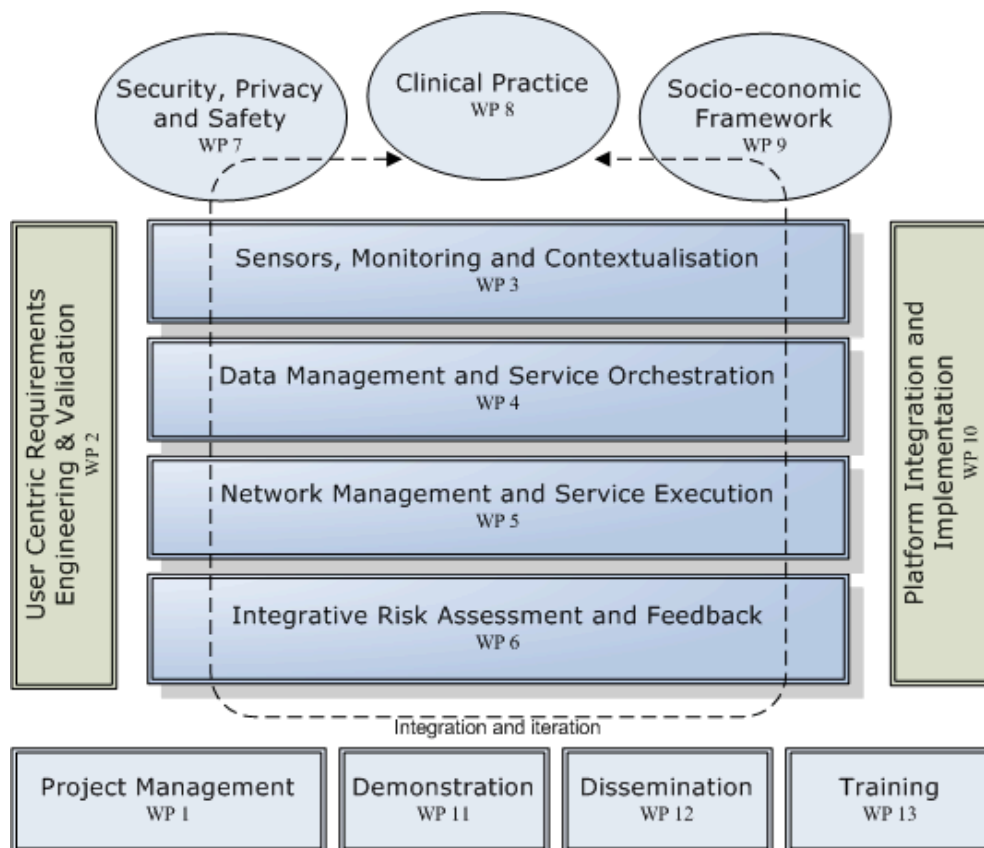
Figure 6 Work package structure

Iterative requirements engineering

The REACTION project seeks to use technology as a tool to foster Human Development, in order to use the great potential that new technologies might have for addressing major societal challenges in coping with the increasing number of citizens suffering from insulin-depending diabetes. The success of the new technological applications depends heavily on the acceptance from end-users, i.e. patients, relatives and professional carers as well as the acceptance from healthcare commissioners, business stakeholders, and regulatory authorities.

The requirement engineering process follows the principles of the ISO 13407 "Human-centred design processes for interactive systems" standard. This standard provides guidance on human-centred design activities throughout the life cycle of computer-based interactive systems.

In accordance with this generally accepted process, the REACTION project has adopted an evolutionary requirements engineering, specification and design methodology underpinned by a strong user-centric development, which comply with the following template in each iteration:
- User requirements engineering and refinement
- Architecture design specification and refinement
- Clinical protocol and medical context planning
- Technologies research and development to implement architecture
- Integration and prototype development and field trial preparation
- Field trials in clinical domains
- Conformance testing, usability evaluation and user acceptance testing
- Lessons Learned and change analysis

The methodology calls for comprehensive iterative requirements and stakeholder analysis based on initial requirements gathered from medical and clinical scenario thinking. These requirements would encompass the needs and priorities of the users as well as the wider exploitability and scalability requirements taking into account the technical constraints as well as the safety, socio-economic and legal acceptance and the deployability of the resulting REACTION platform in real Public Healthcare Systems.

Overview of the iterative approach

The starting point of the iterative design process is a set of domain-specific vision scenarios delivering end-user visions of applications in three different insulin therapy domains: General Ward, Outpatient and Automatic Glucoses Control.

The vision scenarios are used to derive detailed technical and clinical oriented use cases that will be discussed in focus groups with stakeholders. The result of this work in WP2 will be an initial set of requirements specifications for the REACTION platform and applications. From the initial set of requirements, the software experts will specify the initial architectural specification.

The architectural specification then drives the research and development work in WP3 to WP7. At the end of each iterative cycle (corresponding to one calendar year) a prototype of the REACTION platform will be implemented in WP10 with a view to integrate as many as the existing components available at the time and in accordance with the detailed work plan.

The clinical work will be undertaken in parallel to the technical development in WP8. It starts with the establishment of a set of clinical protocols in each of the three domains. The protocols define and drive clinical field trials, which will be performed using the increasingly advanced platform prototypes during the cause of the project. The field trials will be used for validation of the benefit provided for individual users and healthcare organisations in terms of efficiency of closed loop healthcare provisioning in diabetes management and insulin therapy.

In WP9, the socio-economic framework will be analysed with focus on ethics, legal and regulatory framework and the business eco-system for private and public stakeholders.

The validation outcome together with results and requirements stemming from WP will be fed back to the WP2 and drive the requirements re-engineering work.

Timing of the work packages and their components (PERT)

All the workpackages and subtasks are structured according to the methodology as described above. The project follows a logical flow of analysis and requirements engineering, research and development of prototypes, and implementation and testing. The logical structure can be seen from following Pert diagram showing how the clinically oriented WP8 and the supporting WP7 on security and safety and WP9 on socio-economic issues feed information and knowledge (models) into the research and development oriented WP3, WP4 and WP6.
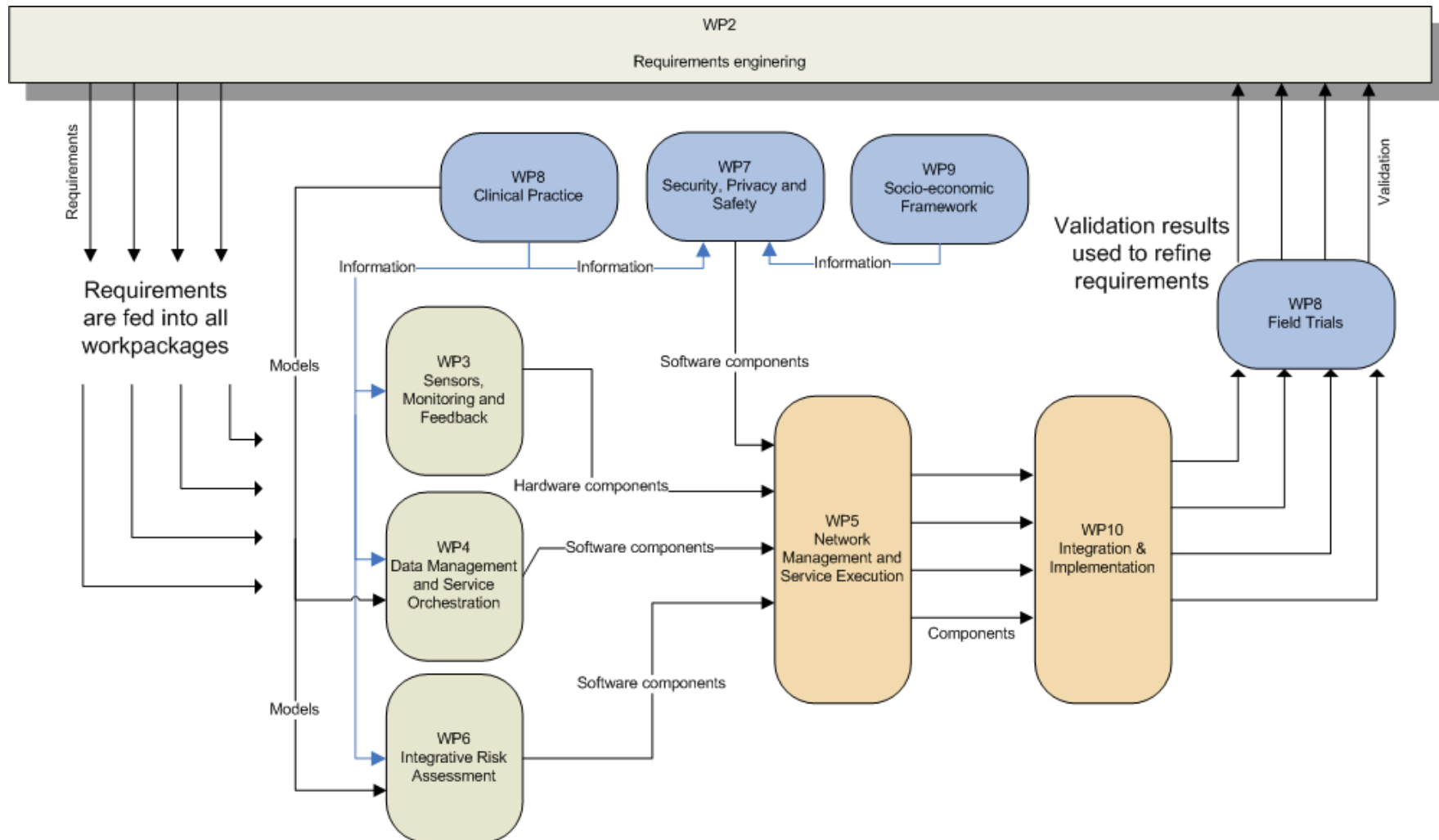
All the WP3, WP4 and WP6 feeds hardware and software components via the production oriented WP5 on network management and service execution. Finally, the integration and implementation in the form of prototypes takes place in WP10 and validation results are fed back to WP8 for field trials and validation. Validation results and Lessons Learned are used to re-engineer requirements in each iteration cycle.

The tasks in the research and development phase runs in parallel and feed prototypes into the demonstrators used for the annual validation the progress of the project and its alignment with project objectives.

Timing of work packages and their components

The overall project time schedule and timing of the 13 workpackages and subtasks is shown in the Gantt chart. A great degree of overlap has been achieved in the different tasks in order to create an efficient workflow with minimal slack.

	Year 1 (M1–M12)	Year 2 (M13–M24)	Year 3 (M25–M36)	Year 4 (M37–M48)
WP1 Project Management				
Task 1.1 Project initiation				
Task 1.2 Overall IP management and co-ordination				
Task 1.3 Project reporting.				
Task 1.4 Knowledge Management				
Task 1.5 Quality Control and Quality Management				
WP2 User Centric Requirements Engineering and Validation				
Task 2.1 Scenario thinking				
Task T2.2 Initial requirements specifications				
Task T2.3 Evolutionary requirements refinement				
Task T2.4 Validation of platform and services				
WP3 Sensors, Monitoring and Contextualisation				
Task T3.1 ePatch body sensor technology				
Task T3.2 Continous glucose monitoring sensors				
Task T3.3 Automatic Glycaemic Control				
Task T3.4 Multiparametric monitoring sensors				
Task T3.5 Graphical User Interfaces				
WP4 Data Management and Service Orchestration				
Task T4.1 Architectural analysis and description				
Task T4.2 Data structures, taxonomies and ontologies				
Task T4.3 Data management				
Task T4.4 Context management framework				
Task T4.5 Rule-based orchestration of services for monitoring and event handling				
WP5 Network Management and Service Execution				
Task T5.1 Network architecture and analysis				
Task T5.2 BAN and PAN network implementation				
Task T5.3 Network Management implementation				
Task T5.4 Network interoperability and service execution				
WP6 Integrative Risk Assessment and Feedback				
Task T6.1 Disease management strategies for diabetes				
Task T6.2 Models for risk assessment				
Task T6.3 Stratifications and multi-parametric health status profiling				
Task T6.4 Knowledge discovery and semantic annotation				
Task T6.5 Integration and implementation with user feedback				
WP7 Security, Privacy and Safety				
Task T7.1 Security requirements				
Task T7.2 Security architecture				
Task T7.3 User empowerment				
Task T7.4 Virtualisation				
Task T7.5 Patient safety and device risk assessment				

REACTION: Remote Accessibility to Diabetes Management and Therapy in Operational healthcare Regimes

	Year 1												Year 2												Year 3												Year 4											
	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18	M19	M20	M21	M22	M23	M24	M25	M26	M27	M28	M29	M30	M31	M32	M33	M34	M35	M36	M37	M38	M39	M40	M41	M42	M43	M44	M45	M46	M47	M48
WP8 Clinical Practice and Field Trials																																																
Task T8.1 General ward RCT	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X												
Task T8.2 Outpatient clinical field trial	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X											
Task T8.3 Automatic Glucose Control (AGC)																									X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
WP9 Socio-economic Framework																																																
Task T9.1 Ethical issues	X	X	X	X	X								X	X	X	X									X	X	X	X	X	X	X	X	X	X	X	X												
Task T9.2 Social issues							X	X	X	X	X	X													X	X	X	X	X	X	X	X	X	X	X	X												
Task T9.3 Legal and regulatory framework	X	X	X	X	X	X							X	X	X	X	X	X							X	X	X	X	X	X	X	X	X	X	X	X												
Task T9.4 Healthcare economics and business models					X	X	X	X	X	X	X	X	X	X	X	X	X	X							X	X	X	X	X	X	X	X	X	X	X	X												
WP10 Platform Integration and Implementation																																																
Task T10.1 Application development platform	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Task T10.2 Device and network integration and testing				X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Task T10.3 Backend integration and testing				X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Task T10.4 Field trials application development					X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X
WP11 Demonstration																																																
Task T11.1 Demonstration																																					X	X	X	X	X	X	X	X	X	X	X	X
WP12 Dissemination and Exploitation																																																
Task T12.1 Dissemination	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Task T12.2 Contributions to standards					X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Task T12.3 Exploitation											X	X	X	X	X	X	X	X	X	X					X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
WP13 Training																																																
Task T13.1 Horizontal project integration						X	X	X	X	X	X	X																																				
Task T13.2 External training						X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Prototyping and field trials

The functionality of each prototype will be determined partly by the development plan for the technological development and partly by the requirements of the clinical protocols to be defined in the project. The requirements will be documented in an annual "Prototype application specification", which serves as a guideline for the development work to be undertaken between the prototypes. The field trials will be used for validation of the benefit provided for individual users and healthcare organisations in terms of efficiency of closed loop healthcare provisioning in diabetes management and insulin therapy.

All results from validation and experiences gathered in the process will lead to refined technical and business oriented scenarios, revised requirements specifications, updated middleware architecture and new prototype specifications.

Evaluation and validation activities will take place on a yearly basis as follows:
> End of year 1: Rapid prototype of closed-loop system to be used in general ward (including some software mock-ups)
> End of year 2: Prototype of outpatient closed-loop system and improved closed-loop system used in general ward (including sensor prototypes)
> End of year 3: Partly/fully functional prototypes of in-hospital and outpatient prototypes including multi-parametric monitoring, risk analysis and full backend interoperability (demonstrators)
> End of year 4: Automatic glycaemic control with closed-loop feedback directly to insulin dosage pumps and field trials with final prototypes
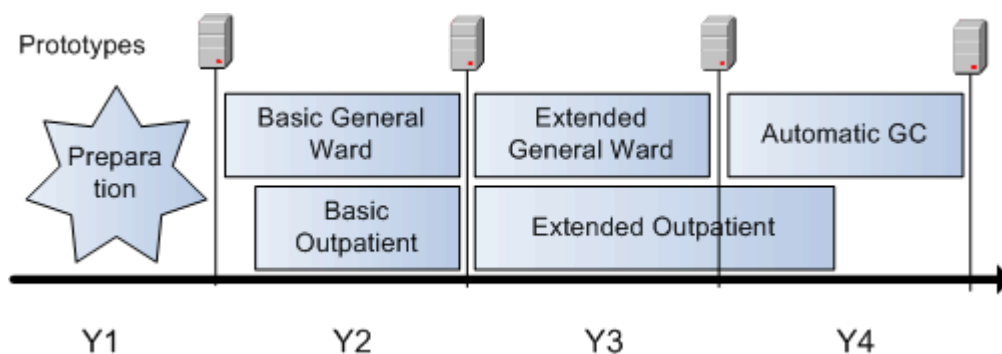
Figure 7 Prototypes and field trials planning

This will help elicit further requirements from the different stakeholders and can be used to refine and enhance the user requirements specifications once a year.

Following the first full validation of the system, the results will be compiled together with latest updates from medical progress reports considered together with updates on user needs from external sources. All this information on evolving requirements will be used to update and refine the user requirements specification, which will then be fed into the architecture design specification and will be used for the re-engineering of the demonstrator prototype.

The last cycle thus coincides with the final prototypes of the project. In the final validation, field trials will be set up to test the health applications on the REACTION platform in realistic settings with representative user populations. The goal is to conclusively prove the validity of the services, to demonstrate the benefit for the healthcare domain, acceptance by patients and other users, and to assess the impact at the European level.

Clinical trials have been designed as explained in the following paragraphs. REACTION project plans to have the following three clinical trials:
- In-hospital glucose monitoring
- Outpatient monitoring and feedback for self-management
- Compliance control and motivation

Trials in humans will be reviewed in ethics committee and will be performed according to GCP and DoH:

- Step 1: Technical evaluation studies
    - o Clinical Research Centre; performance of hardware and software, safety testing, in healthy or diabetic subjects small groups (n<10)
- Step 2: Feasibility studies
    - o Hospital care and/or outpatient setting; in vivo technical performance and usability, safety and side effects small groups (n~20-30), no control group needed
- Step 3: Randomized controlled studies
    - o Hospital care and/or outpatient setting; efficacy, metabolic control and side effects, large groups (n>50), control groups with standard care

B.1.3.3 Work package list /overview

Work package list

WP Number [53]	WP Title	Type of activity [54]	Lead beneficiary number [55]	Person-months [56]	Start month [57]	End month [58]
	LIST OF WORK PACKAGES (WP)					
WP 1	Project Management	MGT	1	86.00	1	48
WP 2	User Centric Requirements Engineering and Validation	RTD	8	85.00	1	48
WP 3	Sensors, Monitoring and Contextualisation	RTD	4	240.50	1	48
WP 4	Data Management and Service Orchestration	RTD	2	194.50	1	48
WP 5	Network Management and Service Execution	RTD	7	96.00	1	48
WP 6	Integrative Risk Assessment and Feedback	RTD	11	145.50	1	48
WP 7	Security, Privacy and Safety	RTD	6	84.00	1	48
WP 8	Clinical Practice and Field Trials	RTD	10	135.50	1	48
WP 9	Socio-economic Framework	RTD	14	77.50	1	48
WP 10	Platform Implementation	RTD	5	136.00	1	48
WP 11	Demonstration	DEM	2	30.00	36	48
WP 12	Dissemination and Exploitation	OTHER	8	43.00	1	48
WP 13	Training	OTHER	13	21.00	6	48
			Total	1,374.50		

B.1.3.4 Deliverables list

All deliverables marked as "Other", "Demonstrator" and "Prototype" will be accompanied by a report describing the deliverable as part of it.

List of Deliverables – to be submitted for review to EC							
No.	Deliverable name	WP no.	Lead bene-ficiary	Estimated Effort PM	Nature	Dissemi-nation	Delivery date
D1.1	Project Quality & Risk Management Plan	1	ATOS	1	R	CO	M01
D12.1	Project website	12	IN-JET	8	O+R	PU	M01
D2.1	Scenarios for usage of the REACTION platform	2	IN-JET	5	R	PU	M03
D2.5	Initial requirements report	2	FORTH-ICS	24	R	RE	M04
D1.2.1	Interim progress report for the Commission M6	1	ATOS	8	R	CO	M06
D2.4	Market and regulatory-standards watch report	2	ATOS	4	R	PU	M06
D4.3	Technical requirements for medical data management	4	MSG	10	R	PU	M06
D5.1	Communication standards within BAN and PAN	5	FORTH-ICS	8	R	PU	M06
D10.1	AmI test bed	10	FORTH-ICS	5	P+R	RE	M06
D1.3	Plan for managing knowledge and intellectual property	1	ATOS	2	R	CO	M09
D4.2	Initial data structures, taxonomies and ontologies	4	ALL	14	R	RE	M09
D7.5	Safety issues in REACTION applications	7	UBRUN	10	R	PU	M09
D1.4.1	Periodic activity, management and financial reports Y1	1	ATOS	10	R	CO	M12*
D2.7	Validation framework	2	FORTH-ICS	3	R	PU	M12
D3.2.1	First generation e-patch, Report on ePatch technology and integration results	3	DELTA	10	R	RE	M12
D3.3	SOLIANIS Impedance Spectroscopy CGM sensors	3	SOLIANIS	20	P+R	RE	M12
D3.5	IMM IR breadboard device	3	IMM	34	P+R	RE	M12
D3.10	Survey of commercially available CGM devices and insulin pumps + suitability for AGC	3	IMM	8	R	PU	M12
D4.4.1	1st Prototypes of core data, context and event handling management subsystems	4	CNET	56	P+R	RE	M12
D5.3.1	Network Management subsystem implementation & REACTION internal development platform	5	FORTHNET	14	P+R	RE	M12
D6.1	Assessment of existing disease management strategies & Available risk assessment tools and their parameters	6	MSG	24	R	PU	M12
D7.2	Concepts of trust and architectural implications	7	FHG-SIT	24	R	RE	M12
D8.1	Clinical protocol for MDI compliance	8	CHC	11	R	PU	M12
D9.4	Healthcare economics and reimbursements	9	IN-JET	3	R	PU	M12
D10.2	Integration and test plan for BAN/PAN infrastructure	10	DELTA	26	R	PU	M12

No.	Deliverable name	WP no.	Lead bene-ficiary	Estimated Effort PM	Nature	Dissemi-nation	Delivery date
D1.2.2	Interim progress report for the Commission M18	1	ATOS	8	R	CO	M18
D3.1	Concept for disposable ePatch platform	3	DELTA	18	R	PU	M18
D3.8	Report on glucose sensor development	3	IMM	5	R	PU	M18
D7.3	User empowerment, requirements and concepts	7	FHG-SIT	16	R	PU	M18
D9.1	REACTION services in social and cultural contexts	9	FORTH-ICS	15	R	PU	M18
D7.1	Security, privacy and trust requirements	7	ATOS	14	R	PU	M21
D1.4.2	Periodic activity, management and financial reports Y2	1	ATOS	10	R	CO	M24*
D2.2	Clinical watch report	2	UBRUN	4	R	PU	M24
D2.3	Technology watch report	2	CNET	4	R	PU	M24
D2.6	Prototype application specification	2	IN-JET	3	R	RE	M24
D3.11	Relevant integrated algorithms implemented, evaluated and benchmarked in retrospective analysis	3	BTS	23	O+R	RE	M24
D4.1	State of the Art - Concepts & technology for a unified data fusion architecture	4	CNET	26	R	PU	M24
D4.4.2	2nd Prototypes of core data, context and event handling management subsystems	4	CNET	56,5	P+R	RE	M24
D5.2	BAN & PAN networking components and implementation	5	FORTH-ICS	14	P+R	RE	M24
D5.3.2	Network Management subsystem implementation	5	FORTHNET	10	P+R	RE	M24
D6.2	Newly discovered diabetes knowledge in public available datasets	6	MSG	27	R	PU	M24
D6.4.1	1st Prototype Computational kernel for individualized mechanistic models	6	BTS	19	P+R	RE	M24
D8.5	Clinical evaluation of MDI compliance study	8	CHC	6	R	PU	M24
D9.2	Regulatory framework and data protection	9	VUB	24	R	PU	M24
D10.3.1	Prototype of backend infrastructure & Integration and test plan for backend infrastructure	10	FORTHNET	24	P+R	RE	M24
D10.4	Applications for field trials	10	CNET	39	P+R	RE	M24
D12.2	Market and competitor analysis	12	IN-JET	6	R	RE	M24
D13.1	Teaching material for healthcare professionals	13	UBRUN	7	R	PU	M24
D2.8	Lessons Learned and results of usability evaluation	2	IN-JET	7	R	RE	M25
D1.2.3	Interim progress report for the Commission M30	1	ATOS	8	R	CO	M30
D3.6	IMM IR CGM prototype	3	IMM	25	P+R	RE	M30
D3.9	Sensors for glucose measurement for first field trials and second generation e-patch	3	IMM	8,5	P+R	CO	M30
D7.4	Virtualisation in distributed healthcare applications	7	FHG-SIT	20	R	PU	M30
D8.2	Clinical protocol for AGC	8	MUG	20	R	PU	M30

No.	Deliverable name	WP no.	Lead bene-ficiary	Estimated Effort PM	Nature	Dissemi-nation	Delivery date
D1.4.3	Periodic activity, management and financial reports Y3	1	ATOS	10	R	CO	M36*
D3.4	SOLIANIS Impedance Spectroscopy AGC sensors	3	SOLIANIS	10	P+R	RE	M36
D3.7	IMM IR AGC prototype	3	IMM	14	P+R	RE	M36
D3.13	Prototype insulin pumps and pump control for tests	3	IMM	8	P+R	RE	M36
D4.5	Integration with emergency centres, results/experience	4	CNET	32	R	PU	M36
D5.4	Backend network integration	5	FORTHNET	20	P+R	RE	M36
D5.5	Implementation of event handling systems	5	CNET	14	P+R	RE	M36
D5.6	REACTION SDK - Software Development Kit tools	5	CNET	16	P+R	PU	M36
D6.4.2	2nd Prototype Computational kernel for individualized mechanistic models	6	BTS	20	P+R	RE	M36
D8.3	Clinical evaluation of general ward clinical field trial	8	MUG	35,5	R	PU	M36
D9.3	Product liability issues in REACTION applications (including a privacy framework for diabetes monitoring)	9	VUB	14	R	PU	M36
D10.3.2	Prototype of backend infrastructure	10	FORTHNET	18	P+R	RE	M36
D13.2	Workshop teaching material for business managers	13	IN-JET	7	R	PU	M36
D2.9	Updated requirements reports	2	FORTH-ICS	18	R	PU	M38
D9.5	Sustainable business models in diabetes management	9	IN-JET	21,5	R	PU	M40
D13.3	Workshop teaching material for healthcare developers	13	UBRUN	7	R	PU	M40
D1.2.4	Interim progress report for the Commission M42	1	ATOS	8	R	CO	M42
D8.4	Clinical evaluation of outpatient clinical study	8	CHC	38	R	PU	M42
D6.3	Refined risk assessment engine	6	FORTH-ICS	55,5	P+R	RE	M46
D1.4.4	Periodic activity, management and financial reports Y4	1	ATOS	10	R	CO	M48*
D1.5	Final report	1	ATOS	11	R	CO	M48*
D2.10	Final validation report of the REACTION platform (all inclusive: sensors, subsystems, security framework, services)	2	FORTH-ICS	13	R	PU	M48
D3.2.2	Final generation e-patch, Report on ePatch technology and integration results	3	DELTA	12	R	RE	M48
D3.12	Evaluation of integrated systems with best out of prospective evaluation of 2 top-ranked algorithms	3	BTS	23,5	R	RE	M48
D3.14	Report on of multi-parametric monitoring sensors	3	DELTA	21,5	R	PU	M48
D8.6	Clinical evaluation results of technologies for AGC systems (inclusive of sensors, pumps, e-patch)	8	MUG	25	R	PU	M48
D10.5	Final REACTION platform prototype (all inclusive: sensors, subsystems, security framework, services)	10	CNET	24	P+R	RE	M48
D11.1	Feedback from demonstration activities	11	CNET	30	R	PU	M48

No.	Deliverable name	WP no.	Lead bene-ficiary	Estimated Effort PM	Nature	Dissemi-nation	Delivery date
D12.3	Plan for dissemination and exploitation of knowledge	12	IN-JET	29	R	RE	M48
			TOTAL	**1374,5**			

* Deliverables marked with the asterisk (*) can be delivered up to 60 days after the end of the month indicated in the list above.

B.1.3.5 Work package descriptions

WP 1 – Project management

Objectives

The workpackage will provide an effective and efficient management and work process of the project during the contractual period. Its objective is to ensure an efficient management of the project and a consistent high quality of the work to be performed and of the reports produced. Further, it deals with the administrative and financial management of the project.

The main objectives of this workpackage are to:
1. Ensure the delivery of the project on time and within the established budget.
2. Co-ordinate the technological and scientific orientation of the project.
3. Effectively deal with all risks and issues as they arise.
4. Secure high quality of the work and of the delivered documents and software.

Workpackage leader

The workpackage will be led by the coordinator ATOS. Various management activities will be carried out by CNET, UBRUN, MUG and IN-JET.

Tasks and actors in this workpackage

The tasks are specifically formulated to ensure the implementation of the management approach and structures described in section B2.1. Management structure and procedures.

ATOS is the intermediary between the Commission and the Consortium and responsible for the IP project controlling, in particular for the administrative and financial reporting, project time controlling, co-ordination issues and overall IP activities (e.g. dissemination). They are also responsible for the correct application of all EU rules, the overall technical management and co-ordination within and between work packages. ATOS will coordinate all relations with the European Commission and other projects in the Framework Programme (clustering).

ATOS' appointed Project Manager is the direct point of coordination for the working relationships with the Workpackage Leaders. The Project Manager will be supported by the Project Board, the Technical, the Medical Engineering Manager, the Clinical Manager and the Workpackage and Task Leaders.

CNet will assist the coordinator in the day-to-to-day coordination of the IP, while the technical coordination of workpackages will be carried out as part of each individual WP. In addition to this CNet will organise and prepare the technical part of reviews initiated by the commission. Also, it is their responsibility to organise and report to the project Technical Advisory Board meetings as well as participate and report to the PMB on the overall technical progress of the project. Another important task for CNet is to set up the quality procedures and provide the ongoing quality management of the project as Quality Manager. CNet will assist the project coordinator in the review of deliverables. Moreover, CNet will organise and carry out the yearly updates of the DOW. In case competitive calls would be needed, CNet will be responsible for organising the technical part of this. All these activities are conforming to activities described in Article II.16.5 of the Model Grant Agreement.

Regarding the management role of MUG and UBRUN, these two partners are entitled to work in a very close manner with the project Coordinator and the Technical manager, in order to ensure the quality and the accuracy of the medical results. These two partners are in charge of supervising, on one hand that all the medical results are in line and are coherent with the expected results, and on the other hand the quality of the performed work giving feeback for improving the whole processes to get better results. Therefore this participation could be

understood as quality management for medical approach and trials. Additionally to this, UBRUN is responsible of the Knowledge Management task to be carried out within the project.

The work will be carried out in five main tasks:

Task T1.1 – Project initiation

TASK LEADER – ATOS

The first task within this workpackage will be the effective initiation of the project. This will involve the project "kick-off" meeting and setting out a plan for the project including the detailed assignment of roles, responsibilities and resources, the project timetable and description and assignment of each deliverable to be produced together with the project Quality Plan. This will be agreed with all the Project partners at the kick off meeting.

Task T1.2 – Overall IP management and co-ordination

TASK LEADER – ATOS

The focus of this task is project management and co-ordination deploying all the functions, roles, resources and responsibilities. This includes in particular the Project Board, Project Manager, Specialist individual and team project roles, partner managers, Workpackage Leaders and Task Leaders. This task has five very important sub-tasks as follows:

Subtask 1.2.1 Co-ordination and organisation of IP management bodies

ATOS is responsible for the overall co-ordination, administration and organisation of the IP management structure and will deploy the organisational structure and procedures to ensure the smooth and efficient operation of the project from both the strategic and tactical perspectives.

ATOS will ensure that this structure operates in an effective way, that all necessary collaborations and decision-making apparatus are in place and that the necessary liaisons, including both formal and informal meetings, are undertaken so that a truly multi-party, multi-discipline REACTION project environment is efficiently maintained.

Subtask 1.2.2 Operational project management

To ensure efficient working, there will be day-to-day operational Project Management of the project's work overseen by the Project Manager. The Project Manager is the interface between the Project Board and the project, and is overall responsible for the success and smooth running of the project.

Subtask 1.2.3: Technical management and coordination

This subtask is responsible for the co-ordination of the technical part of the project. The main part of the task will be to secure the continuous alignment and integration of the technical work performed in each of the workpackages in order to secure a smooth and trouble-free integration of individual components and continuously alignment of the work with the projects overall objectives. The technical coordination will be provided by the Technical Manager, a Medical Engineering Manager and a Clinical Manager. This subtask will include on-going evaluation of the projects plans and the review and updating of the project plan following the first 12 months of the project and annually thereafter.

Subtask 1.2.4: Workpackage management

This subtask is responsible for the co-ordination and organisation of the workpackage management. Strong emphasis on workpackage autonomy and management will be enforced with clear objectives for the outcome of each RTD workpackage. Interfaces between work-packages have been made simple in order to create transparency and promote responsibility among project managers. The main players involved in workpackage management are the Workpackage Leaders and Task Leaders together with the other project managers.

Subtask 1.2.5: Risk Management

This subtask is responsible for the management of all risks and issues which are identified at the beginning of the project and arise over its course. All project participants and external advisors will be responsible for raising any risk or issue they perceive. All such risks and issues will be registered via the project's risk log. The status and mitigation of each risk identified will be reviewed regularly as a working document and formally at each Project Board meeting. The Project Manager will manage and maintain the risk management log.

Task T1.3 – Project reporting

TASK LEADER – ATOS

The Project Manager will be responsible for producing the formal project reporting deliverables, including the periodic project management reports, the yearly progress reports and the final project report. Highlight and exception reports will be produced as required throughout the project. Each contracting partner will take part in the overall reporting of the project.

Task T1.4 – Knowledge management

TASK LEADER – UBRUN

Knowledge Management is a key objective both within the Consortium and to the outside world, which will start 3 months after start of the project (M3).

Subtask 1.4.1: Knowledge Management

Ensures that relevant project information (technical, process or other) is made available by the generator of knowledge (e.g. via a process) and those who need this knowledge or information have easy access to it. The goal of this subtask is to ensure an appropriate transfer of required information within the project.

Subtask 1.4.2: IPR and Patent filing

This subtask will ensure that IPRs are properly handled and patents are filed where and when necessary, and the required legal advice for handling this, will be provided within this task. If required there will also be advice provided on how to best exploit IPRs and patents.

Task T1.5 – Quality control and Quality management

TASK LEADER – CNET

This task will take the overall responsibility of the quality management and quality control of the project and of its deliverables and other outputs. This quality control is achieved through internal and external reviews. Existing tools (e.g. product definition and quality criteria, checkpoint analysis, milestone tracing, lessons-learned databases) will be used to ensure quality of the project and the results.

A permanent quality control plan will be applied to all deliverables, major other outputs and training courses for external use. The plan will specify timing and scope of internal and external reviews. Internal reviews are carried out by partners not directly involved in the production of the relevant deliverable. External reviews are envisaged for major deliverables that are disseminated to the outside world. In addition to deliverable reviews other reviews may be planned, e.g. mid term audits, milestone reviews, technological audits.

Workpackage description

Workpackage number:	WP 1	Start date or starting event:						Month 1		
Work package title:	Project Management									
Activity type:	MGT									
Participant number:	1	2	3	4	5	6	7	8	9	10
Participant short name	ATOS	CNET	DELTA	IMM	FORTH-ICS	FHG-SIT	FORTHNET	IN-JET	ALL	MUG
PM per participant:	67,0	16,0								1,0
Participant number:	11	12	13	14	15	16				
Participant short name	MSG	CHC	UBRUN	VUB	BTS	SOLIANIS				
PM per participant:			2,0							

Objectives
- ensure the delivery of the project on time and on budget.
- coordinate the technological and scientific orientation of the project.
- secure the quality of the work to be undertaken and of the delivered documents and software.
- management of knowledge
- risk management and contingency planning

Description of work (broken down into tasks) and role of partners

T1.1 Project initiation: The effective initiation of the project involving the production of a project Initiation Document and Quality Manual (internal Milestone M1)

T1.2 Overall IP management and co-ordination: The co-ordinating partner will conduct the operational management of the project on a day-to-day basis.

T1.3 Project reporting: The formal project reporting deliverables, including the annual progress and financial reports and the final project report. Also interim project progress reports will be prepared for the commission.

T1.4 Knowledge Management: Ensures that relevant project knowledge is made available to those who need and that IPR is properly handled and patents are filed where and when necessary.

T1.5 Quality Control and Quality Management: Responsible for implementing and maintaining a quality control scheme that is applied to all deliverables, major other output and training courses.

Deliverables (brief description) and month of delivery
D1.1 Project Quality & Risk Management Plan (M1)
D1.2.x Interim progress reports for the Commission (M6 – M18 – M30 – M42)
D1.3 Plan for managing knowledge and intellectual property (M9)
D1.4.x Periodic activity, management and financial reports (M12 - M24 - M36 - M48)
D1.5 Final Report (M48)

WP 2 – User Centric Requirements Engineering and Validation

Objectives

The work in WP2 will manage and undertake the work in carrying out the iterative engineering of requirements, which special focus on the engineering process of initial requirements and after the end of each iteration cycle.

The aim of this workpackage is thus to maintain a continuous discovery and analysis of user centric requirements, needs and prospects, to be used in the design, development, implementation and validation of platform and services. Moreover, the aim is to plan and manage user validation activities and to collect, analyse and document the results.

The work package will finally investigate all external drivers for service oriented remote health and home care environments and its deployment in European healthcare systems using a holistic approach to health status monitoring, assessment, improvement and maintenance.

The specific methodologies that will be used include evolutionary design and refinement re-engineering. Lessons Learned obtained during project progress will be used to arrive at adjustments to the initial requirements incorporating and inclusion of emergent requirements. The workpackage is responsible for continuously informing the workpackage partners of the requirement engineering process in order to enable the necessary and timely modification of design specifications and possible re-engineering of affected modules.

Specifically the objectives of this workpackage are to:
- Elicit the generic and specific domain requirements for the full technical, societal and business realisation of the project results in the domain of Public Health Services.
- Maintain a continuous study of the medical, clinical, technological, legal, regulatory, and market developments affecting the REACTION platform as the project progresses.
- Evaluate the potential clinical value and validate the impact on clinical workflows from REACTION applications and field trials in WP3 and its affect on the requirements.
- Evaluate the early adoption of the platform in relevant healthcare environments taking into account socio-economic and regulatory boundary conditions derived in WP9.
- Re-formulate the specific domain user requirements in terms of updated functionalities from each of the sub-systems. This process will feed back results from all workpackages to the (re)specification phase enabling the re-engineering of requirements for best technical outcome, conformity to user needs, innovation and market potential.

Workpackage leader

The workpackage will be led by IN-JET

Tasks and actors in this workpackage

The work will be carried out in four tasks:

Task T2.1 – Scenario thinking

TASK LEADER – IN-JET

At the beginning of the project, scenarios of clinical protocols and use cases will be developed for the selected user domains. This task will be carried out using the IDON methodology for scenario thinking. A one-day user workshop for each domain will be organised to bring together representative users with appropriate expertise and experience. Representative users from the project user partners as well as end-user representatives from a mix of health and social care providers (public and private providers, healthcare professional, patient organisations,) will be invited to these workshops. The activities carried out focus on identification of *uncertainties* about the future of diabetes control, insulin therapy and integrative care.

The scenarios are constructed from a varied background of knowledge and guesswork about the relevant environment and the trends and discontinuities likely to happen in the future and

affecting the users operations and way of work. The scenarios will draw on both available research and application knowledge in the Consortium and on the opinion of a diverse set of people invited for the workshops. The results of these activities will be documented in a full set of scenarios for each of the domains. Following the prepared scenarios, a set of storylines will be prepared. The storylines provide a research glossary and details of the research approach.

This task will be carried out jointly by IN-JET with the participation of all clinical partners. IN-JET will plan and execute the workshops and FORTH-ICS will assist in the development of scenarios. The work will be documented in deliverable D2.1 Scenarios for usage of REACTION in medical domains and used to formulate an initial requirements specification.

Task T2.2 – Initial requirements specifications

TASK LEADER – FORTH-ICS

This task will aim to achieve a systematic formalisation of all relevant stakeholder requirements and subsystem functionality requirements. The functional user requirements are derived from user workshops.
- Functional requirements - what is required from different user perspectives?
- Security and safety requirements – based on the security analysis and device risk analysis from WP3, which include the formulation of a set of security policies.
- Business requirements – what is required to live up to market and business needs, what are required to satisfy existing and new stakeholder involvement and how will current business practices be supported?
- Societal requirements - including requirements related to ethics, inclusion, quality of use, professional liability, regulatory needs, etc.

Subtask 2.2.1: Functional requirements

Functional requirements are related to the use of the REACTION platform in clinical settings. It will be based on the user scenarios and derived storylines that involve the most important aspects of user expectations. Demands for closed loop feedback and seamless interoperability and mobility will be integrated in the functional requirement specification. The aim of this work is to capture functional requirements in such a way that they can drive architectural and technical decisions and be used to validate the various sub-systems and the entire architecture.

Subtask 2.2.2: Security and safety requirements

The scenarios will be used as the basis for a security and patient safety analysis to be performed in WP3. Security requirements workshops will be performed to stimulate discussion regarding common security criteria, metrics, models and protocols and negotiations and conclude the security requirements for the REACTION scenarios in such a way as to provide a private, secure and trusted healthcare environment.

Subtask 2.2.3: Ethical and legal requirements

The aim of this subtask is to capture non-functional requirements related to ethical and legal realms originating from WP9. Several areas will be targeted for requirements gathering. This subtask will be concerned with the collection and structuring of requirements on the socio-economic framework. Aspects of inclusion and data protection requirements, i.e. ensuring that the individual should have the possibility to control access to his or her personal information and to construct his or her own public persona, will also be investigated. Finally, important requirements derived from liability analysis and IPR issues will be included.

Subtask 2.2.3: Business requirements

Present stakeholders in the diabetes market may seek - or be forced into - new roles as the convergence of Internet communication, on-line services, and content evolve into the Internet of Things and Services. Interoperable services on the REACTION platform must be accompanied by sustainable business cases for all stakeholders, including healthcare providers, device manufacturers, pharmaceutical companies, and service providers. The requirements for supporting this ecosystem of heterogeneous stakeholders will be analysed and the impact on functional and non-functional requirements will be elicited.

The requirements will be identified and verified together with each WP leader. ATOS, FORTH-ICS, CNET and IN-JET will lead the engineering work, which includes evaluation of relevance, realism and consistency as well as resolving conflicts and bridging gaps. MSG and ALL will provide input for the integrative risk assessment and BTS on data model requirements and design for optimal data analysis and closed loop control. DELTA, IMM and SOLIANIS will participate on sensors, MUC and CHC will provide the clinical practice views from the users. FHG-SIT will be responsible for performing the security and safety analysis, VUB for the ethical and legal requirements and IN-JET for the business requirements.

Task T2.3 – Evolutionary requirements refinement

TASK LEADER – IN-JET

After the successful completion of a prototype cycle, each RTD work package will analyse and report their development results, RTD experiences, lessons learned in the development and integration work and other relevant knowledge gained during the development cycle. Moreover, knowledge gained from formal testing and system integration will be collected together with latest development in technology, regulatory affairs and markets, which influence the Hydra middleware and its exploitability. The task will include the following subtasks, with the aim of continuously pushing the project's advancement of the state-of-the-art:

Subtask 2.3.1: Lessons learned collection and analyses

Lessons are learned during project RTD work, during testing and integration, as a part of the validation of project prototypes and during literature search and technology watch-reports. Lessons can thus be learned throughout the project work. As such, lessons learned constitute both individual and organisational knowledge and understanding gained by experience, either negative (missed targets, solutions that do not work as expected, wrong choice of technology) as well as positive (easier implementation than expected, faster response time, more interoperable devices than expected).

Subtask 2.3.2: Medical and clinical watch

This subtask will maintain a continuous observation of emergent and disruptive medical and clinical advances in CGM and diabetes therapy with a view to assess their impact on the functionality and usability requirements of project subsystems. It will make available periodic reports to feed into the re-engineering refinement process.

Subtask 2.3.3: Technology watch

This subtask will maintain a continuous observation of emergent and disruptive technology developments with a view to assess their impact on the requirements. It will make available periodic reports to feed into the re-engineering refinement process.

Subtask 2.3.4: Market and regulatory-standards watch

This subtask will maintain a continuous observation of emergent and disruptive market and regulatory-standards developments with a view to assessing their impact on the functionality integration and requirements of project subsystems. It will make periodic reports to feed into the re-engineering refinement process and exploitation planning.

Subtask 2.3.5: Requirements re-engineering

From the lessons learned, validation results, and watch reports, relevant new and/or updated requirements will be extracted. The identification, formulation and validation of requirements will be performed by a WP2 team together with the Technical Manager and relevant WP leaders.
The Project Manager, the Technical Manager and the WP2 manager will evaluate and describe the impact on the future development work arising from the re-engineered requirements and report this in the recurrent deliverables. The evaluation will take place both in the context of scientific and technological progress, adherence to the projects' overall vision and impact on the overall project plan. CNET will provide the technology watch.

Task T2.4 – Validation of platform and services

TASK LEADER – FORTH-ICS

The objective of the validation work will be to obtain feedback of the applied technologies from all stakeholders involved in order to evaluate the potential clinical value and validate the impact on clinical workflows from the REACTION applications with special focus on validating feedback and sensor performance as well as potential for interoperability and scalability.
A validation framework will be developed, as it is important to have a well-defined structure for the testing and evaluation already in the beginning of the project which is agreed by all partners. The validation framework will include definition of appropriate metrics and guidelines for usability testing, refinement of the initially defined success criteria, and measurement.

During platform development, validation is carried out to detect possible deviations from the original plan and to provide feedback to the development team and to the Project Board for early corrective action. To this end, project progress is assessed in yearly intervals throughout the project to allow tight, results-oriented monitoring of project status.

Validation will be concluded with the field trials defined in WP8, which will demonstrate the benefit provided for individual users and healthcare organisations in terms of efficiency of closed loop healthcare provisioning in diabetes management. The field trials will be used to evaluate the potential validity of the clinical applications, and the benefit for the healthcare domain, acceptance by patients and other users, and to assess the impact on the organizational level.

Validation activities will focus on impact on patients, their relatives, healthcare personal and other individual users as well as on organizational processes (e.g. in primary and secondary care as well as nursing care), with appropriate weight given to either aspect according to the phase of project progress. Hence, the validation will mostly centre on organisational workflows and stakeholder interaction as observed during the field trials. Traditional clinical research and validation of the clinical protocols is outside the scope of the project. However, the REACTION platform will be available for one full year after the end of the project thus allowing the clinical partners to carry out limited clinical research in that time.
The validation work will be carried out in three subtasks:

Subtask 2.4.1 – Validation planning

The validation framework is a well-described methodology to serve as a baseline on how, when and by whom validation is going to take place. The framework guides the collection of information about the project specific objectives, requirements and constraints on user validation (different methods measure different quality dimensions). The validation framework will provide guidance for carrying out the validation activities and for making the decisions about redesign, error correction, start of implementation etc, on the basis of the validation results.

Subtask 2.4.2 – Application field trials

Usability will be tested in the field trials in WP8 with a small number of users to detect user problems and deficiencies of the prototypes early in the development process and to feed these back to the development teams. This subtask will report the conclusions of the clinical trials in order that common assessment criteria are adopted to allow aggregation and analysis of data.

Subtask 2.4.3 – Deployment preparation

Knowledge gained through the clinical trials will be used to develop a road map for describing key elements to the process of Public Health Systems implementations including user requirements, operational and technical requirements as well as how to address safety, regulatory and socio-economic requirements. In this way the project will promote the use of the REACTION platform to a wide range of stakeholders addressing the specific needs of diabetes management and therapy.

The work in the task will be managed by FORTH-ICS and IN-JET. IMM, SOLIANIS and DELTA will validate sensor performance and reliability. ATOS and FHG-SIT will validate the security framework. The clinical partners MUG and CHC will carry out the validation of clinical workflows separately in WP8, but will be involved in WP2 with validation of relevant technological parameters, i.e. usability.

Workpackage description

Workpackage number:	WP 2	Start date or starting event:						Month 1		
Work package title:	User Centric Requirements Engineering and Validation									
Activity type:	RTD									
Participant number:	1	2	3	4	5	6	7	8	9	10
Participant short name	ATOS	CNET	DELTA	IMM	FORTH-ICS	FHG-SIT	FORTHNET	IN-JET	ALL	MUG
PM per participant:	5,0	10,0	4,0	5,0	10,0	6,0	6,0	11,0	3,0	5,0
Participant number:	11	12	13	14	15	16				
Participant short name	MSG	CHC	UBRUN	VUB	BTS	SOLIANIS				
PM per participant:	3,0	5,0	8,0	2,0	2,0					

Objectives
- perform scenario thinking for overview and analysis of the usage of different types of storylines in different domains.
- elicit the generic and specific requirements.
- systematic formalisation of all initial stakeholder requirements and functionality requirements.
- maintain a continuous study of the medical, clinical technological, regulatory-standards and market developments
- evaluate the potential clinical value and validate the impact on clinical workflows
- perform evolutionary requirements refinement based on lessons learned and watch reports

Description of work (broken down into tasks) and role of partners

T2.1 <u>Scenario thinking</u>: Elicit the generic and specific domain requirements by using scenario thinking techniques.

T2.2 <u>Initial requirements specifications</u>: Derive initial functional requirements, trust, privacy and security requirements and societal and business requirements. An internal milestone is set at M6 to check the status of Initial requirements, specifications and concepts established. Additionally, first internal versions of the clinical, technological, Market and regulatory-standards watch reports will be available at M6.

T2.3 <u>Evolutionary requirements refinement</u>: Use the results obtained during project progress to arrive at a re-formulation of the initial requirements incorporating any emergent requirements to be fed back in order to enable the necessary modifications of the design specifications and the subsequent re-engineering and re-validation of the affected modules. Prototype application specifications will be available internally at M9 and M18. Additionally, a first internal version of D2.8 Lessons Learned and results of usability evaluation will be available at M13. Internal versions of the Updated Requirements Reports (D2.9) will be available at M14 and M26. Finally, internal changes request and re-engineering reports will be issued at M13, M25 and M37.

T2.4 <u>Validation of platform and services</u>: Obtain feedback of the applied technologies from all stakeholders involved in order to evaluate the potential clinical value and validate the impact on clinical workflows from the REACTION applications focusing on feedback loops and sensors.

Deliverables (brief description) and month of delivery
D2.1 Scenarios for usage of the REACTION platform (M3)
D2.2 Clinical watch report (M24)
D2.3 Technology watch report (M24)
D2.4 Market and regulatory-standards watch report (M24)
D2.5 Initial requirements report (M4)
D2.6 Prototype application specification (M24)
D2.7 Validation framework (M12)
D2.8 Lessons Learned and results of usability evaluation (M25)
D2.9 Updated requirements report (M38)
D2.10 Final validation report of the REACTION platform, including sensors, subsystems, security framework, services (M48)

WP 3 – Sensors, Monitoring and Contextualisation

Objectives

The *first objective* of this workpackage is to research and develop several types of non-invasive and minimally invasive wearable sensors for continuous monitoring of blood glucose levels.

The *second objective* is to investigate the requirements on measurement accuracy and applicability of several sensor technologies to be used in Automatic Glucose Control systems and optimise the sensor design for such system.

The *third objective* is to develop a set of wearable and portable medical devices that can be coupled seamlessly with the REACTION platform for multi-parametric monitoring and contextualisation of health status. The requirements are focusing on accurate measurements with minimally or non-invasive methods. Sensors are wearable and interconnected with a BAN.

The *fourth objective* is to develop and evaluate a closed-loop control algorithm relying on mechanistic physiologically-based glucose-insulin models in combination with the REACTION sensors and delivery systems.

The fifth objective is to develop suitable user interfaces for feedback to patients.

Workpackage leader

The workpackage will be lead by: IMM

Tasks and actors in this workpackage

The work will be carried out in six tasks:

Task T3.1 – ePatch body sensor technology

TASK LEADER – DELTA

The project will use a special body sensor concept called electronic patch or ePatch, i.e. a small body sensor embedded in a skin friendly adhesive. With the ePatch concept, this task will develop several multi-parametric monitoring ePatch sensors to be worn by the patient.
The ePatch sensor is a small body sensor, which senses physiological signals and is embedded in a skin-friendly adhesive.

It can contain various types of miniaturised body sensors to measure physiological parameters, micro-electronics for data analysis, a wireless radio module for communication and a battery power source. The skin adhesive of the ePatch ensures optimised for wearability and bio

compatibility. The basis for the adhesive will be hydrocolloid pressure sensitive adhesives. This category of adhesives is extensively used in a number of medical devices like ostomy products, blister patches, wound dressings and for other skin applications.
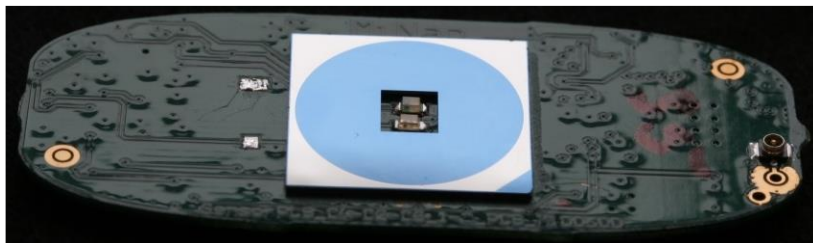
Figure 8 ePatch body sensor for myographic recordings

Wireless communication between sensors and the central node in the BAN: off-the-shelf radio chips will be benchmarked to identify components that optimize the trade-off between bandwidth, reliability and low-power performance. Targeted specifications will include: band-width of (order of magnitude) 100kbps per node, range between 1-10m, low-power performances in order to meet the miniaturization objective while avoiding frequent replacement

of batteries, integrated MAC[22] and flow-control protocols. Radio chip technology developed by Texas Instrument and Nordic for the ISM[23] band appears to be a reasonable starting point. More advanced technologies such as pulsed ultra wide band will also be investigated for future generations: these would allow further reduction of power consumption and the achievement of ultra-low-power performances. Power management electronics will be developed for the wireless sensor node, to enable power optimization at the system-level. Beyond power management, existing battery technology will be investigated to identify suitable power sources for the two REACTION platforms, which will achieve a decent autonomy for the device while exhibiting enough flexibility for integration into e.g. ePatches.

Two ePatch platforms will be implemented. The first platform is for low volume applications and has high flexibility. It will be used to integrate micro sensors and microelectronics into a reusable sensor unit with disposable skin adhesives and batteries. The second ePatch platform will be entirely disposable and will be optimised for low cost, high volume applications.

Subtask 3.1.1: ePatch sensors for professional use

The first development of ePatch designs is targeting the in-hospital application and usage by care professions. These ePatches will be optimises for hospital environments and the work will focus on:
- Integration of multiple sensors and interface electronics in a single reusable sensor unit
- Reliable concept having a reusable sensor unit and a disposable adhesive patch with an embedded battery
- Robust, reliable, cleaning friendly and biocompatible design
- Reliable wireless communication being compatible with the hospital environment having massive wireless equipment with critical life saving signals
- Digital signal processing (DSP) of multiple sensor signals and embedding of software to application specific functions that should be prepared for re-calibration and even adoption to individual patient requirement.

To meet these objectives, commercial off-the-shelf micro-controllers and DSPs will be analysed and compared from a performance point of view (trade-off between computational power and power consumption). The benchmarking procedure will rely on a few sets of algorithms, corresponding to the different services envisaged in REACTION, to 1) evaluate the use of off-the-shelf components for integration within the generic ePatch platform and 2) identify possible bottle-necks in current technologies. Finally, enhancement of existing technologies will be performed to match system requirements.

A single ePatch can perform different measurements simultaneously by integrating several sensors in the same ePatch structure.

The sensors to be developed in this subtask are predominantly spectroscopy and IR sensors for CGM, which are developed in T3.2. The development of ePatch platforms will be carried out by DELTA, who will also develop control and communication systems. IMM will assist on electrode design and packaging and manufacture of IR sensors in their precision manufacturing facilities. SOLIANIS will assist on integrating their pre-manufactured spectroscopy sensors in the ePatch.

Subtask 3.1.2: ePatch sensors for outpatient use

The second ePatch platform is aimed for the outpatient applications and handling by diabetes patient themselves. This ePatches will be a fully disposable ePatch design, targeting ease of use and handling and optimised for out-hospital environment. The development of the platform will focus on:
- High volume and low cost sensor and microelectronic to target the economics of disposable devices. Dedicated micro electronic will be developed to achieve this.
- Develop of design and production process where embedded sensors and microelectronics can be sterilised in an industrial process.

---

[22] Multiply-Accumulate, a common operation in digital signal processing.
[23] The industrial, scientific and medical (ISM) radio bands.

- The adhesives can be tailored to specific applications depending on required time of wear, position at the body and type and size of microelectronic to be embedded.
- Enables multiple sensors having less flexible function than the ePatch platform for in-hospital use.
- Optimum patient comfort and usability must be ensured so patients can wear them for up to one week without being visible or attracting undue attention. It must perform reliable measure for a week without the need for calibration and consume very little power. Minimal power consumption is essential for success of ePatches.
- A patch design and a power system allowing use for a week with reliable functions and no biocompatible issues.

The sensors to be developed in this subtask are predominantly IR sensors for CGM, which are developed in T3.2. The development of ePatch platforms will be carried out by DELTA, who will also develop control and communication systems. IMM will manufacture of IR sensors in their in-house precision manufacturing facilities.

An outline of the work plan in task T3.1 is presented as follows:
M1-M6: Specification and concept development of reusable ePatch platform
M6-M18: Developing of the reusable ePatches
M12-M18: Specification and concept development of disposable ePatch platform
M12-M24: Developing the technologies for disposable ePatch manufacture
M24-M30: Developing disposable ePatches
M36-M48: Technical support for field trials

Task T3.2 – Continous glucose monitoring sensors

TASK LEADER – IMM

Measuring the blood glucose level is vital for good diabetes management and for assessing the insulin dose. Glucose level is typically measured on a droplet of venous blood using a disposable stick and reader. Transcutaneous sensors for continuous measurements blood glucose has been a research topic for the last two decades and many principles have been proposed and evaluated, but none have been generally accepted in practice.

The objective of this task is to evaluate several sensor principles with respect to their suitability for a wearable continuous glucose monitoring device in closed loop operation and to develop and integrate prototypes of two different, non-invasive and minimally invasive principles based on 1) impedance spectroscopy and 2) Infrared spectroscopy.

In particular, one objective of the first clinical trials is to investigate what measurement accuracy is needed for the continuous monitoring, when healthcare professionals are part of the closed-loop system. The focus will be on clinical and endocrinological requirements. Later work will be on evaluating the same requirements for accuracy in Automatic Glucose Control systems.

The problem of accuracy takes several forms and cannot be addressed with a simple answer. It depends on the application (epoch identification, change rates, or as a basis for bolus adjustments). For example, in the hypoglycaemic area below app. 4 mmol/L, the relative measurement accuracy will be extremely critical (much lower than what is achievable today) to make sense in hypoglycaemic episodes, which is much more dangerous than hyperglycaemic episodes.

To the best of our knowledge no current glucose monitoring system achieves relative accuracy better than 15% across the normal range. Moreover, the measurement of glucose performed in vivo (inside of the body) is unpredictably influenced by various substances of the body fluids such as proteins, cholesterol and so on. Therefore, the developed sensors will be evaluated according to the CLSI guidelines (Performance Metrics for Continuous Interstitial Glucose Monitoring (POCT05-A)) for the assessment of CGM system performance with attention towards patient safety in AGC systems. The need to obtain accuracy of the glucose sensors as high as possible may be relevant for patient safety in AGC systems and will be investigated in the project.

To achieve the accuracy of 5% for glucose monitoring the sensor hardware is optimised, by applying micro-precision manufacturing to achieve a precise optical path length, by implementation of tunable or multiple light sources to increase the supporting points for the data if required and by implementation of a reference cell to avoid interference with water bands (method of difference spectra). After development of the individual sensors the accuracy is improved further by taking into account the physiological aspects like temperature stabilisation on body temperature, operation close to the skin surface to avoid light scattering by lymph and application of multiple sensors (IR and Impedance spectroscopy) for cross correlation of the data.

Two sensor principles will be investigated in this task and an assessment of commercially available CGM devices will be carried out:

Subtask 3.2.1: Impedance spectroscopy

Scanning the skins impedance has proven a promising technique for non invasive glucose monitoring. SOLIANIS' non-invasive continuous glucose monitor employs Impedance Spectroscopy to track changes in the glucose levels, combined with additional sensors that allow e.g. perfusion characterisation with optical sensors, GHz sensors for skin hydration monitoring and sweat measurement on skin. These sensors form a multi-sensor concept to address the influence of the perturbing factors, and thereby allows for more reliable monitoring of changes in glucose levels, which may be of great importance when monitoring for e.g. hypoglycaemia.

The multi-sensor technology uses frequencies between 1 kHz and 8 GHz as well as visible light at specific wavelength between 550 and 800 nm to measure the effect of changing glucose levels in blood, cells and interstitial fluid and the resulting changes in the ac and dc conductivity in both hyper- and hypoglycaemic episodes. To yield optimal accuracy additional factors influencing the impedance have to be taken into account, such as temperature, sweat and variations in skin composition. The sensors include a closed control systems and Bluetooth communication.

An outline work plan is as follows:

M1-M3: Define sensor concept and interface
- Define data transfer protocols
- Define data structures and naming
- Define interfaces and data storage routines
- Define mechanical interface to fit into experimental settings

M3-M12: Manufacture of sensors
- Adjustment of FW/SW according to definitions made in section M1-M3
- Testing of introduced FW/SW changes/developments according to respective standards for medical devices
- Realization of mechanical/HW adjustments to be suitable for Reaction trials/requirements
- Realization of SW to allow HCP to operate the system and collect data
- Realize interface to data collection infrastructure to be compatible with rest of technical infrastructure

M12-M24: Sensors used in basic in-hospital field trial
- Training and implementation of system at study site/overall infrastructure
- Data collection and evaluation expertise with respective SW

M25-M27: Evaluation of field trials with special focus on accuracy obtained
o Data evaluation expertise
o Adjust mechanical concept to be feasible for field application
o Optimize battery lifetime to reduce dependency on wired mode of operation
o Realize SW/FW adjustments to be feasible for field application

M28-M36: Manufacture of sensors for Automatic Glucose Control (AGC)
- Adjustment of FW/SW to allow automated data processing, feedback and control
- Testing of introduced changes are required as well as calibration and characterization of respective devices

M37-M48: Tests in Automatic Glucose Control (AGC) systems

- Data evaluation expertise
- Points as provided above

SOLIANIS will provide 20 Multisensor Units that are to be integrated into the ePatch system. The respective Multisensor system will feature a total of 19 sensors that allow wide band biophysical tissue characterization. Devices will be customized and prepared according to the requirements illustrated above. Each device with all 19 sensors will need to be calibrated, characterized and go through a extensive test procedure. At this point in time devices will still be manufactured on a semi handmade bases.

Subtask 3.2.2: Subcutaneous IR sensor

A sensor for the glucose determination based on near-IR spectroscopy will be investigated for transmittance measurement (Jeon2006); (Mäntele2006). The basic idea for this sensor is to measure NIR-absorption inside of a metallic micro-cell based on a micro-structured hollow needle using an optical fibre probe for the in and out-coupling of the light into/from the detection cell respectively. The hollow needle can be inserted beneath the skin. The spectral range of 1100 to 2500 nm including both the combination and overtone bands of glucose absorption will be analyzed to identify most suitable absorption bands. A concentration area of glucose between 40 and 400 mg/dl will be scheduled for this sensor.

The sensor will be composed from two modules:
- a reusable fibre-optical two-way sensor with a reference channel for suppression of the background noise including the possible instability of the light source as well as for the influence of the water and environment. The measurement can be continuous or pulsed;
- a one-way hollow side-gated needle with integrated mirror perpendicular to the axis on the end of needle for attaching to the optical sensor.

The control module of the sensor will be realised separately form the sensor. The communication will be implemented via either Bluetooth or ZigBee protocols.

The work plan will aim at having a prototype ready for the field trials the extended general ward domain to be concluded in M36 and a final prototype ready for the AGC system to be used in field trials in the last year of the project.

The outline work plan is as follows:
M1-M6: Sensor concept and simulations
M6-M12: Realization of the first generation breadboard device (not yet integrated into the e-patch)
M12-M18: Characterization of breadboard device
M18-M30: Optimization of sensor design for clinical field trials, first prototype (second generation e-patch)
M30-M36: Adaptation for Automatic Glucose Control (AGC) systems, manufacture phase
M36-M48: Technical support for field trials using AGC systems

IMM will develop and manufacture five IR sensors in their precision manufacturing facilities for the field trial in WP8 and DELTA will integrate with control system and communication unit into an ePatch design.

Subtask 3.2.3: Evaluation of commercially available CGM devices

This subtask will perform a survey of commercially available Continuous Glucose Monitoring devices and pre-market technologies in this area.

The aim is to produce a survey that can serve as a baseline for evaluation of the achieved performance obtained with the sensors developed in the other subtasks.

A number of sensors will be acquired for further testing and incorporation in the REACTION platform for demonstration of interoperability.

The partners in this subtask are IMM, DELTA and SOLIANIS.

Task T3.3 − Automatic Glycaemic Control

Subtask 3.3.1: Automatic Glycaemic Control - devices

TASK LEADER − IMM

The objective of this task is to design and evaluate a suitable devices for Autonomous Glycaemic Control (AGC) and therapy system where continuously measured glucose level will be used to regulate the devices' own operation as well as external IV insulin pumps. One aim is to study the requirements on CGM accuracy when used in AGC environments.

An external pump delivers insulin to a patient's body. Pump users can adjust their bolus insulin doses according to activity, stress and meals. The objective is to validate the possibility for adjusting the insulin doses automatically.

Over the years compact wearable insulin pumps allowing continuous subcutaneous insulin infusion are used by a substantial group of patients with diabetes and are considered the benchmark for insulin delivery (Jeitler2008).

Commercially available pumps will be evaluated as to whether they can be adapted to be inserted in a closed loop. It is expected that insulin pumps are available on the market, suitable for the REACTION project and that suppliers give access to the relevant communication protocols (has been successfully done in the past at MUG). Potential candidates are the following pumps:

- ACCU CHEK Spirit from Roche, with infrared port for wireless communication

- OneTouch Ping from Animas, with wireless communication

- Amigo from Nipro, communication to be clarified

- Minimed from Medtronic, wireless communication + CGM

The major objective of this workpackage is to optimize the interface between the AGC algorithm and the insulin pump itself, rather than optimizing the pumps performance or their hardware communication interface. Based on the sensor data generated from the individual sensors an optimised insulin dose has to be delivered by the pump. The optimisation of the insulin dose is to be achieved by taking into account the physiological data from clinical studies on diabetes patients, allowing for the development of an AGC algorithm. This work is strongly correlated with WP8. Later on the AGC algorithm has to be evaluated clinically in conjunction with the continuous glucose sensor unit, to evaluate the requirements on the sensor accuracy and to validate the automated adjustment of the insulin dose.

The work plan will aim at having a prototype ready for the field trials of the AGC system to be commenced in the last year of the project.

The outline work plan is as follows:

M1-12: Survey of commercially available insulin pumps and their suitability for automatic glycaemic control
M13-36: Adaptation of insulin pumps and pump control for tests
M37-48: Concept test of AGC system

The work will be undertaken by IMM with the assistance of DELTA.

Subtask 3.3.2: Automatic Glycaemic Control – Closed-Loop Control

TASK LEADER – BTS

A core component of Automatic Glycaemic Control is a closed loop control systems that translates glucose measurements (but also further information about day time, food uptake and activity status; see T3.4) into optimal insulin delivery rates. The major hurdles in closed-loop concepts for diabetes management are the physiological and pharmacological lag-times as well as the intra- and inter-individual variability of both glucose measurement and insulin uptake and response.

To overcome known hurdles and shortcomings of state-of-the-art closed-loop concepts (for a review s. Youssef et al., Algorithms 2009) REACTION will combine several known control theorectical concepts such as Proportional-Integral-Derivative (PID), Model Predictive Control (MPC), and Fading Memory Proportional Derivative algorithms with mechanistic physiologically-based models of glucose-uptake, insulin-delivery and glucose-insulin interaction (see WP6, D6.4.1 and D6.4.2). The parameterization of these mechanistic models is expected to be supported by findings from Task 6.3 where stratification criteria are to be developed.
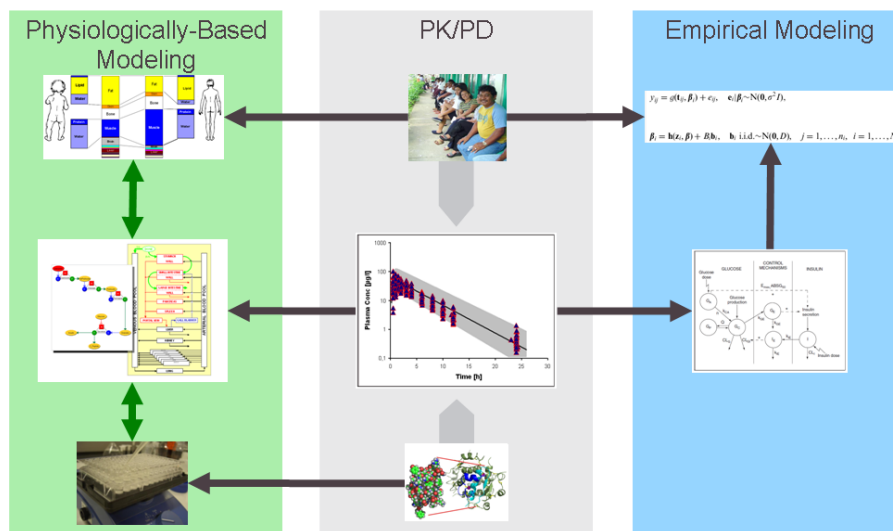
A comparison of "classical" empirical modeling used in closed-loop approaches to insulin delivery, so far, and physiologically-based modeling. The main advantages of physiologically-based models are 1) the explicit distinction between substance and patient properties and the possibility to use use prior knowledge about individuals (generated for example during anamnesis and clinical diagnosis or generated as a result of Task 6.3) to pre-parameterize individualized models and 2) the mechanistic representation of lag-times resulting from lymph and blood flow rates, diffusion etc.

The integrated closed-loop control system (control algorithm + mechanistic model kernel) will be benchmarked against each other by first using historical clinical glucose-insulin challenge data from MUG. This initial evaluation will check the pure predicition performance of the algorithms.

Based on a prioritization of algorithms using their retrospective predictive performance, new glucose-insulin challenge experiments will then be performed using the two top-ranked candidates. This first round of experimentation and algorithm evaluation will use invasive glucose measurement systems established at MUG and closed-loop will either be implemented in a prototype system or be simulated as a quasi-closed-loop with a physician being the interface between glucose measurement, algorithm and insulin delivery system. MUG has already demonstrated the power of this simulation approach in the CLINICIP project. The two closed-

loop approaches will be benchmarked against each other and the potential for further optimization of the algorithm and the mechanistic model kernel will be evaluated. To maximize the applicability of the results of from this initial testing of the algorithm in humans, the expected (lower) accuracy of the minimal invasive REACTION sensor system will be simulated by adding virtual noise to the sensor signal and comparing the insulin delivery signal under optimal condidtions with the control signal under predicted REACTION sensor signal quality.

In year 4 of REACTION the invasive measurement systems established at MUG will be replaced by the newly developed minimal invasive patch system (the clinical insulin delivery pumps will probably be replaced by the system identified in sub-task 3.3.1) and a series of clinical experiments will be performed to evaluate the performance of the integrated system. An optimization of the closed-loop control is intended with an alternation of experimentation and algorithm optimization.

The outline of the work plan is as follows:
M1-12: Implementation of relevant state-of-the-art closed-loop control algorithms
M13-24: Integration with mechanistic physiologically-based model kernel and retrospective analysis and benchmarking of predictive performance
M25-36: Prospective evaluation and benchmarking of two algorithms in new clinical experiments
M37-48: Evaluation and optimization of integrated system.

BTS and MUG will jointly perform the implementation, testing and refinement of the closed loop algorithms using historic data and new clinical experiments. All subtasks, especially the last step of the evaluation of the integrated system, will be performed in close collaboration with subtask 3.3.1 and the corresponding responsible project partner IMM and DELTA. All clinical testing is work to be performed in Task 8.3. The clinical study design is jointly performed in subtask 3.3.2.

Task T3.4 – Multiparametric monitoring sensors

TASK LEADER – DELTA
In clinical treatment of diabetes patients, multiple medical and environmental contextual parameters have to be measured and monitored. For example, changes in blood glucose level causes other physiological effects such as changes in pulse, skin temperature and transpiration and are important early indicators of e.g. hyperglycaemia.

Various medical sensors will be used in order to measure vital signs, related to diabetes such as skin temperature and pulse. Other types of measurements will be acquired continuously from sensors that measure ambient temperature, activity (accelerometers), air humidity, geo-position (GPS) etc. Other sensors will provide discrete measurements such as electronic scales, user questionnaire terminals, etc.

The daily management of correct basal insulin dosing is dependent on the variation in activity. An ePatch activity monitor is able to give the user information if the activity level has been higher then normal or lower then normal. The activity monitor is based on temperature, accelerometer and pulse. Hypoglycaemic alarms are based on measuring skin-impedance, QT-wave morphology, HRV and other EKG parameters.

Within WP3 the GM sensors (Impedance and IR) will be integrated into the e-patch platform. The first generation e-patch will contain only impedance spectroscopy CGM sensors, since these are available from the beginning of the project. The second generation e-patch will contain both, impedance spectroscopy as well as IR CGM sensors.

With the second generation e-patch advanced data analysis, like application of chemometric methods for spectroscopy and cross correlation of the individual sensor data within the AGC algorithm is applied to ensure a high level of predictability. The development of these models again are strongly correlated to WP8, taking into account the physiological data of patients. With the knowledge of this data also calibration models can be generated to account for the patients individual biological profiles.
Calibration models refer to all the models required to make the proper calibrations of the different components integrating the system (to make sure that final measurements are correct

and not biased by errors in devices, measurement systems, etc.).

- The first calibration model that should be defined is the one related to the calibration of the continuous glucose sensors. For this specific case, what will be measured are the parameters related to the device itself (sensitivity variations, selectivity variations, etc.). Other measures that will be taken into account are the secondary parameters, which are other physiologic parameters that varies when the blood glucose varies, is often easier and more reliable to measure compared to continues blood glucose. These parameters are skin temperature, heart rate variations and pulse, skin impendence or galvanic skin response. They are indirect indications of the general condition of the patient. They can also be indications of the reliability of the primary measurement of the glucose sensor. They may also be indications of drift or change of measurement conditions.
- Another model that will be defined is the one correlating the measure of the glucose levels at the skin spot where the value is taken by the sensor with the real value (the one that could be measured in the blood stream).
- Other parameters that will be measured are the ones related to environmental conditions (the temperature and humidity of the environment around the patient) that could give an indicator of the reliability of the primary and secondary sensor signal. The body automatically shorts down or minimise the blood perfusion at the skin surface when the person is freezing and therefore the sensors on the skin surface may measure correctly, but the physiologic parameters measured in tissue near skin surface may not be in correlation with the conditions of the patient.

All these different conditions should be evaluated for their influence on the final decision on what is the dose of insulin the patient should be given. The project aims to investigate the relations between the parameters, evaluate them, and test the reliability and sensitivity of the data concluded on the sensor signal. This work within the project will result in a model for calibration and algorithm controlling the insulin dosing.

DELTA will manufacture the needed ePatch sensors based on in-house knowledge of various sensor principles. with the help of SOLIANIS and IMM for integration of the impedance spectroscopy and IR GM sensors.

Task T3.5 – Graphical User Interfaces

TASK LEADER – FORTH-ICS

Feedback in the form of self-management information to patients or decision support information at the point of care will be presented on multimedia terminals with interactive displays. Interaction with patients can be personalised and will contain feedback and clinical pathway adjustments, automatically generated context aware risk assessments and general material for education and learning of the patient, such as instructions for insulin injection, calculation of insulin dose, etc.

Great importance is attached to the intuitive and adjustable outline of the User Interfaces. Attention is primarily placed on ease-of-use and customization capability. The User Interface on PAN node terminals should ensure that all available functionality is effortlessly within the reach of non-experts and that information display is configurable according to the user's preferences. In general, technology adaptation is a matter of personal preference and in the context of this project it will be treated as such. This subtask will provide the guidelines for User Interfaces.

FORTH-ICS will make the UI specifications together with users and develop the UI framework together with FORTHNET. UBRUN will contribute design methodologies on user involvement.

Workpackage description

Workpackage number:	**WP 3**	Start date or starting event:					Month 1		
Work package title:	Sensors, Monitoring and Contextualisation								
Activity type:	RTD								
Participant number:	1	2	3	4	5	6	7	8	9	10
Participant short name	ATOS	CNET	DELTA	IMM	FORTH-ICS	FHG-SIT	FORTHNET	IN-JET	ALL	MUG
PM per participant:			58	84	10		8			12
Participant number:	11	12	13	14	15	16				
Participant short name	MSG	CHC	UBRUN	VUB	BTS	SOLIANIS				
PM per participant:			4		34,5	30				

Objectives
- research and develop several types of non-invasive and minimally invasive wearable sensors for continuous monitoring of blood glucose levels.
- investigate the requirements on measurement accuracy and applicability of several sensor technologies and optimised the design for AGC systems.
- develop a set of wearable and portable medical devices that can be coupled seamlessly with the REACTION platform for multi-parametric monitoring and contextualisation of health status.
- develop suitable user interfaces for feedback to patients.

Description of work (broken down into tasks) and role of partners

T3.1 ePatch body sensor technology: Develop several multi-parametric monitoring ePatch sensors to be worn by the patient. The ePatch sensors use skin friendly adhesives and incorporates control logic and wireless communication between body-worn sensor nodes and the central node in the BAN. Power management electronics will be developed for the wireless sensor node, to enable power optimization at the system-level. Two ePatch platforms will be implemented: one for low volume applications and high flexibility, the other for disposable sensors optimised for low cost, high volume applications. A first version of the specification and concept for reusable ePatch platform will be available internally at M6.

T3.2 Continuous glucose monitoring sensors: Evaluate several sensor principles with respect to their suitability for a wearable continuous glucose monitoring device in closed loop operation. Develop, manufacture and integrate prototypes of two different, non-invasive and minimally invasive principles based on 1) impedance spectroscopy and 2) Infrared spectroscopy. Survey commercially available Continuous Glucose Monitoring devices and pre-market technologies in this area. Information related to the IMM IR sensor concept and simulations will be included in D1.2.1 Interim progress report for the Commission at M6. Additionally, an internal report on test and calibration of glucose sensors will be available at M30.

T3.3 Automatic Glycaemic Control: Design and evaluate a suitable technology for Autonomous Glycaemic Control (AGC) and therapy system. Measured glucose level will be used to regulate the devices' own operation as well as external insulin pumps. Combine several known control concepts such as Proportional-Integral-Derivative (PID), Model Predictive Control (MPC), and Fading Memory Proportional Derivative algorithms with mechanistic physiologically models of glucose-uptake, insulin-delivery and glucose-insulin interaction to implement a closed-loop algorithm.

T3.4 Multiparametric monitoring sensors: Integrate various medical sensors will be used in order to measure vital signs, related to diabetes such as skin temperature and pulse. Other types will be sensors that measure ambient temperature, activity (accelerometers), air humidity, geo-position (GPS) etc. Other sensors will provide discrete measurements such as electronic scales, user questionnaire terminals, etc.

T3.5 <u>Graphical User Interfaces</u>: Develop comfortable user interfaces for multimedia terminals with interactive displays. Interaction with patients can be personalised and contain feedback and clinical pathway adjustments, automatically generated context aware risk assessments and general material for education of the patient, instructions for insulin injection, calculation of insulin dose, etc. An internal deliverable Design criteria for Graphical User Interfaces will be distributed at M12.

Deliverables (brief description) and month of delivery
D3.1 Specification and concept for disposable ePatch platform (M18)
D3.2.1 1st generation e-patch, report on ePatch technology & integration results (M12)
D3.2.2 Final generation e-patch, report on ePatch technology & integration results (M48)
D3.3 SOLIANIS Impedance Spectroscopy CGM sensors (M12)
D3.4 SOLIANIS Impedance Spectroscopy AGC sensors (M36)
D3.5 IMM IR breadbord device (M12)
D3.6 IMM IR CGM prototype (M30)
D3.7 IMM IR AGC prototype (M36)
D3.8 Report on glucose sensor development (M18)
D3.9 Sensors for glucose measurement for 1st field trials, 2nd generation e-patch (M30)
D3.10 Survey of commercially available CGM devices & insulin pumps + suitability for AGC (M12)
D3.11 Relevant integrated algorithms implemented, evaluated and benchmarked in retrospective analysis (M24)
D3.12 Evaluation of integrated systems with best out of prospective evaluation of 2 top-ranked algorithms (M48)
D3.13 Prototype insulin pumps and pump control for tests (M36)
D3.14 Report on development of multiparametric monitoring sensors (M48)

WP 4 – Data Management and Service Orchestration

Objectives

The objectives of this WP are to research, develop and implement the very complex Data Management structure of the REACTION platform. This work package will design and implement a semantic data management server that will provide the needed information management and service orchestration functionality to support the above REACTION requirements.

The objectives of the WP can be summarised as:
- Analyse and define the overall architecture of the Data Management structure
- Define data structures, taxonomies and ontologies for the service components
- Research and develop a Data Management structure that provides a model-driven architecture for application development and deployment
- Research and develop a service oriented architecture with service ontology with high level concepts to be used in both development and run-time processes.
- Design and implement a context management framework and a context awareness mechanism capable of managing patient and user data across different contexts and situations in the REACTION architecture.
- Research and develop the Network Management subset responsible for physical communication between devices, persons and external repositories.
- Research and develop a rule-based service orchestration engine that allows for the static or dynamic assembly of services and their execution on the REACTION platform. This would be a basis for application-oriented workflows, including event handling and crisis management.
- Develop a resilient and intelligent event handling mechanism that can support crisis management and interface to established emergency centres.

Workpackage leader

The workpackage will be lead by: CNET

Tasks and actors in this workpackage

The work will be carried out in five tasks:

Task T4.1 – Architectural analysis and description

TASK LEADER – CNET
The workpackage is initiated by a state-of-the-art survey. The survey will be used for input to the requirement engineering work in WP2 and serve as a basis for the subsequent design and development tasks on other WP's.

This task will survey and evaluate the state of the art in models, technologies and standards in the context of the REACTION Data Management requirements and service architecture. It will include healthcare standards for messaging and health data representation as well as current approaches to and the adoption of the HISA (Health Informatics Service Architecture) standard across the EU. Further, investigations will be undertaken into the work of the Continua Health Alliance working groups on architecture and interfaces as well as on the application of ontologies to medical terminology and HIS and CIS interoperability. The most important standards groupings in Health Informatics will be selected for future liaisons with the REACTION project.
This healthcare focus should be complemented by an evaluation the relevant generic technologies for messaging protocols, data fusion and mediator architectures, service oriented architectures (SOA) and novel technologies for semantic management of data and services.

The result of this work will be reported in the deliverable D4.1: State of the Art - Concepts and technology for a unified data fusion architecture in REACTION. The deliverable will be updated in the mid-term of the project. The work will be undertaken by CNET supported by ATOS, ALL, FORTH-ICS, UBRUN and IN-JET providing knowledge on medical systems and SoA concepts. FHG-SIT will contribute security architecture.

Task T4.2 – Data structures, taxonomies and ontologies

TASK LEADER – ALL

The Data Management subset manages contextualisation of data and should facilitate a number of decision support functions and risk assessment activities based on mathematical models and backend medical information systems.

Given the advanced knowledge management tasks, the REACTION architecture must be based on a well-founded semantic modelling and knowledge representation framework.

The objective of this task is to define a customizable, comprehensive taxonomy with data mapping for data acquisition, standardisation, comparative analysis and event handling. The taxonomies will be built using existing XML Taxonomy tools that support HL7 clinical taxonomies such as Altova's MapForce or similar.

Moreover, it is the aim to build a set of dynamic ontologies to implement the taxonomies in the dynamic service environment. The solutions will encompass higher level abstractions in the form of ontologies for healthcare concepts and terminologies as well as their mappings to executable objects.

The result of this work will be reported in the deliverable D4.2 REACTION data structures, taxonomies and ontologies. The work will be organised by ALL with contributions from FORTH-ICS and ATOS. CNET will give input on device ontologies and integration with Hydra middleware and general health domain ontologies. MSG contributes to information processing and representation.

Task T4.3 – Data management

TASK LEADER – CNET

The purpose of this task is to design and implement the core data management functionality in REACTION. The work will focus on the design of a device and network-based data fusion/diffusion model providing a semantic integration of a multitude of heterogeneous medical devices and media, information sources and services and communication.

This work will build on the models and structures developed in task 4.2.
Initially the task will analyse the technical requirements for a specific medical data management model, based on the functional requirements derived in WP2. From the requirements, a suitable architecture for the data fusion/diffusion model in a device and network oriented environment and the technology to implement it in the REACTION platform will be specified.

The main work in the task will be the research and development of the software components required to perform the core data management task including data capture, support for contextualisation, data fusion, inferring of knowledge, and invoking of event handling.

The work will partly build on refined results from the HYDRA project by further extending the Hydra middleware and Semantic Model-driven Architecture (SeMDA) researched in this project. It will be complemented by exploiting the Semantic Medical Device Spaces as proposed by the SmartHealth project.

The Hydra middleware incorporates support for self-discovery of devices. When a Hydra enabled device is introduced to the BAN or PAN, the middleware is able to discover and configure the device automatically. Here we see an example of a Hydra device network. Hydra distinguishes between two different devices. More powerful devices are capable of running the Hydra middleware natively and smaller devices that are too constrained or closed to run the middleware. For the latter devices, proxies are used. The proxies are embedded in the BAN or the PAN node, which presumably have more computing power than the device has.
Once proxies are in place, all communication is based on the IP protocol.

The figure below illustrates the two cases. On the right, the terminal can directly incorporate Hydra middleware and is able to establish communication with services on the REACTION

platform. In the situation on the left, the devices cannot operate the Hydra middleware (because they are too resource constrained or have proprietary interfaces). In this case, proxies are created on the BAN or PAN node (in this case a mobile phone). The proxies virtualises the device vis-à-vis the REACTION platform. Any service will think it is communicating with the device, where in fact it is communicating with the proxy.
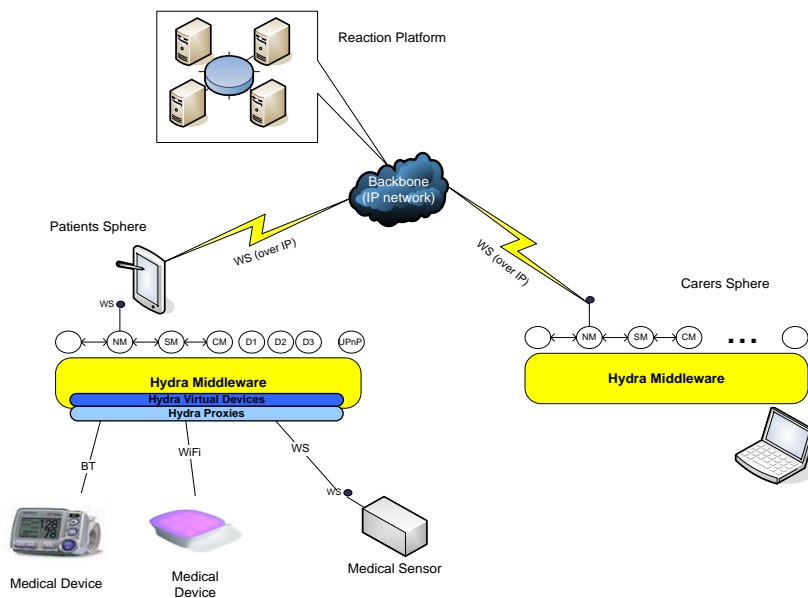
Figure 9 Incorporation of devices using the Hydra middleware

The Hydra middleware provides: 1) Discovery mechanism, 2) Low level protocols, 3) Service execution, 4) Virtualisation (IEEEx73) and 5) security and trust policies which can directly be used by the developer of REACTION applications.

The work will result in a number of core software modules to be implemented in the REACTION architecture. An overview of the modules and their functionalities will be presented in the deliverable: D4.4 Prototypes of core data management subsystem, which will be updated annually in line with the iterative implementation of prototypes. The work will be undertaken by CNET providing refinement of the Hydra middleware to support the semantic models of REACTION. FORTH-ICS will design algorithms for the predictive models and filtering and MSG will work on data management. ATOS will contribute on backend interoperability.

Task T4.4 – Context management framework

TASK LEADER – MSG

The context management will be based on a dynamic and multi-dimensional model of context. It is an important function in the REACTION architecture with the purpose to facilitate semantic integration of data and in monitoring multiple devices and other data sources.

A context-awareness framework will be developed, taking existing approaches to context-management into consideration. The framework will include a REACTION-specific model of context and the required components for the management of that model. A candidate starting point is the approach to context management developed in the Hydra project. The Hydra framework defines a multi-level context model relating providers and consumers of context, to different levels for context sensing, context provision and context linking. A context management architecture specifies the necessary functional components.

This approach, with possible inputs from other approaches, will be adapted and improved to fit the REACTION platform and the specific healthcare requirements derived from the REACTION applications and user models. The basic approach to achieve context awareness is to apply principles and technologies for semantic annotation of device data and data coming from the

patient's (or users') environment. This environment will be dynamically mapped to a set of different contexts and sub-contexts in the REACTION ontologies.

An overview of the context management subsystem will be presented in the deliverable: D4.5, which will be updated annually in line with the iterative implementation of prototypes. MSG will work on context aware information systems and data fusion with FORTHNET contributing to data monitoring. CNET will extend and adapt the Hydra context manager to handle new resources.

Task T4.5 – Rule-based orchestration of services for monitoring and event handling

TASK LEADER – ATOS

Monitoring and event handling are important aspects of REACTION services. Any REACTION applications will be able to react ubiquitously to change in the patients' health state and/or environment and perform pre-defined activities or alarm handling according to pre-programmed rules or through closed loops involving formal and informal carers. To this end REACTION will combine the orchestration of services with an underlying efficient networked-based event management solution.

Subtask 4.5.1: Monitoring and event handling

The REACTION platform will be based on a service-oriented architecture (SOA) supporting a collection of loosely coupled services that communicate with each other. Services in the REACTION environment need to access and control numerous heterogeneous devices at different locations using different access mechanisms. Ensembles of REACTION services are orchestrated by a specific high-level workflow e.g. based on existing orchestration languages (e.g., BPEL) or on a REACTION specific orchestration scheme. The workflow would be specified in the application and interpreted by the REACTION Orchestration Manager. The Orchestration Manager will take care that the right sequence of REACTION services is called. The Orchestration Manager will interface with legacy back end systems such as operational workflow and resource scheduling systems (SAP, EPR systems, etc.)

The services thus orchestrated are based on the underlying event management architecture. An event occurs when a pre-described condition is true: Is the blood sugar level higher than 7.0 mmol/L?" In real life, events are typically combined to yield more accurate assessment of the situation: "Is the blood sugar level higher than 7.0 mmol/L?" AND "Has the patient been eating within the last 20 minutes?" For multi-parametric monitoring, methods for fast, reliable evaluation of complex conditions are essential.

Moreover, the actual software implementation in real deployment of even the simplest event detection can involve up to hundreds of value comparisons:

```
IF (<blood_sugar> IS GREATER THAN <7.0>) AND (<blood_sugar_unit> IS EQUAL
TO <mmol/L>) AND ((<time_now> - <time_last_meal>) IS LESS THAN <20>) AND
(<blood_sugar_monitor_type> IS EQUAL TO <plaster>) AND (<software_version>
IS GREATER THAN <1.5> AND (<application_owner> CONTAINS <NHS>) OR … THEN DO
…
```

In order to provide fast, complex and robust event handling, the REACTION platform will develop an event handling framework based on states. Event handling will be much simplified using well known state machine concepts[24] from the field of control theory.

Monitoring will thus be based on mapping of data into "states". In principle, all data are expressed in the time domain. Dynamic values change as a function of time – also static values are functions of time, although they change less often or never. However the mechanism of event handling becomes much simpler when time resolved data are mapped into states.

The state of a particular parameter represents the result of a logical comparison typically expressed in clinical terms: "Is the blood sugar level higher than 7.0 mmol/L?" The resulting

---

[24] A state machine is a model of behaviour composed of a finite number of states, transitions between those states, and actions

state will be FALSE until the glucose value actually exceeds 7.0 mmol/L. Parameters can then be subjected to complex conditional monitoring rules by simply sequencing their states.

An event occurs when a *transition* (change of state) take place and alarm responses can be initiated by the occurrence and detection of events corresponding to a pre-defined scheme. The alarm handling can take the form of a simple, predefined feedback to the patient: "Your blood sugar level is slightly elevated. You need to adjust your insulin dose at next injection" or more complex medical feedback to healthcare professional. It can also involve physical actions in the Patients' Sphere (ringing a bell, turning on lights) and invoking professional emergency response teams with the inclusion of a complete medical history and contact information.

The work will be managed by CNET. CNET will design rule-based orchestration language and engine and implement components for orchestration and rule execution. FHG-SIT will contribute with orchestration of security services while FORTHNET will develop alarm handling and notification systems using SMS / IM.

Subtask 4.5.1: Alarm handling and crisis management

Hypoglycaemia is the medical term for a pathologic state produced by a lower than normal level of blood glucose. Hypoglycaemia can produce a variety of symptoms and effects but the principal problems arise from an inadequate supply of glucose as fuel to the brain, resulting in impairment of function which can range from vaguely "feeling bad" to coma, seizures, and permanent brain damage or death.

Hypoglycaemia episodes can happen within minutes. Management of hypoglycemia involves immediately raising the blood sugar to normal, determining the cause, and taking measures to hopefully prevent future episodes. The crisis management can seldom be administered by private so it is of the utmost importance to involve professional emergency and crisis teams as quickly as possible. Some researchers believe that the rate of decrease in blood sugar rather than its absolute low mark is what triggers the hypoglycaemia episodes. A REACTION application can detect both absolute low and relative changes in glycaemic levels and performed rules based event handling based on this.

A hypoglycaemia alarm is the most wanted feature in the diabetes community. In this task, a hypoglycaemia alarm will be developed based on multi-parameter techniques (skin-impedance and EKG parameters). Sensitivity and specificity will be optimised during night where it is most important.

A setup involving a crisis management emergency centre will be created. The aim is to demonstrate the ability of the REACTION platform to handle crisis management. Professional alarm handling involves several different states: Event occurred, alarm sent to emergency team, alarm acknowledged, emergency team dispatched, alarm responded, etc. Handling complex alarm schemes like this thus require a state based approach. The demonstration will be performed together with a supplier of safe and effective care solutions and experience in crisis management in the healthcare sector. Since this service is ordinary commercial services, it will be provided for through subcontracting (see section on Sub-contracting for more details).

ATOS and FORTHNET will develop the alarm handling interface and IN-JET will arrange the subcontracting of alarm services. ATOS contributes to alarm systems design and implementation.

Workpackage description

Workpackage number:	WP 4	Start date or starting event:					Month 1		
Work package title:	Data Management and Service Orchestration								
Activity type:	RTD								
Participant number:	1	2	3	4	5	6	7	8	9	10
Participant short name	ATOS	CNET	DELTA	IMM	FORTH-ICS	FHG-SIT	FORTHNET	IN-JET	ALL	MUG
PM per participant:	26,0	72,0			21,0	12,0	8,5	7,0	25	
Participant number:	11	12	13	14	15	16				
Participant short name	MSG	CHC	UBRUN	VUB	BTS	SOLIANIS				
PM per participant:	19,0		4,0							

Objectives
- analyse and define the overall architecture of the Data Management structure.
- define data structures, taxonomies and ontologies for service components.
- research and develop a model-driven Data Management architecture.
- research and develop a service oriented architecture for development and run-time processes.
- design and implement a context awareness framework for patient and user data accross the REACTION architecture.
- research and develop the network management subset responsible for physical communication between devices, persons and external repositories.
- research and develop a rule-based service orchestration engine that allows for the static or dynamic assembly of services and their execution.
- develop an intelligent event handling mechanism supporting crisis management and emergency centre interfaces.

Description of work (broken down into tasks) and role of partners

T4.1 Architectural analysis and description: survey and evaluate the state of the art in models, technologies and standards in the context of the REACTION Data Management requirements. A first internal version of D4.1 State of the Art - Concepts & technology for a unified data fusion architecture will be available at M6.

T4.2 Data structures, taxonomies and ontologies: define a well-founded semantic modelling and knowledge representation framework.

T4.3 Data management: research and development of the software components required to perform the core data management tasks including data capture, support for contextualisation, data fusion, inferring of knowledge, and invoking of event handling.

T4.4 Context management Framework: design and implementation of a dynamic and multi-dimensional framework for context awareness, including a mode of context and architectural components.

T4.5 Rule-based orchestration of services: design and implementation of a service orchestration engine with an underlying networked-based event management mechanism.

Deliverables (brief description) and month of delivery
D4.1 State of the Art - Concepts & technology for a unified data fusion architecture (M24)
D4.2 Initial data structures, taxonomies and ontologies (M9)
D4.3 Technical requirements for a implementation of a medical data management model (M6)
D4.4.1 1st Prototypes of core data, context and event handling management subsystems (M12)
D4.4.2 2nd Prototypes of core data, context and event handling management subsystems (M24)
D4.5 REACTION integration with emergency centres, results and experiences (M36)

WP 5 – Network Management and Service Execution

Objectives

The main objective of this WP is to research, develop and implement the network platform on which REACTION applications can be executed.

The first objective of this workpackage is to research, propose and implement the network platform that allows seamless wireless connectivity and operability between patients' Body Area Networks (BAN) at one end, through Personal Area Networks (PAN) and backend Wide Area Networks (WAN) and the Data Management subsets at the other end.

Connectivity must be network agnostic in order to support plug-and-play monitoring and feedback services, regardless of time, bandwidth, and protocol constraints. Crisis management and other time critical applications must offer real-time connectivity; data handling applications must offer wide bandwidth connectivity on demand; critical monitoring services must offer geographically dispersed, always-on features regardless of heterogeneous network structures and diverse operators across Europe.

The *second objective* is to research and develop the Network Management subset responsible for the physical communication between objects (devices, persons and external repositories). Each PAN node will have its own Network Manager. The Network Manager enables a way to communicate between different devices transparently; building an overlay network in uniquely identified resources (devices, services and contents).

The *third* objective of this WP is to define and develop a resilient and intelligent event handling mechanism that can support crisis management and interface to established emergency centres. The semantically informed and proactive event management architecture will serve as a basis for patient data monitoring and alarm handling.

Workpackage leader

The workpackage will be led by: FORTHNET

Tasks and actors in this workpackage

The work in will be divided in four tasks:

Task T5.1 – Network architecture and analysis

TASK LEADER – FORTHNET

The first step in this task is to perform the analysis of and define the overall network architectural model based on the requirements derived in WP2. The network architecture will have to handle resources and services in heterogeneous networks, and dynamically change performance data of the resources without restricting the domain to IP networks. Analysis on which existing models and standards can be applied and which new developments and standardisation models need to be undertaken will be performed.

In order to ensure last meter communication for REACTION Patients' Sphere, Peer-to-peer networks will be examined. Peer-to-peer (P2P) is a style of networking in which a group of computers communicate directly with each other, rather than through a central server. The P2P overlay network consists of all the participating peers as network nodes. There are links between any two nodes that know each other: i.e. if a participating peer knows the location of another peer in the P2P network, then there is a direct connection from the former node to the latter in the overlay network. Based on how the nodes in the overlay network are connected to each other, P2P networks are classified as unstructured or structured.

An unstructured P2P network is formed when the overlay links are established arbitrarily. Such networks can be easily constructed as a new peer that wants to join the network can copy existing links of another node and then form its own links over time. In an unstructured P2P

network, if a peer wants to find a desired piece of data in the network, the query has to be flooded through the network to find as many peers as possible that share the data. The main disadvantage, which may affect REACTION, is that the queries may not always be resolved. Popular content is likely to be available at several peers and any peer searching for it is likely to find the same thing. But if a peer is looking for rare data shared by only a few other peers, then it is highly unlikely that search will be successful. Since there is no correlation between a peer and the content managed by it, there is no guarantee that flooding will find a peer that has the desired data. Flooding also causes a high amount of signalling traffic in the network and hence such networks typically have very poor search efficiency.

Most of the popular P2P networks are unstructured but in order to ensure collaboration of different P2P nodes in the REACTION Patients' Sphere, the main emphasis in this task will be given to structured P2P networks that employ a globally consistent protocol to ensure that any node can efficiently route a search to some peer that has the desired file, even if the file is extremely rare. Such a guarantee necessitates a more structured pattern of overlay links. By far the most common type of structured P2P network is the distributed hash table (DHT), in which a variant of consistent hashing is used to assign ownership of each file to a particular peer, in a way analogous to a traditional hash table's assignment of each key to a particular array slot.

Since the platform is network agnostic, the applications need to be able to adapt network access and protocols to the specific requirements of the application in question. As a part of the network architectural analysis, the different requirements for network protocols will be analysed from the usage scenarios and the requirement engineering phase derived in WP2 and the most suitable network architecture will be drafted.

Finally, the structure of the backend network to the last meter PAN will be defined in close collaboration with WP4, in order to ensure compatibility and proper interfacing with the Data Management subset and the Service Orchestration system. The wireless communication will be defined to create a basis for the development of PAN core components.

The work will be undertaken by FORTHNET. CNET will analyse and define P2P architecture and distributed device discovery architecture. FORTH-ICS and UBRUN will contribute on data communication. The results will be documented in D5.1 Initial network architectural analysis.

Task T5.2 – BAN and PAN network implementation

TASK LEADER – FORTH-ICS
A Personal Area Network is a data network used for communication among devices, medical sensors, and terminals within a few meters of a person. PANs can be used for communication among the personal devices themselves (intrapersonal communication) or function as a bridge between the BAN and higher-level wireless networks and Data Management subsets.

Overall, this task aims at addressing issues in the communication between PAN and BAN devices on one side and PAN devices and application servers on the other side. The specific research and development goals in this task are to design architectural solutions, interfaces, protocols and techniques for:
- Efficient and robust PAN to BAN communication
- Efficient and robust PAN/BAN to backend communication
- Cross-layer optimisation utilising context and location awareness to improve energy usage, security, QoS, and cost

Subtask 5.2.1 – Efficient and robust PAN to BAN communication
The subtask will start with evaluating the benefits and shortcomings of different protocols for data transmission between devices and sensors. The implementation will focus on seamless switching between available, wireless connections such as WiFi, GPRS, Bluetooth, etc. A key requirement is that the protocol will have to ensure QoS in the BAN while maintaining low power consumption. The actual implementation will encompass software that not only keeps the key device in contact with available networks, ready to switch to them, should the active connection fail, but keeps the power consumption at a minimum, since continuous connectivity reduces a device's standby time significantly. Implementation of advanced keep-alive, polling and power

state management techniques will be deployed. The work in Continua Health Alliance's working group for BAN and PAN interfaces will be followed closely. On the basis of the structure of the BAN, the task will finally develop protocols for power-economic data compression and encryption as well as an integration system for device and sensor management and self-supervision, in support of the security, privacy, and safety framework.

Subtask 5.2.2 – Efficient and robust PAN/BAN to backend communication

A network agnostic infrastructure will be achieved by incorporating Personal Area Network technologies, which allow intelligent and seamless wireless connectivity between patients' Body Area Networks and the personal environment and the REACTION Data Management subset. Current wireless infrastructures cannot support seamless continuous access. The implementation will incorporate relevant Personal Area Networking (PAN) technologies from research projects as well as commercially available infrastructures. An important objective is to create a secure and resilient topology that encompasses the wireless sensors on the patient's body as well as mobile devices in the patient's PAN. The mobile peer-to-peer (P2P) paradigm can be employed to "bridge" heterogeneous networks, especially in cases of intermittent connectivity. The REACTION platform will develop a SOAP tunnel architecture to allow access of BAN devices from application servers, via PAN devices. This will provide a mechanism for both monitoring as well as controlling the BAN devices from application servers. This task will also consider issues related to low-energy transfer (LET) for short-range wireless interfaces within the PAN, at the link and data transport layers. Work in this task will identify robust data transfer protocols with minimal activity on idle-time and lowest possible retransmission as well as specifications and guidelines for LET implementations within the PAN.

Subtask 5.2.3 – Cross layer optimisations

Finally, the work in this task will develop optimised solutions, not only at the network abstraction level, but also by considering cross-layer issues, i.e. insuring seamless interfacing with the surrounding world. Given the sensitivity to transient phenomena related to radio signal, mobility, and traffic demand, a device needs to be able to adapt based on the network conditions and resource availability. Two facets of adaptation will be explored (a) the selection of the appropriate network interface, channel, Access Point, or relay node and (b) the use of a cache instead of accessing directly the Data Management subset. The existence of multiple channels, gateways, relay nodes, and network interfaces can improve the connectivity and robustness of the network. On the other hand, it may increase the energy spending, interference, and, management cost. This subtask will address these tradeoffs and investigate the impact of the network topology on the robustness and performance of the network. Furthermore, since connectivity (with the Data Management Subsystem) cannot always be guaranteed, the system will have provisions for caching data locally for data persistency. The implementation will encompass components that not only keep the key device in contact with available networks, but also keep the power consumption at a minimum, since continuous connection reduces a device's standby time significantly. Data persistence poses a special challenge to the security framework (developed in WP7). Network connectivity will be monitored to optimize the network for the actual service based on reliability, bandwidth, cost, etc.

Overall, the work in this task will result in annual prototypes of BAN and PAN networks to be implemented during the iterative development process. FORTH-ICS will be responsible for the design and implementation. DELTA and CNET will work on hardware/sensors and middleware integration respectively and UBRUN focusing on the data communication standards.

Task T5.3 – Network Management implementation

TASK LEADER – FORTHNET

This task will implement the Network Management architecture. The Network Management subset manages data traffic between the Patients' Sphere and the Carer's Sphere and communication and integrates backend networks to and from backend systems and EHRs with the BAN and PAN components.

The REACTION project combines different networking technologies under a common platform, able to address numerous communication needs, from body and personal to local and wide area

networks. These needs comply with a variety of network parameters that need to be addressed in order to achieve sound collaboration and QoS among REACTION services and applications.

Different QoS methods will be used based on monitoring flow of data records or specific data packets in a flow, based on Flow tools tool and programmes. Flow-tools is library and a collection of programs used to collect, send, process, and generate reports from NetFlow data. The tools can be used together on a single server or distributed to multiple servers for large deployments. NetFlow, will be used in collaboration with N-Top, a simple, open source (GPL), portable traffic measurement and monitoring tool, which supports various management activities, including network optimization and planning, and detection of network security violations. N-Top is a mature passive traffic monitoring application able to be integrated into industrial or home environments and platforms like Reaction.

Furthermore, applications like "NfSen" (Netflow Sensor) or "Webview Netflow Reporter" will be used in order to implement graphical web based front end for the NetFlow data.

Some of the most significant methods used on network and systems' monitoring that will be implemented comprise:

DoS Attack detections: Detection and protection of REACTION servers in case of Denial of Service (DoS) attacks can be achieved by analyzing aggregated statistics based on information from flow records. DoS attacks can be detected when the total number of flows to individual hosts is reported to be unnaturally high. When a host has been identified as being the subject of a DoS attack, individual flow records can be studied and a defence strategy can be devised.

Intrusion detection: Intrusion detection is of high importance to the REACTION platform. Intrusion is the problem of identifying individuals who are using a computer system over a network without authorization. An intrusion attempt often starts with a port scan of the targeted host. This port scan can be detected by analyzing flow records each packet separately.

QoS monitoring: Quality of Service (QoS) monitoring is the passive observation of transmission quality in the network. This kind of monitoring usually requires multiple observation points in the network, while the synchronization of system clock is important.

Accounting is an important application for measurement based systems. The amount of transferred data on the network is recorded for each user separately and this information is then used for further process, such as billing. Using Accounting applications, REACTION may detect the total data traffic per user. This means that the underlying platform that collects the information must have the capabilities for differentiating between types of traffic.

The task will also be concerned with implementation of the REACTION security framework in the PAN according the WP7 outcomes. The security framework in the PAN will allow for secure establishment of connections between devices and networks and support secure and trusted data exchange to backend systems. However, many devices and sensor networks have limited computational or power resources and new concepts of virtualisation and federation as defined and developed in WP7 will be implemented. In some applications existing technologies can be employed to provide secure and trusted connectivity in the uplink from the PAN. The possibilities of implementing e.g. VPN or tunnelling must thus be provided in order to adhere to existing standards for secure uplink connections in medical backend systems.

Finally, the task will implement an instant communication method based on Short Messaging System (SMS), available over GSM networks, which will be used for mobile crisis teams, carers and patients, and other notification means for recipients who will be inside a building (pop up windows on the PC, sound alerts, IM, light switches, etc). The input for the alarm service will be the complex user profiling derived from the REACTION service which will dynamically compose and send alert and notification messages to the users. A generic event messaging protocol will be designed and implemented in close cooperation with WP4, considering message model, coordination actions and network interfaces.

The development work in this task will thus encompass:

- Develop support for handling multi-connectivity when several wireless connections are available.
- Develop a backend structure of communication from the REACTION servers, through cabled networks and out to the "last mile" using existing wireless technologies.
- Implement network security with distributed parts of the REACTION security framework.
- Implement an alarm communication system for mobile or fixed users.

FORTHNET will develop and implement annual prototypes of the Network Management subsystem including the relevant detection, debugging, monitoring, QoS and accounting applications. CNET will contribute software components and FHG-SIT will contribute PKI implementation.

Task T5.4 – Network interoperability and service execution

TASK LEADER: CNET

Services in the REACTION environment need to access and control numerous heterogeneous devices at different locations using different access mechanisms. The sound collaboration of different applications and services will be secured using specific Software Development Kit tools, under a common internal network development platform. The communication through Web Services represents the main procedure for communicating between devices in the REACTION architecture. The Web Services are distributed in the network and implemented in different languages (Java and C#). Thus, the Web Service technology provides interoperability in the network, as the way of publishing, discovering and accessing services in a distributed way. Each Network Manager will have an external Web Service based interface, where it can receive data coming from remote Network Managers.

The communication between applications running in different devices will be based on SOAP messages. Usually, SOAP messages are forwarded through TCP connections to the destination. The destination address corresponds to the endpoint contained in the message. Traditional WS architectures are based on client-server architectures, where the server is an always-on end system with a well known endpoint address, which should be known by clients beforehand (using either service descriptors or UDDI registries). Furthermore, actual WS communications require direct connection between the client and the server, being impossible to consume services across networks. Moreover, devices may be presented as UPnP devices, but UPnP discovery information is usually restricted to Local Area Networks.

The SOAP tunnelling approach addresses these problems and proposes a way to replace the client-server architecture for a distributed one, using the Network Manager P2P platform. In this approach, all the peers will act as clients and servers at the same time.

P2P networks are often used to avoid the expense and delay of handling huge traffic volumes at the server. An important goal in P2P networks is that all clients provide resources, including bandwidth, storage space, and computing power. Thus, as nodes arrive and demand on the system increases, the total capacity of the system also increases.

As a complement to the network transparent SOA tunnelling, event based communication will be provided in support of higher level data monitoring and alarm signalling. The REACTION platform will support an event-driven messaging architecture. The core of this architecture will be a specific component, the event handling engine. This engine and the context manager form the basis for the context-aware multi-parametric monitoring functions and alarm.

The software SoA services will be developed and implemented by CNET. FHG-SIT will contribute PKI implementation.

Workpackage description

Workpackage number:	WP 5	Start date or starting event:						Month 1		
Work package title:	Network Management and Service Orchestration									
Activity type:	RTD									
Participant number:	1	2	3	4	5	6	7	8	9	10
Participant short name	ATOS	CNET	DELTA	IMM	FORTH-ICS	FHG-SIT	FORTHNET	IN-JET	ALL	MUG
PM per participant:		18,0	8,0		8,0	14,0	42,0			
Participant number:	11	12	13	14	15	16				
Participant short name	MSG	CHC	UBRUN	VUB	BTS	SOLIANIS				
PM per participant:			6,0							

Objectives
- research, develop and implement the network platform on which REACTION applications can be executed
- propose and implement the network platform that allows seamless wireless connectivity and operability between patients' BAN, through PAN and WAN to the Data Management subsystem
- develop the Network Management subset responsible for the communication between objects
- define / develop a resilient and intelligent event handling mechanism that supports crisis management

Description of work (broken down into tasks) and role of partners

T5.1 Network architecture and analysis: Perform analysis and define the overall network architectural model based on the requirements derived in WP2 to handle resources and services in heterogeneous networks. Peer-to-peer networks will be examined. Analyse different requirements for network protocols and proper interfacing with Data Management and Service Orchestration systems. An internal document describing the Initial network architectural analysis will be available at M6.

T5.2 BAN and PAN network implementation: Incorporate relevant Personal Area Networking (PAN) technologies from research projects as well as commercially available infrastructures with provisions for caching data locally for data persistency. Implement the PAN and develop optimised solutions. A first Backend network integration will be available internally at M24.

T5.3 Network Management implementation: Implement the Network Management architecture with the REACTION security framework proposed under WP7. Implement an instant communication method based on Short Messaging System (SMS).

T5.4 Network interoperability and service execution: The communication through Web Services represents the main procedure for communicating between devices in the REACTION architecture. Implement in each Network Manager an external Web Service based interface, where it can receive data coming from remote Network Managers. Implement SOAP tunnelling approach and event based communication in support of higher level data monitoring and alarm signalling. A first Implementation of event handling systems & interface to crisis management and the initial REACTION SDK - Software Development Kit tools will be available internally at M24.

Deliverables (brief description) and month of delivery
D5.1   Communication standards within BAN and PAN (M6)
D5.2   BAN & PAN networking components and implementation (M24)
D5.3.1 Network Management subsystem implementation & REACTION internal development platform (M12)
D5.3.2 Network Management subsystem implementation (M24)
D5.4   Backend network integration (M36)
D5.5   Implementation of event handling systems & interface to crisis management (M36)
D5.6   REACTION SDK - Software Development Kit tools (M36)

WP 6 – Integrative Risk Assessment and Feedback

Objectives

The work in this workpackage will focus on developing integrative tools for analysis and correlation of the multi-parametric data with established biomedical knowledge and expertise to derive clinically relevant and useful information. It will develop strategies and tools for personalization of the disease management including the continuous control of insulin dosing that will be founded on evidence based knowledge for the patient population as well as individual anamnesis information and biomarker measurements.

"Integrative risk assessment" will be implemented in the REACTION platform as a synthesis of several components. Multi-parametric data about patient health status (from real-time observations and direct patient inputs regarding e.g. exercise status) and health history (from data storages and EHR repositories) will be combined with user preferences (from patients and healthcare professional) in order to create the patients "Health Status Profile". Prior knowledge about healthy physiology and patho-physiological conditions common to diabetic patients will be used to set-up mechanistic models that support and structure the modelling and data analysis process. This generated "patient footprint" can then be used to investigate various risk assessment models and services.

The *first objective* is to develop and implement tools to promote physiological and context parameters to knowledge about the patient and the illness with the aim to provide a risk assessment based on her/his current health state and history. The tools will allow for integration between instantaneously measured data from sensors, historic data from EPR's, statistical data from stratification studies and statistical database and evidence based case management repositories. A continuous update and calibration with independent off-line measurements of relevant biomarkers and diagnostic tools is possible.

Predictions, risk assessments, risk profiling are among the various techniques that medical professionals increasingly rely on to improve the ability to provide early diagnose in patients with elevated risks and to slow down the rapid increase in prevalence of chronic diseases. For the purpose of focusing the work in the REACTION project, we define some fundamental aspects of the forecasting methods.

> The term *prediction* involves a statistically significant claim of a certain situation to occur in the future. Diabetes therapy predictions come from glucose measurements, insulin delivery data and specific patient parameters, and result in advice on how to adapt individual therapy in order to obtain more stable disease control in everyday life. Predictions are focused on providing insight into the *most likely* situation to occur and will provide relatively specific instructions on how to eliminate or reduce the effect of the situation. Predictions are most accurate in the short term.
> The term *risk assessment* involves assessing the overall statistical probability of certain situations to occur in the future. Medical risk assessment may provide probabilistic statements as to the likelihood that certain complications may occur given the present and historic health status. Risk assessment is most useful in the medium to longer term range.
> *Risk profiling* practices refer to the process of construction and application of health risk profiles based stratification of population health data in large populations. Risk profiling methods (e.g. pattern recognition) are used to find or test knowledge in the form of statistical patterns between data. Individual health profiles can be classified based on data matching and risk profiles can be derived.

The *second objective* of this task is to provide contextualised and personalised feedback to patients and carers. Whereas the sensors provide the first leg of the clinical management loop, the final leg is covered by feedback mechanisms to be used at the point of care.

The third objective is to integrate mechanistic physiology-based models of insulin and glucose kinetics and their physiological feedback loop with statistical models for prediction and risk

assessment. The mechanistic models will be used for direct individualization using patient characteristics (e.g. anthropometric data like height and body-mass-index) and biomarkers like plasma lipid and protein levels and blood flow measurements. The individualized models for pathophysiological conditions have already been successfully be applied to other non-diabetic applications like renal impairment, cirrhosis, congestive heart failure and cystic fibrosis. Their integration shall facilitate the optimization of therapies at the level of the individual.

Workpackage leader

The workpackage will be led by MSG

Tasks and actors in this workpackage

The work in will be divided in five tasks:

Task T6.1 – Disease management strategies for diabetes

TASK LEADER – MSG

Healthcare professionals in diabetes are beginning to explore more fully the tremendous potential of disease management. Disease management is a system wide strategy for proactively managing diabetes across the entire continuum of care. National disease management strategies guide diagnoses and treatments based on scientific advancement. The strategies direct decisions in optimising patient care and demonstrate the dedication to practice medicine that is both evidence-based and humane.

This task will survey European national strategies and approaches for diabetes management. In particular, the work will be build on and draw from existing good practice, including national strategies, such as the "National Service Framework for Diabetes: Delivery Strategy"[25] of the UK NHS and its implementation through hospital and primary care services as defined in the "Quality and Outcomes Framework"[26] and the National Institute for Health and Clinical Excellence (NICE) [27]. Special emphasis will be put on the use and factors influencing acceptance of ICT technologies and multi-parametric risk assessment methods in different diabetes management approaches (D6.1).

The results will be documented in at deliverable on systematic assessment of existing disease management strategies, with special emphasis on ICT and multi parametric risk assessment usage. This work will be carried out by MSG assisted by UBRUN and SST. ALL will contribute knowledge of diabetes management systems. BTS will contribute by identifying relevant components of existing disease management programs that allow a physiological interpretation and can be used in a mechanism (i.e. physiology) based approach suited for hybrid modelling and data analysis of data generated in other workpackages and tasks (e.g. in WP 8).

Task T6.2 – Models for risk assessment

TASK LEADER – MSG

The concept of a medical risk score is to determine the weight that should be applied to each data variable on a patient to predict likelihood of developing disease (or complications) given their present and historic health status.

Although some have faith in a stringent risk assessment approach, research over the years has not shown this to be a particularly productive route, other than reinforcing the obvious or what is known from epidemiological studies.

---

[25]http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4003246
[26]http://www.diabetes.nhs.uk/
[27]http://www.nice.org..uk/

The purpose of this task is to study existing assessment diabetes models as well as comparative models from the literature such as Framingham and UKPDS for cardiovascular events[28]. Unfortunately their data comes from epidemiological studies, and it has never really been shown, that the modification of a risk factor (like stopping smoking) really modifies the risk to the extent as calculated by these formulas.

The task will survey the different readily available risk assessment scores for persons with diabetes and their evaluations. Based on the published literature, methodology used to develop models will be systematically assessed and accuracy of models for wide spectrum of outcomes in different populations will be systematically assessed. Most promising methods, parameters and models will be identified and provide basis for the further development of multi-parametric risk assessment in the REACTION platform.

Predictions from individualized physiology-based in-silico models will be used to rationally (and non-linearly) transform patient "raw data" and will be integrated into to the analysis as additional covariates. A special focus shall lie on physiology-based transformations of patient input like exercise status, food uptake and other relevant varying non-biomarker factors.

Most promising models will be implemented, and if needed externally evaluated with additional already published studies and with publicly available data sets like Diabetes Control and Complications Trial (DCCT) for a wide variety of outcomes of interest.

During the project, a huge amount of laboratory and clinical data will be collected from different sources and integrated. Those data will together with readily publicly available data build a basis for further development and refinement of the REACTION risk engine.

Finally, the task will implement the chosen, potentially complex, multivariate models for risk assessment as REACTION services.

A report will be produced with a systematic assessment of currently available different risk assessment tools and their parameters (D6.2)

MSG will be working on risk assessment approaches supported by ALL on mathematical modelling. FORTH-ICS will contribute with the design of algorithms for predictive models. BTS will supply physiology-based models suited for personalization that can be used to predict additional input covariates for risk assessment models and will support the data analysis.

Task T6.3 – Stratifications and multi-parametric health status profiling

TASK LEADER – MSG

The aim of this task is to define the data set of incoming data from monitoring devices and health status information to build new models to estimate risk. Data from different sources will be made available and used by the risk assessment models.

The data set will be used to construct health risk profiles based on stratification of population health data in large populations. Risk profiling methods (e.g. pattern recognition) are used to find or test knowledge in the form of statistical patterns between data. Individual health profiles can be classified based on data matching and risk profiles can be derived.

The task will apply data mining methodologies and heuristic algorithms to large well defined datasets (such as held by primary care in the UK or other publicly available data) to evaluate the multi-parametric health status profiling approach. Task T6.3 will apply results from task T6.4 in the clinical domain. Report on the newly discovered diabetes knowledge in publicly available and REACTION datasets will be published in the project deliverable D6.3.

---

[28] Framingham and UKPDS risk scores are clinically useful for long-term primary prediction of coronary heart disease (CHD) events. Both Framingham and UKPDS risk scores are predictors of the prevalence and extent of coronary plaque.

MSG, together with UBRUN will perform this task. BTS will support the data mining with hybrid modelling technologies.

Task T6.4 – Knowledge discovery and semantic annotation

TASK LEADER – ALL

From the information systems perspective, integrative risk assessment and personalised feedback involves data from several sources to be combined using semantically based information management tools.

The quality of the personalised feedback depends on the quality of collected data and significant effort in this task will be devoted to data preparation including the application of intelligent methods for semantic annotation.

A central activity in this task is knowledge discovery aimed at analysing the collected data (e.g., qualitative and quantitative data such as data from real-time observations, direct patient inputs and health history). A modification rule approach, especially those based on subgroup similarity will be analysed and implemented. Approaches leading to the detection of useful complex features that can help in improved system characteristics, improved decision making for the professional carer as well as better education of the patient will be tested using state of the art machine learning, statistical, and data mining techniques (e.g. Support Vector Machine, regression models, and artificial neural networks, natural language engineering methods).

The formalisation of pre-existing clinical knowledge and the discovery (e.g. with semantic data mining techniques) of new elicited knowledge represent one of the main innovations in the REACTION project. Accurate, homogeneous and long-term data acquisition will allow the construction of evidence databases that can provide knowledge beyond the existing published clinical guidelines.

A semantic structure will be built in such a framework that is able to
- represent the current state of relevant biomedical knowledge,
- represent in an integrated manner data from different sources providing information about the dynamics of the disease and the physiological state of the patients

This type of semantic structure allows for the problem-oriented interpretation of data in a unified semantic platform.

The following tools will be developed in Task 6.4:

(i) Module to develop the above mentioned semantic structure (including a method for the representation of the relevant biomedical knowledge and data)
(ii) Module to map the data into the structure.
(iii) Module for problem-oriented query and retrieval of the data based on the structure.
(iv) Method for discovering new cause-effect relations in the case base in order to introduce new pieces of evidence or to modify the existing ones.

This work will be carried out by ALL providing methods for the semantic analysis of natural language texts as well as methods for discovering new pieces of knowledge on the basis of the data mentioned. MSG will assist with artificial neural network design and fuzzy logic engines in a medical ontology.

Task T6.5 – Integration and implementation with user feedback

TASK LEADER – FORTH-ICS

This task will integrate the assembly of a "Health Status Profile" with a series of REACTION services. "Health Status Profile" makes risk assessment using models developed in T6.2 and refined by results of T6.3 and T6.4 readily available to other REACTION services and components. Emphasis will be put on usability and clearness of personalized feedback. This will allow easy and readily available risk assessment tool to both clinicians and patients, which can be customized according to user needs and preferences. "Health Status Profiles" will thus be not

only essential tool for clinical decision making but also for patient empowerment and shared decision making between patients and physicians.

The aim of this task is thus to close the feedback loop from continuous measurements of the patient's health status to knowledge enriched personalised feedback to the patient for improved control and better education.

The implementation will be carried out by FORTH-ICS assisted by ALL, CNET. FORTH-ICS will be implementing the user feedback environment, including user-friendly interfaces.

Workpackage description

Workpackage number:	**WP 6**	Start date or starting event:					Month 1		
Work package title:	Integrative Risk Assessment and Feedback								
Activity type:	RTD								
Participant number:	1	2	3	4	5	6	7	8	9	10
Participant short name	ATOS	CNET	DELTA	IMM	FORTH-ICS	FHG-SIT	FORTHNET	IN-JET	ALL	MUG
PM per participant:					22,0				33,0	
Participant number:	11	12	13	14	15	16				
Participant short name	MSG	CHC	UBRUN	VUB	BTS	SOLIANIS				
PM per participant:	41,0		10,5		39,0					

Objectives
- develop integrative tools for analysis and correlation of the multi-parametric data with established biomedical knowledge and expertise to derive clinically relevant and useful information
- develop and implement tools to promote physiological and context parameters to knowledge about the patient and the illness with the aim to provide a risk assessment
- provide contextualised and personalised feedback to patients and carers

---

Description of work (broken down into tasks) and role of partners

T6.1 Disease management strategies for diabetes: Survey European national strategies and approaches for diabetes management. Emphasis will be put on the use and factors influencing acceptance of ICT technologies and multi-parametric risk assessment methods in diabetes management approaches.

T6.2 Models for risk assessment: Study existing assessment diabetes models as well as comparative models. Survey the different readily available risk assessment scores for persons with diabetes and implement the most promising models. The description and material related to the study of the Mechanistic whole-body model of insulin-glucose interaction and kinetics will be included in D1.4.1 Periodic report for the Commission at M12.

T6.3 Stratifications and multi-parametric health status profiling: Define the data set of incoming data from monitoring devices and health status information to build new models to estimate risk. Construct health risk profiles based on stratification of population health data.

T6.4 Knowledge discovery and semantic annotation: Develop knowledge discovery aimed at analysing the collected data. Approaches leading to detection of useful complex features will be tested.

T6.5 Integration and implementation with user feedback: Integrate the assembly of a "Health Status Profile" with a series of REACTION services. Close the feedback loop from continuous measurements of the patient's health status to knowledge enriched personalised feedback to the patient for improved control and better education. Documents describing the Architectural design of REACTION risk assessment engine will be available internally at M15 and the Implementation of the REACTION risk assessment engine will be available at M22.

Deliverables (brief description) and month of delivery

D6.1 Assessment of existing disease management strategies including available risk assessment tools and their parameters (M12)

D6.2 Newly discovered diabetes knowledge in publicly available and REACTION datasets (M24)

D6.3 Refined risk assessment engine (M46)

D6.4.1 1st Prototype computational kernel for individualized mechanistic models (M24)

D6.4.2 2nd Prototype computational kernel for individualized mechanistic models (M36)

WP 7 – Security, Privacy and Safety

Objectives

The objective of this workpackage is to develop a visible and controllable distributed security and privacy model, based on the concept of trust as a multilateral relation between stakeholders in a community of patients, informal carers and formal healthcare providers.

People who use electronic/mobile health applications and services share a responsibility to assure the value and integrity of the networked health systems by exercising judgment in using the services, and by providing meaningful feedback about health information.

Because health information, products, and services have the potential both to improve health and to do harm, organisations and individuals that receive and provide health information remotely using internet communication technologies, have obligations to be trustworthy, provide high quality solutions, protect users' privacy, and adhere to standards of best practices for online professional services in healthcare.

In particular, the workpackage will carry out the following activities:
-   Security requirements engineering
-   Concepts of trust and architectural implications
-   Patient empowerment
-   Virtualisation development

The solutions targeted will draw on insights from the result of the previous EU-funded projects in the field of security and trust models such as Hydra and PRIME.

Autonomous regulation of the devices' own operation poses instrumental safety risks that need to be addressed in terms of merit, resilience, repudiation, and most importantly, liability.

Whereas this workpackage deals with the theoretical foundation of security and privacy and the formulation of suitable models for distributed applications, the implementation and adoption of security models and policies are present in each of the technical workpackages.

Workpackage leader

The workpackage will be lead by: FHG-SIT.

Tasks and actors in this workpackage

The work will be carried out in five tasks:

Task T7.1 – Security requirements

TASK LEADER – ATOS
This task includes conducting security requirements workshops to specify healthcare scenarios with partners and invited experts to stimulate discussion regarding common security criteria, metrics, models and protocols and negotiations and conclude the security requirements for the REACTION scenarios in such a way as to provide a private, secure and trusted healthcare environment for the home, office, mobile spaces as well as hospitals and healthcare clinics. The output of this task is the REACTION security requirements specification. Requirements gathering will be performed through focus group risk analysis, which will provide the basis for further analysis of threats and risks. The analysis includes the identification of involved actors as well as of different types of assets in the REACTION scenarios. The actors are assigned roles and the assets are assigned to these roles. In the second part possible threats to the assets are identified, which leads to the required protection goals. Finally, the specific security and privacy implications are identified and a full set of requirements can be formulated and fed to WP2.

A further objective is to analyse and prioritise implications of standardisation activities to the security requirements engineering process and monitor the implications on security

requirements from major European and national activities such as the eHealth Cards and general purpose ID cards. The findings of ICE Integrated Clinical Environment will be considered, even if ICE is still a draft.

The work will be carried out ATOS focusing on security analysis and FHG-SIT on security management.

Task T7.2 – Security architecture

TASK LEADER – FHG-SIT

Personal health data in particular may be very sensitive, and the consequences of inappropriate disclosure can be grave. If trust is lacking, e.g. if a larger group of citizens lack confidence in the security enhancing technologies of a healthcare application, such a group will prevent or at least significantly slow down the adoption of these applications. The fear of privacy loss can represent a significant barrier for the acceptance of healthcare applications based on the REACTION platform. Patients have the right to expect that their personal health data will be kept confidential.

To protect users, REACTION will take reasonable steps to prevent unauthorised access to or use of personal data, to make it easy for users to review personal data they have given and to update it or correct it when appropriate, to adopt reasonable mechanisms for tracing how personal data are used and to tell how the provider stores users' personal data and for how long those data are stored. People who use the REACTION healthcare applications also need to know that the services are described truthfully and that information they receive is not presented in a misleading way. It should be forthright the efficacy, performance, or benefits of products or services.

REACTION aims to integrate OpenID with SAML. Using SAML will enable implementation of single-sign on and enable distributed transactions by making the client application retrieve its security assertions from a trusted authority and sending it to the other end of the transaction or making the other end of the transaction look for the required assertions before the completion of the transaction.

An OpenID-enabled site can ensure that for a given identity URL, only the person owning that URL can authenticate, and nobody else can fake that identity. Additionally, this prevents the ability for a malicious site author to extract a person's identity without their effort and consent. Also emerging specifications, like Web Single Sign-On Metadata Exchange (Web SSO MEX) Protocol and Web Single Sign-On Interoperability Profile (Web SSO Interop Profile), will be of great relevance. OpenID allows linking the identity of the user with an URL. In order perform a transaction in a server, the user sends his request along with the identity URL, DSA signature, and assertion timestamp, and the server can then verify the signature using either its cached version of the ID server's public key, or get it directly from the ID server URL. Alas, currently OpenID does not work with WS security and SAML.

SAML, (Security Assertions Markup Language) may contribute to provide a solution for distributed identity management in an open environment. SAML is designed to work with several communication protocols, such as HTTP, Simple Mail Transfer Protocol, file transfer protocol and several XML frameworks, including SOAP. It provides a standard way to define user authentication, authorization and attribute information in XML documents. While SAML makes assertions about credentials, it doesn't actually authenticate or authorize users. The security module will take charge of that. SAML just links back to the actual authentication and makes its assertion based on the results of that event.

An Identity Security infrastructure (with minimum overhead) is required to block actions from identities. Differences emerge where we focus on the security and risk balances when moving into transactions incorporating liability. The problem is that any communication entails risk and liability to some extent; particularly payments which do the most. The security paradigm attempts to mitigate risk using third parties and upfront collection of "proof" meaning no privacy, risk of identity theft, commercial feudalism (gatekeepers) etc.

This task also includes extending the technical device descriptions with an abstract modelling of security models incorporating issues and elements like traceability path, accountability path, dispute initiation and legal base, network and devices security contexts. Further, the work will include mapping and brokering between security models, user and client devices profiling management, mapping and usability between trust domains, and semantic standards and generalisation ontologies development.

The work will be carried out by FHG-SIT assisted by ATOS.

Task T7.3 – User empowerment

TASK LEADER – FHG-SIT

Patients have the right to be informed that personal data may be gathered, and to choose whether they will allow their personal data to be collected and whether they will allow it to be used or shared. And they have a right to be able to choose, consent, and control when and how they actively engage in a commercial relationship. Hence the REACTION platform must allow applications to clearly disclose if there are potential risks to users' privacy and support that data are not collect without obtaining the user's specific affirmative consent to collect, use, or share personal data in the ways described.

To assure that users understand and make informed decisions about providing personal data, REACTION will support clear and accurate indication of what data are being collected, who is collecting it, and how the healthcare provider will use those data.

This task will develop support for user empowerment and implementation of data protection and privacy regulations into the REAACTION platform, in particular the EU directive on Data Protection and concepts of informed consent are of importance.

The work will be carried out by FHG-SIT assisted by ATOS. VUB will provide input on patient rights and international law.

Task T7.4 – Virtualisation

TASK LEADER – FHG-SIT

In REACTION we distinguish between various types of identities such as virtual identities, federated identities with respect to different domains. In this task we will combine identity virtualisation with infrastructure-based accountability negotiations, which are very efficient but also complex. REACTION will assess the feasibility of an approach, which incorporates a context server. This can be combined with a client device layer that will take care of device and identity virtualisation and security adaptation to context.

With the increase of cross-boundary services that span over several organizations or web sites and involve multiple agents, the need for a distributed way to manage the user identity becomes an increasingly concerning issue. This problem is closely related with single-sign on solutions, and a strong desire to reduce the amount of login operations that users must undergo. Currently several solutions exist that provide a solution for this problem, but none of them is fully satisfactory. A lot of other distributed identity systems are not actually distributed, having one or more parts centrally controlled.

Virtualisation of devices is an important method to protect devices from attacks and balance users' security risks and ensure damage control. Both devices and users can operate with virtual identities. Two devices with respective users can thus connect based on semantic security description according to the security model.

This task will undertake the specification of the privacy model and the development of support for virtualisation of devices and users for secure connectivity and delegation of services, as well as user centric enabled authentication and authorisation.

REACTION will combine identity virtualisation with infrastructure-based accountability negotiations, which are very efficient but also complex. We will assess the feasibility of an

approach, which incorporates a context server, which will take care of next generation session initiation. This can be combined with a client device layer that will take care of device and identity virtualisation and security adaptation to context.

In addition identity management will need a way to transfer between trust domains. Certain security technologies (and protocols) fail here particularly for some specific needs; for example Kerberos, which is a trusted network authentication system, but not all network participants trust it or can interpret its security protocol. This implies it is a costly sophisticated infrastructure with which it is not possible to extend operations dynamically in order to encompass new resources; nor allow control over a shared resource.

The work will be carried out by FHG-SIT.

Task T7.5 – Patient safety and device risk assessment

TASK LEADER – UBRUN

ICT systems, and in particular when it involves automated closed-loop glycaemic control, must be rigorously monitored for possible adverse effects on human beings. Rigorous risk analysis will be undertaken of the entire REACTION platform and its subsystems and components.

The device risk assessment will be undertaken using existing risk management methodologies and frameworks. Where possible it will include existing standards and industry best practice. We will expect to apply the draft standards "IEC/ISO JWG7 Risk Management for networks with medical devices (IEC/ISO 80001)" and "Devices within the Integrated Clinical Environment (ICE)[29] under the auspices of ASTM subcommittee F29.21. All medical devices will, in Europe, also have to comply with EU Council Directive 93/42/EEC of 14 June 1993 concerning medical devices.

Of specific concern will be the safety of the closed loop glycaemic control system. The risk assessment analysis will include the use and the location of use of the device. For example for in-patient use, risk may be reduced as patients are in general under close observation, however they may have more severe illness than in home use of the system.

The task will start with risk assessment in the in-patient case in a more controlled setting and only with highly compliable patients. Later, it will be expanded to the out-patient use, incorporating further risk cases that do not apply in the hospital.

The problem of product liability when devices from two or more manufacturers are integrated, will be further analysed in WP9.

The task will be led by UBRUN, and will coordinate the activities of the medical device manufacturers to perform specific risk analysis on the components and a total system risk analysis.

The work will be carried out by UBRUN who will coordinate the activities of the medical device manufacturers in WP3 to perform specific risk analysis on the components level as well as a total system risk analysis. CHC and MUG will provide clinician input and VUB will analyse legal and regulatory demands.

---

[29] http://mdpnp.org/ICE.html

Workpackage description

Workpackage number:	WP 7	Start date or starting event:						Month 1		
Work package title:	Security, Privacy and Safety									
Activity type:	RTD									
Participant number:	1	2	3	4	5	6	7	8	9	10
Participant short name	ATOS	CNET	DELTA	IMM	FORTH-ICS	FHG-SIT	FORTHNET	IN-JET	ALL	MUG
PM per participant:	9,0					37,0				4,0
Participant number:	11	12	13	14	15	16				
Participant short name	MSG	CHC	UBRUN	VUB	BTS	SOLIANIS				
PM per participant:		3,0	22,0	9,0						

Objectives
- develop a visible and controllable distributed security and privacy model
- develop concepts of trust and architectural implications
- define patient empowerment and provide mechanisms for exercising it
- develop virtualisation
- perform device risk assessment and investigate aspects of patient safety

Description of work (broken down into tasks) and role of partners
T7.1   Security requirements: Security requirements workshop, metrics, models and protocols and   development of security requirements specification, implications of standardisation activities. A first internal version of D7.1 Security, privacy and trust requirements will be available at M9.
T7.2   Security architecture: The objective being to define the security architecture to be used in REACTION.
T7.3   User empowerment: Support that data are not collect without obtaining the user's specific affirmative   consent.
T7.4   Virtualisation: Protect devices from attacks and balance users' security risks and ensure damage control through virtualisation of devices and users
T7.5   Patient safety and device risk assessment: Develop a safety framework to make sure that devices don't cause bodily harm.

Deliverables (brief description) and month of delivery
D7.1   Security, privacy and trust requirements (M21)
D7.2   Concepts of trust and architectural implications in healthcare environments (M12)
D7.3   User empowerment - requirements, principles and concepts (M18)
D7.4   Virtualisation in distributed healthcare applications (M30)
D7.5   Safety issues in REACTION applications (M9)

WP 8 – Clinical Practice and Field Trials

Objectives

The overall aim of this work package is to assess the effectiveness of the REACTION platform in three treatment scenarios addressed by the project, namely (i) within a hospital environment, (ii) outpatients under therapeutic control and for (iii) patients who are self-managing their disease. The goal is to conclusively prove the validity of the applications, demonstrate the benefit for healthcare providers and provisioning authorities, gain acceptance by patients and other users and to assess the impact at the organizational level. The work package has the following four broad tasks:

- To design and conduct iterative technical feasibility studies of the REACTION platform
- To design randomised controlled trials (RCTs) based on the optimised REACTION platform
- To conduct RCTs to assess the optimised REACTION platform as described in the overall work package aim
- To disseminate the results, in particular to the medical community and to develop a compelling strategy for routine implementation

Three clinical studies have been selected based on their importance in terms of mortality, morbidity, clinical importance, potential widespread impact as well as today's lack of suitable technologies and care processes to address the issues. The three clinical studies are:

In-hospital glucose monitoring: The goal is to facilitate wide spread TGM in patients with diabetes, demonstrate closed-loop feedback involving special diabetes team and integration with workflow systems. Potential impact can extend to also preventing stress induced diabetes in normal patients.

Outpatient monitoring and feedback for self-management: Intelligent management of patients with hypertension and type 2 diabetes; a common case of co-morbidity. The goal is to introduce easy application development of remote multi-parametric monitoring and personalised feedback and support for life-style changes.

Compliance control and motivation: Problems of non-compliance with prescribed medicine (insulin) plans are wide spread and causes unnecessary medical complications as well as high costs. The aim of this study is to use intelligent pens and devices to measure compliance and to evaluate the impact on the patient's health status.

A further task has been made with the aim to evaluate technological and medical requirements for building AGC systems, in which sensor data from continuous glucose measurements are used to control the working of fluidic pumps for infusion of insulin. The study will in particular evaluate the achieved accuracy of REACTION CGM sensors and the security and resilience of the REACTION platform and its impact on patient safety and liability.

Each task will coordinate the activities and the conclusions of the clinical evaluations in their specific domain in order that common assessment criteria are adopted to allow aggregation and analysis of data. They will also cooperate to produce the final analysis of the clinical evaluation.

The work undertaken in this workpackage will be provided to the other workpackages for clinical guidance and for implementation of the platform.

Workpackage leader

The workpackage will be led by MUG

Tasks and actors in this workpackage

The work will be carried out in three tasks corresponding to the tree domains:

Task T8.1 –General ward RCT

TASK LEADER – MUG

The objective of this task is to specify and validate in an inpatient environment a suite of multi-parametric monitoring services designed to facilitate the close monitoring of diabetic patients by remote dedicated diabetes experts and so enable more widespread use of TGC. Aggressive treatment of stress-induced hyperglycaemia has shown remarkable results in recent years. In a randomized, controlled study conducted in a surgical intensive care unit (Vandenberghe2001), strict control of blood glucose levels with insulin reduced morbidity and mortality, significantly reducing in-hospital mortality from 11 to 7 percent in the entire study population. Strict glycaemic control also decreased morbidity from bloodstream infections by 46%, acute renal failure requiring dialysis or hemofiltration and critical illness polyneuropathy.

The common general ward workflow for good glucose control requires that blood samples be taken, identified and transported to the central laboratory. After analysis, the results are transmitted to the physician or nurse for evaluation and validation. Often, dedicated insulin therapy specialists, with training in handling control algorithms or guidelines for therapy, need to be involved in the validation. Only then can the therapy be safely applied. This procedure causes delays of hours and even days, which is highly problematic considering that TGC ideally requires measurements to be made every 3-4 hours.
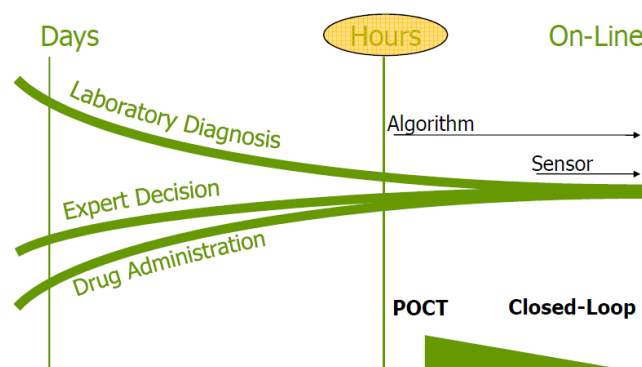
Figure 10 In-hospital workflow for glucose control

The entire process is moreover subject to errors, a situation that is compounded by the changing of the treating physician.

In the general ward RCT, a REACTION application will continuously monitor a range of vital parameters including blood glucoses, skin temperature as well as measures of nutritional intake. The data will be contextualised in the Data Management component and mathematical algorithms will be used to calculate the required insulin doses. Results will be fed to dedicated diabetes experts specialised in glycaemic control (usually located in a specialist diabetes centre) for verification and evaluation. Their appraisal will then, on-line, be fed back to the physicians and nurses at the point of care in the patients ward.

Subtask 8.1.1: Work flow analysis and compliance surveys

MUG will provide access to two inpatient departments for planning and work-flow analyses during the early stage phase of the project. To ensure compliance with the new system by health care professionals, comprehensive surveys will be performed amongst clinicians and nurses. Prior to enrolment, patients will be fully informed and asked to sign a statement of consent. Ethical approval will be obtained from the Austrian clinical board prior to the study commencement.

For the work-flow analysis and compliance surveys two inpatient departments of the University Hospital will be selected. In a first step the "state of the art" inpatient glucose control will be analyzed using a semi-structured interview. In the first part information from nurses and medical staff will be obtained to understand work-flow patterns for inpatient care, the current use of information about actual glucose control, status of medical decision-making and related problems and risks. In the second part of the survey improved work-flow models and validated glucose control algorithms will be discussed with the medical staff and nurses.

After informed consent, 50 inpatients with established diabetes mellitus or with newly diagnosed elevated blood glucose will be analyzed to obtain information about actual number of glucose

measurements (POCT, central lab), mode of diabetes treatment, use of insulin, algorithms of dose adjustments and overall quality of diabetes control. Subjects will be interviewed to understand patients' expectations and experience.

For the implementation of the new REACTION application, hospital systems will need to be adapted and hospital and ward-wide protocols for administration and monitoring of blood glucose levels and insulin infusions will be required. Besides that, and for risk mitigation purposes, protocols for risk management of hyperglycaemia will be established.

Subtask 8.1.2: Technical feasibility studies

In the first 18 months, for clinical evaluation of the newly developed sensor systems in the REACTION platform, intravascular microdialysis (ivµD) will be established as a reference method for continuous glucose monitoring. Intravascular microdialysis will not only serve as a reference method for continuous glucose monitoring, it will also provide the ideal matrix for the glucose sensor development based on impedance spectroscopy or infrared spectroscopy within the REACTION platform (T3.2).

The first technical feasibility study will be performed in 12 healthy subjects in the Clinical Research Center of the Medical University of Graz. After approval of the Ethical Committee and after informed consent commercially available microdialysis probes will be inserted into the anticubital vein. On the contralateral arm an intravenous catheter will be inserted and the arm will be placed in hot box to obtain arterialized blood for frequent blood glucose measurements. A variable glucose infusion will be administered to achieve various glucose levels (euglycaemic and hyperglycaemic clamp method). Glucose measurements will analysed with appropriate statistical methods.

The second technical feasibility study will include 12 inpatients in the Department of Endocrinology with elevated blood glucose. Technical feasibility for intravascular microdialysis as a reference method will be established using similar methods as in healthy subjects. Data from continuous monitoring obtained from intravascular microdialysis will be compared to frequently measured glucose levels using POCT and central lab.

In order to avoid the occurrence of technical problems during the main RCT and consequently an unacceptable level of data loss, all devices and associated software tools will be tested under conditions close to those that will prevail during the RCT. For this purpose, appropriate technical feasibility trials will be devised in close cooperation with the developers. To ensure timely identification of problems, these trials will be conducted to as great an extent as possible in parallel with the development process.

Subtask 8.1.3: Clinical protocol and inpatient RCTs

In the first 6 months of the project, clinical protocols will be established for inpatient implementation of the REACTION system. Based on the results of the work flow analysis and on the feasibility data of intravascular microdialysis, a clinical protocol for an algorithm driven randomized controlled trial (RCT) targeting for tight glycaemic control in hospitals will be developed. Until recently, glycaemic control in hospitalized patients has not been a major therapeutic focus, partly because of a lack validated targets, partly because evidence demonstrating improved overall outcomes as the result of improved glycaemic control is only just emerging. Despite national and local efforts, widespread implementation of improved glycaemic control for inpatients has remained an elusive goal for many medical centres.

So far, only few clinical trails have focused on optimal management of inpatient hyperglycaemia in the noncritical setting, and no definition of adequate glycaemic control exists. In the planned clinical trial in wards, adequate glycaemic control will be defined as 1) satisfactory glycaemic control (e.g. average blood glucose 5,5-8,9 mmol/l (100-160 mg/dl), 2) without clinically relevant hypoglycaemic events, 3) in affordable time for medical staff.

Accordingly, we will develop a prospective, randomized controlled study protocol to compare the efficacy and safety of a new algorithm-driven glucose control regimen based on or to be implemented on the REACTION platform with that of optimized standard care in patients with

diabetes mellitus in internal medicine wards. Power calculation to assess the needed patient number will be performed. The proposed trial protocol will be submitted to a peer review process to obtain external feedback and input. Outcome parameters will include average glycaemic control, risk of hypoglycaemia, diabetes treatment, concomitant diseases, overall inpatient mortality and morbidity, workload for medical staff, acceptance of patients and staff, and costs/effectiveness analysis.

UBRUN will run an RCT in Hillingdon Hospital[30] in which half the wards will be equipped with the Abbott glucose monitor system. This is currently installed and in use. This system stores all glucose readings for each patient (identified using scan of patient wrist band barcode) and are uploaded to the EHR every time the device is docked. Often this might only be once every 24 hours and so does not currently allow immediate response to glycaemic conditions. The current system is therefore used for audit and allows analysis of performance for satisfactory glycaemic control. In the RCT, half of the wards will instead be equipped with wireless glucose monitors, able to transmit readings as they are taken. This offers possibility for automated checking and provision for monitoring and intervention by the diabetes team. Audit will determine whether the technology improves glycaemic control. Hillingdon Hospital has 12 wards and there are around 100 diabetic patients on the wards at a given time. We would anticipate that we will audit of up to 1000 diabetic patients over a 12 month period.

We believe the design of the study allows direct comparison of performance of with and without the enhanced technology and the benefit of prompt readings on which automated protocols can prompt intervention.

The outcome of field trial will be assessed by level of intervention required (percentage of the group requiring intervention) and the number of patients enabled to bring control parameters within defined target levels. The patients may be their own control.

Also user acceptance surveys will be performed in association with the clinical field study.

Subtask 8.1.4: Data analysis, conclusions and outlook

This subtask is dedicated to the analysis of the data generated by the RCT, i.e. an analysis of the clinical data on glucose control using the novel control system vs. data on state of the art glycaemic control, analysis of user acceptance, safety and efficacy of the newly developed system.

Subtask 8.1.5: Data dissemination and development of an implementation strategy

The study data will be disseminated through the REACTION programme website, peer-reviewed publications and through presentations (conference and invited). As well as this, a protocol for implementation of the system in other centres will be formulated. Courses will be organized to provide diabetes carers from these centres with in depth information concerning the REACTION system in order to prepare the way for evaluation in these centres.

The work in this task will be carried out by MUG. MSG will perform the technical and workflow analysis.

Task T8.2 – Outpatient clinical field trial

TASK LEADER – CHC

In general, the approach to manage outpatients with diabetes in the community is different to the acute in the hospital. The aim is to improve long term management, with its associated impact on reducing the likelihood of developing long term complications (vascular disease, ulceration, amputation, blindness). This is achieved through improved management programmes.

---

[30] The expert who will analyse the data will be engaged by UBRUN and also the costs of installation will be paid by UBRUN.

The objectives of this task are to specify and validate a suite of services aiming at simultaneous monitoring of blood glucose, blood pressure and physical activity to achieve comprehensive protection against diabetic complications and promote pro-active disease management. A small clinical development program will be initiated and performed in two main sections: Data monitoring, validation and interactive algorithm identification and clinical assessment of the capacity of multi-parametric monitoring.

Careful monitoring of multiple parameters may represent a useful integrated basis for achievement of strict and sustained glucose control that will provide a better opportunity to reduce diabetic complications and improve patients' quality of life. Devices for glucose and physical activity monitoring will be used to determine whether multi-parametric monitoring provide a reliable measurements as compared to classical mono-parametric monitoring.

The REACTION platform will also support medication compliance, adherence to clinical pathways, education, and self management health services for diabetes related conditions. Furthermore, clinical intervention for patients can be targeted to those with need; those that are well controlled will have less need for routine check up, and those above guidance levels will receive pro-active timely intervention.

The subtasks examine a multi-dimensional approach, including: impact of education to improve compliance and modify lifestyle; enhancing primary care management with monitoring; and improving risk assessment to determine those likely to develop disease and complications.

Subtask 8.2.1: Work flow analysis and field trial preparation

CHC, as a primary care health centre, will deploy and validate the REACTION applications to provide intelligent management of patients with hypertension and type 2 diabetes and determine clinical models and assess them for their effectiveness for long term control. This subtask will prepare the trials including managing multi-modality data for patients with co-morbidity by developing multivariate algorithms for management of these patients. Patients will be fully informed, given access to all data and asked to sign a statement of consent before being enrolled. Ethical approval will be obtained from the UK clinical board prior to commencement.

Subtask 8.2.2: Clinical outpatient field trials

Many patients present with co-morbidities of several diseases, e.g. diabetes and hypertension. This increases risk from either of the diseases and the risk from the complications of both and the patient must also be managed in an integrated way. This task also explores the issues of managing these patients.

This field trial will validate clinical system design methodology and tools to define generic architectures that can be localised. It will build on existing research on patient care pathways. It will focus on testing the utility of simultaneous monitoring of blood glucose and physical activity in the daily management of diabetes.

The field trial will be initiated and performed in a realistic user environment under the supervision of physicians and clinicians at CHC. This program will be divided in two main sections:
- Data monitoring validation and interactive algorithm identification
- Clinical assessment of the utility of multi-parametric monitoring in the daily management of diabetes
- Determine clinical outcomes and measure differences in access to health services
- Determine clinical intervention strategies

An RCT of 100 patients managed long term using home based monitoring with a further 100 in the control arm will be used to assess the effectiveness of the approach. Daily monitoring of blood glucose will identify at risk patients and, using clinical intervention, appropriate changes to management to be made. HbA1c measured every three months will be used to determine clinical effectiveness for patients, as measured by those brought within target values. The number of clinical interventions will be used to determine the effect on clinical services of such a clinical strategy. We anticipate most patients will be brought within target within 8 weeks and

monitoring can be withdrawn for patient with diabetes type II. In this way, we can cycle monitoring and recruit a larger cohort. We wish to determine how long the effect lasts, and we wish to continue "passive" monitoring for a further 12 months followed by a further cycle of monitoring. Where indicated monitoring would be resumed for patients no longer within target levels. The trial will therefore extend for 24 months (within the project duration) to encompass at least two cycles of monitoring. Clinical effectiveness will be measured by the percentage of patients kept within target values and mean reduction in HbA1c. Impact on clinical services will be determined by recording relevant clinical intervention and determining the percentage of the cohort receiving intervention. Outcome parameters will include average glycaemic control, risk of hypoglycaemia, diabetes treatment, concomitant diseases, overall inpatient mortality and morbidity, workload for medical staff, acceptance of patients and staff, and costs/effectiveness analysis.

Clinical management will require an integrated approach to diagnosing, monitoring and managing patients, combining delivery of healthcare service to the patient in several health domains, and the task will undertake clinical validation based on exploitation of healthcare services close to the point of need of the patient to deliver intensive disease management and response. The study will build on existing UK frameworks for managing patients in primary care and will seek to determine effectiveness of pro-active management and self-management to achieve and sustain target levels and determine effect on complications.

The education of patients is a key issue in diabetes management. How the patient is capable of changing lifestyle is a key question, which will be analysed in the field trials. A REACTION application will be set up to continuously monitor a range of vital parameters as well as measures of nutritional intake and lifestyle behaviour. The data will be contextualised in the Data Management component and mathematical algorithms and semantic searches in medical backend expert systems will be used to derive risk assessment. The contextualised information will be fed back to the patients and the informal carers in their social environment.

Subtask 8.2.3: Multiple Daily Injection compliance

The objectives of this subtask are to establish a compliance monitoring application for MDI (Multiple Daily Injection) insulin pens therapy and assess its impact on the patients' clinical pathway.

Monitoring will take different forms. In one application, the patient will be warned of missing insulin intake. In another application, the patient will be unaware of the missing intake, but the non-compliance pattern will be logged. 100 patients will be enrolled in a clinical study and divided in two groups. One group will be reminded by personalised alerts when noncompliant. The other group will not. All patients will be tested for glycosylated hemoglobin A1c every two weeks. The Hb_{A1c} level is proportional to average blood glucose concentration over the previous four weeks to three months and will thus represent an aggregated quality measure of the patient's level of glycaemic control. Development in Hb_{A1c} levels over a 9 month period will be analyzed and compared to the patient case history, with particular focus on registered hyper- and hypo-glycaemic episodes.

The compliance monitoring will be established using prototype insulin pens from Novo Nordisk with build in wireless communication devices. The pens are capable of registering time and dose of insulin intake and communicate the results via the patients BAN and a personal node, such as a mobile phone, to dedicated monitoring applications on the REACTION platform. Novo Nordisk is the only European company that can offer an insulin injection device which can accurate record the time and dose of insulin intake. However, in the case that Novo Nordisk will not join the project and this pen will not be available, the compliance study will be carried out with manual recording of time and dose of the insulin injection and the patient will be instructed to use the smart phone (or similar user terminal) to send the data to the REACTION platform.

This subtask identifies patients that are unstable in their diabetes control. These patients ought also to be equipped to transfer their regular blood glucose readings (as control is about the balance between ingested food and insulin delivery) as well as injections.

It seems that compliance and control is a much greater problem in type II diabetes. An alternative possibility is to undertake a questionnaire to such a patient group to supplement the community based study in order to determine actual compliance issues. In such a project we should send to several thousand patients. We can then identify compliance issues compared to management issues.

An option would be to build the 11073-10472[31] (medication monitor) standard into these pens. We can approach such manufacturers through efforts of the project CONTINUA.

The clinical aim of this study is to:
1) evaluate the impact on the patient's health status from TGC based on compliance monitoring;
2) assess the potential cost/benefit from using insulin pens with wireless communication capabilities for compliance monitoring;
3) evaluate the ability of the REACTION platform to launch personalised, easy to use compliance monitoring applications using commercially available insulin pens and standard mobile phones or smart phones, and
4) study the benefit of having applications embedded in the communication networks rather than embedded in millions of single products.

The clinical work in this subtask will be performed by CHC. Novo Nordisk will supply FlexPen® MDI pens and insulin and IN-JET will evaluate the economic benefits and usability aspects.

Subtask 8.2.4: Data analysis, conclusions and outlook

In all cases, data registration will be obtained via the REACTION platform and will be validated against reference readings obtained by classic monitoring before and after meal ingestion, before and after standardised physical exercise, and during sleep. The data obtained will be analyzed in an integrated manner in order to identify algorithms for individualization of interaction between blood glucose changes, physical activity, and treatment.

Data about hypoglycaemic events rate, postprandial glucose excursions and glucose variability will be collected and compared between the different monitoring strategies to evaluate the contribution of the different approach at the daily diabetes management and glucose control. Moreover, a sequence period analysis will be done to evaluate the educative implication of the multi-parametric monitoring approach.

The methodology can be used as a design tool, an implementation tool in order to determine clinical service elements that need to be put in place, and an analysis tool to compare effectiveness of the implementation for the integrated approach to be used for general healthcare provisioning by the Primary Care Trusts and other national healthcare providers. Consequently, clinical practice in different Member States as well as aspects of cross-border healthcare issues will be analysed.
The work in this task will be carried out by CHC. UBRUN will perform the technical and workflow analysis. IN-JET will research the cross-border healthcare issues.

Task T8.3 – Automatic Glucose Control (AGC)

TASK LEADER – MUG
The aim of this task is to evaluate paradigms for control of devices for autonomous regulation of the delivery of insulin to patients by considering changes in health status, calorific intake, response to treatment and through blood glucose measurement, in order to personalise and optimise care.

A reference implementation will be made, in which a CMG sensor will continuously measure the glucose level. Other data on treatment response will be collected and the combined data will be used within an algorithm to determine the level of insulin delivery.

---

[31] Note that ISO/IEEE 11073-10472 Medication Monitor provides standard way to record when medication is taken or administered and this should be adopted within devices built for reaction so that all can be integrated, including 11073-10417 glucose monitor.

Data analysis will be used to identify improvements in the algorithms and physiological models (which are part of the algorithm) and individualization of interaction between blood glucose changes and treatment response. The evaluation is expected to establish the basis for more appropriate treatment guidance and for designing actual AGC systems.

Within this task there will be a stepwise approach:
A physiological model of glucose control based on ingested food and insulin delivery will be developed in Task 3.3.2 using information from the literature and based on measurements performed using the continuous blood glucose measuring sensor developed within the Reaction project (Task 3.3.1). The physiological models will be validated against the data from several patients to determine inter-person differences between parameters to determine those parameters that must be calibrated individually and those that can be tuned through automatic parameter adaptation or managed by the feedback control. The physiological model will become the basis for simulation experiments to determine the sensitivity of parameters to change and to develop robust and reliable control algorithms that react appropriately and can be determined to fail safe.

The basic physiological model is to be built from clinical data, taking into account glucose levels and the physiological parameters as a function of time as well as the insulin doses delivered during the measuring cycle. It is expected that individual patients require adapted physiological models, therefore, requiring an adaptation of the physiological model, based on the REACTION sensor platform data. The adaptation of the physiological model may not be made in an automated closed loop fashion but rather has to be verified by the carer. In this way the individual biological profile of the patient can be addressed.

Initial work will be based on testing and improving the physiological models/algorithms by providing clinical data. In parallel the glucose sensors which will be developed in the REACTION project will be clinically tested (sensor workshops). In the next step the algorithm will be adapted and tested based on the performance of the sensors.

After successful integration of the three essential components of the automated glucose control system - glucose monitoring, computing insulin dosing by an algorithm based on a physiological model and insulin delivery – and if successfully evaluated in a simulated environment using real patient data, the whole automatic glucose control system will be tested with inpatients in a clinical environment.

Schematic of the AGC Algorithm
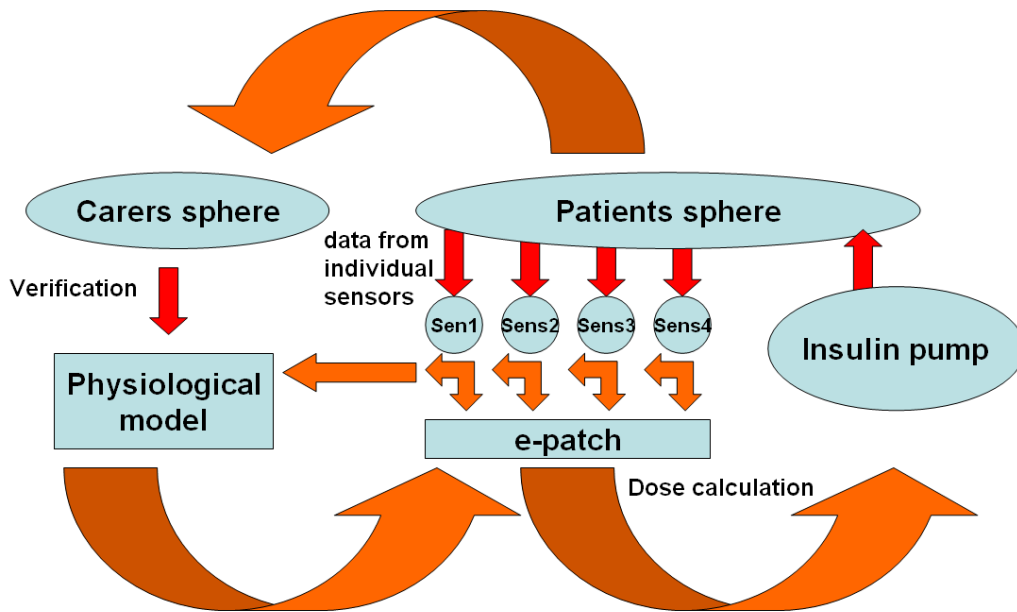
Figure 11: Schematic representation of the AGC Algoriithm

A general overview of the system is shown in Fig.11 including the direct feedback control from physiological measurements and the context from indirect information to support personalisation and safety interlock from user and carer verification. The purpose of the automatic glucose control (AGC) algorithm is to calculate insulin delivery rate from available physiological data and deliver this via an insulin pump. The closed loop algorithm calculates the insulin delivery rate based on the continuous glucose monitoring via the CGM sensor, together with additional physiological parameters using the sensors in the e-patch platform.

Workpackage description

Workpackage number:	WP 8	Start date or starting event:							Month 1		
Work package title:	Clinical Practice and Field Trials										
Activity type:	RTD										
Participant number:	1	2	3	4	5	6	7	8	9	10	
Participant short name	ATOS	CNET	DELTA	IMM	FORTH-ICS	FHG-SIT	FORTHNET	IN-JET	ALL	MUG	
PM per participant:						2,0		7,0		40,5	
Participant number:	11	12	13	14	15	16					
Participant short name	MSG	CHC	UBRUN	VUB	BTS	SOLIANIS					
PM per participant:	16,0	30,0	31,0			9,0					

Objectives
- assess the effectiveness of the REACTION platform in three areas:
    - In-hospital glucose monitoring
    - Outpatient monitoring and feedback for self-management
    - Compliance control and motivation
- design and conduct iterative technical feasibility studies
- design randomised controlled trials (RCTs) based on the REACTION platform
- conduct RCTs to assess the REACTION platform

Description of work (broken down into tasks) and role of partners

T8.1 <u>General ward RCT</u>: Specify and validate in an inpatient environment a suite of multi-parametric monitoring services designed to facilitate the close monitoring of diabetic patients by remote dedicated diabetes experts and so enable more widespread use of TGC, perform technical feasibility studies and perform an inpatient RCTs. A Common clinical assessment criteria for medical domains will be available internally at M3. Additionally, the clinical protocol for general ward clinical field trial will be available internally at M6. Finally, a first clinical evaluation of general ward clinical field trial will be available internally at M24.

T8.2 <u>Outpatient clinical field trials</u>: Specify and validate services aiming at protection against diabetic complications and promote pro-active disease management. Perform clinical outpatient field trials with patients with co-morbidities and investigate self-management and life-style change. This task will also consider studies on Multiple Injection Compliance. A Common clinical assessment criteria for medical domains will be available internally at M3. Additionally, the clinical protocol for outpatient clinical field trial will be available internally at M6. Finally, a first clinical evaluation of of outpatient clinical study will be available internally at M24.

T8.3 <u>Automatic Glucose Control (AGC)</u>: Evaluate paradigms for remote control of devices for autonomous regulation of the devices' own operation, in order to personalise and optimise care. A reference implementation will be made in which a CMG sensor will continuously measure the glucose level and control data which are transmitted to a fluidic micro-pump simulating an insulin pump.

Deliverables (brief description) and month of delivery
D8.1 Clinical protocol for Multiple Daily Injection (MDI) compliance (M12)
D8.2 Clinical protocol for Automatic Glucoses Control (AGC) (M30)
D8.3 Clinical evaluation of general ward clinical field trial (M36)
D8.4 Clinical evaluation of outpatient clinical study (M42)
D8.5 Clinical evaluation of Multiple Daily Injection compliance study (M24)
D8.6 Clinical evaluation results of technologies for Automatic Glucose Control (AGC) systems including sensors, pumps, e-patch (M48)

WP 9 – Socio-economic Framework

Objectives

A general trend in Europe is the emphasis on providing for chronically ill in their own home in response to patients' and their families' wishes. Such developments depend to a great extent on well functioning services but even more on the acceptance by patients and users.

The objective of this workpackage is to investigate and provide overview of the ethical, social, legal, regulatory, and economic aspects of the REACTION platform in order to provide the best possible framework for the successful deployment of REACTION applications in the future. The workpackage delivers important input to the requirements engineering, the continued development of user interaction components and the final integration and validation phase.

Workpackage leader

The workpackage will be lead by: VUB

Tasks and actors in this workpackage

The work will be carried out in four tasks:

Task T9.1 – Ethical issues

TASK LEADER – VUB

ICT in healthcare echoes value conflicts in the provision of healthcare. As pointed out already by the European Group on Ethics and New Technologies in its opinion No.13 of 1999 conflicts include the need to know and share patient personal health data in order to provide good quality of care *versus* creating situations of shared secrecy which may compromise confidentiality. Privacy may be traded for certain collective goods for prevention and independence, planning or for benefiting the population at large research, administration, planning. There are concerns that quality assurance standards may restrict or diminish professional autonomy. There are issues of fairness concerning access to innovative procedures independently of economic considerations.

Subtask 9.1.1: Ethical analysis of the overall REACTION vision

This subtask will first carry out an ethical analysis of REACTION services, philosophy, and vision against the background of the European Charter of fundamental Human Rights, Opinions of the European Group of Ethics, European Science Foundation Policy Briefings, ethical rules in FP7, etc. Special focus will be put on medical surveillance, the meaning of human dignity and threats to people's autonomy.

Subtask 9.1.2: Privacy

The private digital space could be considered as an extension of the private home. Currently, the law guarantees neither the establishment nor the protection of an online private space in the same way as the private space in the physical world is protected. The European Convention on Human Rights and Fundamental Freedoms states that the individual has the right to enjoy the privacy of his own home. There is consensus among scholars that this principle should be extended to digital types of personal space such as the PAN (Personal Area Network), which will need to be defended against any invasion as fervently as we now defend our homes.

Subtask 9.1.3: Accessibility and inclusion

In Europe the digital divide is real. According to the CEC 2005 Benchmarking Report, only 38% EU citizens are regular users of the Internet, and only 8% of people 65+ are regular users. Furthermore, ICT uptake is considerably lower in the southern European Member States than in the northern. Accessibility of REACTION services implies a problem of justice and in this subtask we aim to study how REACTION applications may be developed in different cultural contexts.

The task will be implemented by desk search and text comparative analysis combined with meetings between the project partners and focus groups in different EU regional areas. Results

and summaries from group meetings will be published. VUB will be managing the ethical studies jointly with ATOS and IN-JET. FHG-IST will be involved in privacy analysis. MUG, CHC will provide input on clinical ethical standards.

Task T9.2 – Social issues

TASK LEADER – FORTH-ICS

Social and cultural factors related to REACTION services are going to play an important role in public acceptance.

ICT has an important social impact since such technologies afford diversified modalities of interaction. Ljungberg and Sørensen (Ljungberg2000) characterise interaction modality by two dimensions drawn from Schmidt and Simone's work (Schmidt1996): unobtrusive vs. obtrusive and ephemeral vs. persistent. Interaction can be "more or less obtrusive dependent on how strictly it imposes obligations to notice or react". In their influential book, Nass and Reeves (Reeves1996) demonstrate convincingly that interactions with ICTs are identical to real social relationships.

One of the startling consequences of Nass and Reeves' argument is that research is needed about the "personality" of different technologies and their applications. People automatically extrapolate personalities from little hints. The creation of personality for an ubiquitous computing system is not primarily an issue of artificial intelligence. Virtually all human-machine interfaces have a personality. This literally applies to anything that interacts with the user, especially where words are presented. Personality can creep in everywhere: the language in error messages, user prompts, methods for navigating options, and fonts chosen. The ability to design ICT personalities will become a crucial element in public acceptance of new technologies.

Marc Pesce, one of the early pioneers in Virtual Reality, speaks of 'techno-animism' to describe a world pervaded by computational objects (Pesce2000). Humans have a deeply intuitive tendency of projecting human features onto non-human aspects of the environment, and we commonly perceive intentional agency even in inanimate objects. Animism is a feeling/belief that our environment is saturated by invisible communication between the things that surround us in our daily lives. That is, things have the ability to observe, gather knowledge, to communicate and perform actions in the real world.

ICT and literacy skills may actually serve as "barriers" for the attainment of good health and are important for proper case management. Hence information provided in closed-loop applications must on the one hand be targeted to users' literacy skills to avoid missing a large number of the patients.

This subtask will be implemented by convening four focus groups in four different EU regional areas. Results of the focus groups will then be analysed, formulated in terms of functional and non-functional requirements, and forwarded to the iterative requirements engineering process managed by WP2. The work will be carried out by FORTH-ICS assisted by IN-JET and VUB.

Task T9.3 – Legal and regulatory framework

TASK LEADER – VUB

The objective of this task is to describe which legal perspectives are applied to the REACTION service platform. The task covers a wide range of legal and regulatory aspects.

Subtask 9.3.1: Data protection

Data protection is a set of rules designed to ensure that the individual should have the possibility to control access to his or her personal information and to construct his or her own public persona. Generally speaking, REACTION services should respect data protection fair information principles. More in particular the following issues will be addressed in this task:
- Informed consent
- Freedom of choice
- Individual participation principle

- Data minimization
- Purpose Limitation
- Security of data
- Right to access
- Profiles or decisions based on inadequate criteria
- Compensation
- Function creep
- Inter-operability

Subtask 9.3.2: Patients' rights

As freedom of movement becomes established in the European space, European healthcare providers are ready to move with them to provide cross border healthcare to their patients. At the EU level, the building block can be found in article 35 of the EU Charter of Fundamental Rights, which states: "Everyone has the right of access to preventive healthcare and the right to benefit from medical treatment under the conditions established by national laws and practices. A high level of human health protection shall be ensured in the definition and implementation of all Union policies and activities". Although a specific EU Charter of patients' rights does not exist, the 2008 European Patients' Rights day sought to give a boast to put article 35 principles in practice. The Active Citizenship Network, an NGO active in Italy, for example, has drawn up a 14 point patients' rights charter which include access to health service and to timely information tailored to the individual, as well as rights to consent, choice, innovation, privacy, to make complaints and to be spared unnecessary suffering and pain. Several aspects of patients' rights will be studied such as: Change in interactions between practitioner and patient, Third parties access, Standards and Remote electronic systems and reported.

Subtask 9.3.3: Product liability

Many different producers and service providers will provide parts of the final REACTION application. When a defective device or an erroneous feedback causes damages, it could be very difficult to determine which producer or provider to hold liable for the damages caused and whether this producer has committed a fault that caused the damage. Council Directive 85/374 on the approximation of the laws, regulations, and administrative provisions of the Member States concerning liability for defective products stipulates that producers are jointly and severally liable for defective products. However, the directive does not apply to services and it is unclear whether it applies to software or hardware and whether the Directive could be altogether invoked in the case of ICT products. In addition, the directive does not provide that a product is defective when it insufficiently protects against privacy violations or when it easily allows identity theft. Other questions concern whether the provider of the software can be held liable and to what extent this liability can be waived in general contractual terms and conditions. Questions of liability will be tackled focussing on *direct liability* and *indirect liability.* In terms of direct liability, the question to be coped with is whether liability covers the case in which the ICT system fails to provide feedback to the caregiver or it provides wrong indications. In terms of indirect liability, the question concerns a situation in which responsibility for payment or satisfaction may arise in the future, after the adoption of the technology.

Subtask 9.3.4: Intellectual property rights and DRM

Intellectual property rights (IPRs) such as copyrights, patents, etc., provide the legal protection upon which stakeholders rely to protect knowledge, which becomes openly accessible through the REACTION platform. Digital technologies allow unlimited copying and dissemination of knowledge so without adequate protection and enforcement authors may not make their knowledge available. The legal framework for digital content IPRs in the EU is established by the Directive on the Harmonisation of Copyright and Related Rights in the Information Society (2001/29/EC). The Directive also addresses the use of Digital Rights Management[32] systems (DRMs) that can be used to enforce usage rules set by right holders or prescribed by law for digital content. They can also facilitate legal copying and reuse of content by establishing a secure environment in which right-holders are remunerated for private copying, on-line content

---

[32] DG Information Society, Commission Factsheet 20, September 2004.

is paid for, and illegal copying is prevented. This subtask will establish IPR strategies for the REACTION stakeholders and define suitable DRM systems to be included in the REACTION

The work in this task will mainly be carried out by VUB. ATOS and FHG-SIT will participate on security and data protection, VUB will contribute on patient rights and IN-JET and BTS in IPR and DRM.

Task T9.4 – Healthcare economics and business models

TASK LEADER – IN-JET

The objective of this task is to develop a viable and sustainable business framework for deploying the REACTION platform that alignes with realities of healthcare economic and reimbursement schemes.

The provisioning of long-term healthcare and home-care differs between the EU Member States and this task aims to define the socio-economic foundation for sustainable implementation of REACTION remote monitoring services across Europe. In France, "hospitalisation at home" has been introduced; in the UK rehabilitation care is increasingly being carried out at community level or at home rather than at hospitals; and Kaiser Permanente in the US, one of the earliest adaptors of telemedicine, has developed the concept of "Home as the Hub". Just to name a few of the many healthcare organisations working with remote monitoring and telemedicine, who have realised sustainable business cases for achieving acceptable cost-benefit ratios with these new services.

A solid economic foundation is required for a similar successful integration of REACTION applications into healthcare systems in Europe. A suitable framework for analysis of value creation and business modelling will be developed, which will allow accurate and viable metrics for cost-effectiveness, organisational adaptation and sustainable business and cost-benefit models for the stakeholders. Clinical and medical scenarios will be used to capture parts of the service concept idea and to contribute to a common understanding between stakeholders. Moreover, the business cases will be an integral part of the scenarios for the purpose of user validation. It is thus important that the scenarios are also capable of capturing parts of the service value model and not just focus on functionalities and other inherent attributes.

The development and implementation of ICT in healthcare requires willingness to invest large sums without expecting to see the economic benefits immediately. The eHealth Impact[33] project has demonstrated that there is at least a 4 years payback period of ICT investments in eHealth. After this period, there will be a 2:1 ratio between costs and benefits, thus illustrating the overall benefits of investing in ICT in healthcare. Most governments are adapting this view and beginning to see ICT investments as long term investments a major priority in order to ensure an efficient and cost-effective healthcare system in the future.

In the trail of the extensive ICT developments within the healthcare systems in Europe in recent years, there is a fertile environment for the introduction of yet more comprehensive services for improving healthcare and make healthcare providers more effective. But the valorisation of new ICT service in healthcare is becoming more and more focused on real value creation. Every new product has to provide a viable cost-benefit to the healthcare provider or it has to provide real, measurable advances in medical practice in a prioritised area.

The situation is even more obscure as seen from the supply chain of manufacturers, service providers and operators, pharmaceutical companies and suppliers of healthcare products, etc. The ubiquitous nature of the REACTION infrastructure and the dynamisms of services orchestration are the core features of the future Internet of Things and Services. Understanding the business framework in this ecosystem is an essential prerequisite for the successful deployment and exploitation of new services and applications.

---

[33] eHealth-Impact, EU funded project under the 6th Framework Programme, www.ehealth-impact.org

This task will therefore focus on analysing the business system and its stakeholders, modelling different potential ecosystems and developing sustainable business cases for important actors. The work will include:
- Develop a suitable framework for business modelling
- Identify actors and roles and the value created
- Derive and validate viable business cases for the medical domains
- Provide sustainable business models to support deployment of REACTION platforms

REACTION will adopt an ontological perspective on the exploration of innovative service concepts and for quantifying value creation (Thestrup2008). The chosen approach is called e^3value, and is based on the analysis of economic value creation, distribution. The initial work on the e^3value concept was done by Jaap Gordijn at Vrije Universiteit Amsterdam (Gordijn2002).

The e^3value ontology is organized in viewpoints, where actors exchange objects of value. The value exchange can be analysed in terms of value proposition and profitability. The challenge is to identify exactly what is the value in REACTION healthcare applications and what kind of value exchange can be expected in order to provide a real value proposition to actors. By adopting the ontology consistently over the business landscape, a complete value model can be developed. The method also allows for a complete mapping of dynamic value constellations, which again will form the foundation for the REACTION business cases.

New models of business constellations will be explored including private public partnerships, collaboration pharmaceutical companies as innovation drivers and bringing together payers, providers and patients in new constellations. Special emphasis will be placed on how to share proprietary information across organisational barriers, involve and transform the patient from a passive health information provider to an active information user, and safe handling of the massive flow of information and intellectual property rights to healthcare information. The business system can be seen hierarchical structure with four value levels. At each level, selected actors and stakeholders have been identified for further analysis:

The Concept Owner licenses the right to use the REACTION concept to one or more healthcare commissioning bodies or service providers. The Concept Owner develops the concept in a suitable form, based on open standards as end-to-end solutions based on open standards. In dedicated (proprietary) REACTION applications, concept owners may be found among pharmaceutical companies or in healthcare organisations. In open systems, concept owners can be software service providers or system houses.

The Service Providers are organisations that establish the commercial REACTION platform and offer the REACTION applications to health commissioners or healthcare providers. The Service Providers may charge an initial license fee plus a usage fee for the right to use the service.

The **Healthcare** system consists of healthcare commissioners and healthcare providers and other professional actors working with delivering healthcare services.

Healthcare Commissioners in the tax-based healthcare systems in Europe mainly takes the form of public bodies providing and managing healthcare services. Public bodies often act as both providers and commissioners (purchasers) of health services, although the National Health System in the UK has created special bodies for healthcare commissioning.

Healthcare Providers are usually divided into three groups: primary, secondary and tertiary care providers. Primary is general healthcare where patients first seek assistance from the healthcare system. Secondary care covers hospital care (in-patient and outpatient services), while tertiary care is the highly specialised care offered in specialised (or university) hospitals with sophisticated technological facilities and support.

Patients and carers are people actually using the REACTION applications including patients, and informal carers as well as healthcare professionals and administrators, etc.

The work will be carried out by IN-JET assisted by ATOS. UBRUN and MSG will assess cost/benefits in healthcare regimes.

Workpackage description

Workpackage number:	WP 9		Start date or starting event:					Month 1		
Work package title:	Socio-economic Framework									
Activity type:	RTD									
Participant number:	1	2	3	4	5	6	7	8	9	10
Participant short name	ATOS	CNET	DELTA	IMM	FORTH-ICS	FHG-SIT	FORTHNET	IN-JET	ALL	MUG
PM per participant:	6,0				9,0	6,0		17,0		2,0
Participant number:	11	12	13	14	15	16	17			
Participant short name	MSG	CHC	UBRUN	VUB	BTS	SOLIANIS				
PM per participant:			5,0	30,5	2,0					

Objectives

- investigate and provide overview of the ethical, social, legal, regulatory, and economic aspects of the REACTION platform
- formulated functional and non-functional requirements derived from social analysis
- describe and analyse all legal and regulatory perspectives applied to the REACTION services
- develop a viable and sustainable business framework for deploying the REACTION platform

Description of work (broken down into tasks) and role of partners

T9.1 <u>Ethical issues</u>: Ethical analysis of the overall REACTION vision and special analysis of privacy, accessibility and inclusion. An internal document presenting an overview of ethical issues in diabetes monitoring applications will be available at M12.

T9.2 <u>Social issues</u>: Results of focus groups will then be analysed, formulated in terms of functional and non-functional requirements, and forwarded to the iterative requirements engineering process.

T9.3 <u>Legal and regulatory framework</u>: Describe legal perspectives applied to the REACTION service platform including data protection, patients' rights, product liability and intellectual property rights and DRM. An internal document on IPR issues and DRM solutions in REACTION applications will be available at M40.

T9.4 <u>Healthcare economics and business models</u>: Develop a viable and sustainable business framework for deploying the REACTION platform that aligns with realities of healthcare economic and reimbursement schemes. New models of business constellations will be explored based on values. An internal document describing Business modelling concepts will be available at M30.

Deliverables (brief description) and month of delivery
D9.1 REACTION services in different social and cultural contexts (M18)
D9.2 Regulatory framework and data protection including patient rights (M24)
D9.3 Product liability issues in REACTION applications including a privacy framework for diabetes monitoring (M36)
D9.4 Healthcare economics and reimbursements (M12)
D9.5 Sustainable business models for actors in diabetes management (M40)

WP 10 – Platform Integration and Implementation

Objectives

This WP deals with the integration of all the parts of the REACTION platform, the technical testing of its functionality and the setting up of prototypes to be used in the clinical field trials in WP8, including population of user domain data. The development of applications to be used in field trials in preparation for the validation of performance and applicability to user requirements will also be undertaken. A suitable development environment for rapid application development will also be implemented.

The main objectives to be achieved in this workpackage are:
- To use the Software Development Kit (SDK) that will allow developers to rapidly create new applications on the REACTION platform.
- To integrate the developed sensor networks and the data management and service orchestration subsystems with backend healthcare information systems.
- To set-up the prototypes of the REACTION platform in the various phase of the evolutionary design with the integration of the various services, seamless connectivity to heterogeneous networks, context awareness, risk assessment, and crisis management.
- To develop prototype applications based on the clinical protocols developed in WP8, populate the ontologies and perform testing of the platform prior to field trials.
- To carry out the deployment (installation, configuration and training) of the integrated prototype platform for the field trials in WP8.

The prototypes which will be assembled are:
a) Rapid prototype of closed-loop system used in general ward (including some software mock-ups) (end of year 1)
b) Prototype of home/on-the-move closed-loop system and improved closed-loop system used in general ward (including sensor prototypes) (end of year 2)
c) Partly/fully functional prototypes of in-hospital and home/on-the-move prototypes including multi-parametric monitoring, risk assessment and full backend interoperability (end of year 3)
d) Automatic glycaemic control with closed-loop feedback directly to insulin dosage pumps and field trials with final prototypes (end of year 4)

The partners responsible for the actual research and development of the component in question are responsible for performing technical testing of the individual components and the entire platform prior to deployment for field trials. The following testing requirements are adopted:
- There must be a complete test plan that identifies the tests to be undertaken.
- The test plan shall contain a schedule of test to be undertaken with a test script detailing the test to be performed.
- A test log is maintained showing the test to be performed and the progress against their performance and the testing outcomes with a note of any corrective actions necessary.

The parts of the REACTION platform will be installed in a "smart" space test bed located at the premises of ICS-FORTH before being rolled out for field trials. A test plan will be developed as the basis for the testing process. It formalises a set of actions including any procedure, process, equipment, material, activity or system that will help to understand whether the system performances meet the required specifications and quality attributes.

After thorough test (using simulations, wherever appropriate) and quality inspection, the platform will be populated with the use cases and clinical protocols (in-patient and home/on-the-move), and the platform will be rolled out for use in the field trials at the respective clinical uses' locations. This process is designed, because field trials involve real patients. Any technical malfunctioning of the prototype platform is likely to cause interruption of the field trials and should thus be minimized.

Workpackage leader

The workpackage will be lead by FORTH-ICS

Tasks and actors in this workpackage

The workpackage involve most of the partners. The work will be carried out in five tasks:

Task T10.1 – Application development platform

TASK LEADER – CNET

The REACTION Software Development Kit (SDK) will allow developers to rapidly create new networked applications on the REACTION platform. The generalised platform will support cost-effective development of a broad range of innovative healthcare applications, so a user-friendly development platform is warranted. The SDK will provide solution developers with a high-level interface for innovative monitoring applications with embedded intelligence and closed loop feedback provisioning using the REACTION platform.

The task will initially develop a specification guide for the functionality and the selected platform for the SDK. The development of specific modules will continue throughout the project in line with the needs arising from the evolutionary development of prototypes.

All parts of the REACTION platform will be installed and integrated in a test bed located at the "Ambient Intelligence" premises of FORTH-ICS, where they will be used to integrate, test and demonstrate the platform's technical environment before being ported to the field trials.

The work will be undertaken by CNET providing components from WP3, WP4 and WP5 and FORTH-ICS implementing the "Ambient Intelligence" premises. FORTHNET will set up the projects internal, integrated development environment (servers).

Task T10.2 – Device and network integration and testing

TASK LEADER – DELTA

This task deals with the integration of sensors and parts of BAN and PAN networks, as well as, the technical testing of their functionality. The main objectives to be achieved are:
   - To assemble and test sensors, BAN and PAN infrastructure.
   - To integrated the sensors, devices, software components and Web Service modules.
   - To implement and test the security framework in the distributed networks.

A detailed integration plan will be described describing how the different sensors, subsystems, networks and software modules developed in WP3 and WP4 will be integrated into a common platform so that they can easily interoperate. The integration plan will be described at the beginning of this task in order to start the integration as soon as possible.

The work will be carried out by DELTA and IMM with FORTH-ICS delivering infrastructure and CNET software components.

Task T10.3 – Backend integration and testing

TASK LEADER – FORTHNET

This task deals with the integration of the BAN and PAN networks through heterogeneous backend communication structures to the backend healthcare information systems. It also performs integration of the Data Management and Service Orchestration subsystems. Finally, the central security framework will be installed and tested.
This task also deals with the implementation of the risk assessment modules and their integration into the Service Orchestration Subsystem.

A detailed integration plan will be developed describing how the different networks and software modules developed in WP4, WP5 and WP7 will be integrated into a common platform so that they can easily interoperate. The integration plan will be developed at the beginning of this task in order to start the integration as soon as possible.

The work will be carried out by FORTHNET with assistance from FORTH-ICS on infrastructure. FHG-SIT will work on implementation of security modules. ATOS will perform interoperability and integration with HIS. BTS will supply computational model kernels for use in feedback systems and analyze the performance of the integrative risk assessment approach based on clinical performance data generated in WP8.

Task T10.4 – Field trials application development

TASK LEADER – FORTH-ICS

Following the integration tasks, this task will develop the various prototypes of REACTION applications to be used in the field trials. The applications will be guided by the clinical protocols developed in WP8. The applications will be developed to a level where they can demonstrate the full functionality of the REACTION platform and serve as validation objects for the validation phase.

Application development involves the following generic activities:
- Analyse and customise the scenarios, which will be used for field trials
- Build the necessary ontologies and populate with instances of user specific data.
- Customise the Web Service framework on PAN nodes for data management.
- Customise the security and trust framework.
- Customise the Data Management subsystem for the specific application and install clinical semantic Web Services.
- Develop applications for risk assessment
- Develop the alarm handling and crisis management applications
- Implement the applications in the AmI environment test bed
- Prepare the scenarios for field trials.

This sequence of work will be repeated for each prototype cycle and subsequent field trials.

All parts of the REACTION platform will be installed in a "smart" space test bed located at the premises of ICS-FORTH. This smart space will emulate an everyday home environment, comprising several Ambient Intelligence (AmI) technologies, such as computer-controlled electronic appliances and devices, dynamic lighting, various types of sensors, computer vision, etc. In addition, the smart environment will exhibit the potential of simulating the installation of the REACTION platform in certain types of work environments, thereby increasing the likelihood of success during the field trials.

The work will be carried out by FORTH-ICS assisted by FORTHNET, CNET, DELTA, ALL and UBRUN in their respective fields. The clinical partners CHC and MUG will assist in the population of ontologies and implementation of the clinical protocols.

Workpackage description

Workpackage number:	WP 10	Start date or starting event:						Month 1		
Work package title:	Platform Integration and Implementation									
Activity type:	RTD									
Participant number:	1	2	3	4	5	6	7	8	9	10
Participant short name	ATOS	CNET	DELTA	IMM	FORTH-ICS	FHG-SIT	FORTHNET	IN-JET	ALL	MUG
PM per participant:	5,0	15,0	15,0	9,0	32,0	10,0	12,0		4,0	6,0
Participant number:	11	12	13	14	15	16				
Participant short name	MSG	CHC	UBRUN	VUB	BTS	SOLIANIS				
PM per participant:		5,0			23,0					

Objectives
- integration of all the parts of the REACTION platform
- technical testing of its functionality
- setting up of prototypes to be used in the clinical field trials
- develop prototype applications based on the clinical protocols making use of the SDK
- carry out the deployment
- coordinate test plans and testing

Description of work (broken down into tasks) and role of partners

T10.1 Application development platform: Use a Software Development Kit (SDK) which allows developers to rapidly create new networked applications on the REACTION platform. All parts of the REACTION platform will be installed and integrated in a test bed at FORTH-ICS

T10.2 Device and network integration and testing: Integration of sensors and parts of BAN and PAN networks, as well as the technical testing of its functionality. Develop a detailed integration plan.

T10.3 Backend integration and testing: Integration of the BAN and PAN networks through heterogeneous backend communication structures to the backend healthcare information systems. Implementation of the risk assessment modules and their integration into the Service Orchestration Subsystem.

T10.4 Field trials application development: Develop the various prototypes of REACTION applications to be used in the field trials. Manuals and deployment plans for the field trials of the medical domain applications will be produced and released for internal use at M12 and M24.

Deliverables (brief description) and month of delivery
D10.1 AmI test bed (M6)
D10.2 Integration and test plan for BAN and PAN infrastructure (M12)
D10.3.1 1st Prototype of backend infrastructure including integration and test plan for backend infrastructure (M24)
D10.3.2 2nd Prototype of backend infrastructure (M36)
D10.4 Applications for field trials (M24)
D10.5 Final REACTION platform prototype including sensors, subsystems, security framework, services (M48)

WP 11 – Demonstration

Objectives

The validation activities will be broadened out to include a limited demonstration to external users. This is necessary to ensure that the Consortium takes a broader view of the potential user community. These limited activities will be treated as demonstration as they are part of the process of taking the project message to a wider community. It further paves the way for subsequent exploitation of project results by the partners.

The demonstration activities are designed to prove the viability of the REACTION platform before it can be commercialised, e.g. testing of product-like prototypes. This type of activity goes beyond the validation activities internal to the project, which will be based on prototypes with limited functionality.

The target groups for the demonstrations are healthcare providers, public and private healthcare organisations, health insurance companies, public decision makers, pharmaceutical companies, medical equipment and device manufacturers, research organisations, and the general press.

Demonstration will be performed towards the end of the project when a stable version of the REACTION prototype with sufficient functionality will be available. The demonstration platform will be available for individual exploitation one year after the project ends.
Demonstration of the prototype will be performed jointly by the technical and the medical partners and the lessons-learned will be documented in a report for each application domain.

Workpackage leader

The workpackage will be lead by: CNET

Tasks and actors in this workpackage

The workpackage partners are: Industrial partners and authorities. The work will be carried out in one task:

Task T11.1 – Demonstration

TASK LEADER – CNET
The work in this task will consist of developing a demonstration plan for the external demonstrations to be performed in the project. Further, the task will organise the external demonstration activities, arrange hands-on workshops and prepare site-surveys and application analysis for potential uses and customers of the REACTION platform. Further, the feedback from external users and the lessons learned will be documented for internal use in the project.

The following demonstration activities are foreseen:
- IN-JET will demonstrate the platform to Danish healthcare providers, regional healthcare authorities and patient associations as an advanced multi-parametric monitoring system for diabetes patients. Longer term, the platform will be demonstrated as a generic monitoring platform for other chronic diseases.
- IN-JET will demonstrate the platform to the Danish market segments of healthcare organisations, private healthcare providers and device manufacturers. The demonstration may be organised in cooperation with the Danish Federation of Industries, who have a stated interest in promoting innovative ICT technologies for healthcare to their members.
- UBRUN and CHC will demonstrate concepts to the NHS, specifically within the framework of Connecting for Health (CfH), which manages the IT services of the NHS, and within the NHS networks (Telecare Advisory Network) established to disseminate information on IT approaches to healthcare.
- CNET and FORTHNET will demonstrate the concept to national customers at an early stage to get feedback that can be incorporated into the project.

The demonstration activities will be closely coordinated with the dissemination, exploitation and use the training material already developed to the furthest extent possible.

Workpackage description

Workpackage number:	WP 11	Start date or starting event:					Month 36			
Work package title:	Demonstration									
Activity type:	DEM									
Participant number:	1	2	3	4	5	6	7	8	9	10
Participant short name	ATOS	CNET	DELTA	IMM	FORTH-ICS	FHG-SIT	FORTHNET	IN-JET	ALL	MUG
PM per participant:	4,0	9,0	10,0			2,0	3,0	2,0		
Participant number:	11	12	13	14	15	16				
Participant short name	MSG	CHC	UBRUN	VUB	BTS	SOLIANIS				
PM per participant:										

Objectives
- develop a demonstration plan for the external demonstrations
- perform demonstration activities designed to prove the viability of the REACTION platform before it can be commercialised directly
- arrange hands-on workshops and prepare site-surveys and application analysis for potential uses and customers
- collect feedback from external users and the lessons learned
- create a demonstration platform for demonstrating REACTION functionalities to potential users

Description of work (broken down into tasks) and role of partners

T11.1 Demonstration: organise the external demonstration activities, arrange hands-on workshops and prepare site-surveys and application analysis for potential uses and customers of the REACTION platform, provide feedback from external users and lessons learned. A demonstration plan will be available internally at M36.

Deliverables (brief description) and month of delivery

D11.1 Feedback from demonstration activities (M48)

WP 12 – Dissemination and Exploitation

Objectives

The overall objective of this work package is to provide an active and professional dissemination of the project results according to the dissemination strategy described in section 3.2 Dissemination and/or exploitation of project results. Further, it is the objective to develop an effective and realistic exploitation strategy for the project results.

The dissemination objectives are in particular to:
- Define, agree and execute a comprehensive dissemination strategy.
- Supervise that the knowledge created in the project is properly captured, managed and re-used.
- Ensure that the knowledge created in the project and the results are properly disseminated to the appropriate target audiences.
- Facilitate that results are being presented to relevant standardisation bodies.
- Coordinate the dissemination activities.
- Further, the exploitation objectives are:
- Ensure the best possible foundation for an appropriate academic and commercial joint exploitation of the project results after the project has finished.
- Facilitate that all results of the project are fully exploited through development of effective exploitation plans.

Workpackage leader

The workpackage will be lead by: IN-JET

Tasks and actors in this workpackage

All partners will engage in normal dissemination activities within their areas of expertise. partners will work together for identifying and carrying out dissemination activities within specific areas, such as conferences and workshops, exhibitions, policy conferences, etc.: CNET, FORTHNET, IN-JET and FORTH-ICS will disseminate technical results related to ICT technologies and infrastructures, DELTA, IMM and SOLIANIS on advancements in sensor technology, ALL, MSG and BTS on biomedical modelling, MUG, MSG, CHC, and UBRUN on clinical and medical results, and VUB and IN-JET on ethical, legal and regulatory matters.

The work will be carried out in three tasks:

Task T12.1 – Dissemination

TASK LEADER – IN-JET
The overall objective of dissemination is to maximise the transfer of knowledge to the outside world, as well as within the project Consortium itself. Strong coordination and targeted approach to selected strategy elements are keys to success.

The specific dissemination strategies and dissemination plans for the project are described in details in section 3.4. This task is concerned with the *coordination of dissemination* of project results. It sets up the framework for implementation and execution of the project's dissemination strategy and plans and covers:
- Define and agree a comprehensive dissemination strategy with measurable goals
- Coordinate the disseminating activities in the project to the appropriate target groups
- Follow-up on dissemination goals and report outcome to the Project Board

The task will be initiated by the development of a dissemination plan setting out an agreed approach to dissemination throughout the project. The dissemination strategy is intended to optimize dissemination of project knowledge and results to scientific and medical communities, companies and healthcare organisations. The Consortium will approve the dissemination strategy and the detailed dissemination plan before any dissemination takes place.

The dissemination goals will be achieved by various other means, including but not limited to: Courses of various types, conferences and workshops, printed documents, web sites, CDs, etc. The results of the technological research work conducted in the development workpackages of the project will be submitted for publication to international, peer-reviewed journals according to the established dissemination plan (see section 3.4).

The task shall set up a scheduling system for dissemination that enables other WPs to keep track of related activities in order to submit contributions at the right time and right place. The task shall also contribute to promoting knowledge and specifications developed within the WP. For this purpose the task shall set-up a knowledge base and a knowledge management system. There are already a number of tools available to set-up sophisticated knowledge management systems. This support task will therefore not develop new tools.

A rich project website will be set up, providing up-to-date information about the project and its results to the public. Goals will be established and followed re visitor statistics and a database of registered users will be established and used for dissemination.

This dissemination coordination will be performed by IN-JET. All partners participate in dissemination as part of their project work, i.e. only activities for the actual dissemination have been budgeted in this WP.

Task T12.2 – Contributions to standards

TASK LEADER – UBRUN
This task is concerned with the coordination of contribution of project results to relevant European and international standardisation bodies as set out in great details in section 3.1.3. The task will coordinate the identification for standardisation needs and the partners' access and affiliation with the relevant standardisation bodies in the following areas:
- Medical standards
- Wireless networks
- Security
- Web services

The task is thus supporting the entire project and will undertake the following activities:
- Maintain list of standardisation bodies and standards relevant for the project
- Identify important standardisation bodies and trigger participation by Consortium partners and ensure timely input into standardisation bodies
- Organise and coordinate participation by the Consortium partners in standardisation work
- Coordinate standardisation activities and provide a list of standards influenced / produced by the project
- Apply for membership of the Continua Health Alliance

The IPR and knowledge manager will routinely identify needs and opportunities for influencing and contributing to international standards based on the knowledge resulting from the research work undertaken in the project.

Partners UBRUN and FORTH-ICS are members of major standards organisations (ISO/CEN/IEEE /HL7) and will work to bring relevant developments to the technical working groups. UBRUN currently serves on CEN TC251 and ISO 215 committees for medical devices. UBRUN is also on the development committee IEEE 11073. FHG-SIT is chair of the Special Interest Group "Security & Trust" of the Wireless World Research Forum (WWRF) and a member of ACM's SIGMobile. The work will be performed by UBRUN with contributions from CNET on software and FHG-SIT on security.

Task T12.3 – Exploitation

TASK LEADER – IN-JET

The realisation of exploitation plans for the results of individual participants and for the Consortium as a whole will be the main activity in this task. They will be created in order to ensure that the developed technologies have a significant impact in the market and that they do not stay as theoretical developments that never provide their benefits to potential users. The major outcomes of the exploitation work package are the Market and Competitor Analysis and the Exploitation Plan.

In order to actively promote the project and its potential results, different activities will be undertaken. It will be important to establish liaisons with other relevant projects, standard organisations, and institutions that can be of benefit for the project. The different partners will establish contacts with other companies outside the Consortium, thus preparing the market for the technology adoption. These derived contacts, potential users and exploitation potentials will be documented in a final version of the Exploitation Plan. The task involves the following activities:
- Investigate the project's commercial potential in terms of user needs, market analysis and business models. Provide the necessary marketing material and demonstration platform for presenting the results to potential users
- Provide information about the potential products, competitors and the technology benchmarks, define REACTION market position and identify the potential market segments. Refined information will be provided after the platform architecture has been defined, business issues have been clarified and realistic business models have been developed.
- Coordinate and develop business plans for each of the partners involved in commercial exploitation and scientific exploitation plans for the non-commercial partners.

This exploitation work will be coordinated by IN-JET.

Workpackage description

Workpackage number:	WP 12	Start date or starting event:						Month 1		
Work package title:	Dissemination and Exploitation									
Activity type:	RTD									
Participant number:	1	2	3	4	5	6	7	8	9	10
Participant short name	ATOS	CNET	DELTA	IMM	FORTH-ICS	FHG-SIT	FORTHNET	IN-JET	ALL	MUG
PM per participant:	2,0	2,0	2,0	2,0	1,0	2,0	2,0	16,0	2,0	2,0
Participant number:	11	12	13	14	15	16				
Participant short name	MSG	CHC	UBRUN	VUB	BTS	SOLIANIS				
PM per participant:	1,0	3,0	3,0	1,0	1,0	1,0				

Objectives
- ensure that the results of the project are properly disseminated
- provide contribution of project results to relevant international standardisation bodies.
- ensure that the results of the project are properly prepared for exploitation

Description of work (broken down into tasks) and role of partners

T12.1 Dissemination: Define a comprehensive dissemination strategy. Disseminate knowledge from the project to the target groups. Develop a detailed plan for the demonstration of the REACTION platform. Information related to the dissemination strategy, activities and plans will be included in all Periodic Reports (deliverables D1.4.x) for the Commission at M12, 24, 36 and 48.

T12.2 Contributions to standards: Provide contribution of project results to relevant international standardisation bodies. Information related to the activities for contribution to standardisation work will be included in deliverables D1.2.1 Interim progress report for the Commission at M6.

T12.3 Exploitation: Investigate the commercial foundation in terms of user needs, market analysis and business models. Develop exploitation plan and prepare market introduction. Information related to the exploitation strategy and plans will be included in D1.4.2 and D1.4.3 Management reports at M24 and M36.

Deliverables (brief description) and month of delivery

D12.1 Project website (M1)
D12.2 Market and competitor analysis (M24)
D12.3 Final plan for dissemination and exploitation of knowledge (M48)

WP 13 – Training

Objectives

The training dimension of the REACTION project is essential to guarantee the project long-term impact and hence, several training activities have been planned. Some are directed towards Consortium members and offer inside training in use of technology and software tools. Most activities are directed towards external developers developing healthcare systems.

The REACTION project will produce a set of professional course material in the form of websites, lecture notes and other printed and multimedia material. The first set of course materials to be produced will be targeted at healthcare solution developers. This material will be derived from the project internal technical training courses.

Workpackage leader

The workpackage will be lead by: UBRUN

Tasks and actors in this workpackage

The work will be carried out in two tasks:

Task T13.1 – Horizontal project integration

TASK LEADER – IN-JET

Experience has shown that horizontal integration is enormously enhanced if all partners in a Consortium implement the project at their own sites. To be able to do that, sufficient operational knowledge of all system requirements and components must be available at each site. To allow all researchers in the project to collaborate effectively and efficiently a number of internal training courses are foreseen. These will be intensive courses in which all disciplines will be covered by advanced introductions. Also, the researchers in the project will get hands-on experience with the software components that are available at the time of the course.

The first course, which will take place shortly after the kick-off meeting, is intended to lay the foundation for successful collaboration in the Consortium. Subsequent courses will emphasise the software components and sensor technologies developed in the course of the project. One project internal course is planned for each year of the project. Senior researchers in the project will teach the project internal courses.

This task will be performed by IN-JET with training support from CNET on technical content and MSG and UBRUN on medical technology content.

Task T13.2 – External training

TASK LEADER – UBRUN

External training activities will take different forms, depending on the target audience.

Subtask 13.2.1 – Training courses for healthcare managers

A set of courses will address managers in healthcare providers and healthcare organisations. At least three seminars will be organised to learn how to think in terms of device networks and monitoring of chronic disease management as well as the clinical and economical benefits that can be realised with the REACTION platform. We would anticipate these will be integrated with existing events (e.g. World of Health IT) to maximise audience.

Subtask 13.2.2 – Training courses for software developers

One set of training courses will aim at solution developers in healthcare companies or regional healthcare centres. The training topics will be the full range of disciplines related to the various technologies covered by the REACTION platform.

Subtask 13.2.3 – Training courses for business developers

Researchers and healthcare managers often find it difficult to agree on the opportunities and threats of disruptive technologies and completely new applications. The REACTION project plans three courses for this target group, in the second, third and fourth year.

The training seminars will be organised by UBRUN and IN-JET with support from all partners.

Workpackage description

Workpackage number:	WP 13	Start date or starting event:						Month 6		
Work package title:	Training									
Activity type:	OTH									
Participant number:	1	2	3	4	5	6	7	8	9	10
Participant short name	ATOS	CNET	DELTA	IMM	FORTH-ICS	FHG-SIT	FORTHNET	IN-JET	ALL	MUG
PM per participant:				3,0		2,0		8,0		2,0
Participant number:	11	12	13	14	15	16				
Participant short name	MSG	CHC	UBRUN	VUB	BTS	SOLIANIS				
PM per participant:		1,0	5,0							

Objectives
- guarantee the projects long-term impact through comprehensive training
- produce high-class training material
- conduct internal and external training activities

Description of work (broken down into tasks) and role of partners

T13.1 Horizontal project integration: Horizontal project integration through intensive technology workshops and courses. Produce professional course material in the form of text and multimedia material. The first milestone of this task corresponds to the production of internal workshop teaching material on software development at M6. A second milestone corresponds to the production of internal workshop teaching material on sensor development at M9.

T13.2 External training: Plan and organise training courses for managers in healthcare providers and healthcare organisations, developers in healthcare companies or regional healthcare centres and business developers and managers. Production of professional course material in the form of books and multimedia material.

Deliverables (brief description) and month of delivery
D13.1 Workshop teaching material for healthcare professionals (M24)
D13.2 Workshop teaching material for business managers (M36)
D13.3 Workshop teaching material for healthcare solution developers (M40)

B.1.3.6 Efforts for the full duration of the project

Indicative efforts (man-months) per Beneficiary per Work Package													
Beneficiary number and short-name	WP 1	WP 2	WP 3	WP 4	WP 5	WP 6	WP 7	WP 8	WP 9	WP 10	WP 11	WP 12	WP 13	Total per Beneficiary
1 - ATOS	67.00	5.00	0.00	26.00	0.00	0.00	9.00	0.00	6.00	5.00	4.00	2.00	0.00	124.00
2 - CNET	16.00	10.00	0.00	72.00	18.00	0.00	0.00	0.00	0.00	15.00	9.00	2.00	0.00	142.00
3 - DELTA	0.00	4.00	58.00	0.00	8.00	0.00	0.00	0.00	0.00	15.00	10.00	2.00	0.00	97.00
4 - IMM	0.00	5.00	84.00	0.00	0.00	0.00	0.00	0.00	0.00	9.00	0.00	2.00	3.00	103.00
5 - FORTH-ICS	0.00	10.00	10.00	21.00	8.00	22.00	0.00	0.00	9.00	32.00	0.00	1.00	0.00	113.00
6 - FHG-SIT	0.00	6.00	0.00	12.00	14.00	0.00	37.00	2.00	6.00	10.00	2.00	2.00	2.00	93.00
7 - Forthnet	0.00	6.00	8.00	8.50	42.00	0.00	0.00	0.00	0.00	12.00	3.00	2.00	0.00	81.50
8 - IN-JET	0.00	11.00	0.00	7.00	0.00	0.00	0.00	7.00	17.00	0.00	2.00	16.00	8.00	68.00
9 - ALL	0.00	3.00	0.00	25.00	0.00	33.00	0.00	0.00	0.00	4.00	0.00	2.00	0.00	67.00
10 - MUG	1.00	5.00	12.00	0.00	0.00	0.00	4.00	40.50	2.00	6.00	0.00	2.00	2.00	74.50
11 - MSG	0.00	3.00	0.00	19.00	0.00	41.00	0.00	16.00	0.00	0.00	0.00	1.00	0.00	80.00
12 - CHC	0.00	5.00	0.00	0.00	0.00	0.00	3.00	30.00	0.00	5.00	0.00	3.00	1.00	47.00
13 - UBRUN	2.00	8.00	4.00	4.00	6.00	10.50	22.00	31.00	5.00	0.00	0.00	3.00	5.00	100.50
14 - VUB	0.00	2.00	0.00	0.00	0.00	0.00	9.00	0.00	30.50	0.00	0.00	1.00	0.00	42.50
15 - BTS	0.00	2.00	34.50	0.00	0.00	39.00	0.00	9.00	2.00	23.00	0.00	1.00	0.00	110.50
16 - SOLIANIS	0.00	0.00	30.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	31.00
Total	86.00	85.00	240.50	194.50	96.00	145.50	84.00	135.50	77.50	136.00	30.00	43.00	21.00	1,374.50

Indicative efforts per Activity Type per Beneficiary

Activity type	Part. 1 ATOS	Part. 2 CNET	Part. 3 DELTA	Part. 4 IMM	Part. 5 FORTH-I	Part. 6 FHG-SIT	Part. 7 Forthne	Part. 8 IN-JET	Part. 9 ALL	Part. 10 MUG	Part. 11 MSG	Part. 12 CHC	Part. 13 UBRUN	Part. 14 VUB	Part. 15 BTS	Part. 16 SOLIANI	Total
1. RTD/Innovation activities																	
WP 2	5.0	10.0	4.0	5.0	10.0	6.0	6.0	11.0	3.0	5.0	3.0	5.0	8.0	2.0	2.0	0.0	85.0
WP 3	0.0	0.0	58.0	84.0	10.0	0.0	8.0	0.0	0.0	12.0	0.0	0.0	4.0	0.0	34.5	30.0	240.5
WP 4	26.0	72.0	0.0	0.0	21.0	12.0	8.5	7.0	25.0	0.0	19.0	0.0	4.0	0.0	0.0	0.0	194.5
WP 5	0.0	18.0	8.0	0.0	8.0	14.0	42.0	0.0	0.0	0.0	0.0	0.0	6.0	0.0	0.0	0.0	96.0
WP 6	0.0	0.0	0.0	0.0	22.0	0.0	0.0	0.0	33.0	0.0	41.0	0.0	10.5	0.0	39.0	0.0	145.5
WP 7	9.0	0.0	0.0	0.0	0.0	37.0	0.0	0.0	0.0	4.0	0.0	3.0	22.0	9.0	0.0	0.0	84.0
WP 8	0.0	0.0	0.0	0.0	0.0	2.0	0.0	7.0	0.0	40.5	16.0	30.0	31.0	0.0	9.0	0.0	135.5
WP 9	6.0	0.0	0.0	0.0	9.0	6.0	0.0	17.0	0.0	2.0	0.0	0.0	5.0	30.5	2.0	0.0	77.5
WP 10	5.0	15.0	15.0	9.0	32.0	10.0	12.0	0.0	4.0	6.0	0.0	5.0	0.0	0.0	23.0	0.0	136.0
Total Research	51.0	115.0	85.0	98.0	112.0	87.0	76.5	42.0	65.0	69.5	79.0	43.0	90.5	41.5	109.5	30.0	1,194.5
2. Demonstration activities																	
WP 11	4.0	9.0	10.0	0.0	0.0	2.0	3.0	2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	30.0
Total Demo	4.0	9.0	10.0	0.0	0.0	2.0	3.0	2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	30.0
3. Consortium Management activities																	
WP 1	67.0	16.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	0.0	0.0	2.0	0.0	0.0	0.0	86.0
Total Management	67.0	16.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	0.0	0.0	2.0	0.0	0.0	0.0	86.0

4. Other activities																
WP 12	2.0	2.0	2.0	2.0	1.0	2.0	2.0	16.0	2.0	2.0	1.0	3.0	3.0	1.0	1.0	1.0	43.0
WP 13	0.0	0.0	0.0	3.0	0.0	2.0	0.0	8.0	0.0	2.0	0.0	1.0	5.0	0.0	0.0	0.0	21.0
Total other	2.0	2.0	2.0	5.0	1.0	4.0	2.0	24.0	2.0	4.0	1.0	4.0	8.0	1.0	1.0	1.0	64.0

| Total | 124.0 | 142.0 | 97.0 | 103.0 | 113.0 | 93.0 | 81.5 | 68.0 | 67.0 | 74.5 | 80.0 | 47.0 | 100.5 | 42.5 | 110.5 | 31.0 | 1,374.5 |

B.1.3.7 List of milestones and planning of reviews

Milestone number	Milestone name	Work package(s) involved	Lead Beneficiary number	Expected date	Expected Results and Achievements
MS1	First set of sensors developed	WP3	4	M12	1st generation IR breadboard device, IS sensors and e-patch developed & available [D3.2.1, D3.3, D3.5] (at least 2 different sensor concepts realised as breadboards & fully characterised), implementation of relevant state-of-the-art closed-loop control algorithms. Survey of commercially available CGM devices & insulin pumps + suitability for AGC [D3.10].
MS2	First set of prototypes for data, context and event handling management approved	WP4	2	M12	Running prototypes available allowing data management and service orchestration [D4.4.1].
MS3	Second set of data management prototypes developed and Network management first implementation approved	WP4, WP5, WP10	2	M24	Running prototypes available allowing data mgt & service orchestration [D4.4.2]. BAN & PAN components and event handling system 1st implementation, B-E network integrated, SDK tools ready & B-E 1st infrastructure prototype developed [D5.2, D5.3.2, D10.3.1, D10.4]
MS4	Clinical first evaluations realised	WP3, WP8	10	M24	Definition of closed loop control system for optimal insulin delivery [D3.11], Evaluations of general ward clinical trial, outpatient clinical study and MDI compliance study available [D8.5]
MS5	Second set of sensors developed	WP3	4	M30	Prototype of IR sensors for CGM available & 2nd generation e-patches ready for first trials [D3.6, D3.9]. 1st version of fully integrated e-patch platform available and characterised
MS6	Final set of sensors developed	WP3	4	M36	IS and IR sensors for AGC available. Insulin pump prototype and pump control ready for tests (D3.5, D3.9, D3.14). Evaluation and benchmarking of two algorithms in new clinical experiments.

Milestone number	Milestone name	Work package(s) involved	Lead Beneficiary number	Expected date	Expected Results and Achievements
MS7	Network management second implementation approved	WP3, WP5, WP10	2	M36	Fully functional sensor platform available for clinical trials in WP8. BAN and PAN components and event handling system 2nd implementation, Back-end network integrated, SDK tools and B-E 2nd infrastructure prototype developed [D5.4, D5.5, D5.6, D10.4]
MS8	Final REACTION platform prototype and final validation report submitted	WP2, WP10	2	M48	Integrated REACTION platform available [D10.5] and validated [D2.10]. End of project.

Tentative schedule of Project Reviews			
Review number [65]	Tentative timing	Planned venue of review	Comments, if any
RV 1	12	Brussels	
RV 2	24	London	
RV 3	36	Madrid	
RV 4	48	Gratz	Within M48+2

B2. Implementation

B.2.1 Management structure and procedures

Management structure

The REACTION project's management structure and supporting procedures have been designed to specifically deal with the strategic and operational management requirements of a highly technical and multidisciplinary research project with many partners. Such type of project calls for a strong management structure with strong focus on objectives and milestones, highly knowledgeable technical management skills and strong focus on risk management. REACTION implements the project management activities along these guidelines in WP1.

The project management activities will ensure that the project properly coordinates its multi-party, iterative approach and that the work is completed within the terms of the contract with the European Commission. This will include ensuring that:
- Appropriate agreements and management framework are in place between the partners,
- All the projects activities are properly coordinated with appropriate levels of legal, contractual, ethical, quality, financial and administrative management of the Consortium
- Proper operational project management is provided throughout the project and the project's work is completed to the expected timescales, resource usage and quality levels
- Appropriate reporting to the European Commission is undertaken.

An experienced management team from the co-ordinating partner ATOS and the technical partner CNET has been identified for the project. The individuals involved have successfully run many past European Research projects, and have many years of project and management experience.
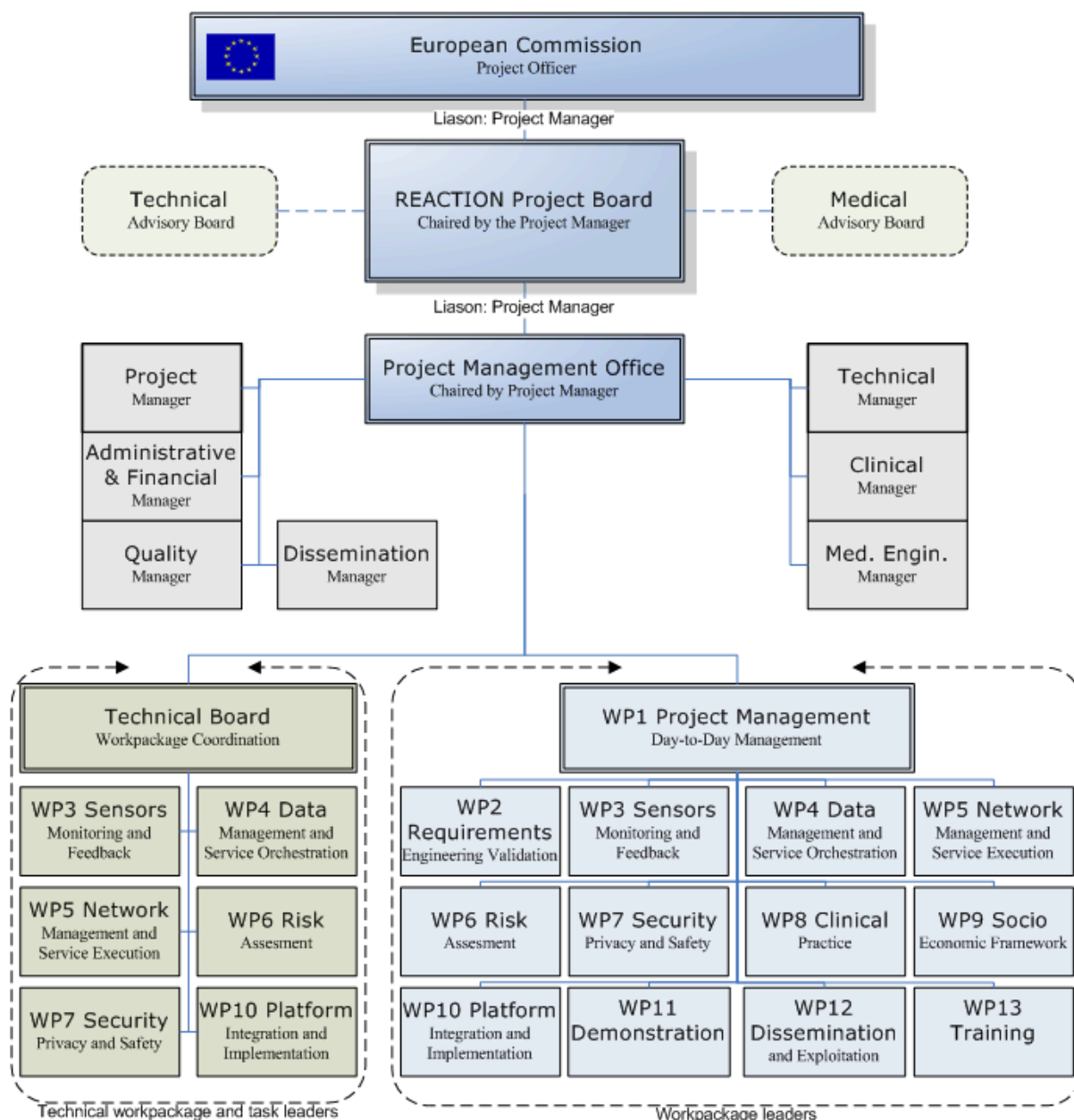
Project organisation

The co-ordinating partner within the Consortium will undertake the management of the project. The project organisation will comprise an overseeing Project Board along with supporting teams. The overall co-ordination of the project will be the responsibility of the REACTION Project Manager under the authority of the Project Board. The Project Manager will be responsible for liaison with the European Commission, co-ordinating the project activities of the Consortium members and for the production of deliverables to time, quality and budget. Day-to day operational project control will be ensured primarily by the Project Manager supported by the project teams at operational level.

Multi-disciplinarity is a key feature of the project and therefore co-ordination needs a team approach. Whilst the Project Manager's role is to ensure the operational management of the project he also needs support from the team to ensure achievement of the project's objectives through strategic and tactical management.

Each partner will work very closely with the Project Manager, the Technical Manager and the Medical Engineering Manager on all project technical and medical matters and will be responsible for work and resource allocation at the partner level under the specific task that has been allocated to this activity under the WP1.

The Project Board supported by the project management structure presented in Figure 12 will ensure this function:

Figure 12 Project management organisation

To ensure effective project management, the identified roles will be maintained over the whole course of the project. Each of these roles will advise the Project Board and provide operational support to the Project Manager in undertaking his role. The roles will be assigned as follows:

Role	Organisation
Project Board	1 person with executive authority from each Consortium Partner
Chair of Project Board	Lydia Montandon - ATOS
Technical Board	Project Management and each Workpackage Leader
Chair of Technical Board	Jesper Thestrup – IN-JET
Project Manager	Lydia Montandon – ATOS
Technical Manager	Peter Rosengren – CNET
Clinical Manager	Thomas Pieber - MUG
Medical Engineering Manager	Malcolm Clarke - UBRUN
Administrative Manager	Blanca Jordán - ATOS

Role	Organisation
Quality Manager	Matts Ahlsén – CNET
Dissemination Manager	Katja Gjørup Kristensen – IN-JET

Table 3 Identified management roles in REACTION

The project roles will be maintained throughout the project and their effectiveness reviewed with the Project Board on an on-going basis. Any changes found necessary to the established roles or any changes arising in the Consortium participants will be appropriately reflected in the management organisation of the project. Leaving participants will have their roles replaced by assignment to other participants. New participants will have representation on the Project Board and engage in the organisational structure of the project's management in a manner appropriate to their project roles and expertise. The Consortium Agreement will set out the basis upon which changes may be made.

Project Board

The Project Board will be the executive authority for the overall management and running of the project, the resolution of any major problems that may arise and will decide on the use of the common knowledge resulting from the project. It will comprise one executive member from each partner. It will be chaired by the Project Manager Lydia Montandon. Each partner represented on the Project Board will have an equal say in the project. Where necessary, decisions will be taken by voting, when each of the members will have one vote. In cases of equal numbers of votes, the Chairman' decision will prevail. Additional members, e.g. Workpackage Leaders may attend the meetings as agreed but without voting power. The Project Board will meet quarterly.

Technical Board

The Technical Board will be the executive authority for technical management and coordination of the project and resolution of any major technical issues that need cross-project resolutions. Moreover, the role of the Technical Board will be to secure that the technical solutions developed in the project is supporting the projects vision and the scientific and technological objectives in all aspects and in all of the involved areas of research.

The Technical Board will approve major architectural solutions and technological components of the REACTION components, which has a direct impact on the projects vision and the exploitability of the results. It will identify potential areas suitable for patent protection, assess the exploitability of the IPR, and recommend proper causes of action to the Project Board.

The Technical Board will comprise the Technical Manager and all Workpackage Leaders, Task Leaders and team members as necessary. The Project Manager, the Clinical Manager, and the Medical Engineering Manager will participate as needed. The Technical Board will be chaired by Jesper Thestrup from IN-JET in the capacity of "Vision Owner" and WP2 manager of the requirement engineering process. Each participant will have an equal say in this forum. If issues cannot be resolved in an amicable way, the matter will be taken to the Project Board for resolution, if the Chairman, one of the project's managers or two or more Partners request it. The Technical Manager is responsible for preparing and presenting the case to the Project Board. The Technical Board meets at least quarterly in connection with the Project Board meetings.

The Project Manager

The consortium has designated Lydia Montandon ATOS as Project Manager of the project. Lydia Montandon holds a Master of Science in Learning and Teaching Technologies from the University of Geneva, Switzerland. She has 12 years of experience in managing RTD projects in the fields of Technology-enhanced Learning, eInclusion, International Cooperation, including Integrated Projects. She is currently coordinating the work various Atos Research and Innovation units with activities in eInclusion, eHealth, eLearning, and International Cooperation.

The Project Manager will be responsible for delivery of the overall project objectives through:
- Definition and implementation of the management structure and procedures to be adopted throughout the project, and the maintenance of detailed project plans

- Co-ordination at Consortium level of the management, technical and quality activities, working closely with the project's Technical Manager and Medical Engineering Manager, and ensuring co-operation among partners, anticipating and managing potential conflicts
- Project Reporting and coordination of management material, managing change control and provision of appropriate guidelines for each of the participants
- Coordination of cost statements and audit certificates.

The Project Manager will work in close consultation with the other members of the Project Board and will handle all operational relations with the Commission. She will work closely with the project's partners and the technical and quality management functions to ensure that the objectives are achieved. Each Consortium partner will designate a Participant Manager who will liaise with the Project Manager on all project management matters relating to their partner.

Technical management

The consortium has designated as Technical Manager of the project Peter Rosengren from CNET, an experienced researcher and industrialist in computer science and a specialist in intelligent ICT services and semantic interoperability. The Technical Manager will have the responsibility of the overall coordination of the project's technical progress. The main tasks of the Technical Manager will be to secure the continuous alignment of commonly understood and agreed project results with the projects vision and the overall technical objectives. The Technical Manager will also perform the coordination and integration of the technical work performed in each of the workpackages in order to secure a smooth and trouble-free integration of components.
Other specific tasks will include, but are not limited to, the following:
- Provide day-to-day co-ordination of the technical aspects of the project
- Provide technical leadership and team management support for the work package leaders
- Organise technical meetings and secure that all technical issues and risks are identified and managed and that decisions are properly recorded
- Support the Project Manager in validating that the project's technical objectives are fully met
- Support the Project Manager in co-ordination with other EU-funded or other international projects
- Advise the partners, the Project Manager and the Project Board on the projects technical aspects throughout the project

The Technical Manager will report to the Project Manager, be supported by the Workpackage Leaders and work very closely with the Chairman of the Technical Board.

The consortium has designated Prof. Thomas Pieber, MD and head of the Division of Endocrinology and Nuclear Medicine at MUG and an opinion leader in the field of diabetes, as Clinical Manager. The Clinical Manager will have the responsibility of the coordination of the project's progress in clinical practice and to ensure that the technological developments continuously support medical and clinical objectives and with the projects vision and overall objectives. The Clinical Manager will be responsible for overseeing that medical ethics and safety requirements are properly addressed in all field trials. The Clinical Manager will report to the Project Board and will chair the Clinical Advisory Board.

The consortium has designated Malcolm Clarke, PhD in Medical Engineering, from UBRUN, as Medical Engineering Manager. The Medical Engineering Manager will have the responsibility for coordinating the project's progress in medical engineering and to ensure that the developed applications will be deployable in real life healthcare systems, and that regulatory boundary conditions are adequately addressed and considered. The Medical Engineering Manager will report to the Project Board.

Finally, the project has appointed a Dissemination Manager, Katja Gjørup Kristensen from IN-JET, who is responsible for coordinating the widespread dissemination of the knowledge coming out of the project. The Dissemination Manager will report to the Project Manager and will maintain the coordination tools created for coordinating partner's dissemination activities.

Workpackage and task direction

Due to the size of the project, strong emphasis on workpackage autonomy and management will be enforced. Clear objectives has been established for the outcome of each of the RTD workpackages

and interfaces to other workpackages have been made as simple as possible in order to create transparency and promote responsibility among project managers. The work in each workpackage is under the responsibility of a single partner who designates a Workpackage Leader to lead the work. The workpackages are split into a set of tasks; the main responsibility for each main task will reside with a single partner with each task being assigned a Task Leader. The Workpackage Leader organises the work on the tasks between the concerned partners and is responsible for achieving the objectives and producing the workpackage deliverables on time.

The Workpackage Leader organises workshops and meetings within the workpackage in close liaison with the other RTD workpackages and with the supporting workpackages. Meetings will be called as often as needed for ensuring effective work progress; however electronic conferencing facilities will be used as much as possible to limit travel expenses. Other meetings will be organised at task level by participants involved in the task. The Technical Manager continuously oversees that integration of the different components of the overall REACTION platform is progressing according to plan and that overall project objectives are achieved.

Technical and Medical Advisory Boards

The REACTION project will create two Advisory Boards before the end of the first year, each consisting of an independent group of five to eight technology and healthcare experts in the appropriate fields of activity.

The task of the Technical Advisory Board will be to ensure that the project remains aligned to healthcare technology trends and market and exploitation movements during the course of its execution and that the projects results are always aligned with the newest scientific trends. The Technical Advisory Board will be chaired by Jesper Thestrup from IN-JET. The Chairman decides the agenda for the meeting. The Technical Manager has the task of presenting relevant scientific and technological solutions for discussion. The Project Manager and other managers may participate in the meetings.

The task of the Medical Advisory Board will be to ensure that the project remains aligned to medical and clinical trends and movements in regulatory and economic healthcare provisioning during the course of its execution and that the projects results are always aligned with medical and organisational trends. The Medical Board will be chaired by the Clinical Manager. The Chairman decides the agenda for the meeting. The Medical Engineering Manager has the task of presenting relevant scientific and medical solutions for discussion. The Project Manager and other managers may participate in the meetings.

The Advisory Boards will not make any decisions on behalf of the project, but can make recommendations. The Chairmen will secure that recommendations from the Advisory Boards are properly recorded and fed back to the workpackage leaders. The Chairmen may organise, in cooperation with the Quality Manager, external peer review of project deliverables by members of the Advisory Boards. The Advisory Boards convene at least every twelve months. If needed, the Chairmen can call more frequent meetings.

Quality management

A Quality Plan will be produced at the start of the project and this document will govern the quality procedures for the whole project. It will define a set of rules for the organisation of the day-to-day work, including the procedures to be used, the reporting mechanisms, the organisation of meetings, and the preparation of documentation for submission to the Commission. It will also contain a process description for project deliverables, with the procedures for internal review and the quality criteria against which the deliverable will be assessed. As an important part of the quality work, the Project Board may engage a set of external, independent scientific reviewers appointed from the project's Advisory Boards. The external reviewers will focus on the independent evaluation of the project's on-going work. Their role will be to review the project's deliverables and outcomes, make recommendations and advise the Project Board. To ensure impartiality of the quality assurance process the Quality Manager will report to the Project Board.

Administrative and financial management

The project Administrative Manager is Blanca Jordán from the co-ordinating partner. She will be responsible for the administration of the internal Consortium structure and the financial administration of the project, including ensuring the proper completion and consolidation of the cost claims. The Administrative Manager will act as a support to the Project Board and will attend its meetings.

Planning and internal reporting

The project will be executed according to an established and proven project management approach based on a Project Quality & Risk Management Plan and a detailed project plan to be updated every year.

The Quality & Risk Management Plan will define the activities and resources necessary to ensure that the quality requirements of the project are met. It will define quality standards, quality requirements, quality assurance methods, quality assurance activities and configuration management. It will also define policies for identifying threats on the project and for implementing corrective actions.

The project plan will cover 18 months and will be refined and agreed with the European Commission each year. It will contain a detailed work plan setting out the duration and inter-dependencies of work packages and tasks defined for the period, and the anticipated resources required to complete each task within a particular timescale. Each Workpackage Leader will be responsible for preparing and managing a detailed workpackage plan and to submit it to the Project Manager and the Technical Manager, who check the overall coherency across workpackages.

Progress control

The Project Board will meet as necessary and agreed, usually every three months, and as a minimum at the key milestones of the project such as completion of each workpackage. The Project Manager will report progress control to the Project Board.

For each period the Project Manager will submit a detailed progress and financial report to the European Commission together with cost statements and audit certificates as required under the contract. Furthermore, in addition, the project will submit quarterly progress reports to keep the European Commission and external reviewers informed of the overall progress.

The delivery of major deliverables in the project has been aligned with the expected external project reviews. A first review will be held at month 12 by which time a number of key technical deliverables will have been produced. Further reviews will be held every 12 months. The project will actively seek to arrange a pre-review already in month 8 to align the projects direction with the Commission's expectations.

Communication

The REACTION participants will install a web-based project extranet to support collaborative working. It will contain workspaces for partners to share materials and knowledge and a web-based Wiki space, allowing participants to work cooperatively, to report and to monitor progress. The extranet, together with the project website, will provide the focal point for project management and co-ordination activities including the project's library with all deliverables and documents, the wiki space for collaborative working and sharing, and the website with forum, news groups, and meetings and events planning for project discussions and planning of key topics and issues.

A project management package will be used by all Workpackage Leaders to plan the activity of the various workpackages; it will enable homogeneous organisation and reporting to the Project Board and the effective management of the detailed project plan.

Project risks and risk management

The following key project risks have been identified prior to project start and remedial actions foreseen as set out in the table below. A much more detailed risk analysis will be performed during the course of the project.

Risk	Impact	Preventative and remedial actions
BAN is unstable with wireless communication	**Medium** The wireless networks may interfere or be unstable	The BAN is based on wireless communication and has been demonstrated before. The risk of interference is real, but can be solved using e.g. adaptive radios.
PAN integration with BAN and other sensors is unstable	**Low** The PAN cannot connect to the devices needed	The PAN is based on mature technology and is known to work. The concept of the PAN with nodes and device connectivity is important for the REACTION concept.
CGM sensors cannot be manufactured in ePatch technology environment	**Low** CGM cannot be attached and worn comfortably	The ePatch technology is mature at DELTA. A range of sensors have been manufactured including skin temperature and electromyography.
The accuracy of the wearable CGM sensors fails to reach the necessary level	**High** Low accuracy makes use of CGM for TGC and therapy difficult and prevents reliable hypoglycaemic episode alarm	Sensing methods based on impedance and IR-detection of blood glucose level measurement have been demonstrated before. Additional use of optimised algorithms for glucose control can help alleviate the problem. Even without high absolute accuracy we will combine CGM with discontinuous calibration and biomedical modelling for stabilisation of glucose levels.
SOA etc. is not applicable on PAN	**Medium** The functionality at the PAN level can't be implemented	The partners have great experience in SOA services and distributed intelligence and will use common standards and tools for the development. Resources constraints will be addressed with virtualisation of devices.
Platform fails to integrate to backend HIS	**Medium** Integration with other backend systems fails	Failure of integrate to HIS due to unavailability or technical interface problems. Every effort will be made to secure this functionality and ATOS has deep insight into this area. Stubs and demons will be used for non-essential legacy systems.
Biomedical modelling does not yield sufficient statistical evidence to support longer term risk assessment (and predictions of conditions) in self-management for individual patients	**Medium** The risk assessment cannot be used by patients directly in the self-management schemes.	While risk assessment and therapy optimization for individual patients' personalized therapy is the ultimate goal, the clinical evidence from a large population of diabetic patients can be used by clinical practitioners to provide improved disease management strategies to be developed and thereby ultimately benefit the individuals too.
Clinical validation shows inconclusive or negative results	**Low** Remote monitoring does not provide improvements	Many studies have proved that there are clinical benefits connected to remote monitoring. The clinical field trials will be carefully planned to show correct results.
Ethical and social analysis shows considerable user dissatisfaction	**Medium** Uses are not comfortable with the concept	Users have different attitudes to remote monitoring. Studies in the SENIOR project reveals that many of the problems of privacy can be solved with the proper design of technology personalised to the user.

Risk	Impact	Preventative and remedial actions
The legal analysis fails to point out conclusive answers to problems of liability	**High** Product liability issues will prevent the platform from being accepted in the market	The technical design must comply with legal requirements. The iterative process takes this into account. Designs must be changed in order to comply with requirements.

Table 4 Identified risks and remedial actions

During the cause of the project, all project participants, and in particular the project managers, will be responsible for raising any material or perceived risk as part of the normal reporting. All risks and issues will be registered in the project's risk log and the status and mitigation of each risk element will be reviewed regularly as a working document and reported at each Project Board meeting. The Project Manager will manage and maintain the risk management log.

The project plan, updated each year, will also contain an updated Risk Management Plan, which will report the project's strategic and technological risks and the identified corrective actions.

Risk Mitigation and Contingency plans for sensors development

The following table contains specific data in relation to the risks related to sensors development.

WP3 Tasks	Risk description	Probability	Severity	Criticality	Action type	Countermeasure Action	Who?
Task T3.1-ePatch body sensor technology							
Sensor integration	Integration of optical components into the e-patch not possible due to space reasons	2	4	8	A	Adaptation of the e-patch geometry	Delta, IMM
Disposability	Optical sensor head might not be disposable	4	1	4	A	Change concept of sensor head by separating the needle from the permanent optical parts	IMM
Power consumption	Size of the ePatches must be small to be convenient to ware and should monitor continually for many days. The optical sensors for CGM will use relatively more power and battery size would be unacceptable	3	3	9	A	design of optical sensor for low power and designing the measurement applications for lowest possible on-time of optical sensor system	IMM and DELTA
ePatch materials and bio-compatible design	Patients in intensive care who has traumas also have very strung sweating, this might call for a new and critical design of the skin adhesive system of the ePatch	3	4	12	A	Specific investigation on the matter of adhesives and adhesion on trauma patients	DELTA
Disposable ePatch platform	The disposable ePatch platform should be low cost and based on the new fibre-optical CGM sensor. The fibre-optical sensor could be too costly for disposable use	3	3	9	A	design of optical sensor for low cost and automatic production	IMM and DELTA
Task T3.2 - Continous glucose monitoring sensors							

WP3 Tasks	Risk description	Probability	Severity	Criticality	Action type	Countermeasure Action	Who?
sensitivity	Sensitivity and specificity not high enough when measuring only in one wavelength band	3	5	15	A	Apply tunable light source	IMM
light source fluctuation	Instability of wavelength and intensity of the source especially at longer acquisition times	3	4	12	A	choose acquisition time as fast as possible and reference the light source	IMM
ISF composition	variation of ISF condition such as changes in temperature, chemical composition (e.g. uric acid, medications), causing interference of the glucose IR-spectrum, day-to-day changes in the vasculature, the aging process, diseases and the person's metabolic activity-lack of transferablity of calibration from one part of the body to another	4	5	20	A	Extensive validation and testing of the glucose prediction equation is needed to determine if the glucose correlation is consistent in all clinically important conditions in all types of patients	IMM, Medical partners
physical interference	Sensor lacks specificity due to substantial chemical and physical interferences with skin (sensor type 1).	4	4	16	A	Use chemometric modelling, applying multivariate regression analysis. Large amounts of data should be used to build the glucose model, taking into account the sampling environment and other factors involved during the analysis. Application of a different sensor concept (sensor type 2).	IMM, medical partners
influence of bilogical condition	Influence of individual biological condition on the sensor output (Tissue changes: blood supply for body fluid, medications, day-to-day changes in vasculature, aging processes, personal metabolic activity)	3	3	9	A	Individual calibration of the e-patch sensor device before first usage, including implementation of a calibration routine.	Delta
Integration with epatch	The fibre-optical GCM-sensor must penetrate the skin and be placed in the tissue. As well the optical measurement could require an optical system higher than few mm.	3	4	12		design of the fibre-optical system should be optimised for integration in an ePatch platform	IMM and DELTA
Sensor accuracy	Accuracy of the developed sensors not as good as specified	3	3	9		Follow different independent concepts from the beginning of the project, combine IR and IS sensors to increase accuracy, check on alternative COTS sensors	

WP3 Tasks	Risk description	Probability	Severity	Criticality	Action type	Countermeasure Action	Who?
Task T3.3 - Automatic Glycaemic Control							
Pumps	Either pumps may not be available on the market or details about the available pumps (see also Task 3.3 description for an overview) may not be given by the suppliers of the pumps	2	3	6		The risk of non-availability of insulin pumps is estimated to be very low, since a lot of pumps are on the market (IMM discussed e.g. availability of Roche pumps directly with Roche). However, it might be possible that pump suppliers may not give all the required informations (interface communication protocols) to the consortium for adequate control of the pump for legal concerns. But this scenario is also unlikely, since MUG in the past worked with external insulin pumps and never had problems to receive communication protocols from the suppliers. In case this might be a problem IMM is experienced to take the characteristic curve of the pumps and build a controller.	IMM
Task T3.4 - Multiparametric monitoring sensors							
Specs of multi sensor	The specification of the multiparametic sensor that will be made as an ePatch is not known. It might be that the specification cannot be met by known sensors	3	3	9		The performance of the Multiparametric sensors should be specified early in the project to ensure that useful sensors exist	DELTA, IMM and clinical experts
Sensor components Risk analysis estimation	A supplement of a single risk assessment for each of the MGMS (Multisensor Glucose Monitoring System) components was performed			0		See the details in the paragraphs below this table	
Task T3.5 - Graphical User Interfaces							

WP3 Tasks	Risk description	Probability	Severity	Criticality	Action type	Countermeasure Action	Who?
Specs of multimedia terminals	The specification of the multimedia terminals will be too wide with too many O.S. and display size and resolutions	3	2	6		More appropriate selection of multimedia terminals with O.S., display size and resolutions, trying to target the most diffuse in the world market	FORTH, UBRUN and users

Probability:		Severity:	
Probability of the risk.		The severity of impact of the risk on the project.	
5	Risk will occur (has to be invented)	5	Sensor will not function (must have)
4	Risk is likely to occur (has already been done elsewhere)	4	Sensor function is likely to be significantly impaired/reduced (should have)
3	Risk has 50/50 chance to occur (has already been done by the project partners)	3	Sensor function is likely to be partially impaired/reduced (good to have)
2	Risk is unlikely to occur (project partners state of the art)	2	Tolerable inconvenience to users (nice to have)
1	No risk (requires a several of events to occur)	1	Tolerable impact in manufacturing (not necessarily required)

1. <u>Classification of the device</u>

As our device Multisensor Glucose Monitoring System will be used for registering the bio-physical skin characteristics and will not display any glucose values during this trial, the device may be considered as a Class IIa medical device in accordance with Rule 10 to Directive 93/42/EEC.

2. <u>Supplement to the Risk analysis (document version 01)</u>

An assessment of the single risks described in the Risk analysis document was performed.

Sweat/moisture sensor

Biocompatibility	The risk is reduced after applied actions (FDA approved materials, limited skin exposure, gold coating) for warning or passable assessment?
Infection risk	The risk is eliminated after applied actions (no use of invasive methods, cleaning protocol for sensors)
Device labelling	The risk is eliminated after applied actions (proper labelling of devices, study information and training)
Displayed data	The risk is eliminated after applied actions (no displayed information for the study subjects)

The risk of **sweat/moisture sensor** for the patient is judged as acceptable.

Acceleration Sensor

Device labelling	The risk is eliminated after applied actions (proper labelling of devices, study information and training)
Displayed data	The risk is eliminated after applied actions (no displayed information for the study subjects)

The risk from **acceleration** sensor for the patient is judged as acceptable.

Optical Sensor

Biocompatibility	The risk is reduced after applied actions (FDA approved materials, limited skin exposure, minimized contact between optical fibres and skin) for warning or passable assessment?
Infection risk	The risk is eliminated after applied actions (no use of invasive methods, no direct skin contact of LEDs)
Device labelling	The risk is eliminated after applied actions (proper labelling of devices, study information and training, harmless and low intensity light emittion)
Displayed data	The risk is eliminated after applied actions (no displayed information for the study subjects)

The risk of **optical** sensor for the patient is judged as acceptable.

Dielectric Spectroscopy Sensors

Biocompatibility	The risk is reduced after applied actions (FDA approved materials, limited skin exposure, gold coating, cytotoxicity tests, low field intensity) for warning or passable assessment?
Infection risk	The risk is eliminated after applied actions (no use of invasive methods, cleaning protocol for sensors)
Device labelling	The risk is eliminated after applied actions (proper labelling of devices, study information and training)
Displayed data	The risk is eliminated after applied actions (no displayed information for the study subjects)

The risk of **dielectric spectroscopy sensors** for the patient is judged as acceptable.

Temperature and Humidity Sensor

Biocompatibility	The risk is eliminated after applied actions (FDA approved materials, limited skin exposure and not in direct skin contact)
Infection risk	The risk is eliminated after applied actions (no use of invasive methods, not in direct skin contact)
Device labelling	The risk is eliminated after applied actions (proper labelling of devices, study information and training)

Displayed data	The risk is eliminated after applied actions (no displayed information for the study subjects)

The risk of **temperature and humidity sensors** for the patient is judged as acceptable.

Algorithm Development

Data storage	The risk is reduced after applied actions (device testing, data handling procedure described in study protocol, site personnel training, backup procedures) for passable assessment
Infection risk	The risk is eliminated after applied actions (no use of invasive methods, not in direct skin contact)
Device labelling	The risk is eliminated after applied actions (proper labelling of devices, study information and training)
Displayed data	The risk is eliminated after applied actions (no displayed information for the study subjects)

The risk of **algorithm development** for the patient is judged as acceptable.

The risk analysis of the single sensor applies as well to the complete Multisensor. The remaining risk of biocompatibility (different sensors) have a warning or passable assessment. The biocompatibility risk is currently manifested as a light skin irritation, in case of skin sensitive patients. The data storage risk has a passable assessment after application of risk reducing actions.

The general risk of the complete Multisensor for the patient is judged as acceptable.

Consortium Agreement

Before the project commences, the Consortium members will sign a formal Consortium Agreement in which roles, responsibilities and mutual obligations will be defined. It is a prerequisite of Consortium membership that every participant must sign the Consortium Agreement before the start of the project. The agreement will be based on the DESCA model for IP consortium agreements and will include:
- Management of knowledge generated by the project, and rules for knowledge transfer
- Specific arrangements concerning intellectual property rights to be applied among the participants and their affiliates, in compliance with the general arrangements stipulated in the contract (see section 3.3 on IPR management principles);
- The internal organisation of the Consortium, its governance structure, decision-making processes, reporting mechanisms, controls, penalties and management arrangements;
- Arrangements for the distribution of funds among participants and among activities;
- Provisions for the settlement of disputes within the partnership.
- Rules and procedures for partners joining and leaving the Consortium

Partners may change the Consortium, provided that appropriate agreements and contract amendments are followed and that all responsibilities and obligations have been reassigned. Partners may also be asked to leave in case of defaulting on their obligations.

B.2.2 Beneficiaries

Partner 1: Atos Origin [ATOS]

Atos Origin is an international information technology services company. Its business is turning client vision into results through the application of consulting, systems integration and managed operations. The company's annual revenues are more than EUR 5 billion and it employs over 46,000 people in 40 countries. Atos Origin sae is the Spanish branch of this leader European IT services Company and a founding member of the European Technology Platform NESSI (Networked European Software and Services Initiative). Atos Research & Innovation, ARI (http://www.atosresearch.eu), node of R&D of Atos Origin in Spain, is focused in projects which combine the most advanced technological developments and the economic exploitation of results in R&D. Our aim is to lead our knowledge and experience acquired to concrete projects with clients. The Biotechnologies & Healthcare Unit within ARI is composed of a group of engineers, biologists, bioinformaticians, mathematicians, and doctors specialised in applied research and development of bio and health related projects. Our unit participates in several European and Spanish projects. The Unit's expertise is supported by its involvement in different European projects, and also supported by their professional careers in technical divisions of other companies. The key area of contribution in REACTION will be in the area of system architecture and interoperability of services (WP4), security analysis (WP7) and exploitation (WP12). Atos Origin also participates in other technology platforms like the European and Spanish platform of Nanomedicine, eMOV for mobility, eSEC for security, PROMETEO for embedded systems, INÉS for software and services.

In addition to the managerial tasks associated to the coordination of the project Atos is also involved in RTD activities as integration of the system with backend HIS systems and security analysis.

Atos has previous experience in these activities as it is stated in the list below:
- Management Subsystem: Projects EuropaNet, C-MONITOR and TELECARE. They are Telemedicine projects in which Atos designed and developed the systems following the specifications launched by medical professionals.
- Exchanging information with HIS. Projects LIQUID, SMARTIE, C-MONITOS and pEHR: Atos involvement was related to Medical Knowledge Management, some of them multilingual aspects and search engines of medical documentation with semantic capacity was developed.
- Medical Images management: Projects NewRoentgen and DynCT. Atos developed algorithms for medical image processing (particularly TAC), user interfaces for medical images systems and software integration.
- Decision Support Systems:Project SMARTIE. Atos worked on the analysis of algorithms founded on Evidence-Based Medicine, design and development of software application for PC environment as well as for web based and PDA including multilingual aspects, integrating this environment with the HIS.
- Remote monitoring systems : Projects C-MONITOR, TELECARE and DAPHNET. Atos worked on the design of the complete service, design and development (jointly with a partner) of communication protocol and design and development of storage facilities for medical signals and other medical applications.
- Electronic Health Record (Project pEHR): Design and participation in Electronic Health Record applications able to be customised by the patient.

Security analysis: Atos Origin within the MASTER project provides methodologies and infrastructures that facilitate the monitoring, enforcement, and audit of quantifiable indicators on the security of a business process, and that provide manageable assurance of the security levels, trust levels and regulatory compliance of highly dynamic service- oriented architecture in centralized, distributed (multidomain), and outsourcing contexts. To this extents MASTER has identified new innovation components in terms of key assurance indicators, key security indicators, protection and regulatory models and security model transformations coupled with the methodological and verification tools for the analysis and assessment of business processes. MASTER is being

demonstrated by a proof-of-concept implementation in the IT systems of Hospital San Raffaele, a healthcare institution with multiple initiatives on patient care, health care research and application of information technology to health care.

Security management: ATOS Origin developed the security solutions management mechanism in this project within the SERENETY project, a run-time framework to support monitoring of events and resources at different levels (operating systems, middleware, application and users) and to support adoption of proper reaction policy/strategies to threats/attacks. Regulatory compliance assurance and risk assessment: ATOS within the TrustCoM has developed a framework for trust, security and contract management in virtual organizations in which regulatory compliance, assurance and risk assessment aspects have been addressed.

Key persons involved in the REACTION project:

Lydia Montandon: is currently working at Atos Origin Spain as co-ordinator of the Societal Applications area, being responsible of the area strategy and the day-to-day management of several international RTD, innovation and cooperation projects, focused on the development and implementation methodologies of new technologies enhancing human learning and social inclusion. Before joining Atos Origin, she worked as edutainment applications designer in a Spanish Multimedia production firm. Her professional background includes 10 years of experience in communication, graphic and multimedia design, with references from a wide range of International customers. She studied Educational Technology at the Faculty of psychology and educational sciences, University of Geneva, Switzerland, and graphic/industrial design in Milan, Italy. She is fluent in English, French, Italian, Spanish, German and Greek.

Blanca Jordán: is the Head of the Biotechnologies & Healthcare Unit within Atos Research and Innovation group. She is a Master Engineer in Telecommunications from the Polytechnic University of Madrid, specialised on Mobile Communications. In 2000 she started a degree on Sociology in the Universidad Nacional de Educación a Distancia. She worked for Atos from September 2000 dealing with IST European projects in technical and managerial tasks. From November 2003 to March 2005 she worked as account manager for a Spanish SME specialised in technology outsourcing services. She re-joined ATOS Origin in March 2005 where she is working in managerial tasks for different research projects of the European Commission. Blanca is also working as Ethical Reviewer for the European Commission since 2007.

Carlos Cavero is technical consultant of the Biotechnologies & Healthcare (B&H) unit. He was born in 1977 in Spain. He has a Degree in Computer Science Engineering from the Autonomous University of Madrid (Spain). He also has a Degree in Philosophy from the National University of Distance Education (Spain). He joined the Atos Origin former, Sema Group sae, in October 1999 as a Junior Programmer in Public Sector working in national projects. In 2006 he joined the B&H unit in the Atos Research and Innovation department (ARI) participating since then in the realisation of international projects delivering software solutions and system integration, working on several projects for the European Commission where Atos Origin has consolidated a strong partnership with many public and private institutions from all European Countries. He has developed this technical work mainly in the DAPHNET and SENSACTION-AAL Projects, within the B&H Unit.

Partner 2: CNet Sweden AB [CNET]

CNet is a leading-edge software house specialising in semantic technologies for content and knowledge management in networked embedded environments. Our long-term vision is to contribute to establishing the Internet of Things and Services. We are developing systems and middleware to acquire, organise, personalise and share the knowledge embedded in devices, web, databases and multimedia content. Our technologies achieve semantic interoperability between heterogeneous devices, information sources and services, and allow our customers to maximise automation of the knowledge life cycle.

The core in our offering is Visual Net Server, a semantic annotation server. It is used to capture knowledge from raw information and multimedia content in webs and other distributed repositories

to turn poorly structured information into machine-processable knowledge. This allows our customers to improve their workflow efficiency and streamline business processes reducing their costs. Our semantic technologies also allow our users to organise their digital assets and deliver tailor-made information products and services to their customers. Other products include NewsToBuy for knowledge and content management as well as Termado for the management of ontologies and terminology catalogues.

Recently we have started addressing the smart home area offering energy efficiency solutions for home owners by providing seamless access to and control of home appliances using semantic-based middleware. Our initial strategy is to work through established home suppliers like energy providers rather than sales directly to home owners. Some relevant customer projects are Storuman Energi (smart metering), Swedish Building Society (building modelling) and Securitas/Jourmontör (building/appartment maintenance). These customers together with results from our projects EU-Domain and Hydra form the basis for our investments into smart home offerings. We plan to expand this business line to also include personal health monitoring which we see as a natural and innovative extension to our current offerings in the smart home area.

CNet have previous experience of e-health solutions from the STREP project EU-Domain (FP6), which developed solutions for remote monitoring of vital signs such as blood pressure as one of the important use cases. In the Integrated Project Hydra (IST-2005-034891) in which we are technical coordinators for, e-health is also an important use case dealing with accessing and controlling medical devices such as glucose meters and blood pressure meters. CNet personnel has also been involved in European standardisation activities in medical informatics (CEN-TC251) and in previous European RTD in distributed electronic healthcare records (EHCR).

CNet is a spin-off company from Swedish IT research and was originally founded by a research group from SISU, Swedish Institute for Systems Development. We still keep close contacts and collaborate with different R&D partners in Europe. We are currently researching and developing middleware technology for Service-oriented Architectures and Semantic Web Services as well as ambient intelligence solutions for mobile wireless applications like healthcare and facility management.

Key persons involved in the REACTION project:
Peter Rosengren, Msc, Tech. Lic: is the managing director of CNet Sweden and one of the founders of the company. He has a Master's degree and a degree of Licentiate of Technology in computer science from the Royal Institute of Technology, Stockholm. He is one of the architects and developers behind Visual Net Server, an XML-server for semantic-based knowledge and content management. His current R&D interest is focused on ambient intelligence, semantic web and interoperability, ontologies, mobile and wireless collaborative applications. He is currently the technical coordinator of the Integrated project Hydra (IST-2005-034891), focusing on middleware for networked embedded systems for ambient intelligence applications in eHealth and home automation. He has long-time experience in service oriented architectures and has been the architect behind several of the largest XML-based web services in Sweden. He has been involved as a project manager for projects in application domains like education and e-learning, media and publishing, building and construction. He was the technical coordinator of the Multimedia Broker project (IE2093) within the FP 4 for R&D in Information Engineering. The results of the project is now being commercialised by CNet. Prior to founding CNet he was a research director at Swedish Institute of Systems Development, SISU. There he managed the Human Computer Interaction research group 1990-92 and the research group Interaction&Communication, 1994-1995. He was also responsible for developing and implementing several new research programmes. He leads numerous of projects in the areas of multimedia information retrieval, knowledge management and business intelligence, mobile applications and collaborative work.

Matts Ahlsén, BSc, Lic.Phil: CNet associate with responsibilities in project management, consultancy and European projects. Main expertise includes systems modelling and semantic interoperability, systems architecture design and XML-based systems implementations. Extensive experience of participation in EU research projects in the ESPRIT, Telematics and IST programmes.

Representing CNet in FP6 projects Hydra and eu-DOMAIN and FP5 project METIS ("Multimedia Interactive Environments for Distributed Teamwork Promotion in Schools"). Previous work areas have included e-health standardisation, distributed healthcare records, object-oriented software engineering, databases and federated information systems, information systems architecture, multimedia databases and co-operative work. Degree in Computer and Systems Science 1983 Univ. of Stockholm. Assistant Researcher and Lecturer at the Dept. of Computer & Systems Sciences (Univ.of Stockholm), 1983-1988. Licentiate of Philosophy degree Univ. of Stockholm 1995. Research Engineer at the Swedish Institute for Systems Development (SISU) starting 1985. Senior Analyst, Head of the Information Systems Architecture Lab, and member of SISU management 1995 –1998. RTD manager at SITI, The Swedish IT Institute 1998-1999.

Mathias Axling: is currently working at CNet Svenska AB with product development. Since joining in 2001, he has worked as architect, analyst, developer and mentor in various software development projects, primarily using XML related technologies, dotNET platform and Java. Previously he was a Ph.D. student, analyst and project manager at the Research Corporation for Media and Communications Technology (FRAMKOM), the Swedish Research Institute for Information Technology (SITI) and the Swedish Institute for Systems Development (SISU). Prior to that, he was a consultant at Enator (now TietoEnator) developing computer telephony integration platforms. EU funded RTD projects he has worked on includes METIS (IST 25175), RITE (P22078), Multimedia Broker (IE2093) and IMPRIMATUR (IE20676). He holds a M.Sc. degree in computer science and technology from the Royal Institute of Technology in Stockholm (KTH) and is currently pursuing a B.Sc. in business administration and economics at Stockholm University.

Peeter Kool: is one of the founders of CNet. He is an architect and developer behind several of CNet's products, including Visual Net Server and adEtransact. His expertise is in semantic web service development, solutions for semantic interoperability and ambient intelligence solutions for mobile work. He has deep knowledge about several development languags and platforms like C, C++, C#, .net, Java. He is also skilled in database technologies and regularly develops solutions based on MS SQL, Oracle and Tamino. Prior to CNet he was working at Swedish Institute of Systems Development and holds a MSc in Computer Science and Engineering. He has participated in several EU projects, including Intutive (FP4), HOD (FP4), IRISPOL (FP4), Multimedia Broker (FP4), Metis (FP5), EU-Domain and Hydra (FP6).

Partner 3: DELTA [DELTA]

DELTA is a technology provide within electronics, microelectronics, acoustics and optics. DELTA provides development services for electronic system developers and is well know for a history of more than 60 years in testing electronic systems. DELTA has 230 employees and has its main income from providing services to the industry end OEM-components with in optical systems and microelectronics. A minor part of the turnover is on technology transfer project mainly based on contracts with the Danish government.

DELTAs microelectronic division has its main business in developing applications specific microelectronics (ASIC) and has a design group of 20 people, and tested and supported more than 10 million ASIC components in 2006. The main part of these ASICs are for mobile electronics and DELTA focus its competences on mobile sensor application. The micro system group in DELTA's microelectronics division has worked on micro sensor applications for the last 15 years, and has today facilities to develop and manufacture prototypes of micro sensor based products. Since start of 2006 the 15 people of the micro system group have focused on building up competences on body sensor development. The effort is on developing medical devices body sensors and especially focus is on developing capabilities for developing and supplying body sensors imbedded in skin friendly adhesives. This new ePatch technology will be further developed in the REACTION project and is expected to be a platform for future development and supply of application specific ePatches as OEM products.

DELTA has participated in and managed numerous EU and national funded projects includes PROSPECT (development of one of the first virtual classrooms, EU funded), ASH (development of a virtual control room for simulated space missions for students, EU funded) and Apparater.dk (research on different ways of web and net enabling of machines and services, national funds).

Key persons involved in the REACTION project:

Jens Branebjerg: is manager of DELTA's micro system activities. He received his Bachelor degree in electronic engineering from the Technical University of Denmark DTU, Lyngby, in 1981 in the area of electromechanics. He was employed as R&D engineer at Radiometer A/S in Copenhagen from 1982 to 1988 working in the area of development of electrochemical medical sensors based on thick film technology and hybrid microelectronics, and was responsible for building up and managing the R&D facility for prototyping of hybrids and ceramic sensors. In 1989 he was employed as research engineer at the Laboratory for Semiconductor Technology (the later Microelectronics Centre, MIC) at DTU and worked on research projects for development of processes for semiconductor manufacturing. From 1989 to 1997 he worked as R&D engineer in the corporate research department of Danfoss A/S, Nordborg, Denmark. During first 3 years he worked on his PhD. project on actuators in micro technology and got his PhD. degree in 1991 in micro technology from MIC, DTU, Denmark. During his employment at Danfoss A/S he was stationed at MIC, DTU and responsible for Danfoss' activities concerning Microsystems at MIC. From 1991 to 1997 he was project manager for a research project on micro machined components and systems for flow control and micro chemical analysis systems. Since 1997 he has worked as project manager at DELTA with the responsibility of developing and supplying Microsystems services in the areas of packaging, testing and reliability. He is currently managing the micro system group of 15 people and the focus of the group have the last 1½ years been on body sensor development and especially on the new concept of ePatches.

Morten Wagner: is M.Sc. Computer Science and Cognitive Science from University of Copenhagen. He has been employed by DELTA since 1996, where he has been involved in research in distance education; computer supported collaborative work and distributed computing. Morten has been working with Java, one of the two most popular object-oriented programming languages, almost since its inception. He has experience with server-side, client-side, embedded- and mobile java and also has several years of teaching experience in the field. Now, embedded Internet technologies, mobile computing and intelligent sensors are amongst Morten's interest areas. Additionally, Morten is also a specialist in electronic, distributed learning environments, human factors and human-computer interaction, and has been in the board of the Danish branch of ACM SIGCHI for several years. He has been workpackage-leader in a recent EU research project on new learning technologies, and active contributor to several EU research projects. In DELTAs micro system group Morten is responsible for concept development of Body Areas Network solutions, and is currently project Task Leader in at national project on ePatches.

Irvin Jacobsen Manwiza: is R&D hardware engineer working within the microelectronics area in DELTA. Irvin has a solid theoretical background in electronics, physics and technology and practical experience in product development, technological projects and quality assurance. He is M.Sc EE from Syddansk university of Denmark Odense, has an Honour in electronics from Zimbabwe and a Marketing Diploma from London Chamber of Commerce and Industry. He is an experienced engineer in hardware and software design, power electronics, microcontrollers, smd , emc/emi type approval, wire less applications, analogue sensors, amplifiers etc. He has been working with development of new electronic products in a number of companies in Zimbabwe, Botswana and Denmark before he joined DELTA in 2006. He is currently responsible for the development of hardware and mechanics for the ePatches concept.

Partner 4: Institut für Mikrotechnik Mainz [IMM]

IMM is a non-profit research and technology institute having a public service mission, owned by the local government of the German federal state Rhineland-Palatinate. As a service provider, IMM is developing together with industry system technology to solve complex analytical problems in order to achieve principle solutions for biomedical analysis and diagnosis, industrial analytics and environmental analysis. Expertise in the required processes and methods for the realization of microstructures (precision engineering, structuring technologies, surface modifications) as well as their project oriented development are the basis for the success in national and international projects. With a staff of 140 people, IMM has carried out or is currently working on more than 40 projects funded by the EC in the fields of chemical process engineering, micro-fabrication, micro-fluidics and micro-optics. IMM has broad expertise in design, development and fabrication of

marketable micro-devices. Various methods are available in-house for manufacturing micro structured devices, e.g. mechanical micro-machining, electro-discharge machining, laser material processing and thin-film technologies. The present organizational structure consists of the five R&D departments: Fluidics & Simulation, Mixing & Fine Chemistry, Energy Technology & Catalysis, Micro Structuring & Sensors and Precision Engineering. Based on a platform for rapid lab-on-a-chip development, IMM's expertise in fluidics comprises extraction processes from various types of samples, microfluidic chips for sample preparation, chip-based optical or electrochemical detection, functional integration of different microfluidic tasks onto a single chip, set-up of microfluidic systems for analytic and diagnostic purposes. This is supplemented by expertise in optical detection and sensing technologies.

Within the REACTION project IMM will especially deal with sensor development tasks and has the role of WP leader of WP3. A number of already completed projects or projects that are currently running have created a sound basis for the tasks to be performed in this project – although they are related to diverse application fields such as food industry and cancer diagnostics. These include: **MASCOT** (integrated Microsystem for the Magnetic Isolation and Analysis of Single Circulating Tumour Cells for Oncology Diagnostics and Therapy Follow-up) and **SAFER** (Isolation of foetal cells from maternal blood) require isolation of a very few cells from a comparatively huge amount of blood and, thus, represent a real challenge with respect to all micro- to macro-interfacing issues. In **CD-MEDICS** (Development of an integrated system comprising polymer chip, control device, and data processing for the multiparametric diagnosis of celiac disease) IMM deals with aspects of hardware integration and sensor realisation, in particular amperometric and impedance sensors. The integrated project **SMARTHEALTH** (Smart Integrated Biodiagnostic System for Healthcare) is an example of an elaborate multi-analyte screening approach. In **POSSEIDON** (Progressive Oil Sensor Systems for Extended IDentification ON-line) IMM is developing solutions for the online analysis of lubricants used with ship motors. Essential components of the online sensor system are NIR sensors, realized as transmission or ATR cells for the detection of contaminations like water, or micromechanical sensors allowing to measure viscosity via shear forces. In **CD-CHEF**, a gladin sensor has been developed based on ELISA with optical detection (absorbance and fluorescence) in the VIS spectral area. The detection module has been integrated into a micro-fluidic network of the sensor system and the one-way chip includes free-space optical elements for the in and outcoupling of the light signal.

Dr. Thomas Klotzbuecher: studied physics at the Rheinisch-Westfälische Technische Hochschule in Aachen with the main focus on solid state physics and laser technology. During his employment at the Lehrstuhl für Lasertechnik from 1995 to 1998 he worked on the field of thin film deposition and spectroscopic surface analysis. In 1999 he received his PhD with a work on laser based deposition of superhard thin films. Since 1998 he has been employed at the IMM Institute of Microtechnology Mainz GmbH, where he is head of the Lasertechnology & Optical Sensors group. His current fields of research are the laser micro- & nano-structuring, optical sensors for fluid analysis and integrated polymer optics.

Dr. Ines Frese: received her diploma in Optics from the University of Tashkent, Soviet Union in 1983. She researched at the Lomonosov University on fiber-optical sensors between 1985 and 1992. She received a PhD degree in Polymer Physics from the University of Saarland, Germany in 1999. After PhD studies at the Max-Planck-Institute for Polymer Research in Mainz she joined the Institute of Microtechnology Mainz (IMM), Germany in 1998. Her research interests are micro-optical systems for bio-medical and chemical sensing technologies.

Dr. Lhoucine Ben Mohammadi received his diploma in electrical engineering from the University of Kénitra in Morocco. Afterwards he studied physics at the University of Darmstadt where he also received his PhD on the field of light generation and laser activity in nanopourous dye-loaded molecular sieve composites. He has a long year experience in microoptics, non-linear optics and laser physics during his employment in the group of Prof. Tschudi at the University of Darmstadt. In 2006 he joined IMM and since then worked in different EU projects in the field of micro optical sensors for chemical and biomedical analysis.

Markus Holzki studied Applied Physics at the University of Applied Sciences in Wiesbaden. Since then he is employed at IMM, first working in the Precision Engineering Department, developing electromechanical systems mainly in the field of medical engineering and hybrid optical systems. Thereby he gained experience in designing precise robot-, handling and gripper-systems for the automated assembly of optical components. After joining the Microstructuring and Sensors Department he was involved in the development, characterization and improvement of various optical sensors for chemical on-line analysis.

Susanne Sigloch has a degree in Applied Physics and works on the development of microtechnical components at IMM since several years. Her main interests are microoptics and sensors. She has large experience in the field of development, assembly and testing of prototypes and small series of microtechnical products. She also has operating knowledge in micromachining and measurement technologies. She has been working successfully in interdisciplinary teams in several industrial and EU-funded projects. Before she joined IMM, she worked at the Max-Planck-Institute of Microstructure Physics in the field of thin film deposition and characterisation.

Partner 5: Foundation for Research and Technology – Hellas (FORTH-ICS)

The Foundation for Research and Technology - Hellas (FORTH) is one of the largest research centres of Greece, with well organised facilities and a highly qualified staff. It is a private non profit research organization that operates under the supervision of the Greek Ministry of Development. The Institute of Computer Science at FORTH (FORTH-ICS), since its establishment in 1983, is a pioneering contributor towards the deployment and adoption of Information Society Technologies in Greece. FORTH-ICS has a relatively long history and recognized tradition in conducting basic and applied research, developing applications and products, providing services, and playing a leading role in Greece and internationally. The activities cover important research and development areas, taking into consideration new perspectives, emerging fields of research and technological challenges worldwide. The FORTH-ICS main group involved in the current proposal is the Biomedical Informatics (BMI) Laboratory. The Laboratory was founded in 1985 by Professor Stelios Orphanoudakis (1948 - 2005) who led the laboratory until March 2005. BMI Lab's R&D work is carried out in collaboration with health professionals and is supported by 7 researchers, 8 senior s/w & telecommunications engineers, 28 systems & s/w engineers and a varying number of graduate students & undergraduate trainees. The research activities of the BMI Laboratory focus on the development of innovative computer methods and tools in the area of biomedical informatics, medical imaging and bioinformatics. Research in machine learning and data mining for biomedical knowledge discovery, is an additional important activity of the Laboratory.

The BMI Lab has also developed special purpose autonomous clinical information systems which have integrated into a hospital-wide information system, regional pre-hospital health emergency systems, e-Health and m-Health systems and services and computer supported co-operative work environments for medical tele-consultation and remote patient management. Last, the BMI Lab has developed Integrated Care Products such as the Integrated Electronic Health Record (I-EHR) which is widely acceptable in Greece and Ireland. Today the BMI Lab of FORTH-ICS guides production level implementation efforts in other regions of Greece.

Another group which will be involved in this proposal is the Ambient Intelligence (AmI) group which has the goal of improving the quality of life of all citizens of the emerging Information Society through the creation and provision of safe, efficient and user-friendly AmI technologies, which support and cater to the needs of each and every individual user in a seamless, unobtrusive and invisible way.

The long experience in the design, development and support of HYGEIAnet, the Health Telematics Network of Crete, provides the necessary background to FORTH-ICS's contributions towards the activities and goals of the current proposal. HYGEIAnet provides an environment of strengthened privacy protection, builds on a regional healthcare information infrastructure in order to improve the quality and accessibility of healthcare and to enable the delivery of integrated healthcare services. Such a health working environment has been the foundation for the design and development of

integrated user-oriented telematic services, which ensure prompt and secure access to information resources, given that proper authorization is available.

Key persons involved in the REACTION project:

Dr. Ing. Franco Chiarugi: received the degree, magna cum laude, in electronic engineering from the University of Pisa in 1983 and in the same year he got the qualification to practice as an engineer. He has been working in the field of biomedical engineering for about 20 years (in industries and research centres) with special focus to biosignal processing and communication protocols. In 1999, he joined the Biomedical Informatics Laboratory at FORTH-ICS, working on teleconsultation systems, homecare platforms, emergency care and clinical information systems. Dr. Ing. Chiarugi has contributed to JUST, PICNIC and TWISTER IST R&D projects. Since 2002, he has been managing the OpenECG portal and providing development support to companies implementing the SCP-ECG standard for electrocardiographs. He has been FORTH's Scientific Responsible for the HEARTFAID IST FP6 STREP project. His last significant achievement is the collection of the 3 out of the 4 prizes at the PhysioNet Challenge 2004 in Chicago with the study "Predicting the End of an Atrial Fibrillation Episode: The PhysioNet Challenge".

Dr. Ioannis Tsamardinos: is an Assistant Professor at the Department of Computer Science at University of Crete, an Adjunct Assistant Professor at the Department of Biomedical Informatics at Vanderbilt University, and an Affiliated Research Scientist, at FORTH-ICS. He received his Ph.D. in 2001 from the Intelligent Systems Program of the University of Pittsburgh and worked as an Assistant Professor at the Dept. of Biomedical Informatics at Vanderbilt University between 2001 and 2006. He has developed several state-of-the-art algorithms and systems for Machine Learning, Data Mining, Bayesian Network learning, Variable Selection, and Causal Discovery with over 35 publications in international journals and conferences. He has also participated in several analysis projects of biomedical data, including clinical, epidemiological, microarray gene-expression, proteomics and text-categorization.

Dr. Angelina Kouroubali: received her PhD from the University of Cambridge, Judge Business School, UK and a masters degree in Medical Informatics from Columbia University, USA. She is an affiliated research scientist at the Biomedical Informatics Laboratory at FORTH-ICS and a lecturer on medical informatics at the University of Crete Medical School. Her research interests include social and organizational issues in ehealth; emergency care services; emergence of practice cultures in eHealth; impact of eHealth on quality and outcomes of health services. She is the principal investigator for FORTH for the EHR-IMPLEMENT project studying social and organizational aspects of EHR national implementations across Europe, and HEALTHWARE. In 2005, she received Best Paper prize at the10th International Symposium for Health Information Management Research (ISHIMR 2005) for the paper "Innovation practices in the Emergency Medical Services in Crete" (authors: A.Kouroubali, D. Vourvahakis, M. Tsiknakis)

Dr. Ioannis G. Tollis: is a Professor of Computer Science at the University of Crete and the head of the Biomedical Informatics Laboratory at FORTH-ICS. He received his Ph. D. degree in Computer Science from the University of Illinois at Urbana-Champaign in 1987. He joined the faculty of the University of Texas at Dallas in 1987, where he was a Professor of Computer Science until 2004. He has published 7 books, over 130 journal and conference papers, and has given more than 60 invited lectures worldwide. He is editor-in-chief of the electronic Journal of Graph Algorithms and Applications and was a member of the editorial board of the IEEE Transactions on Computers (2000-2004). He is the chair of the Digital Patient working group of ERCIM, and just finished co-editing a special issue of the ERCIM News magazine devoted on the "Digital Patient". His current research interests include algorithms for the analysis and visualization of biomedical data, such as, epidemiological, gene expression, protein interaction, etc.

Partner 6: Fraunhofer SIT [FHG-SIT]

The Fraunhofer-Gesellschaft zur Förderung der angewandten Forschung e.V.(FhG) is an autonomous research organisation with a decentralised organisational structure, which currently maintains 56 research institutes in locations throughout Germany. Whilst the administrative headquarters are in Munich, the legally non-independent research institutes operate from different locations in 15 of the

German states. A staff of approximately 12,500 works with an annual research budget of about 1.2 billion Euro. Commissioned by customers in industry, Fraunhofer scientists provide rapid, economical and immediately applicable solutions. Work focuses on specific tasks across a wide spectrum of research fields including communications, energy, microelectronics, manufacturing, transport and the environment.

The Fraunhofer Institute for Secure Information Technology (SIT) is dedicated to provide scalable IT security in conformance with the needs of the marketplace. SIT is one of the pioneers within the field of IT-Security in Germany and Europe and has experience in development and promotion of security technologies and in embedding of security technologies into already established applications to make them trustworthy. Comprising about 100 employees SIT offers highly reliable and individual services in assuring the protection of infrastructures and networks that are enterprise-critical.

The Fraunhofer Institute SIT has numerous partners from business and industry – such as DoCoMo EuroLabs, Vodafone, and Siemens in the mobile and wireless area – and participates extensively in networking for scientific research, e.g. Wireless World Research Forum (WWRF) – a global pre-standardisation body. SIT's current major project in the area of secure platforms for embedded wireless and mobile devices is HYDRA, funded by the European Community in FP6.

During the last four years SIT was heavily involved in building the new IT infrastructure for the German health system. Both smart cards used by this system, the patient data card and the health professional card, have been specified by SIT. The institute has contributed to the architecture of the system and has expert knowledge on all key aspects, e.g. connecting the health professional to the infrastructure, the ticket system, privacy, anonymization, pseudonymization.

Key persons involved in the REACTION project:
Michael Herfert: is head of the research area transaction and document security at Fraunhofer SIT. His main areas of work are Public Key Infrastructures, long term security and security architectures. He worked in a multitude of national and international security projects. In the Makosi project (management of complex security mechanisms, funded by the German ministry of research) he worked on the model based definition, enforcement and evaluation of security policies. In the last three years he worked in three of the four major projects in order to build the new eHealth infrastructure in Germany. At the moment he works for the German ministry of Health on improvements and practical realisations of this infrastructure.

Dr. rer. nat. Matthias Enzmann: receives his PhD from the computer science department of University of Darmstadt in 2007. His main areas of work are privacy (PhD-Thesis: *Methods to Improve Privacy and Loyalty in Online Commerce*), Public Key Infrastructures (e.g. project NSI – New Security Infrastructures, funded by the German Ministry of Science) and eHealth, where he was involved in the introduction of Germany's new patient data card ("eGK") and the new health professional card ("HBA"). Within the institute he is a specialist for virtualisation solutions specific to security aspects, in particular for Linux hosts.

Frederik Franke: is a graduate computer scientist. His background includes long term data security, protocols for mobile devices (PDAs and mobile phones) and forensics. In the last time his research work was focused on statistical methods to detect privacy problems in networks. Further he worked on a patented algorithm to handle passwords in a secure, efficient and user friendly way.

Ulrich Waldmann: is a graduate computer scientist. Since 2002 he is a member of the working group "Smart devices and embedded security". His working fields are RFID, smart cards, standardization, design and implementation of cryptographic protocols, specification of card applications for the German health card and health professional card. He was engaged in projects of card performance tests and development of secure card application systems, and has contributed to several technical reports.

Partner 7: FORTHNET [FORTHNET]

FORTHNET S.A. is a leading provider of broadband network services in Greece. The company was established in 1995 to be the first commercial Internet Service Provider in the country. Starting from the Internet access services arena in 1995 up to today, FORTHNET has entered both the telecommunications and network services business, being a convergent services provider offering from voice telephony to Internet and value-added services. The company has a total of 450.000 subscriber lines and FORTHNET customer base comprises a major part of the Greek Internet community and the market of alternate voice telephony & network providers. FORTHNET utilises and integrates technological solutions on the basis of the latest telecommunications prototypes to develop and provide new services on the Network.

FORTHNET S.A. has established its Research & Development department in the Science & Technology Park of Crete. It designs, develops and evaluates the application of modern services management through operation support systems, as well as security management systems. It also develops information systems for the SMEs and for the realisation and provision of eServices. Core server technology, integration capability and web interface customization are within the technological skills of the R&D team, based upon object-oriented development with C++, Java/J2EE on various operating platforms. FORTHNET – through its R&D activity - has 10-years of experience in European projects, either as a coordinator or a contractor.

FORTHNET is currently participating in EC funded projects in the areas of eHealth such as HEARTFAID (STREP - IST FP6) aiming at the development of a knowledge based decision support system for improving the medical-clinical management of heart failure within the elderly population. Biopattern is an Network of Excellence (NoE – FP6) and Rural Wings an Integrated Project (IP – Aeronautics & Space FP6),) project that proposes to develop an advanced eLearning platform through satellite DVB-RCS and terrestrial wireless technologies.

Key persons involved in the REACTION project:

Manolis Stratakis: holds an MSc by research in Computer Networks and Digital Communications and a BSc in Electronic Computer Systems, both from the University of Salford, UK. He is currently the Head of Research Projects in the R&D department of Forthnet S.A., where he is managing several European and National research projects, primarily related to Internet and web applications and the development of Value Added Services in the areas of Mobile Internet, Advanced Messaging Systems, mobile Learning, Electronic Commerce, Teleworking, eHealth, Telemedicine and 3G Technologies. Some of the projects in which he has participated or co-ordinated are TEMeTeN, Intercare, Guidefree, groupSMS, CTN, AD-HOC, MoTFAL, ADOL, Inlet, Ypaithros, Biopattern, Rural Wings, Heartfaid, Talos, Diamouses, COLLAGE, Science-Café, Metaverse1 and several other national and regional projects. He has worked from 1992 to 1997 at the Institute of Computer Science, Foundation for Research and Technology - Hellas (FORTH), where he was mainly involved in the design and development of digital computer systems. He has also worked as a visiting professor in the Technological Education Institute of Heraklio, School of Technological Applications, from 1993 to 2000. Since 1994 he has delivered a number of Internet related courses in the Cyprus International Institute of Management and several other academic establishments. His research interests include integrated services computer networks, new technologies and applications over the Internet, mobile Internet, intelligent and personalised messaging services, real life links with advanced technology and regional development.

Antonis Miliarakis: was born in Crete, Greece on 27 June 1978. He holds an MPhil degree by the Systems Engineering Department, at BRUNEL University, UK. He graduated with honors from the Electrical Engineering Department of the Technological Educational Institute of Crete, Greece, in 2002. Since October 2000 he has worked at Forthnet S.A. where his main responsibility is the technical management of ICT research projects and the design of mobile service platforms and wireless networks. During his activities at the research and development department he has participated in the implementation of many European and national IT projects. Since September 2004 he has been lecturing Computer Systems Architecture, Medical Informatics and Microprocessors at the Applied Informatics and Multimedia department of Technological Education Institute of Crete. As a web services designer, he has designed and implemented applications for

desktop and mobile platforms like Pocket PC and Palm OS, using a variety of tools like C, VB6.0, eVB3.0, eVC++, VB.NET and ASP.

Dimitrios Maglaras: holds an MPhil by research in Software Engineering from University of Glamorgan, UK and a BSc in mathematics from the University of Crete, Greece. He is currently a Software Engineer of the Network Applications Development Unit within the R&D department of FORTHnet S.A. He is leading the development of research projects mainly in the area of Mobile Communications and Service-Oriented Systems. At the same time he is a visiting professor in the Technological Institute of Heraklion and the author of some scientific papers in the area of Software Engineering and Heterogeneous System Environments.

Partner 8: In-JeT ApS [IN-JET]

In-JeT ApS was established in 1997 and has developed to become a renowned research and innovation firm in the field of technology development and exploitation. In-JeT has developed a effective tools for technology assessments, defining technology strategies, developing business models and business cases and exploiting innovative technology solutions in such divers areas as healthcare and industrial services.
In-JeT has increasingly been incorporating socio-economic and cross-disciplinary research tasks in technology development and is working with sociologists and anthropologists to define boundary conditions and analyse and integrate ecosystems in healthcare development. We have also pioneered methodological techniques such as scenario thinking for deriving comprehensive user requirements and value modelling for developing viable business models.

In-JeT ApS has been engaged as concept and technology developer in Ambient Intelligence and Pervasive Computing since 1998 and has extensive knowledge about wireless technologies, networks, Semantic Web Services, ontologies, and Knowledge Management. Since 2000, In-JeT has specifically since 2000 been working with various kinds of eBusiness and eHealth services in heterogeneous networks and has worked as. concept and technology developer in Pervasive Healthcare since 2003. In- JeT is currently involved with a demonstration eHealth platform (Healthcare Innovation Lab) in Denmark together with the Center for Sundhedsinnovation (Center for Halthcare Innovation) at Herlev Hospital and several other hospital and medical companies.

In-JeT has also worked as an advisor to the Federation of Danish Industries on ICT and healthcare and has participated in various working groups with regional and national healthcare innovation bodies, including Øresund Regionen, Eastern Birmingham PCT and IBM.

In-JeT has increasingly been incorporating socio-economic and cross-disciplinary research tasks in technology development and is working with sociologists and anthropologists to define boundary conditions and analyse and integrate ecosystems in technology development. We have also pioneered methodological techniques such as scenario thinking for deriving comprehensive user requirements and value modelling for developing viable business models.

In-JeT ApS is marketing and operating a service platforms in Denmark for various distributed service networks. The present customers include municipalities for eGovernment services, including home networks, but the intention is to expand the platform with eHealth services for the Healthcare Innovation Lab.and is currently rolling out a demonstration eHealth platform in Denmark.

In-JeT has participates in the Danish research project "Enabling Pervasive Computing in Reality" (EPCiR) which involved Pervasive Healthcare functions, and several EU funded projects. The FP6 STREP project eu-DOMAIN developed a client-server platform for context aware service provisioning on heterogeneous networks and one focus area was in eHealth. In-JeT was technical coordinator and the results are now in commercial exploitation. Later, In-JeT was involved in the Hydra IP project, which develops middleware for heterogeneous networked embedded systems, where In-JeT was responsible for eHealth, one of the three user domains. The results will be used in the REACTION project. Finally, the project "SENIOR, social ethical and privacy needs in ICT for older people: a dialogue roadmap", is a FP7 Support Action which aims to provide a systematic assessment of the

social, ethical, and privacy issues involved in ICT and Ageing. The results of SENIOR will also be used to facilitate the ethics work to be undertaken in the REACTION project.

In REACTION, In-JeT is manager of the iterative requirement engineering process, vision owner, business modelling lead partner and chairs the technical board.

In-JeT's role in the REACTION project will be to lead the requirement engineering phase and secure that the technical implementations align with the projects conceptual vision at all times. Further, it is In-JeT's role to perform socio-economic analysis, define regulatory and policy framework and develop sustainable ecosystems in healthcare and coordinate all dissemination activities.

Key persons involved in the REACTION project:

Jesper Thestrup: received his MSc. in EE from the Technical University of Denmark in 1974 and later obtained degrees in business administration from the Copenhagen Business School and INSEAD. He worked for a number of years in for a leading medical electronics company in Denmark and in the USA. From 1987 he was Managing Director of a global electronics research company in scientific instrumentation. He founded In-JeT ApS in 1997 and is presently President and principal shareholder. He has been involved in IST programme activities for over 10 years, including ESPRIT, CRAFT, eTEN, FP6 and FP7 projects. He was Technical Manager of the eu-DOMAIN and presently manages the requirement engineering process in the Hydra project. He has done extensive work on concepts for healthcare and telemedicine solutions and has authored and co-authored papers on business modelling.

Trine F. Sørensen: has a master degree in Gender, Culture and Modernity from the Sociology Department, Goldsmiths College, University of London. She later received a MSc. in Anthropology from Copenhagen University. She has been working intensively with social and societal issues and has participated in several comparative project studies, especially in the healthcare sector. Her professional experience includes employment with governmental committees, private organisations and companies. She joined In-JeT in 2005 and is currently working with ethical and societal issues of the ICT applications in the SENIOR project and socio-economic modelling in the Hydra project.

Mette Bjørn-Andersen: has a master degree in political and economical sciences. After her graduation, she was employed in the Danish Enterprise and Construction Agency where she was responsible for analysing and consulting on public procurements, good service practice, economic models and environmental guidelines. From 2005 to 2008, Mette was a senior consultant at the Federation of Danish Industries working in the section of ITEK "IT, telecommunications and electronics". Her job is to perform industry analysis and input to formulation of national ICT strategies for healthcare, promote Public-Private Partnerships and to organise the subsection of the federation on "ICT in healthcare". Mette Bjørn-Andersen joined In-JeT on a part time in October 2009.

Partner 9: Applied Logic Laboratory [ALL]

Applied Logic Laboratory (ALL) is a Hungarian R&D SME company established in 1986. Its main research areas include computer science, artificial intelligence, cognitive systems, modelling of systems of high complexity, medical and biological informatics. The company unites expertise in system modelling and design, knowledge engineering, signal processing, neural computing, data analysis and data mining, natural language processing, and decision support.

ALL has started its research and development activity in medical informatics in 1988. Among others ALL has contributed to establishing the IT infrastructure of patient-centred new healthcare institutions. It has developed web-based information systems for virtual hospital department which support physicians to work together efficiently, share data, information and knowledge which are accessible at any point or time regardless of where and when the data was recorded. ALL is intensively working on IT application in healthcare that can be used in order to support diagnosing and treatment selection activity on the net. Technologies include efficient knowledge management, efficient reasoning and argumentation methods. Some of the works are related to the theoretical underpinning of complex clinical reasoning while others focus on developing health record and

information systems complemented by intelligent decision support services. Moreover ALL has developed methods to organise and combine information coming from different sources. The proposed methods provide solutions for (i) representation and organisation of knowledge, (ii) integration of different data, information and knowledge bases, (iii) combined use of various data mining and knowledge acquisition tools.

ALL was a member of the project co-financed by the EU FP5, Multi-Access Services for Telematic Management of Diabetes Mellitus (M2DM) with the aim to provide a sustainable service care to residential and mobile diabetic patients and to increase the quality of patient's care through improving communication between patients and caregivers.

ALL has worked out an insulin treatment fixation supporting program for the doctors of the Péterffy Sándor Street Hospital in 2007.

ALL is planning to launch most probably by the end of 2009 - beginning of 2010, its Diabetes Management Support System and Service aimed to provide direct support to the insulin dependent patients with the everyday management of their illness. ALL has worked out an "Intelligent Information System for Traumatological and Emergency Care" for the OBSI Traumatology Department, Budapest.

ALL is specialised for developing knowledge based systems such as digital assistants, decision support systems, high performance knowledge bases and distributive and co-operative intelligent systems e.g. in different medical consultation and critiquing services.

Key persons involved in the REACTION project:

Dr. Tamas Gergely: is a mathematician, Ph.D., D.Sc, and Fellow of the Russian Academy of Natural Sciences. He is also the director of Applied Logic Laboratory. His research areas include computer science, artificial intelligence, cognitive systems, modelling of systems of high complexity, medical and biological informatics. He is active in development of various methods of plausible reasoning including statistical, logical and fuzzy logic methods, case-based reasoning and methods based on analogy. These methods are used to realise abduction, deduction and induction for reasoning. The reasoning methods developed and applied includes several methods for data mining and knowledge extraction such as statistical methods (used in geological and medical expert systems), plausible logical methods (used in pharmacological design system and diagnostic system). He suggested a special approach that allows to synthetise the processes of cognitive reasoning from the various reasoning operators. He also works in the area of medical and biological informatics with the application of intelligent tools in various medical information systems. This includes the development of intelligent assistant systems for various medical disciplines. He has gained substantial experience in medical informatics system analysis, system design, development and implementation as project manager. In the REACTION project his role will be to coordinate the ALL's team and to lead ALL's efforts on mathematical modelling and knowledge discovery.

Akos Levay: has a MSc in Physics from Eotvos University. Parallel to his Physics PhD studies, he started to work with application development in the ICT industry. During that time he has led a number of mid-sized projects developing database driven web portals for prestigious clients. From the beginning of 2004 he is at Applied Logic Laboratory, his research area is in the application of the newest ICT technologies for Health. Currently he is leading the team of ALL for the development of ALL's diabetes management system. He has lead the developments at ALL in the MORE project (www.ist-more.org) co-financed by the EU FP7 and he is responsible for the application of the MORE technology for diabetes care. Earlier, he has been a participant of ALL's team for the development of a decision support system for a biomedical laboratory later deployed for the Athens 2004 Olympic Games by the NATO troops. He was also a participant of ALL's work in the project "Intelligent Information System for Traumatological and Emergency Care". He has experience with the full cycle development of the software development from planning through design till maintenance. He has system integration experience with CORBA, J2EE, DPWS, SOA and Web Services, He has experience with ontologies and related software tools including those operating on OWL, RDF and XML

represented data. In the REACTION project he will be responsible for the integration of ALL's semantic technology into the risk asssessment engine.

Dr. Miklós Szőts: is chief research fellow, Applied Logic Laboratory, Budapest. He holds a MSc, BME in civil engineering, a MSc, ELTE TTK in mathematics, and a PhD in computer science. He has been interested in theorem proving, knowledge representation, logic programming, semantics of programming languages. Has worked in modelling tasks, design of software systems; and has practice in SSADM, the UML based Unified Process technologies, OO modelling. He is also an expert in the field of theoretical and practical problems of ontologies and natural language processing. In the REACTION project his main responsibilities will be to lead ALL's effort on semantic technologies. He is a key person in the EC FP6 co-funded ImportNET project (http://www.importnet-project.org/) with idea of idea to provide an ontology-based methodology, as well as software solution bridging between different engineering domains and allowing a fast and flexible semantic integration of proprietary systems.

Partner 10: Medizinische Universität Graz [MUG]

Founded in 2004, Medical University Graz (MUG) is a young university, comprising 16 Research Institutes and 23 Clinical Departments as well as a Center for Medical Research. MUG is embedded in a 1600 bed University Hospital located in Graz, Austria with over 6000 employees. The division of Endocrinology and Nuclear Medicine at the Department of Internal Medicine offers extensive outpatient services and a 20-bed inpatient general ward with special emphasis in the treatment of diabetes and associated metabolic disorders. Research interests of the division of Endocrinology and Nuclear Medicine focus on areas, such as overall metabolic control, pathophysiology of late complications, cardiovascular endocrinology, vascular biology and on the investigation of new pharmaceutical approaches for the treatment of diabetes mellitus. The division has considerable experience with EC-projects, e.g. ADICOL (FP5-IP), CLINICIP (FP6-IP), CAREMAN (FP6-IP), NanoBioPharmaceutics (FP6-IP) and Survive ICU (FP6-Marie Curie Actions-IIF).

MUG will contribute to the REACTION project mainly within WP8, Clinical Practice, with provision of clinical access to the 20-bed inpatient department for the planning and conduct of work-flow analysis during the early stage phase of the project, performance of healthcare professionals compliance surveys, establishment of protocols for in-patient implementation of the system and planning and conduct of clinical field studies, data analysis and dissemination.

Key persons involved in the REACTION project:

Thomas Pieber MD: is head of the Division of Endocrinology and Nuclear Medicine, is opinion leader in the field of diabetes. From 2005 to 2008 he has been the Medical Director of the University Hospital Graz and currently head of a multidisciplinary team of 140 employees, approximately half researchers, half healthcare professionals working in the field of diabetes and associated disorders. Recent scientific contributions include: (Pachler2008), (Kulnik2008) and (Plank2006).

Lukas Schaupp: Ph.D in Electro- and Biomedical Engineering, holds a working position as senior scientist at the Division of Endocrinology and Nuclear Medicine at the Medical University Graz. After a postdoctoral stay at the Technical University of Graz he has scientifically worked in the field of continuous glucose monitoring and body interfaces, contributing to the project CLINICIP (FP6-IP) with the objective to develop a metabolic control system for patients at an intensive care unit.

Stefan Korsatko: MD, is consultant for general medicine and responsible for strategic planning and coordination of clinical and experimental trials within the division of Endocrinology and Nuclear Medicine at Medical University Graz. Recent scientific contributions include: (Korsatko2008).

Partner 11: Joanneum Research, Institute of Medical Technologies and Health Management [MSG]

The Institute of Medical Technologies and Health Management (MSG) – located in Graz, Austria – is an institute of the non-profit technology centre JOANNEUM RESEARCH (JR). JR is concentrating on

applied R&D with a highly qualified staff of more than 400 people. JR has provided the necessary know-how and manpower for setting up and running national competence centres as well as numerous large international projects including R&D activities on a European level, co-ordinating and participating in several IST/ICT projects in FP4, FP5, FP6 and FP7. The content spectrum of MSG reaches from technology development in the medical domain to organizational and public health concepts and software development for the healthcare system. With a strong background in the combination of classical information systems, digital media and communication technologies, health technology assessment, data management and quality of care in the field of diabetes and biostatistics, MSG develops tailored applications for regional and national disease management programmes, patient care and epidemiology. MSG has strong experience in workflow modelling and implementation of information systems in healthcare for administration, decision support, information retrieval, quality management and interoperability.

In close cooperation with local health authorities MSG works on the improvement of administrative and clinical processes in medical care, patient-oriented care and the optimisation of data management. MSG performs cost analyses and evaluations of health care interventions. MSG has developed the information system for a nation-wide implementation of Disease Management in Austria und currently works on the implementation of the Styrian Health Information System – GeISt.

MSG will mainly contribute as work package leader of WP 6 Integrative Risk Assessment and Feedback. This WP contains the development of integrative tools for analysis and correlation of the multi-parametric data with established biomedical knowledge and expertise to derive clinically relevant and useful information.

Key persons involved in the REACTION project:

Peter Beck MSc: studied Computer Science "Telematics" in Graz, Austria and Stockholm, Sweden and graduated in 2000. He has 9 years working experience in health management research, design and development of medical informatics systems, service oriented architecture and project management. Peter Beck is head of medical informatics and health management departments of the MSG.

Ivo Rakovac, PhD: obtained PhD in Computer Science ("Telematics") in Graz, Austria. He has 9 years of research experience in the fields of medical informatics, quality of diabetes care, medical data management and biostatistics.

Louise Schmidt, MSc: awarded BSc from University of Bristol (economics and sociology) and Masters degree from Department of Public Health and Primary Care at University of Oxford (2002). She has several years experience in health services research, particularly in the areas of outcomes measurement, health economics and health technology assessment.

Stephan Spat, MSc: studied "Technical Mathematics" in Graz, and specialized in knowledge management and information retrieval. He has 5 years of working experience in the fields of knowledge management and biostatistics.

Partner 12: Chorleywood Health Centre [CHC]

The Chorleywood Health Centre was established in the 1920s and has been serving the community in Chorleywood and its surrounding villages in Hertfordshire and Buckinghamshire ever since. The purpose-built surgery was opened in 1997 and provides comprehensive general medical services including treatment and prevention of illness, health promotion and screening services. We are active in medical and nursing research, training and education.

The practice works within the National Health Service and is a member of the Watford and Three Rivers Primary Care Trust who manage the provision of general practice in the area.

UBRUN is very closely associated with CHC, which will bring its expertise as one of the foremost centres for telemedicine research. CHC will provide expert medical advice on chronic disease management and conduct trials of outpatient applications and devices developed within the project in a primary care setting.

Key persons involved in the REACTION project:

Professor Russell Wynn Jones: graduated from Cardiff in 1971 and after various junior hospital posts, entered general practice in 1977. He is senior partner of the Chorleywood Health Centre in Hertfordshire and has an associate chair in the Department of Information Systems and Computing in nearby Brunel University. His continuing involvement in the application of technologies to healthcare grew from an interest in computerised electrocardiography when he was an honorary research fellow in cardiology at St. Mary's Hospital and in occupational medicine the London School of Hygiene and Tropical Medicine, London. It was at that time that the partnership developed with Dr Malcolm Clarke – a research student then at Imperial College. Dr Jones has collaborated on AIDMAN, an EU funded project that led to the present work, and was a collaborator on three further EU projects, ProEHTEL, Telecare, and E-Vital. He is a former chair and present member of the Hertfordshire LREC; until recent changes he was chair of the Hertfordshire CHD implementation group; cardiology, primary care collaborative, and R&D lead on the Watford & 3Rivers PCT executive and now involved in practice based commissioning; member of the Hertfordshire LMC; chairman of the UKeHealth Association; and a RCGP assessor of research practices and member of the PCRTA management committee.

Partner 13: Department of Information Systems and Computing, Brunel University [UBRUN]

The Department of Information Systems and Computing at Brunel University is one of the largest departments of its type in the UK and members of the Department were awarded a rating of '5' in the last Research Assessment Exercise (RAE).

The vision of UBRUN is to be one of the best centres of excellence for research in the exploitation, development and use of advanced information technologies by individuals within organisations and the society. The department is particularly known for three key areas underlying this vision: advanced information technology, interaction between human and computer, and information systems. There is a critical mass within each area that makes significant progress on its own, and importantly, the synergy and interaction between the three areas have enabled fundamentally challenging issues across traditional boundaries to be addressed in an interdisciplinary way.

In the REACTION project UBRUN will provide expertise in telemedicine, networks and system integration. It will use the recently established MATCH centre, a research establishment that provides rapid evaluation techniques for medical devices in its recently built telemedicine laboratory. It will also use its specialist telemedicine laboratory to conduct the controlled laboratory measurements for performance in simulated telemedicine environments.

Regarding expertise on device safety, UBRUN have been participating in the development of "BS EN ISO/IEC 80001-1 Application of risk management for IT-networks incorporating medical devices Part 1: Roles, responsibilities and activities", and "ASTM F29.21 Integrating the Clinical Environment". Furthermore, clinical risk assessment is made within each of the IEEE 11073 device standards towards which UBRUN has contributed.

Key persons involved in the REACTION project:

Malcolm Clarke: is a Senior Lecturer in telemedicine and eHealth Systems in the Department of Information Systems and Computing, Brunel University. He gained his PhD in medical engineering at Imperial College in 1984, developing and using a computerised 40 lead ECG acquisition system for total body surface potential mapping in ECG stress exercise testing. He then developed an ultrasound system for intra-arterial scanning. He moved to Brunel University in 1989 where he developed and led a Master's programme for data communications until 1999. He recently developed the first Master's programme in Telemedicine and eHealth Systems. He is currently

involved in two European funded research projects, Telecare and eVital. Telecare is developing small devices to allow continuous ambulatory monitoring in the community, with alarms and data being transmitted wirelessly to a monitoring centre. eVital investigates the services to support monitoring in the community, including the organisation and role of each of the key players in primary care to manage such a service. He is chairman of the American Telemedicine Association Special Interest Group in Technology and is on CEN and ISO committees working on standards for medical devices. Dr Clarke has a unique combination of expertise in communications, engineering and systems design with experience in the medical field for 20 years.

Additionally, Brunel University will collaborate with Dr Rowan Hillson, at Hillingdon Hospital, and who is the UK "diabetes tsar", ie she advises DoH and UK government on diabetes policy.

Partner 14: Vrije Universiteit Brussel [VUB]

The Vrije Universiteit Brussel (VUB) interdisciplinary Research Group on Law Science Technology & Society (LSTS) was founded in November 2003, and is devoted to analytical, theoretical and prospective research into the relationships between law, science, technology and society. The research group focuses on legal issues and questions and counts 10-15 researchers, mostly with a legal background. LSTS senior members teach in different legal disciplines and different universities both at graduate and post-graduate level. LSTS has laid a strong focus upon legal aspects of information technologies (e.g. data protection, privacy, copyright), as well as upon more reflexive aspects of the relationships between law and technological development.

LSTS has participated as partner and/or coordinator in the following research projects: FIDIS: The future of identity in information society, a FP6 Network of Excellence (NoE); SWAMI: Safeguards in a world of ambient intelligence, a FP6 Specific Support Action (SSA); REFGOV: Reflexive Governance in the Public Interest, a FP6 Integrated Project (IP), in close cooperation with VUB's Institute for European Studies (IES); SENIOR, social ethical and privacy needs in ICT for older people: a dialogue roadmap, a FP7 Support Action which aims to provide a systematic assessment of the social, ethical, and privacy issues involved in ICT and Ageing; and SPICE: Service Platform for Innovative Communication Environment, a FP6 IP, in close cooperation with VUB's department of communication sciences. Other projects in which LSTS has/is been involved include: FLEmish E-publishing Trends (FLEET), an interdisciplinary research project granted by the Institute for the Promotion of Innovation by Science and Technology in Flanders, IWT-SBO; International Interuniversity Attraction Poles (IAP) Phase V.16 research project The loyalties of knowledge: The positions and responsibilities of the sciences and of scientists in a democratic constitutional state, and, more recently, Law and automatic computing. A mutual transformation process, a Geconcerteerde OnderzoeksActie (GOA) Concerted Research Program (CRP) funded by the Flemish Government and the VUB-research Council.
- LSTS was in charge of the legal aspects of the Prituis - tender project : Privacy and Trust in the Ubiquitous Information Society – Analysis of the impact of convergent and pervasive information and communication technologies on privacy and data protection and needs and options for development of the legal framework (Reference: SMART No. 2007/0011)
- five LSTS members are experts in the COST Action (IS0807) Living in Surveillance Societies (LiSS) which a European research programme designed to increase and deepen knowledge about living and working in the surveillance age. Gutwirth is member of this COST-action's Management Committee

Key persons involved in the REACTION project:

Paul De Hert: is a core member of LSTS. He currently holds the chair of Human Rights, Legal theory, (European and Constitutional) Criminal Law of the VUB, where he also leads the Research Group on Human Rights (HUMR). Additionally, he is an associated-professor at the internationally renowned Tilburg Institute of Law and Technology at Tilburg University (TILT) and is generally involved in national and international legal or multidisciplinary projects about issues such as ambient intelligence, identity, service platforms, profiling, data protection, intellectual property rights, etc, in which he notably provides for fundamental insights with regards to participatory Technology Assessment (pTA), accountability and transparency, the singularity of legal regulation, human rights

and human dignity. He has studied law, philosophy and religious sciences, defended a Doctorate in Law at the VUB, published several books and carried out research for the Flemish Funds for Scientific Research, the Belgian Justice Department, the Department of Interior Affairs and the Brussels University Research Council.

Serge Gutwirth: is a professor of human rights, legal theory, comparative law and legal research at the Faculty of Law and Criminology of the Vrije Universiteit Brussel (VUB), where he studied law, criminology and also obtained a post-graduate degree in technology and science studies. He also holds a part-time position of lecturer at the Faculty of law of the Erasmus University Rotterdam where he teaches philosophy of law. Since October 2003 Gutwirth is holder of a 10 year research fellowship in the framework of the VUB-Research contingent for his project 'Sciences and the democratic constitutional state: a mutual transformation process'. Gutwirth founded and still chairs the VUB-Research group Law Science Technology & Society. He publishes widely in Dutch French and English. Currently, Serge Gutwirth is particularly interested both in technical legal issues raised by technology (particularly in the field of data protection and privacy) and in more generic issues related to the articulation of law, sciences, technologies and societies.

Eugenio Mantovani: graduated in law at the University of Trento, Italy, and obtained a Master in International and Comparative Law (LL.M.) from the Vrije Universiteit Brussel. He is currently working at the Vrije Universiteit Brussel as a PhD student and as a researcher for LSTS in the EU funded SENIOR project. As a PhD student, his research focuses on human rights and the elderly, digital divide and positive obligations. He is also interested in the philosophy of international law, international relations, and legal traditions.

Partner 15: Bayer Technology Services GmbH [BTS]

Bayer Technology Services GmbH offers fully-integrated solutions along the life cycle of chemical/pharmaceutical plants – from development through engineering and construction to process optimization for existing plants. BTS also offers a broad range of products and services for all stages of diagnostics and drug research and development. Examples include nanophosphors, the pharmacokinetics simulation software PK-Sim®, and data-mining and modeling technologies. The Bayer subsidiary employs nearly 2,600 experts worldwide at its headquarters in Leverkusen and other German locations, as well as in regional offices in Baytown, Texas, USA; Antwerp, Belgium; Mexico City, Mexico; Mumbai, India; and Shanghai, People's Republic of China. 2007 sales totalled approx. EUR 400 million.

Bayer started the development of proprietary in-silico models of pharmacokinetic processes in the mid 1980s. After the establishment of Bayer Technology Services GmbH in 2003 the physiology-based biological modelling software suite comprising PK-Sim® and MoBi® was released and offered to the external market. Since then the activities of the Competence Center Systems Biology have been extended to modelling of all levels of biological systems ranging from molecular interaction networks to whole-body models of disease progression and pharmacotherapy. A special focus is on individualization of mechanistic models including the in-silico representation of pathologies like renal impairment, cirrhosis, cystic fibrosis and type I and II diabetes. Bayer Technology Services is offering consultancy to pharmaceutical companies and biotechs and is successfully applying its modelling expertise to clinical trial design and therapy individualization. The competence center Systems Biology is a partner in several publicly funded consortia aiming at the optimization of pharmacotherapy and the non-invasive and invasive assessment of biomarkers including the German HepatoSys initiative and the ForSys partner program (http://www.systems-biology.com/refs/public-funding.html)and has filed several patent applications in the field of open- and closed-loop control systems for pharmacotherapy (WO/2005/033334, DE102005028080A1, WO/2005/116854, EP1722839, WO/2007/147539).

Key persons involved in the REACTION project:

Jörg Lippert: studied physics at Aachen and Paris and received his PhD in computational neuroscience at the University of Technology Aachen. At Bayer he worked on statistical learning and data mining before he became responsible for the strategic projects in the area of computational

systems biology. Since its establishment Jörg Lippert is heading the competence center Systems Biology at Bayer Technology Services (www.systems-biology.com) with its 20 scientists and he heads the global competence field Biology & Fermentation. Jörg Lippert's responsibilities include the systems biology and PBPK modelling software platform consisting of PK-Sim® and MoBi® as well as consultancy services in the area of systems biology. He has gained experience in the application of computational modelling in more than hundred application projects ranging from discovery to late clinical development together with more than a dozen of pharmaceutical companies and biotech partners.

Hans-Ulrich Siegmund: studied chemistry and received his Ph.D. in Biochemistry at the Universität zu Köln. After a postdoctoral training at the U.S. National Institutes of Health in Bethesda (Maryland), he joined Bayer AG and worked on biosensors. He took part in the development of the biosensor product "Ascensia Dex" (Glucometer), and did scouting work on continuous and non-invasive blood sugar monitoring. Afterwards, he led a project to establish a proteomics platform for several business groups of Bayer. After his transfer to Bayer Healthcare, he provided target proteins for high throughput screening. He then joined computational biology at Bayer Technology Services where he currently works on modelling biological processes, primarily centered around the blood coagulation system.

Stefan Willmann: studied physics at the Universities of Düsseldorf and Connecticut and received his PhD in medical laser physics from the University of Düsseldorf. In the Biophysics group of Bayers Central Research he developed physiologically-based pharmacokinetic simulation models for pharmaceutical and agrochemical applications and was responsible for the development of the commercial software tool PK-Sim. Since the establishment of the competence center Systems Biology at Bayer Technology Services, he has worked as a consultant for numerous pharma and biotech companies in the area of pharmacokinetics and systems biology. His scientific record includes more than 30 publications in peer-reviewed journals and 10 patent applications. Since 2008 Stefan Willmann is also teaching graduate courses in clinical pharmacy at the University of Düsseldorf.

Partner 16: Solianis Monitoring AG [SOLIANIS]

Solianis Holding AG is a medical devices company developing a non-invasive Continuous Glucose Monitor (CGM) for self-monitoring patients with diabetes, within the broader range of physiological monitoring. Solianis was incorporated in May 2005, and it is funded by private investors and the Pioneer Fund of the Cantonal Bank of Zürich.

Solianis' non-invasive continuous glucose monitor employs Impedance Spectroscopy to track changes in the glucose levels and the effect of changing glucose levels in blood, cells and interstitial fluid. In a clinical-experimental trial, conducted in cooperation with the University Hospital Zurich, Solianis has shown that its multi-sensor technology tracks glucose changes in patients with diabetes as well as healthy subjects. In these trials, the subjects have gone through glucose challenges under various conditions designed to test the impact of the additional effects, thus simulating real life conditions. The results of these trials with healthy subjects as well as patients with diabetes look exciting – proof of concept is reached.

Key persons involved in the REACTION project:

Dr. Andreas Caduff: has a BSc degree in chemistry, an MSc degree in biotechnology and a PhD in biophysics/biosensors. He has been a driving force in the industrial development of non-invasive sensor technology for physiological monitoring, in particular glucose monitoring techniques and involved physiological processes, combining the expertise in various fields relevant to the research and development work at Solianis. Presently, he holds the position of Chief Technology Officer.

Dr. Mark Talary: is Director of Research and has a BEng/MEng in Electronic Engineering and PhD degree in Biophysics, with an extensive knowledge of the influence of electric fields on biological materials. His previous work in the field of life sciences includes gaining expertise at a bio-tech start-up company in Silicon Valley.

Hans-Joachim Krebs: is Director Development & Manufacturing and has a MEng in Electronic Engineering and a long-standing experience in research and development of medical device technology, e.g. as head of development for digital x-ray systems and sophisticated hospital equipment. Previously he worked with KW+P as a consultant focusing on the coordination of international R&D activities, the optimization of manufacturing processes and the implementation of R&D concepts into final products.

B.2.3 Consortium as a whole

The REACTION Consortium represents an extraordinary partnership of highly multidisciplinary industrial, academics and technology providers; experts in sensors, microelectronics and large scale manufacturing of medical devices; software companies, HIS integrators, network specialists and operators; experts on security; and last, but not least, medical and clinical experts, pharmaceutical companies, sociologist, lawyers and economists. Project partners, besides offering scientific capacity, experiences and skills to successful perform the project's tasks also ensure that remarkable advancement of the state-of-the-art in intelligent multi-parametric diabetes monitoring and management with closed-loop feedback applications can be achieved. Further, the number of industrial partners, including technology providers, assures a real professional orientation towards exploitation of the project results.

The REACTION consortium consists of 16 organisations from nine different countries (Spain, United Kingdom, Germany, Switzerland, Belgium, Denmark, Sweden, Hungary, and Greece representing a wide taste of Europe in terms of population, culture and economic power including partners from North, Central and South Europe. The consortium unifies a number of research groups that have a world leading position in their respective fields. All of the partners have been involved in international R&D projects before. Most of the partners have worked together in one or more prior projects and will bring their collective knowledge gained in these projects into REACTION.

Consortium strengths

The REACTION Consortium presents profound strengths in several respects. The Consortium brings together strong research groups with a background in fundamental academic research, academic and independent research labs in the field of applied science, and R&D laboratories of large commercial companies. Several SMEs will be deeply involved in both the R&D and the deployment and exploitation of the results of the project. Organisation with strong ties to relevant standardisation bodies ensures direct channels of communication and influence.

The partners in the consortium cover widely different sectors which will ensure that the project will provide highly relevant and directly applicable results of major economical and societal impact. In particular:

- In the sensor area, leading industrial companies and research organisations with high innovation capabilities will ensure that innovative solutions are developed and utilised and that the results will be exploited in the academic area. IMM is a world recognised leader in development and fabrication of micro-devices. IMM have in-house methods available for manufacturing micro structured devices for CGM and IV pumps as well as broader lab-on-a-chip devices. DELTA is the leading institute in Scandinavia for microelectronics and sensor miniaturisation. They have a corporation with Coloplast, the world's largest manufacturer of Ostomy Care products and leading the development in medical adhesives plaster technology. SOLIANIS is a rising star in the medical device business for CGM with one of the most promising technological inventions in this area.
- Software providers ATOS, CNET, ALL, FORTH-ICS and IN-JET will ensure that results from other EU projects, notably the eu-DOMAIN project and the Hydra middleware project will be incorporated into the REACTION architecture, in particular semantic Web Services Architecture, dynamic ontologies and interoperability of HIS applications. These partners are well known for their expertise in ubiquitous computing, software architecture, XML based content and web service applications, semantic annotation, knowledge management and system integration. FORTH-ICS is also well known for its long-term scientific achievements in

the area of eHealth, health telematics, biomedical decision support systems, and biomedical device technologies
- Biomedical modelling experts from BTS, ALL and MSG will secure that integrative risk assessment based on multi-parametric health status monitoring and biomedical models can improve the health monitoring and feedback objectives.
- In networks and infrastructure, FORTHNET is the leading convergent Internet Service Provider in Greece and has extensive research in networks infrastructure and security related issues including smart home environments.
- Security experts from FHG-SIT and ATOS will complement other partners with their expertise in security analysis and distributed security and trust models.
- The medical partners are crucial for the successful outcome and deployability of the REACTION platform. The medical partners in REACTION are all prestigious academic research institutions, with world recognised expertise in their fields. The division of Endocrinology and Nuclear Medicine at the Medical University of Graz is a well known leader in areas such as overall metabolic control, pathophysiology of late complications, cardiovascular endocrinology, vascular biology and on the investigation of new pharmaceutical approaches for the treatment of diabetes mellitus. Their work on glycaemic monitoring and control in ICU has received world recognition. CHC is one of the foremost UK centres for telemedicine research and has expert medical expertise on chronic disease management and outpatient applications and devices in the primary care setting. Both clinical partners are intimately working with their respective technology providers: MSG and UBRUN, who are experts in risk and patient safety, healthcare usability and validation methods, which will be used in the field trials.
- As research has shown, the deployability of closed-loop monitoring and feedback applications such as REACTION depend entirely on the social compatibility of the solutions in relation to user acceptance and organisational, regulatory and economic compatibility with existing healthcare systems. To this end, the Consortium includes European-wide recognised researchers from VUB, with experts in ethics, socio-economics and legal frameworks. They provide excellent expertise in the area of socio-economic framework and have close connections with regulatory bodies in Belgium and abroad. IN-JET and ATOS, with their documented experience in business modelling and healthcare economics, will complement this group.

Since all partners have considerable experience in large European projects, they know, respect and trust each other. This will facilitate a smooth start of the project and ensure that the partners will collaborate, efficiently and in a positive atmosphere throughout the project period.

Multidisciplinary skills provided by partners

The following table shows roles and functions of each participant in the Consortium and show how the partners are suited for the roles assigned to them:

Participant	Type	Main functions	Value to the Consortium
(1) Atos Origin ATOS	Industrial Company (ES)	Project management & project administration Service oriented Architecture and software design Interoperability of Data Management subsystem with backend HIS systems Security analysis	Vast experienced EU project coordinator. Large knowledge in HIS and interoperability. Strong skills in decision support in clinical systems. Large pool of experts in software architecture, design and security.
(2) CNet Svenska (CNET)	Industrial Company SME (SE)	System architecture SoA and ontology modelling Hydra middleware implementation General service orchestration Rule-based orchestration of services and event handling Workflow integration Backend integration Technical management	Extensive experience in XML based content and web service application development. Substantial knowledge in web-based meta data creation and model based architectures. Main link to the Hydra project Experience in interactive environments for geographically distributed organisations. Many years of expertise in managing technical research projects at EU and company level.
(3) DELTA (DELTA)	Research Institution (DK)	Design. development and implementation of sensors for BAN and PAN networks Development of ePatch technologies and subsystems	Leading in body sensor development. Vast experience in application specific microelectronics (ASIC). Pioneered ePatch technology and micro sensor applications.
(4) Institut für Mikrotechnik Mainz (IMM)	Research Institution (DE)	CGM IR sensor design, packaging and manufacturing Design of fluid control pump systems for adaption to IV pumps	Development of optical sensors for bio-chemical applications Manufacturing capabilities, in-house precision manufacturing facilities Large expertise in fluid control (e.g. pumps, valves) Expertise in electrode design and packaging including lab-on-a-chip
(5) FORTH-ICS (FORTH-ICS)	Research Institution (GR)	Development and integration of biomedical devices at PAN level Semantic annotation Development of risk assessment models and MIS integration Integration and implementation of platform	Expert experience in algorithms and multi-parametric medical informatics. Recognised research in the areas of machine learning, data mining, networks biomedical decision support. Has build AmI facility to be used as test-bed for implementation and testing.
(6) Fraunhofer SIT (FHG-SIT)	Research Institution (DE)	Trust, security, and identity management concepts and design Model simulation and evaluation specific to security aspects. Virtualisation specific to security aspects.	Pioneer in IT-Security. Developer of security system for the German health card. Outstanding experience in design, modelling, and realisation of holistic security concepts and privacy enhancing technologies.

Participant	Type	Main functions	Value to the Consortium
(7) FORTHNET (FORTHNET)	Industrial Company (GR)	Provide server and network infrastructure Integrate network and edge technologies (PAN/BAN) Design core server services Implement service execution and security infrastructure	Leading provider of broadband network services and convergent services provider. Vast experience in core server technology. Expert in security management systems.
(8) In-JeT ApS (IN-JET)	Industrial Company SME (DK)	Scenario thinking and user requirements engineering process Concept development, Vision Owner and chair of Technical Board Leading in business modelling and contributor to ethical and social analysis Dissemination coordination	Substantial experience in user oriented requirement specifications based on Scenario Thinking. Documented expertise in system concepts and integration related to AmI systems for healthcare / HIS. Wide experience in business modelling, business cases and ethical and social analysis of ICT. Strong communication skills.
(9) Applied Logic Laboratory (ALL)	Industrial Company SME (HU)	Data structures and ontologies Diabetes Management system Models for risk assessment	Extensive knowledge in ontologies. Long experience in clinical management systems Strong knowledge in mathematical modelling
(10) Medizinische Universität Graz (MUG)	University Hospital (AT)	Requirements, clinical testing and validation of platform in general ward domain Clinical Manager Assessment of clinical needs for TGC and AGC. Performance of randomized clinical field trials	World known reputation of the work in TGC in ICU patients. Opinion leader in new pharmaceutical approaches for the treatment of diabetes. General internal medicine ward with concentration on endocrine diseases and diabetes mellitus. Large diabetes outpatient clinic.
(11) Joanneum Research, Institute of Medical Technologies and Health Management (MSG)	Research Institution (AT)	Information processing and representation Integrative risk assessment Context management	Leader in medical information systems and processing Strong experience in data management and representation. Experts in biomedical modelling Technology partner for MUG. Development of Austrian national diabetes disease management programme together with MUG.
(12) Chorleywood Health Centre (CHC)	Hospital (UK)	Requirements, clinical testing and validation of demonstration platform in outpatient domain Expert medical advice on chronic disease management	Chair of UK association of telemedicine Large outpatient population of diabetes patients Leader in innovative pathway monitoring

Participant	Type	Main functions	Value to the Consortium
(13) Brunel University (UBRUN)	University (UK)	Device risk assessment and patient safety Integration and of context aware environments for outpatients Design of data communication Leading in standardisation work Medical Engineering Manager	Leading position in advanced information technology, interaction between human and computer, and information systems. Large expertise in telemedicine, networks and system integration, Member of several standardisation working groups.
(14) Vrije Universiteit Brussel (VUB)	University (BE)	Legal and regulatory studies on patient rights, liability and IPR Analyse ethical and social dimension in healthcare	World class expertise in Law, Science, Technology and Society cross field. Strong expertise in analysis of technology in sociology, ethics and philosophy terms
(15) Solianis Monitoring AG (SOLIANIS)	Industrial Company SME (CH)	CGM Impedance Spectroscopy sensor design and manufacturing	Leading edge technology provider in CGM sensor development and manufacturing
(16) Bayer Technology Services GmbH (BTS)	Industrial Company (DE)	Physiology-based concepts and models Hybrid modelling and data analysis based using mechanistic kernels and machine learning Definition of data model requirements	Largest mechanistic modelling and simulation group in pharmaceutical industry Strong expertise in data mining and software development. Developer of software standards in physiology-based modelling

Table 5 Partners functions and complementary value to the Consortium

Industrial involvement and SME's

The consortium has a strong industrial representation with seven industrial partners. The industrial companies represent various business sectors and activities, but the all have a direct strategic and commercial interest in pursuing the REACTION project.

ATOS, the coordinator of the project and large contributor of security analysis is also a very large industrial company. BTS is part of one of the world's largest chemical and pharmaceutical giants with strong market position in diabetes. FORTHNET has more than 1 million customers for broadband internet access. The other industrial partners are all innovative SME technology providers, who will provide leading technology developments in their respective areas of software, modelling and device development and manufacturing. They will greatly benefit from cooperation with the large companies, research institutes, universities and healthcare providers, in order to secure rapid uptake of their new technologies.

The Consortium thus represents a true involvement from SMEs and industrial companies with an ideal combination of market skills and commercial experience. The Consortium is also well suited for rapid exploiting the results across Europe.

Academic and medical involvement

There are five technological research institutions and two medical research institutions (a hospital and a university hospital) as well as a national healthcare authority involved.

For the research institutions, the REACTION project provides excellent opportunities for participating in multidisciplinary research work and creates excellent networks of industrial partners for uptake of their innovative sensor, healthcare and security technologies. The industrial and medical expertise in

the project assures a professional, experienced and knowledgably platform for direct application of their research results.

The medical institutions are involved to get further insight in medical and clinical opportunities by using emerging and disruptive ICT tools and services as well as new, technology supported case management. For the clinical partners as well as the national health provider, REACTION provides unique opportunities to study new ways of managing medical knowledge and how it can be transferred to clinical practice. Another pharmaceutical company is planning to join in M12.

The pair composed by Chorleywood Health Centre and Brunel University has a long standing expertise in clinical and preclinical diabetes research. They also have experience on operation of a diabetes outpatient clinic and diabetic/endocrinological ward. They have around 6.000 patients with 170 registered as diabetic.

They also count on one stop diabetic clinic (podiatry, retinopathy, blood) for primary care and also with in home monitoring pilot for diabetes management.

The out-patient diabetic expertise for the involved medical partners could be showed as the collaborations to be created with different experts in the field. To this respect, **Brunel** is to collaborate with Dr Rowan Hillson, diabetes consultant at Hillingdon Hospital, and who is currently the "diabetes tsar", and provides top level advice to the government and Department of Health on diabetes management. Expertise includes knowledge of in-hospital risks and management and care of complex and unstable diabetes in the community. For **Chorleywood** Dr Jones is senior partner at Chorleywood Health Centre and has been practicing primary care physician for more than 30 years, with extensive experience of managing diabetic patients. The practice has recently completed a large trial on diabetes management using home based monitoring demonstrating significant improvement in blood glucose and Hb1Ac level.

Publication: J Fursse, M Clarke, R Jones. Early Experiences of the Use of Remote Patient Monitoring for the Long Term Management of Chronic Disease. Journal of Telemedicine & Telecare 2008; 14; 122-4.

Medical University Graz, together with Joanneum Research, has a long standing experience in clinical and pre clinical diabetes research and clinical care. At the MUG, there is a 35 bed specialized endocrinology and nuclear medicine ward with special focus on diabetes mellitus. MUG operates a large outpatient diabetes clinic, with more than 8000 outpatient contacts per year and provides diabetes related consultations to all departments of the Medical University Graz, with more than 80,000 inpatient admissions yearly. Furthermore, MUG operates a large clinical research centre (www.healthsite.at) with special focus on diabetes. MUG and MSG employees are recognized experts in field of diabetes research and clinical care, with over 100 peer reviewed publications in the fields of diabetes, cardiovascular diseases and impaired glucose tolerance, and serve as peer reviewers for numerous diabetes medical journals. Several employees are members of the Cochrane Collaboration and the European Association for Study of Diabetes. They were also involved in the design of Austrian national disease management programme for Diabetes Mellitus, and serve as consultants to national ministry of health. Prof. Thomas Pieber was associate editor of the Journal *Diabetic Medicine*, was president of Austrian Diabetes Association, and was involved in the development of numerous national and international diabetes guidelines. He organized numerous diabetes conferences and post graduate education courses and is one of Europe most recognized diabetes experts.

The soft issues such as ethical and socio-economic challenges, privacy, patient safety, liability and IPR related to deployment of monitoring services are seriously studied by the scholars at the academic and research level in cooperation with security and healthcare experts. All partners in this regime benefit from working together on the issues and with real users.

Complementarity

The consortium members cover a wide range of research disciplines, which will be tightly integrated by virtue of the collaboration in the project.

Together, the members of the consortium cover all skills and expertise, as well as the critical mass that are required to achieve the objectives of the project. At the same time, the project partners complement each other extraordinarily well and jointly they form a multidisciplinary project team with excellent complementarity. The Consortium partners are thus able to provide precisely the required skills and expertise for performing the work while eliminating costly redundancies.
The following table shows a summary of the skills and experiences required for successful execution of the REACTION project and who provides these skills.

Project stages	Required knowledge	Provider(s)
Requirements specifications (WP2)	Scenario Thinking User-centric requirements specifications engineering	IN-JET FORTH-ICS
Multi-parametric sensors. monitoring and feedback (WP3)	Medical sensor technology Low power sensors and BSN Skin adhesive technologies Precise micromanufacturing Optical and MEMS sensor technologies IR sensor technologies IS sensor technologies	DELTA - - IMM - - SOLIANIS
Data management and service orchestration (WP4)	SoA and dynamic ontologies Semantic resolution Workflows and web service orchestration Data structuers and ontologies	CNET - ATOS ALL
Network management and service execution (WP5)	PAN and backend networs Network service access Core server technologies	FORTHNET - -
Integrative risk assessment and health profiling (WP6)	Health Information System integration Knowledge discovery Predictive modelling Biomedical models	MSG FORTH-ICS ALL BTS
Security, privacy and safety (WP7)	Security requirements analysis Concepts of trust Patient empowerment and virtualisation Device risk assessment and patient safety	ATOS FHG-SIT - UBRUN
Clinical Practice (WP8)	Inhospital glucoses control Chronic disease management (diabetes)	MUG CHC
Socio-economic framework (WP9)	Ethical and social issues Regulatory framework Healthcare economics	VUB - IN-JET
Implementation and validation (WP10)	Implementation and testbed Clinical evaluation, inhospital Clinical evaluation, outpatient	FORTH-ICS MUG CHC
Project management and process (WP1, WP2)	Management of large collaborative international projects Technical management Requirements engineering process	ATOS - CNET IN-JET

Table 6 Required knowledge and partner match.

Clustering

The REACTION consortium has very strong ties to a number of EU projects relevant for the work to be undertaken. CNET, IN-JET and FHG-SIT are prominent partners of the Hydra project. MSG is coordinator of the CLINICIP. VUB and IN-JET are partners in the SENIOR support action. CNET, IN-JET and FORTH-ICS were partners in eu-DOMAIN. MSG is technical coordinator in the CLINCIP project. The high level of clustering in other EU projects not only secures a high degree of cooperative spirit, but also substantial savings in project costs due to effective knowledge transfer.

IP integration accomplishments

An IP instrument project must accomplish different types of integration. Vertical integration of the full "value-chain" of stakeholders from those involved in knowledge production through to technology development, and into practical healthcare provisioning. In REACTION, all stakeholders

in the value chain are involved from technology knowledge and manufacturing over medical research to healthcare providers and regulators. Horizontal integration must be achieved with a range of multidisciplinary activities. The Consortium is also highly multidisciplinary; integrating research activities from across the full research spectrum (ICT, sensors and medical and supplemented with other relevant types of activities (social, economic).

Project management skills

The co-ordination of the REACTION project is the responsibility of Lydia Montandon from ATOS, who has extensive experience and skills in the coordination and operational project management of large collaborative research projects in both the public and private sectors, from a national and pan-European perspective. Lydia Montandon holds a Master of Science in Learning and Teaching Technologies from the University of Geneva, Switzerland. She has 12 years of experience in managing RTD projects in the fields of Technology-enhanced Learning, eInclusion, International Cooperation, including Integrated Projects. She is currently coordinating the work various Atos Research and Innovation units with activities in eInclusion, eHealth, eLearning, and International Cooperation.

The technical management has been vested with Peter Rosengren from CNET, who has a degree of Licentiate of Technology (PhD) in computer science from the Royal Institute of Technology, Stockholm. He has been involved as a project manager for projects in application domains like education and e-learning, media and publishing, building and construction. He was the technical coordinator of the Multimedia Broker project (IE2093) within the FP 4 for R&D in Information Engineering and is presently Technical Manager of the FP6 IP project Hydra. Prior to founding CNET he was a research director at Swedish Institute of Systems Development, SISU where he managed the Human Computer Interaction research group and the research group Interaction & Communication.

The Clinical Management has been vested with Dr. Thomas Pieber, MD, head of the Division of Endocrinology and Nuclear Medicine at MUG. From 2005 to 2008 he has been the Medical Director of the University Hospital Graz and currently head of a multidisciplinary team of 140 employees. Prof. Pieber is one of the world's leading experts in in-hospital management of diabetes and TGC in ICU.
The Medical Engineering Management has been vested with Dr. Malcolm Clarke from UBRUN, who has a PhD in Medical Engineering from Imperial College and is currently head of the BRIGHT research group for health technology as well as board member of the UK eHealth Association (UKeHA) and the American Telemedicine Association (ATA) and has worked in many EU projects.

Sub-contracting

Subcontracting amounts to €76.250 for the cost of producing audit certificates for the partners.

Another €10,000 has been set aside for arranging trials with an emergency and alarm organisation. The cost will cover alarm handling operations during the course of a couple of months, which has not been deemed to be sufficiently important to warrant the alarm organisation becoming a full member of the consortium.

Subcontracting of healthcare economics and regulatory work for WP2 and WP9 (IN-JET, 25'000 €):
Due to temporary absence of one employee with one of the contractors (IN-JET) the project needs to subcontract a part-time temporary resource for the first six months of the project. The subcontractor should be knowledgeable about the healthcare domain ecosystems, telemonitoring services and national and European regulatory landscape in healthcare. The work will be for a maximum period of 187 hours to be delivered between the start of the project and until 1st July 2009. It is foreseen that the successful subcontractor will be willing to seek permanent employment with the contractor (IN-JET) after the end of the subcontracting period and continue to work on the REACTION project. Applications from subcontractors will be accepted on these terms and the best subcontractor will be awarded the work.

Subcontracting of alarm and crisis management services for WP4 (IN-JET, 10'000 €):
The project needs a subcontractor able to cover the needs for specifying and testing alarm handling and crisis management functionalities in the REACTION platform. During event monitoring of diabetes patients, the REACTION platform will detect dangerous events such as hypoglycaemia, where immediate response from first aid or crisis teams is necessary, often within minutes. The REACTION platform must be able to forward an alarm safely and securely to a crisis management team using the infrastructure which is in place for standard rescue services or social care services (ambulance, fire, home nurse, etc.). In order to specify the alarm signalling protocols and conditions and test the final alarm interface in trials, a professional alarm and crisis management centre is needed for a limited period of time. Therefore bids will be opened to select the most appropriate candidate offering alarm signalling, 7/7 alarm services or home care health services. The subcontractor should allow alarms to be submitted to its monitoring and alarm centre and have its personnel perform pre-described actions, such as those normally prescribed for alarm and rescue services. The subcontractor shall be willing to provide open specifications for the signalling and participate in performance monitoring, evaluation of services and reporting. However, language skills in either German or English will be required. The subcontractor/s will be selected based on the "best value for money", but also based on their interest in supporting/sponsoring projects like REACTION.

New participants

The REACTION Consortium is planning to include Novo Nordisk as a partner in the project in M12. The Multiple Daily Injection (MDI) compliance study was proposed by Novo Nordisk, but for company internal reasons, Novo Nordisk wished to wait to join the consortium until the end of 2010. Consequently, the trial has been planned to take place then and a reserve of efforts has been made in the budget to fund Novo Nordisk when they joint the project as expected in M12. Appropriate funds have been allocated with the responsible partner UBRUN. Novo Nordisk is the only European company that can offer such a device to facilitate accurate and automatic recording of the time and dose of insulin intake. Novo Nordisk can also enhance the dissemination of project results. In the case that Novo Nordisk does not joint the project as partner, an attempt will be made to convince Novo to supply the needed MDI pens and insulin for the trials and participate in the evaluation at their own expense. If this also fails, the trials will be conducted with standard MDI devices and the patient will record time and dose manually and upload data via a smart phone.

The REACTION Consortium Agreement provides a procedure for the termination of a participant's role and the take-on of new participants. The take-on of new participants will be a competitive process whereby the requirements for new participation will be clearly specified.

WP leaders will identify the need for new partners and describe the skills and knowhow needed in the project in a document, which is presented to the Project Board. If the need relates to technical developments in the project, the Technical Manager will be asked to comment on the proposal. If the Project Board decides to invite a new partner to the consortium, the necessary funds need to be raised within the consortium. When all procedures are fulfilled, the Project Coordinator will start the process of finding the new partner based on the exact requirements approved by the Project Board. The successful candidate must be willing to accept all provisions of and sign the Grant Agreement and the Consortium Agreement. When the procedure is successfully completed, the Project Coordinator forwards the proposal to the Project Officer for approval.

Third country participants

No other countries except EU Member States and Associated States (CH) are involved in the REACTION Consortium.

B.2.4 Resources to be committed

The resources required for performing this project have been budgeted using a bottom-up approach. The budget shows a balanced project, both in terms of efforts and costs, with efficient utilisation of resources, yet sufficient efforts to complete the required tasks successfully.

The project's work plan has been broken down in workpackages, tasks and individual work elements of each task. Each task has been time scheduled in details and each partner's effort has been budgeted in person hours per activity type.

The result of these efforts is a very accurate planning of the partner's efforts needed to complete the project and achieve the objectives. Reference is made to the table of project efforts, which was presented in the section "Summary of staff effort" on page 135.

In order to solve the REACTION challenges, the best actors in Europe have been brought together. The best are not the cheapest, which is reflected in the cost of the REACTION project. With a total budget of €16.3 million, it is somewhat more ambitious than ordinary IP projects. On the other hand, the aim is to, convincingly, bring about the ultimate eHealth monitoring platform where every aspect for a successful implantation in real healthcare systems has been considered and taken into account. REACTION is expected to have massive impact on diabetes care and healthcare delivery efficiency which warrants the large investment.

In order to secure that large public funds are spend cautiously and correctly, a significant, world leading coordinator such as Atos Origin has been chosen to manage the project and at the same time contribute strong technical knowledge about healthcare architectures and interoperability to the consortium.

The consortium has been very carefully put together so that there is no overlap and duplication of resources, as can be seen from Table 5. With an overall resource volume of 1374,5 person months equally spread over 4 years, and with 16 very strong RTD and user partners in the consortium, REACTION undoubtedly has the critical mass required to accomplish its goals. Further, by analysing the way in which the total RTD resources are distributed among the different workpackages and partners, one observes that each workpackage will mobilise the required critical mass required to successful complete its work and reach its objective.

Table 7 shows the distribution of the resources and costs over the different work areas:

Full duration of project	Months	%	Costs	%
WP 1: Project management	86,0	6%	785.835	5%
WP 2: User Centric Requirements Engineering and Validation	85,0	6%	962.525	6%
WP 3: Sensors, Monitoring and Contextualisation	240,5	17%	3.956.944	24%
WP 4: Data Management and Service Orchestration	194,5	14%	2.010.879	12%
WP 5: Network Management and Service Execution	96,0	7%	1.013.112	6%
WP 6: Integrative Risk Assessment and Feedback	145,5	11%	1.681.645	10%
WP 7: Security, Privacy and Safety	84,0	6%	887.174	5%
WP 8: Clinical Practice and Field Trials	135,5	10%	1.473.896	9%
WP 9: Socio-economic Framework	77,5	6%	752.206	5%
WP 10: Platform Implementation	136,0	10%	1.674.158	10%
WP 11: Demonstration	30,0	2%	362.696	2%
WP 12: Dissemination and Exploitation	43,0	3%	468.236	3%
WP 13: Training	21,0	2%	235.710	1%
Total	1374,5		16.265.016	

Table 7 Distribution of efforts and costs

The distribution of efforts demonstrates that the REACTION project is effectively investing the resources in RTD and user related activities. The distribution of costs reflects the fact that different partners have different cost structures, so that distribution of costs is slightly different from the distribution of efforts.

At the partner integration level, the budget shows the very well structured and perfectly integrated resource budget with large and almost equal contributions from the large technology partners, a medium person months contribution from each of the partners in the clinical and application knowledge providers group, and 45-40 person months from each of the specialised technology and knowledge providers.

All partners involved in WP12 Dissemination and Exploitation will reserve a small part of the EC funding (2-3%) for this WP for clustering meetings and requested participation in other events.

Justification of costs

RTD costs

The RTD work requires 1194,5 person months, which is fully justified with the ambitious goals of the project and the many, multidisciplinary aspects being brought into focus in the project. In fact, the efforts needed for realising the very complex and ambitious software infrastructure of REACTION platform is being greatly helped by the large amount of knowledge that can be brought in from other EU projects, in particular from the Hydra, the eu-DOMAIN and the CLINICIP projects, which has helped to keep some of the RTD efforts down.

Still, the bulk of the project work (71,5%) goes into design and development of the REACTION platform (WP2 – 7) and implementation and integration (WP10). Non-ICT development related activities accounts for 15,5% of effort in including clinical trials and medical validation of prototype functionality (9,9%) and socio-economic framework analysis (5,6%).

In relation to work focus, the highly technology oriented WP3 (Sensors, Monitoring and Contextualisation), WP4 (Data Management and Service Orchestration) and WP5 (Network Management and Service Execution) represent a strong resource pool of 531 person months, equivalent of around 10 full time researchers for the full duration of the project. A further 229,5 person months (5 full time persons) is available for integrative risk assessment and security and patient safety. 136 person months (3 full time persons) is available for implementation and integration. This means that the core research team consists of nearly 18 full time researchers and developers.

The medical user functions are equally well equipped to fulfil their roles. Clinical trials and socio-economics experts (WP8-9) are allocated 213 person months corresponding to 4 full time staff.

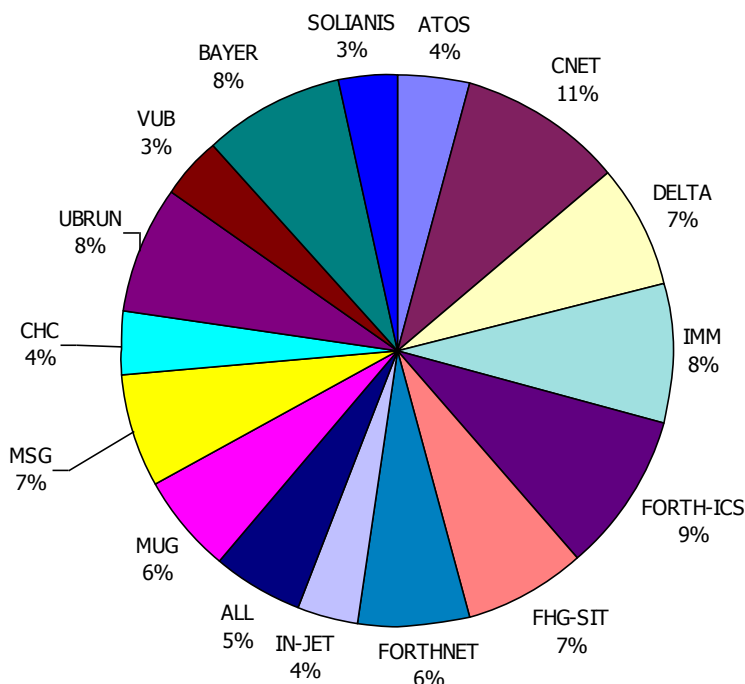The distribution of *RTD* activities on partners is show in Figure 13.

RTD Efforts

Figure 13 RTD efforts per partner

Management and other costs

Although management of such a large consortium, with its complex structure, is not an easy task, total management costs, travel cost and cost of audit certificates, have been kept around 7% of total EU funding. The WP management roles have been strengthened in the management structure, allowing for a lean project administrative and technical management. The management cost for personnel is just 5% of cost reflecting. The total effort for management is 86 person months, or a little less than 2 full time persons.

94 person months, are allocated to demonstration, coordination of dissemination and exploitation, and training. The dissemination activities relate only to coordination activities and actual dissemination, not to the work undertaken to produce the knowledge being disseminated.

Durables

The project has a low budget for durable equipment, because infrastructure equipment will be provided by the partners at no cost to the project. One spectrum analyser and control station will be invested for the GCM sensor production. The investment amount will be €6.500 with depreciations amounting to €4.000.

Consumables

The project has a large budget of €341.506 for consumables. This amount includes €212.497 for precision manufacturing of glucose devices in several runs and sourcing of other devices to be used to validate the REACTION platform in clinical trials. IMM, SOLIANIS and IMM share these costs. A further €98.000 is allocated to actually carry out the trials by CHC and MUG including possible compensation to patients, sourcing of medicine and utensils.

The remaining 31.000€ is planned for various software licences (Matlab licenses), training material, and brochures. The breakdown of consumables per work package is shown in the following table.

WP 1		WP 8	98.000
WP 2	5.000	WP 9	
WP 3	212.500	WP 10	
WP 4	5.000	WP 11	
WP 5		WP 12	9.006
WP 6	10.000	WP 13	
WP 7	2.000	WP 14	
		Total (€)	341.506

Travel costs

The travel costs amount to €425.736, which amounts to 3% of the overall costs. Compared to other international projects of this size it is perceived to be very reasonable, despite 16 partners located from Stockholm to Heraklion. The management travel costs account for €38.500 while the rest is related to RTD activities and validation.

The breakdown of travel costs per work package is shown below.

WP 1	38.500	WP 8	38.625
WP 2	58.667	WP 9	25.235
WP 3	45.925	WP 10	44.036
WP 4	53.600	WP 11	
WP 5	34.298	WP 12	6.600
WP 6	44.000	WP 13	5.000
WP 7	31.250	WP 14	
		Total (€)	425.736

Travel for technical meetings will be kept as low as possible by planning back-to-back meetings and through the use of electronic communication, group working tools (BSCW and wiki) and Skype audio conferencing.

Other clarifications about consortium costs

In this section other aspects related to project costs will be clarified. In particular regarding the justification of the level of indirect costs for partner 4 Institut fuer Mikrotechnik Mainz GMBH (IMM) this partner cost model is "real indirect cost".

In its EC proposal preparations and EC interim cost statements for a year completed and as long as the real overhead rate for a year completed is not yet known (as the annual financial audit is not yet completed) IMM calculates its indirect costs taking 1.9 times the direct personnel costs of the respective EC project. The same overhead rate has been used by IMM in FP5- and FP6-project proposals already and is continued to be used by IMM in all FP7 project proposals where IMM participates. The way the indirect costs are calculated by IMM has been checked and approved along the time several times by independent auditors and has been accepted by the European Commission services for the other projects IMM participates. In determination of this rate of indirect costs one has to take into account not only the IMM bureau offices in Mainz, but also a broad range of technology and workshops. Nearly half of the site at IMM is high technology laboratory space, including more than 800 square meters clean room, plus chemical laboratories, (bio-) fluidic laboratories, analytical and measurement laboratories, optical laboratories, precision engineering workshop, etc. All these facilities are cost intensive and therefore lead to the rate of indirect costs.

Costing and planning of trials

General ward study	Outpatient	Outpatient compliance
Total personnel: 34.5 pmos	Total personnel: 44 pmos	Total personnel: 10 pmos
Cost of personnel: 209.1 K€	Cost of personnel: 254.9 K€	Cost of personnel: 54 K€
Consumables, others: 24K€	Consumables, others: 39K€	Consumables, others: 25K€
Travel: 12 K€	Travel: 12 K€	Travel: 3 K€
Indirect cost: 155 K€	Indirect cost: 171 K€	Indirect cost: 49 K€
TOTAL COST : 300K€	**TOTAL COST : 476K€**	**TOTAL COST : 131K€**

Beneficiaries own contribution

The table below identifies beneficiaries' own contribution to the project realisation, such as durable equipment, laboratories or other relevant resources.

Beneficiary name	Description
ATOS	Durable equipments: Servers, Personnel Computer, Laptops, mobile phones and printers Other relevant resources: IT infrastructure and licensed software
CNET	Other relevant resources: IT infrastructure and licensed software
DELTA	Durable equipments: Systems for design and development of ASICs (Applications Specific Integrated circuits) Laboratories: laboratories for developing, prototype manufacture and testing of electronic patches. Clean room laboratories for chip-scale packaging of microelectronics and micro sensors. Full size facility of failure analysis of microelectronics, packaging solutions and body sensors. Laboratories for test of short range wireless systems. Facilities for performing acceded test of medical devices Other relevant resources: Licensed software for ASIC design and developing of software for wireless systems. Development environment and set-up for development of medical devices including QMS (Quality Management Systems)
IMM	Durable equipments: Thin film Technologies: MEMS processing on SOI-Wafers; Stress optimized PECVD and LPCVD processes; Si wet etching; Advance Silicon Etching (ASE) Deep process; ASE SHALLOW process; Reactive Ion Beam Etching (RIBE); Vacuum evaporator; Mask aligner; Deep UV stepper lithography; X-ray lithography; Spin Coating; Micro electroplating and electroforming; Microwave barrel etcher/stripper; Packaging including wafer-level and flip-chip procedures. Metrology equipment: AFM/SNOM; Ellipsometer; SEM/EDX; Optical-/Mechanical-Profilometer; White light interferometer. Laser Micromachining: Excimer laser ablation; Nd:YAG Laser Micromachining; Laser Welding of Metals and Polymers; 3 dimensional Nanostructuring with fs-Laser Machining. Micro Precision Engineering: CNC turning; 2D/3D micro milling, HSC milling; Micro wire Electrode Discharge Machining (μ-EDM); Micro die-sinking (micro EDM machining); Ultra precision machining with diamond tools. Micro Optics and Micro Fluidics: On-line and On-chip analysis; FTIR spectrometer (NICOLET); NIR-Spectrometer (Axsun); UV-Vis-NIR spectrometer (PerkinElmer); Multi wavelength Refractometer (Schmidt+Haensch); Different optical tables with vibration isolation supports; Optic Simulation software: Zemax and OptiCAD. Laboratories: Clean room class 100-1000 (800 sqm); Fully equipped optical laboratory; Biofluidic laboratory (class 1). Other relevant resources: Interdisciplinary qualified staff with special skills and expertise from physicists, engineers, biochemists to molecular biologists; Modern CAD Software and simulation tools; transfer of macro-scale analytical assay to chip format; Prototyping of automated device for lab on chip application; Biological validation of extraction procedure.
FORTH-ICS	Durable equipments: Servers, Personal Computers, Printers, Laptops, PDAs and mobile phones Other relevant resources: AmI infrastructure, IT infrastructure and licensed software
FHG-SIT	Durable equipments: Servers, Personnel Computer, Laptops, mobile phones and printers Other relevant resources: IT infrastructure and licensed software
FORTHNET	Durable equipments: Servers, Personnel Computers, printers, networks' related hardware and software

Beneficiary name	Description
	Other relevant resources: IT infrastructure and licensed software
IN-JET	Durable equipments: None Laboratories: None Other relevant resources: None
ALL	Durable equipments: Computer and Printers Other relevant resources: Licensed software
MUG	Durable equipments: Blood glucose analyser, freezer, servers, personal computer and printer Laboratories: Standard equipment for laboratory Other relevant resources: ethics committee, insurance for subjects, access to wards, IT infrastructure and licensed software
MSG	Durable equipments: Servers, Personnel Computer and printers Other relevant resources: IT infrastructure, licensed software and services
CHC	Durable equipments: Servers, work stations, and peripherals. Remote patient monitors and digital diagnostics. Tele-consultation Laboratories: Medical services Other relevant resources: Electronic patient records, disease registers, and stable primary care population of patients
UBRUN	Durable equipments: Personal computers, printers Other relevant resources: IT infrastructure, licensed software and services
VUB	Other relevant resources: ample Legal library resources
BTS	Other relevant resources: A physiology and patho-physiology database and a proprietary Modeling & Simulation platform (PK-Sim(R) and MoBi(R))
SOLIANIS	Durable equipments: Developed device according to DoW. PDAs for data collection of Multisensor and computers. Laboratories: Access to manufacturing of HW etc of ext. partners, access to clinical infrastructure at University Hospital. No own lab.

B3. Potential impact

B.3.1 Strategic impact

The impact of the REACTION research work will be visible and remarkable in the area of diabetes management, but it will also be affecting and impacting a wide range of societal, economical and technological areas. It significantly contributes to the fulfilment of the ambitious activity plans for Europe's future and enhances our industrial leadership in several areas, as shall be demonstrated in this section.

The centre of gravity of activities will be in area of ICT but REACTION will make major impact on diabetes care management, clinical workflows, policy and regulatory frameworks and business focus. Relevant regulations will not only be taken into account but will be impacted through the work on patient safety, patient rights, data security and health-economic framework.

The specific area of impact to be addressed in this section will be contributions to the research policy in Challenge 5 of the 2008-10 workprogramme. Secondary contributions may be found on other areas, such as Information Society policy (i2010) and activities related to chronic disease management under the Competitiveness and Innovation Programme (CIP) as well as other Community policies.

The potential impacts of the REACTION project can be summarized as follows:

Expected impact on healthcare

Expected impact on healthcare strategies

The REACTION platform has the potential for greatly impacting national strategies for disease management involving proactively managing diabetes across the entire continuum of care. National disease management strategies guide diagnoses and treatments based on scientific advancement. The strategies direct decisions in optimising patient care and demonstrate the dedication to practice medicine that is both evidence-based and humane.

Implementation of telemedicine programs and eHealth is considered Europe-wide as major instruments for supporting new disease management strategies for chronic conditions, but as has been demonstrated, not many telemedicine projects have been getting passed the pilot phase. The interoperability solutions and ease of which applications can be developed on the REACTION platform makes a prime candidate for technology support for eHealth strategies, provided that the reimbursement systems in the various EU member states recognise this technology as a clinical tool and provide adequate economic compensation to all the involved stakeholders. The REACTION project will not only supply the technology, but also the socio-economic framework that will allow healthcare authorities to make the necessary steps towards economic recognition of the services that can be offered with eHealth solution in diabetes management.

In 2004 the EC issued its communication: COM(2004) 356 final: "e-Health – making healthcare better for European citizens: An action plan for a European e-Health Area" which sets out specific targets for the use of eHealth in several areas, including boosting the deployment of health informatics networks (2004-2008), interoperability standards for EHR and messaging and legal framework (start 2009), all of which will be greatly impacted by the availability of a REACTION platform and the supporting work on legal frameworks. The deliverables from WP9, notably D9.4 Data protection and patient rights and D9.8 Healthcare economics and reimbursements could be developed into policy position papers and used for ministerial conferences.

Expected impact in diabetes care management

The beneficial effects of intensive glycaemic monitoring and therapy in ICU (tight glycaemic control, or TGC) have been widely recognised by experts. J.S. Krinsley at Stamford Hospital in the USA investigated 5365 non-cardiac surgery patients admitted to the adult intensive care unit before and after implementation of TGC. Significant decreases in mortality occurred among medical and surgical patients during the TGC era, but not among trauma patients. Non-diabetics who sustained hyperglycaemia had an especially high risk of mortality, and benefited greatly from treatment (Krinsley2006). The data shows that patients in ICU with mean glucose levels above 10 mmol/l had twice the mortality rate as did patients with lower than 5.5 mmol/l.

The prevalence of hyperglycaemia in diabetes patients admitted to hospitals is alarmingly high. Hyperglycaemia and insulin resistance are common in severe illness and are often associated with physical and mental stress. Stress-induced hyperglycaemia can lead to significant deterioration in glycaemic control in individuals with diabetes and can cause stress-induced diabetes mellitus in non-diabetic patients. In general, poor glycaemic control is accepted to lead to increased morbidity and mortality.

Of the 90% of all patients are admitted to general wards, 40% are believed to have either diagnosed diabetes or unknown/pre-diabetes or are in the risk of developing stress-induced diabetes. According to 1998 results of the ECHP[34], 10.1 % of Europeans have experienced hospitalisation during the last 12 months (9.1 % of men and 11.0 % of women). The proportion ranges from 5.9 % in Portugal and in Greece to 14.2 % in Austria and 12.1 % in Germany. These figures indicate - with caution - that as many as 10 million patients in Europe would benefit from tight glycaemic monitoring and therapy annually.

The potential for reducing the risk of hyperglycaemia in diabetes patients is thus very high, although difficult to quantify. Introducing the REACTION platform in general wards will allow hospital to extend TGC not only to ICU patients but to all patients in risk of hyperglycaemia. A typical metropolitan healthcare region, such as the Greater Copenhagen Region, has 250,000 annual admissions. According to the data, more than 30,000 of patients annually are in risk of developing hyperglycaemia, which may lead to confusion, poor healing, and impairment of cognitive functions. The cost of the prolonged stay in hospital and poor clinical pathway is staggering compared to the cost of installing the REACTION platform in 10-15 regional hospitals.

While REACTION outpatient monitoring devices will allow better management of diabetes to reduce the burden of chronic diabetic complications, technological aids are needed to improve prevention of diabetes itself. Although pharmacologic prevention cannot be excluded in the next future, lifestyle modification will remain a necessary (and powerful) tool. Installing the REACTION context aware environment, with e.g. movement sensors, calorie balance, scales, etc. to the medical information sensors, will allow health management applications to monitor lifestyle modifications.

The proper use and integration into the REACTION platform of existing methods for metabolic monitoring and control, together with the systematic deployment of such platform in healthcare systems, is expected to greatly help reducing the risk of developing complications in general, and in particular hyper/hypoglycaemic events and the rate of hospital admissions. Taking into consideration that hospital admissions accounts for more than 55% of diabetes-related cost, the use of sophisticated, but friendly, user technology can be easily appreciated as cost valuable.

Typical areas of improvement are blood glucose reading and insulin therapy feed-back. The technology for spot measurement of blood glucose levels is available but not directly transferable to insulin dose modification because of open-loop system. The REACTION platform, however, is expected to close the loop. This approach is, obviously, of great importance for insulin-dependent type 1 diabetic patients. Nonetheless, technology is likely to introduce better opportunity for type 2 diabetes as well. While in Type 2 diabetes, punctual blood glucose readings may not necessary

---

[34] European Community Household Panel, Version December 2001,

trigger therapeutic changes, analysis of blood glucose profiles over the time may allow early detection of trends thus allowing timely treatment adjustments. This approach can easily go beyond glycaemic control to include monitoring of multiple cardiovascular risk factors (ECG, blood pressure, lipids, inflammatory parameters, coagulation, etc.). It is indeed proven that significant reduction of cardiovascular events can be achieved with multi-factorial intervention.

Expected impacts listed in the work programme

The Challenge 5 supports highly interdisciplinary research aiming at improved productivity of healthcare systems, continuous and more personalised care solutions, addressing the informed and responsible participation of patients and their informal carers in care processes as well as realising savings in lives and resources by focusing on prevention and prediction.

The REACTION project will first and foremost aim at continuous and personalised care solutions, but it will also aim at a noticeable and lasting improvement in productivity of healthcare systems. The REACTION platform provides better integrated care (including support for joint care and shared care programmes), dynamic management of chronic diseases at the point of need, full integration with clinical workflows, and quicker transfer of knowledge to clinical practice.

The expected impacts from projects under the objective ICT-2009.5.1 "Personal Health Systems" are:

> *Reduced hospitalisation and improved disease management and treatment*
> *at the point of need, through more precise assessment of health status*

The REACTION platform will use accurate wearable CGM sensors a closed-loop feed back system which will support tight in glycaemic control (TGC), which is important in order to reduce microvascular complications and prevent hypoglycaemic episodes. It will provide direct, on-line feedback to spot measurements of glucose levels combined with multi-parametric context awareness. This approach is, obviously, of great importance for insulin-dependent type 1 diabetic patients but it is likely to introduce better opportunity for type 2 diabetes as well. The multi-parametric monitoring, combined with risk assessment profiling, will allow for a much more precise assessment of patients' health status and improved disease management.

Studies have predicted that remote monitoring of diabetes can lead to a reduction of 2.5% in hospital admittances/bed stays or a cost reduction of 5% for diabetes treatment in the primary care[35].

> *Economic benefits for health systems without compromising quality of*
> *care. New business models for health service providers and insurance*
> *sectors.*

The REACTION will have a direct impact on the productivity of healthcare delivery systems in Europe and contribute to the stabilisation of cost, in the light of massive increases in number of chronically ill patients suffering from diabetes type 1 and 2. The potential for impact becomes clear when considering that 5% of inpatients (many with long-term conditions) at hospitals account for 42% of overall inpatient stay.

In the UK alone, diabetes care takes up about 5% of the entire national NHS costs whereas the prevalence (diagnosed diabetes) is around 3%. The cost of treating diabetes is thus over-proportional to the number of patients frequenting the health care systems, in particular due to complications from diabetes.

One REACTION outcome is to point to healthcare solutions with cost/benefit ratios attractive to healthcare authorities in diverse healthcare system in Europe. Another outcome will be viable (profitable) business cases for suppliers of services, technologies, and pharmaceuticals.

---

[35] The eu-DOMAIN project http://www.eu-domain.eu.com

The precise form of the ecosystem and the business cases cannot be foreseen at the time of writing, but previous work in this area indicates that studies of value creation and value models can provide good results in areas influenced by non-monetary expectations and demands (Thestrup2008). The special aspects of healthcare, where citizens are accustomed to receiving perceived "free" benefits, calls for unorthodox thinking and open minded assessment of how healthcare services shall be valued and delivered.

The REACTION project will thus greatly impact the way we perceive healthcare services and value the economic benefits. Concretely, the impact will be in a suitable framework for business modelling activities based on value created in terms of improved health, quality of care and commercial benefits and derive and validate viable business cases for the medical domains in selected countries.

> *Reinforced leadership and innovation of the industry in the area of*
> *Personal Health Systems and medical devices. Where appropriate,*
> *demonstrated potential for patents and spin-offs.*

The number of industrial partners and leading and trendsetting academic partners will facilitate a high visibility of the REACTION project which will - all other things being equal – allow the consortium to strive for major impact on reinforcing the personal health industry in Europe.

The results in wearable sensors and ePatch technology are directly applicable in a range of other sensor networks outside the project. The work on improving CGM sensors will greatly reinforce European leadership in diabetes related sensor technology and medical devices and could very well lead to patentable inventions. The REACTION Service Orchestration concept allows rapid development and deployment of innovative telemedicine and eHealth applications, which will promote innovation in European healthcare industry, particularly among SME's where containment of development cost is critical.

Finally, the need for standardisation in this enormous market (consuming 8.5% of GDP in Europe) goes without saying. The impact in standards from REACTION will be comprehensive and effective and is described in section Contribution to European and global standards.

> *Improved links and interaction between patients and doctors facilitating*
> *more active participation of patients in care processes*

REACTION will provide a platform for improved and wide spread self management of diabetes and other chronic diseases. The REACTION workflow and data management subsystem combined with integrated risk assessment facilities will stimulate better case management by integrating expert knowledge, general medical knowledge and case history, and will allow professional cares to improve the speed and quality of decisions on e.g. drug administration and therapy.

REACTION will also make a major impact on how patients perceive remote monitoring and surveillance. To patients, aspects of privacy, trust, convenience, comfort, inclusion, discretion, ethics and many other non-functional requirements are more important than technological inventions and cost effective healthcare. By including these important aspects solidly in the REACTION project, the impact on frameworks and guidelines for successful deployment is secured.

Over an about the cost aspects mentioned above, REACTION will impact the way people perceives self management of their disease or their likelihood of contracting a disease.

There are several prerequisites which must be met in order to ensure efficient self-management of chronic conditions, such as education, understanding of complications and familiarisation of the clinical pathway laid out by the carer. The REACTION platform allows self management applications and services to be delivered to the point of need of the patient. With the massive focus on functional and non-functional (quality) requirements in the REACTION project, the patient satisfaction and acceptance is in focus (the project will be validated against these criteria), which will have a substantial impact on the active participation of citizens in illness prevention and care management.

The legal studies could directly impact policy making in areas such as patient safety and privacy of distributed telemedicine and eHealth remote monitoring applications.

> *Accelerating the establishment of interoperability standards and of secure,*
> *seamless communication of health data between all involved partners,*
> *including patients*

The protection and confidentiality of patient data is crucial to patient's willingness to take up new methods and technology. The REACTION platform will make a considerable impact by incorporating support for security, privacy and trust models throughout a distributed infrastructure; from sensors to backend Health Information Systems.

Expected impacts on European industries

The health domain and its three main industries, pharmaceuticals, medical devices and eHealth, are dominant economic sectors with respect to employment creation and growth. The eHealth market is estimated at €20 billion, and is experiencing double digit growth.

The REACTION service orchestration and model based ontology concept allows rapid development and deployment of innovative telemedicine and eHealth applications, which will promote innovation in European healthcare industry. It is of particularly interest to innovative SMEs where containment of development cost is critical. The open SDK toolkit for model-driven development of applications that use the REACTION platform is a major tool for developing new telemedicine or eHealth applications or for device manufacturers wanting to make their devices interoperable.

Since anything related to healthcare is expected to be free (or covered) for patients in Europe –i.e. there is no traditional "consumer" with choice and buying power in healthcare, new business concepts will have to be realised based on value creation and value exchange in a world with non-monetary value constructs.

The new models of business constellations, private public partnerships, pharmaceutical companies as innovation drivers and bringing together payers, providers and patients in new constellations, will greatly impact European industries and the way they see the business potential in eHealth. Provided the policy framework and reimbursement recommendations developed in REACTION are actually followed by real life implementation, the market for eHealth services will be even more stimulated than today, where most focus is in care improvements and cost reductions. The REACTION framework will be point also to revenue driven eHealth.

B.3.2 Plan for the use and dissemination of foreground

Dissemination and/or exploitation of project results

Dissemination and exploitation activities are completely embedded in the different workpackages of the project reflecting the intimate and fast transfer of knowledge from the projects research results to public dissemination and commercial exploitation.

Dissemination strategies

The REACTION dissemination strategy is to progressively increase dissemination efforts as project results are obtained, in order to assure a wide awareness of the REACTION project and favourable conditions to facilitate exploitation after the end of project. The dissemination strategy is intended to optimise dissemination of project knowledge and results to companies and organisations, which share an interest in the scientific results and the applications or are potential service providers of REACTION.

The dissemination of the results of the project will take several forms and use a variety of media. To ensure that dissemination objectives are met in a form agreeable to the Consortium and beneficial

for the business interests of individual participants, the Consortium will approve a detailed dissemination plan before dissemination starts.

The dissemination effort for the project begins from day one with the establishment of a rich web site for publicity purposes. This will store technical developments, events and invitations to join a dedicated mail group/interest group. The site will also display any papers and presentations given by consortium members, whether at European conferences or workshops. The members of the project will also write academic and technical papers, to be presented at conferences and trade shows, and published in leading academic and technical journals.

Realising the dissemination strategic objectives will include the following methods:

Time	Objective	Methods
Year 1	1) Create awareness about the REACTION project. 2) Dissemination in strategic boards of participants. 3) Prepare powerful scientific standing in professional clusters.	- Publication of support material, brochures and the web site. - Attendance in seminars and congresses. - Organise European conference on Remote Accessibility - Press releases and liaison with health authorities
Year 2	4) Continue to build awareness of the REACTION results in academic and scientific circles, both within ICT and within healthcare. 5) Verify opportunities to apply the REACTION components in various healthcare environments and involve other stakeholders.	- Aligning events with similar EU or national projects. - Preparation of pre-commercial brochures. - Visit to healthcare communities. - Web site enrichment. - Peer reviewed papers in international journals. - Conference and workshop papers.
Be-yond	6) Prepare to integrate REACTION in a existing health environment 7) Promote the early exploitation of a REACTION platform and individual components.	- Preparation of a commercial brochure. - Newsletter to potential users - Take-up of ePatch components - Take-up of CGM sensor components - Take-up of semantic services components - Demonstration the REACTION platform

Table 8 Dissimination objectives and methods

Dissemination plans

The results of the scientific research work will be continuously submitted for publication to international, peer-reviewed journals and conference proceedings. Each partner will continuously monitor the published conferences in their field and report it to a central repository for dissemination coordination. The Dissemination Manger will establish annual targets for number of conferences to be attended and will monitor the progress. Joint papers will be sought whenever possible and feasible.

REACTION will also organise a number of seminars, aimed at healthcare officials, healthcare providers and the European healthcare industry. Partners will disseminate internally the project through their internal bulletins and by presentations at internal and external meetings and events.

Further, dissemination will be undertaken through a rich project website, various printed and electronic brochures, newsletters and press information.

There will be clear acknowledgement of EC funding in all disseminations activities, at any media or event.

The following dissemination activities have been planned:

Website:
The powerful project website will be established at the beginning of the project. This site will contain information about the project as well as relevant news and events. The website will be kept updated with news, public deliverables, articles and material from participation at events (e.g., slides of presentations, keynote speeches, and conference proceedings).

Marketing:
A brochure will be produced during the first 6 months of the project in order to disseminate the objectives and the expected results and impact of the project.

The project will produce a quarterly newsletter describing results obtained and planned activities.

Conferences:
Dissemination will be targeted at important medical and computer science conferences, both recurrent and ad hoc. The following annual conferences and events will be targeted:

Medical conferences
- Annual Diabetes Technology Meeting (http://www.diabetestechnology.org/)
- European Association for Study of Diabetes (EASD) annual meeting (www.easd.org)
- American Diabetes Association annual meeting (www.diabetes.org)
- Diabetes Technology Meeting (www.diabetestechnology.org)
- MIE (Medical Informatics Europe) conferences .
- Workshops might be run at the STC 2010 conference of the European Federation of Medical Informatics (EFMI) to be held in Rejkavik in June 2010 to look at state of the art for data mining information on risk factors for diabetes and its complications and also on remote monitoring for management of patients.

Computer science conferences
- UBICOMM (http://www.iaria.org/conferences2008/UBICOMM08.html)
- IEEE SECON (http://www.ieee-secon.org/2009/index.html/)
- WSEAS International Conference on Computers (http://www.wseas.org/conferences/ 2008/greece/iccomp/)
- International Conference on Health Informatics HEALTHINF (http://www.healthinf.org/Healthinf2009)
- World of Health IT (http://www.worldofhealthit.org)

Trade shows etc.
- CeBIT (www.cebit.de)

The IEEE/EMBS events will be considered as well, as this attracts a strong technology attendance.
- UBRUN will look to propose a mini-track or session at IEEE/EMBS in 2010 on continuous glucose monitoring techniques in order to explore state of the art.
- UBRUN will look to propose a mini-track or session at IEEE/EMBS in 2011 on feedback control of blood glucose to explore the state of the art.

Additionally, the Annual Diabetes Technology Meeting will be targeted, as this attracts a strong technology and clinician attendance. We will present results and determine state of the art..

The project will aim to make its first global appearance at the Ninth Annual Diabetes Technology Meeting to be held 5-7 November 2009 in San Francisco, USA. This is the worlds premiere event with the world's top diabetes technology professionals discussing the latest high-tech tools in diabetes care. Special focus will be on episodic and continuous Glucose Monitoring and Alarm Performance in Continuous Glucose Monitors; two major topics for REACTION.

The REACTION project will arrange an annual European conference on "Remote Accessibility to Diabetes Management and Therapy". The first conference will be organised in September 2010 and leading scientists will be invited as key speakers. The target audience will be healthcare providers, healthcare providers, health professionals, service providers, pharmaceutical companies. The main aim of the conference will be demonstrate European advances in the field of "Remote Diabetes Management and Therapy", but it will be also a major event for dissemination of REACTION results. The conference will be aligned with other major academic groupings in Europe in order to minimise overlap.

Journals:
The results will also be disseminated to the academic computer science and healthcare communities through academic publication, and conference and workshop participation. Important media for publications are:

Medical journals
- Diabetes (diabetes.diabetesjournals.org)
- Diabetes Care (care.diabetesjournals.org)
- Diabetologia (www.diabetologia-journal.org)
- Diabetes, Obesity and Metabolism (http://www.wiley.com/bw/journal.asp?ref=1462-8902)
- Diabetic Medicine (http://www.wiley.com/bw/journal.asp?ref=0742-3071)
- Diabetes/Metabolism Research and Reviews (http://www3.interscience.wiley.com/journal/122459774/grouphome/home.html)
- Diabetes technology and therapeutics (http://www.liebertpub.com/products/product.aspx?pid=11)
- Journal of Diabetes Science and Technology (http://www.journalofdst.org/)

Computer science and software journals:
- IEEE Pervasive Computing (http://www2.computer.org/portal/web/pervasive/home)
- Pervasive and Mobile Computing journal (http://www.elsevier.com/wps/find/journaldescription.cws_home/704220/description#description)
- Ubiquitous Computing and Communication Journal (http://www.ubicc.org/)
- IEEE Computer (http://www.computer.org/computer/)

Demonstrations:
Experience and best practice will be disseminated to the healthcare community and policy makers through membership of the whole site demonstrator action network (WSDAN) and the Telecare Action Network (TAN) and through existing links with DoH and CfH, and including close links with the UK Diabetes Tsar, Rowan Hillson, based at Hillingdon Hospital, and to be involved in the work of UBRUN.

Demonstrations and site visits will inform policy makers and other NHS organisations planning implementation. Financial and service benefits will be disseminated by the commissioners. Where appropriate, findings will be disseminated through membership of standards bodies (ISO, CEN, IEEE, HL7), professional and trade bodies, including the American Telemedicine Association (ATA), the Telecare Services Association (TSA), and the Continua Alliance.

Results of ethical and social studies will be disseminated to relevant communities active in eInclusion policies, patient organisation and special social interest groups. Likewise, legal and regulatory considerations will be disseminated through policy and position papers. Business

modelling strategies and cases will be disseminated to the business community of device manufactures, pharmaceutical companies and healthcare service providers.

Concertation:
The project partners will actively participate in concertation activities with other ICT funded projects related to the area of the project and organised by the European Commission. The project will be involved in info days, expert groups, IST conferences and other events organised by the EC when relevant. The project may also represent the Commission at some international events as required.

At M30 a clustering event titled "Ambient Intelligence in the support of healthcare" will be organized at FORTH with the participation of other EU projects operating in the healthcare domain which make use of the ambient intelligence. During this event each project will perform demonstration and/or presentation of the implemented solutions. The REACTION platform prototype integrated in the AmI facility of FORTH-ICS will be demonstrated and a round table will be set-up in order to discuss the benefits which AmI can provide in delivering healthcare in different environments starting from home to primary and secondary healthcare settings. The event will be largely promoted and mass media will be invited to attend this clustering event.

Project exploitation plan

The main objectives of the exploitation in REACTION are:

- Identification and description of the innovative components of the REACTION results.
- To assess the exploitation potential of these "products".
- To produce a realistic exploitation plan, solidly anchored in the partners' own strategies.

The demographic trend across Europe indicates that life expectancy is increasing every year. Responding in an adequate manner to the growing need for flexible and adaptive healthcare and social care solutions presents a number of significant challenges to service provision, which REACTION can help to address. The eHealth market is presently estimated at €20 billion, and is experiencing double digit growth, thus creating an extremely important market for the industrial partners and the research institutions.

The EU Members States have already showed their commitment in promoting eHealth strategies and initiatives. By the end of 2005, each Member State has developed a national or regional roadmap for eHealth addressing the challenges of providing citizen-centred healthcare services. There is therefore great potential for the commercial exploitation of REACTION because it is precisely capable of meeting these challenges.

A Project Exploitation Plan will be developed describing joint and individual partner's exploitation strategies. The Exploitation Plan will provide information about the potential products, competitors and the technology benchmarks. It will define the REACTION market position and identify the potential market segments as well as the specific academic and commercial strategies to be implemented. In particular, the Exploitation Plan will include:

- A benchmarking analysis between the REACTION model and other platforms.
- A specific analysis to evaluate the potential market segments.
- Specific industrial partners exploitation strategies and commercial promotion actions.
- Specific academic partners exploitation strategies and academic promotion actions.

The market analysis will be performed by the industrial partners. It will offer new and updated information on users/customer needs in order to provide the scientific partners with useful feedback on the marketability of REACTION products and provide a comprehensive background for each partner's individual exploitation and business plan.

The REACTION partners have a priori defined some joint exploitation targets for bringing the REACTION platform and services to the market within 24 month of project completion.

Technology providers

The technology providers are all commercial partners that will constitute the main thrust for the exploitation of the whole system. The commercial nature of these partners will underpin the quest to bring out commercially viable products and services. The exploitation strategies will be greatly assisted by the various business models, which will be identified during the project.

The main principle for exploitation of the REACTION platform will be for the technology providers to create and operate the platform as PAAS (Platform as a Service). The partners will, in different constellations as explained below, undertake setting up data centres and developing the services and applications needed for their respective markets. Depending on the customer requirements, they will also undertake to deliver sensors and devices in cooperation with selected medical device manufacturers.

The target customers are health authorities (national, regional, local), hospitals, care centres. Revenues will be derived as licensing fees for the software components that constitute the platform, development and customization of services and applications and consulting and training activities.
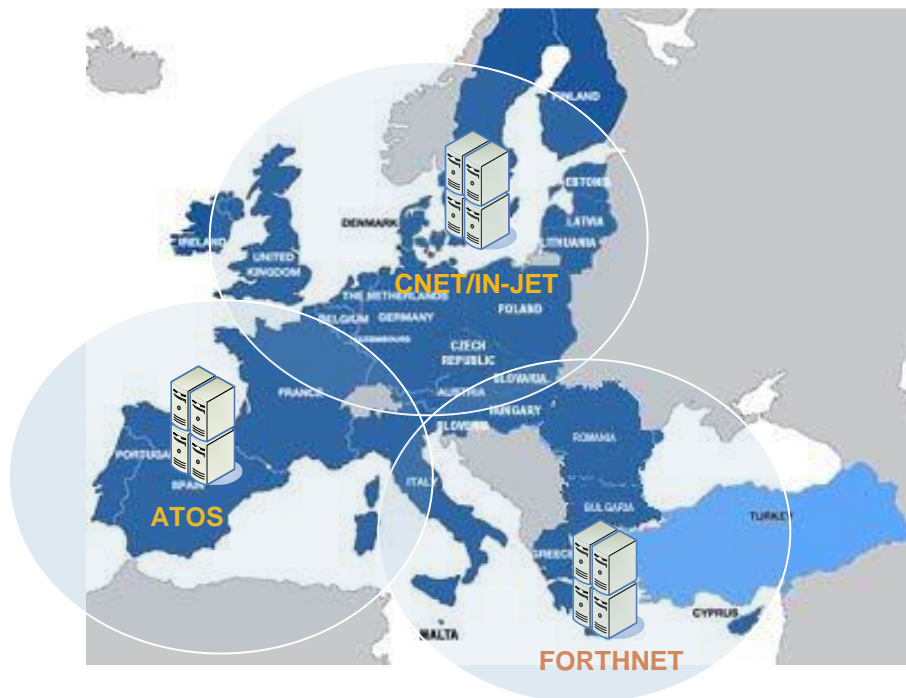
Figure 14 Commercial exploitation of the whole REACTION platform

Different ways of exploiting the REACTION system can be considered. One possibility is to have separated individual exploitations by partners, and another option is to exploit the system jointly, involving part of, or the whole, consortium.

As far as the provided systems and services would be offered jointly the consortium would investigate and reach an agreement on exploitation.

As it can be seen in the map the interactions among the most important commercial partners in the different geographical areas is considered as a key point for wider final commercialization and adoption of the reached solutions.

The exploitation of the system as a whole would be defined following the proper actions as described in upper paragraphs of this section however, at this stage the following points have been already identified:
-   Potential clients of the final system: Hospitals, Healthcare authorities and Care centres.

- Possible business models: Licensing of software components, service development, consulting, training and sensors.
- Creating and operating the platform as PAAS (*Platform as a Service*): Setting up data centres, developing applications, delivering sensors and device.

The figure above shows how the partners plan to roll out REACTION services as PAAS in Europe from three central locations.

IN-JET and CNET are planning to become joint service providers first in the Scandinavian markets. IN-JET is already in contact with regional healthcare authorities in Denmark and Sweden to supply services and will implement the REACTION platform during the last field trial together with CNET. CNET also plans to exploit REACTION software through existing product lines and sales channels as they become available. The platform fit perfectly with their existing workflow interoperability solutions, such as AdeTransact. The REACTION platform will eventually be able to cover national markets in Northern and Eastern Europe.

In Greece, FORTHNET (with the assistance from FORTH-play an active role in the exploitation as service provider authorities. FORTHNET is developing a private broadband which will provide widely distributed networks for applications in Greece. FORTHNET has more than 100 major cities and towns of Greece in which the service can devices can be bought. ICS) will work to for local health network in order REACTION retail shops in all be promoted and

ATOS is a major player in Health Information Systems and is planning to operate the REACTION platform as a PAAS activity in collaboration with local partners in Iberia, France, and Italy.

The Greek and Spanish exploitation will be carefully coordinated with the Scandinavian platform and may be rolled out to other markets in Europe.

Healthcare providers

Clinical partner CHC is planning to upgrade their remote monitoring base using REACTION, improve their clinical success rates. MUG is expecting to introduce TGC in their patient wards and benefit from improved patient recovery and reduced mortality. Both partners will work very closely with their technical partners UBRUN and MSG and will in-source the relevant technology providers from the REACTION project to install REACTION platforms in their own facilities and in those influenced by them.

All academic partners will increase joint publications and presentations of the clinical results in refereed journals, at international and national conferences and workshops and integrate the project results into their educational activities carried out at the universities (postgraduate courses, further professional education courses).

Knowledge providers

VUB will cross fertilize their research (in particular in the project SENIOR, Social Ethical and Privacy Needs in ICT for Older People) with results from REACTION.

IMM, SOLIANIS and DELTA will use the knowledge from the project to improve their respective design of CGM sensors and ePatch technologies, perhaps in some kind of joint-venture.

Individual exploitation plans

Although joint exploitation is seen as the most promising and preferred way to exploit REACTION results, the Consortium partners have a priori identified individual exploitation objectives. The individual exploitation plans complements the joint exploitation strategy in an attempt to optimise

the exploitability and the impact of the REACTION platform. This approach aims to secure that there will always be a realistic exploitation plan for each partner regardless of the success or failure of joint exploitation plans. The individual exploitation will be aligned with the joint exploitation plans in the third year of the project.

The industrial partners individually can exploit research results by enhancing their existing or creating new products and services. These products and services will lead to a competitive advantage and will create substantial benefits for their customers.

In order for the exploitation to be effective an integrated approach will be necessary within each partner's organisation and according to the organisation's strategies and objectives. The integrated approach will be accompanied by the following activities:
- Transfer of research results into actual developments, products, and services.
- Gain feedback on economic benefits and impact of the research projects especially through focus groups interviews and tests.
- Market examinations for the best use of the research results and for creating new business opportunities.
- Achieving high exploitation through the feedback from large customer groups and other technical and scientific networks of the consortium partners.

Individual exploitation strategies will be developed after the user requirements have been clearly defined and the first prototypes have been validated in field trials. From the exploitation framework, potential target groups in different sectors will be identified, analysed and prioritised according to commercial attractiveness. The commercial exploitation activities will be focused on early adopters among customers, in order to optimise time-to-market.

Industrial partners have summarized their individual exploitation objectives as follows:

ATOS

ATOS believes that one of the best exploitation strategies is the one based on the joint exploitation of the results and for that reason ATOS would work on agreements between the parties to cooperate and be present in the market (therefore extending the contacts network).

During the project lifetime ATOS would create and refine the exploitation strategy in line with the joint exploitation planned by the consortium. Nevertheless, ATOS also considers the possibility of exploitation of the different components and services separately.

ATOS has a large list of clients in the health sector that could be interested in the services and systems developed within the REACTION project and for that reason from the very beginning ARI group would work closely with the commercial and consultancy groups within the company in order to present the project to different clients adding the solution to the company portfolio.

CNET

Our route to exploitation will be to exploit the software of REACTION as a product both at a system level as well as at the component level. We plan to incorporate REACTION software into our current product offerings. Our experience from exploiting results from other European R&D projects (Intuitive, Multimedia Broker and Metis) has shown that the most effective way is if exploitation starts very early, long before the project ends. There are several reason for this - by presenting the concepts at an early stage to customers we get feedback that can be incorporated into the project, the project also gets valuable feedback from testing the software in real commercial applications. The component-oriented development approach of the project will allow us to exploit the project incrementally.

CNET expects that their existing customer base in alarm handling and crisis management will be our first target exploitation markets. Within the first year we will approach selected customers, which we know are early adopters of technology and present ideas for pilot applications. Based on the

experience from this we will refine our exploitation strategy and decide on the final exploitation approach - including licensing fees, ratio license/consulting service, sublicensing to third parties, REACTION as an application service, marketing strategy etc. REACTION will strengthen our position as a provider of solutions for semantic-based knowledge and content systems. We will work closely with IN-JET to explore the Scandinavian market.

IMM

IMM will expedite further customer specific development work based on the knowledge and results gained during the project. Due to its interdisciplinary structure and its broad range of equipment IMM has established itself as a highly productive R&D service provider in the field of microstructuring technologies and microfluidic platform technologies. IMM will use this potential by opening up new R&D projects together with suitable partners in the fields of medical diagnostics, environmental and foodstuff analysis as well as industrial analytics.

FHG-SIT

FHG-SIT Fraunhofer has excellent connections to the German Ministry of Health and to gematik, which is the company responsible for introducing the new IT infrastructure for the health system in Germany. FHG-SIT will extend its knowledge portfolio aimed at practical system security and trust into already established healthcare applications and new concepts of trust.

FORTHNET

FORTHNET, as leading 3-play services provider in Greece has a strong interest in the exploitation of the REACTION services to the relevant user groups. The REACTION platform combines emerging sensor technologies with fast data delivery in order to provide time-critical services to end-users, while FORTHNET utilises and integrates technological solutions on the basis of the latest telecommunications prototypes, in order to develop and introduce to the market innovative services that encourage the use of ICT and broadband networks. Under this scope, mid- and long- term commercial exploitation of the integrated platform will be investigated, as well as the exploitation of the individual software modules. These will derive from the technological expertise that will be gained out of the research activities of the project and could contain services such as vital sign sensing, fusion and early risk diagnosis, integrated with the core competences and business interests of the company.

Furthermore, through its activities, FORTHNET possesses a significant experience in providing large-scale data delivery platforms. Previous experience in combination with FORTHNET's large customer base is expected to benefit the REACTION prototype and provide critical contribution in the exploitation of the project results.

IN-JET

IN-JET has as its core business to market concepts for ICT platforms for applications such as healthcare, security and alarm services.

By 2010, IN-JET will start to market a service platform for clinical trials and the objective is to eventually develop the platform further into a real production platform for healthcare services nd thereby enhance its portfolio of service opportunities.

The detailed exploitation strategy for IN-JET will be defined when the scope of the REACTION platform is established, including functionality and interfaces, system requirements and performance. At that point, our business plans and sales and marketing plans will be updated with the new capabilities offered by REACTION. We will work closely with CNET to explore the Scandinavian market.

ALL

Applied Logic Laboratory (ALL) is developing a web based prototype application for the support of the management of type II diabetes. Part of the application is currently under tests involving patients, as part of the MORE FP6 project activities. This application is planned to be extended to include the support for diabetes type I via the utilization f the results of the REACTION project.

Exploitable results of the project include the methodology and algorithms for the integrative risk assessment of diabetes complications. As ALL, is a contributor, in order to exploit this result, ALL will be work on the joint exploitation strategy of the consortium.

Management of intellectual property rights

The REACTION Consortium will state the ownership of knowledge conditions in the Consortium Agreement at project commencement and may be updated as necessary over the course of the project. In case of debate, the Project Board will have the final say, and any conflicts will be resolved using specific voting mechanisms defined in the Consortium Agreement.

The owner of knowledge will provide adequate and effective protection for knowledge that is capable of industrial or commercial application. The consortium participants may publish information on knowledge arising from the project provided this does not affect the protection of that knowledge. So before any knowledge dissemination that may impact on the exploitation potential of one or more partners takes place, the matter should be agreed with the Project Board.

Participants will also be able to use knowledge, which they own arising from the project, in accordance with the provisions agreed amongst them in the Consortium Agreement. When using knowledge, the consortium partners will make every effort to ensure confidentiality and the need to safeguard the interest of the consortium partners, especially their intellectual property rights.

This process will ensure that all IPRs are properly handled both at a participant and consortium level, that patents are filed where and when necessary, and that proper and appropriate legal advice is obtained at each step along the way.

The REACTION Medical Engineering Manager will oversee this process and advice the project on all aspects of Knowledge Management and Patent filing.

The strategy that the Consortium will implement for managing knowledge and intellectual property comply with the rules defined by the EC for projects of the 7th Framework Programme. They will cover the:
- Management of clear schedules of pre-existing know-how brought into the project by each participant and the rules for its use by each partner for project purposes.
- Management of clear schedules of knowledge generated within the project, including the identification of the partner or partners responsible for generating the knowledge, the use rights of this knowledge of other partners for project purposes and exploitation rights.
- Establishment of contractual agreements between consortium members for the individual and joint exploitation of knowledge generated within the project and, where appropriate, involving the use of pre-existing know-how.
- Proper dissemination of knowledge generated in the project.
- Appropriate protection of any knowledge, including methodologies and technologies, resulting from the project that has identified commercial exploitation potential.

The Technical Manager will be in charge of maintaining a schedule of knowledge produced during the project and, in conjunction with the partners involved, assessing the opportunities to apply for patents or declare copyrights. This activity will comprise the:
- Description of the innovative elements of the work conducted in the Technological R&D;
- Review of existing patents databases and other scientific databases for similar developments; and
- Reporting to the Project Board and to the technical teams about the innovation status of the project results and proposing registration of patents where appropriate.

Depending on the decision of the Project Board and involved technical teams, the result in question could be disseminated without becoming registered as a patent or registered as a patent by the consortium member that has developed the innovation.

IPR intentions of consortium members can be summarised as follows:
1) Any partner having conceived innovative methods and techniques will have the opportunity to protect the new knowledge through a patent.
2) Methodologies and market research studies will be made available free of charge through the dissemination activities of the project.
3) Software developed in the project will remain the sole property of the partner having developed it. Regarding the project orientation towards Open Source in some aspects, the software owner will grant free use rights on software (executable and source code) to any organisation that agrees to:
- Refrain from selling the software to a 3rd party;
- Make clear reference to the REACTION consortium when transferring the software to any 3rd parties; and
- Apply the same Open Source transfer conditions on future software derived from the REACTION software.
4) Software owners retain the right to develop commercial variants of their own products.

Contribution to other policy programmes

Contributions to the i2010 action plan

The first objective of i2010 is to establish a Single European Information Space offering affordable and secure high-bandwidth communications, rich and diverse content and digital services. Action in this area combines regulatory and other instruments at the Commission's disposal to create a modern, market-oriented regulatory framework for the digital economy.

The i2010 Action Plan defines a package of proactive policies to harness the potential of the digital economy to deliver growth, jobs and modern, on-line public services. It is a key component of the EU's renewed "Lisbon" competitiveness strategy[36]. The i2010 Action Plan states that ICT can contribute strongly to improvements in the quality of life. ICT are capable of improving the health of our citizens via new ICT enabled medical and welfare services. In light of the demographic challenges facing Europe, ICT can help make public health and welfare systems more efficient and effective[37].

i2010 has a particular focus on the further development of eHealth strategies and it sets out a interoperability roadmap for greater use of technologies, new services and systems, to create a "European e-Health Area". The roadmap identifies various steps involved in order to reach its goals, of which some are being addressed by REACTION and solutions will be proposed:
- Recommend a set of guidelines to facilitate Member States' decision-making on eHealth interoperability, and to assess what aspects of interoperability are most urgent (e.g., Electronic Health Records, health messaging and patient identifiers);
- Reinforce appropriate collaborations by/with industrial players and public-private partnerships;
- Propose possible legislative or regulatory approaches to eHealth interoperability, including aspects relating to data privacy and security.

i2010 states that trustworthy, secure and reliable ICT are crucial for a wide take up of converging digital services. This statement fully justifies the high focus on security, privacy and trust in REACTION.

---

[36] http://europa.eu.int/information_society/eeurope/i2010/docs/launch/i2010_memo.doc

[37] http://europa.eu.int/information_society/eeurope/i2010/docs/communications/com_229_i2010_310505_fv_en.doc

Coordination with the Competitiveness and Innovation Programme (CIP)

The outcomes of REACTION will be coordinated with the activities related to chronic disease management under the Competitiveness and Innovation Programme (CIP). ICT in FP7 and ICT in the CIP are therefore complementary instruments aiming at both progressing ICT and its applications and at making sure that all citizens and businesses can benefit from ICT.

The ICT Policy Support Programme (ICP-PSP) in the CIP aims to stimulate innovation and competitiveness and accelerate the development of a sustainable, competitive, innovative and inclusive information society. It supports activities to accelerate innovation and implementation of ICT based services and systems through the wider uptake and best use of ICT.

The theme 1 of the CIP-PSP programme focuses on health and ageing. For this theme, the challenge is to enable highly innovative technologies and integrated solutions emerging from research for wider deployment across the EU. The areas share the same aim of a triple win: unlocking the huge business opportunities in Europe and in the global market, containing the costs for society, and improving the quality of life (including good health) in general and in particular for the elderly and disabled.

The REACTION project is still in the research phase with more than five years to market. However, the REACTION platform is extremely well suited for subsequent deployment in the area of chronic disease management. Once the research results are starting to come out of the REACTION project, they often need to be incorporated in pilot actions to test the feasibility of dedicated REACTION applications in real life settings. Later, large a large scale pilot of the entire platform, including high accuracy sensors for CGM, are likely to fit very well into the realm of the ICT-PSP programme.

Contributions to other European initiatives

Another set of issues are relating to the mobility of patients, including the cross border circulation of goods and services, among which eHealth services are of growing importance. Patient mobility is addressed specifically in a Communication from the Commission, COM (2004) 301, entitled "Follow-up to the high level reflection process on patient mobility and healthcare developments in the European Union". In this light, a European strategy is needed – which forms part of the current Communication on patient mobility - to ensure that citizens can exercise their rights to seek care in other Member States if they wish, and that European cooperation can help systems to work together to meet better the challenges they face.

REACTION will address issue of cultural and regional differences and will analyse aspects of health economics in different member states across Europe in support of patient mobility. It will also include aspects of the Service Directive in relation to health care services.

Contribution to European and global standards

Uncertainties due to lack of standards is a major contributing factor for the slow and often unsuccessful uptake of remote monitoring systems. In order to meet its objective of high impact, the REACTION project will be very active in standardisation.

The objective of the standardisation work in REACTION is to liaise with the appropriate standardisation bodies and initiatives and ensure that the project is building upon available and emerging standards and industry specifications to ensure interoperability and enable quick market take-up. Where these standards are not sufficient or are difficult to apply, REACTION will seek influence and contribute to their extension, or where feasible, propose amendments. Impacting on standards is clearly an effort that strongly links to exploitation and dissemination. REACTION will thus also use dissemination through SIG workshops and conferences. The following standards and standardisation bodies are relevant:

Medical standards

Development within REACTION will influence standardisation work in bodies such as ISO TC215 WG 7 (Medical devices), CEN TC251 WG IV (interoperability) and IEEE PHD (personal health data). Also the work in CEN/ISSS eHealth Standardisation Focus Group will be closely followed.

The IEEE 11073 PHD standards for sensor design and development will be impacted by the work undertaken in sensor development and Body Sensor Networks.

Interoperability in Health Information Systems will be implemented using existing standards such as EHRcom, openEHR and HL7 Version 3. Semantic interoperability will be advanced using emerging standards such as OWL.

Dr. Malcolm Clarke (UBRUN) currently serves on CEN TC251 and ISO 215 committees for medical devices. UBRUN is also on the development committee IEEE 11073 and has access to expertise and will feedback to the standard.

Wireless networks

The work on Body Area Networks will influence the design and standardisation of low power, short range wireless technology used for medical applications. Results will be exploited and be used to liaise with the networking groups of the Continua Health Alliance.
FHG-SIT is chair of the Special Interest Group "Security & Trust" of the Wireless World Research Forum (WWRF) and a member of ACM's SIGMobile.

Security standards

Most important for standardisation are the World Wide Web Consortium (W3C), the Liberty Alliance and the Open Mobile Alliance (OMA). The areas of our contributions to standards in the area of trust, privacy and security will be secure identity management, authentication, security, privacy, trust, profiling, personalisation, and socio-legal standards to serve sector-specific agent based platforms, specifically for multi-agency cooperation, personalisation, secure identity management, authentication, privacy control, security contracting and governance.

A further impact as to the security requirements will be on standardisation activities in ISO TC 215, CEN TC 251 and HL7 and European and national activities such as the eHealth Cards. FHG-SIT has also been very active in the standardisation process of the German eHealth Card.

Web services

In the Web Services space, standardisation is being driven mainly by multinational IT vendors working through the World Wide Web Consortium (W3C), and the Organization for the Advancement of Structured Information Standards (OASIS). Any contributions realised in this space will comprise specific extensions of standards and profiles for composing specifications to ensure interoperability. Standards related to ontologies and semantic modelling, e.g. OWL, and standards concerning coordination of service oriented and distributed applications such as WS-Coordination and WSRF are obviously of particular interest for REACTION. Furthermore the experience gained from the RTD efforts will provide input to these standardisation processes.

The individual workpackages will produce input to the standardisation work, such as draft proposals, white papers, specifications, etc.

One major lesson from the past in mobile systems is that privacy and security paradigms are changing so that REACTION needs to be active in the standardisation with a twofold approach. First to monitor the developments and to predict upcoming developments and second to influence these bodies to include the requirements into the ongoing work e.g. in terms of use cases.

CNET, FORTH-ICS and FORTHNET are following the work in W3C very closely.

B4. Ethical issues

Basic principles

The principles of the Charter of Fundamental Rights of the European Union are relevant to the approach adopted by ICT researchers. These principles cover dignity, freedom, equality, solidarity, citizens' rights and justice. The project also complies with existing national legislation, European Union legislation, and it takes into account the Opinions of the European Group on Ethics.

Based on these guidelines, the proposers have come to the conclusion that the REACTION project does not present any ethical issues in any form and no such issues are expected to arise in the project.

Informed consent

The REACTION project further complies with Article 8 of the European Human Rights Convention. Given the pervasive and ubiquitous nature of home networks, the partners have considered the sensitive implications of the project for privacy and autonomy. The partners have carried out a prior assessment of risk and identification of precautionary actions proportional to the potential risk/harm of the proposal as described in the proposal.

The clinical trials to be undertaken in the validation of the REACTION solutions will involve real patients in Austria and the UK. All clinical tests involving real patients will be performed by qualified medical staff with the highest expertise in the practice, which will guarantee a strict conformance with national and international ethics and regulations.

MUG will validate a suite of multi-parametric monitoring services designed to facilitate the close monitoring of diabetic patients by remote dedicated diabetes experts and so enable more widespread use of TGC in an inpatient environment. For this purpose, MUG will provide access to its 20-bed inpatient department for clinical trials.

To ensure compliance with the new system by health care professionals, comprehensive surveys will be performed amongst clinicians and nurses. Prior to enrolment, patients will be fully informed and asked to sign a statement of consent. Ethical approval will be obtained from the Austrian clinical board prior to the study commencement. (see page 105).

CHC will validate a suite of services aiming at simultaneous monitoring of blood glucose, blood pressure and physical activity to achieve comprehensive protection against diabetic complications and promote pre-active disease management.
An RCT of 100 patients managed long term using home based monitoring with a further 100 in the control arm will be used to assess the effectiveness of the REACTION approach. Finally, a Multiple Daily Injection compliance study with 100 patients will be carried out. One group will be reminded by personalised alerts when noncompliant. The other group will not. All patients will be tested for glycosylated hemoglobin A1c every two weeks.

The clinical trials will be performed by the CHC in a primary care setting. CHC is a primary care health centre in the NHS system. Patients will be fully informed, given access to all data and asked to sign a statement of consent before being enrolled. Ethical approval will be obtained from the UK clinical board prior to commencement (see page 105).

A member of the team at the coordinating partner ATOS is also a member of the FP7 ethical board and will secure that ethical standards in REACTION are aligned with the EU policies.

ETHICAL ISSUES TABLE

	YES	PAGE
Informed Consent		
Does the proposal involve children?		
Does the proposal involve patients or persons not able to give consent?		
Does the proposal involve adult healthy volunteers?	X	104-105
Does the proposal involve Human Genetic Material?		
Does the proposal involve Human biological samples?		
Does the proposal involve Human data collection?		
Research on Human embryo/foetus		
Does the proposal involve Human Embryos?		
Does the proposal involve Human Foetal Tissue / Cells?		
Does the proposal involve Human Embryonic Stem Cells?		
Privacy		
Does the proposal involve processing of genetic information or personal data (e.g. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction)		
Does the proposal involve tracking the location or observation of people?		
Research on Animals		
Does the proposal involve research on animals?		
Are those animals transgenic small laboratory animals?		
Are those animals transgenic farm animals?		
Are those animals cloned farm animals?		
Are those animals non-human primates?		
Research Involving Developing Countries		
Use of local resources (genetic, animal, plant etc)		
Benefit to local community (capacity building i.e. access to healthcare, education etc)		
Dual Use		
Research having direct military application		
Research having the potential for terrorist abuse		
ICT Implants		
Does the proposal involve clinical trials of ICT		
I CONFIRM THAT NONE OF THE ABOVE ISSUES APPLY TO MY PROPOSAL		

B5. Gender aspects (optional)

The low number of women in the ICT field is a well-known problem. In REACTION, gender issues and gender mainstreaming will be given due attention. This holds for equal opportunities and working conditions for researchers as well as for the content of the work itself.

The partners have already developed a gender equality action plan with gender aspects in the conduct of the planned work, as well as the relevant principles contained in the European Charter for researchers and the Code of Conduct for their recruitment.

Current position

Of the currently 40 researchers associated with the project, 7 are female and 33 are male. REACTION Project Manager is a woman and the Project Management team is led and composed mainly by women.

Equal opportunities for male and female researchers

REACTION will make every reasonable attempt to involve as many more female researchers and developers in the project as possible. The academic and research partners in REACTION will strive to hire female researchers. In particular, we will:
- Strive to have one or more female researchers for each partner.
- Offer possibilities for part-time contracts (for male as well as female researchers).
- Strive to hire female researchers.
- Involve as many female students and researchers in training programs as possible.

Women's participation in research must be encouraged in REACTION. We will aim always to include an equal number of female and male researchers. All of the REACTION partners have well-established equal opportunity policies.

Gender balanced research

Women's participation in research must be encouraged in REACTION. We will aim always to include an equal number of female and male researchers. All of the REACTION partners have well-established equal opportunity policies. In particular, REACTION will:
- Take care that the gender issues will be covered in the planned workshops and seminars.
- Contribute to changing the techno-centric image of the ICT field by involving female developers in the validation activity.
- Urge female members of the project team to undertake important roles in the project.

Gender balanced products

Of course, human users include male as well as female persons. The tests conducted with end users are very important in REACTION and we will take care that proper gender balance will be taken into account. If differences in behaviour between male and female users in dealing with the REACTION platform will come to light, REACTION architecture will strive to be flexible enough to cater to these differences. In particular, REACTION will:
- Develop an architecture that is flexible to include different user models (also) reflecting differences between male and female users.
- Always include an equal number of female and male users in its validation, and report findings in a gender-disaggregated way.