PROJECT PERIODIC REPORT

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Project acronym:	**p-medicine**
Project title:	**From data sharing and integration via VPH models to personalised medicine**
Funding Scheme:	**Collaborative Project**
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Date of latest version of Annex I against which the assessment will be made:

27 October 2011

Interim report: **1st** ☐ **2nd** X **3rd** ☐ **4th** ☐

Period covered: **from 1 February 2012 to 31 January 2013**

Name, title and organisation of the scientific representative of the project's coordinator:

Prof. Norbert Graf

Universität des Saarlandes

Tel: **+49 6841 1628397**

Fax: **+49 6841 1628302**

E-mail: **graf@uks.eu**

Project website address: **www.p-medicine.eu**

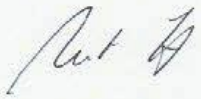
Declaration by the scientific representative of the project coordinator

I, as scientific representative of the coordinator of this project and in line with the obligations as stated in Article II.2.3 of the Grant Agreement declare that:

- The attached periodic report represents an accurate description of the work carried out in this project for this reporting period;
- The project (tick as appropriate) [3]:
  - ☐ has fully achieved its objectives and technical goals for the period;
  - ☒ has achieved most of its objectives and technical goals for the period with relatively minor deviations.
  - ☐ has failed to achieve critical objectives and/or is not at all on schedule.
- The public website, if applicable
  - ☒ is up to date
  - ☐ is not up to date
- To my best knowledge, the financial statements which are being submitted as part of this report are in line with the actual work carried out and are consistent with the report on the resources used for the project (section 3.4) and if applicable with the certificate on financial statement.
- All beneficiaries, in particular non-profit public bodies, secondary and higher education establishments, research organisations and SMEs, have declared to have verified their legal status. Any changes have been reported under section 3.2.3 (Project Management) in accordance with Article II.3.f of the Grant Agreement.

Name of scientific representative of the Coordinator: Prof. Dr. Norbert Graf

Date: 29.03.2013



For most of the projects, the signature of this declaration could be done directly via the IT reporting tool through an adapted IT mechanism and in that case, no signed paper form needs to be sent

[3] If either of these boxes below is ticked, the report should reflect these and any remedial actions taken.

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1 Publishable Summary

Project context and objectives

p-medicine started on 1 February 2011 as a 4-year integrated project. It is an interdisciplinary and collaborative research activity including 19 different academic, industrial and SME partner institutes from nine European countries and Japan who are working together and join expertise in clinical, IT-, legal, ethical and basic research. The aim of p-medicine is to develop and exploit an IT infrastructure that supports translational research in the domain of the Virtual Physiological Human (VPH). All researchers in p-medicine have dedicated themselves to overcome current problems in clinical research and to pave the way for personalized medicine for patients with cancer and beyond. It is the purpose and emphasis of p-medicine to formulate an open, modular framework of tools and services,

- allowing efficient secure sharing, seamless joining, handling and exploitation of large amounts of heterogeneous personalized data sets within the legal and ethical framework to protect the privacy of patients and guarantee data security and safety;
- enabling demanding VPH multiscale simulations (*in silico* oncology);
- building standards-compliant tools and models for VPH research;
- drawing on the VPH Toolkit[1];
- providing tools for large-scale, privacy-preserving data and literature mining;
- developing decision support services to support physicians in decision making in their daily care of patients; and
- fostering patient empowerment.

p-medicine ensures that privacy, non-discrimination, and access policies are aligned to maximize protection of and benefit to patients. The p-medicine tools and technologies will be validated within the concrete setting of advanced clinical research. Education and training activities will ensure the usage of the p-medicine platform by physicians. Pilot cancer trials have been selected based on clear research objectives, emphasising the need to integrate multilevel datasets, in the domains of Wilms tumour, breast cancer and acute lymphoblastic leukaemia. To sustain a self-supporting infrastructure realistic use cases are built that will demonstrate tangible results for clinicians. These use cases are based on scenarios described by clinicians. The project is clinically driven and promotes the principle of open source and open standards.

Work performed since the beginning of the project and the main results achieved so far with special emphasis on the second funding period

All project partners demonstrated a strong commitment and an active enrolment during the two years of the project. Two progress meetings with all partners took place during the 2nd year. In addition to these progress meetings, a number of further very constructive and efficient work package meetings and telephone conferences were held, supported by a steadily increasing e-mail exchange and the p-medicine Wiki. Several meetings of VPH-Share and p-medicine were carried out to exchange information and share knowledge gained in both projects and to adopt a joint strategy for collaboration. Members of VPH-Share[2] attended the p-medicine progress meeting in St. Augustin, Bonn (Germany) in August 2012 and members of p-medicine took part in the consortium meeting of VPH-Share in Madrid (Spain) in March 2013. The main activities for collaboration are related to security interoperability, data integration, clouds and semantics. It was agreed that the p-medicine's Oncosimulator should run within the cloud infrastructure of VPH-Share.

[1] http://www.vph-noe.eu/wp3

[2] http://www.vph-share.eu/

As a result of a strong cooperation between all partners a timely preparation of all scheduled deliverables was possible. An update of user needs and requirements is clinically driven and optimized by a continuous feedback loop with all partners to address end-to-end use cases. These are listed in the p-medicine Wiki[3]. It was agreed in the first year that tools should be built in a modular and general way to guarantee reuse of granular modules in different tools, so these end-to-end tools show first examples of this kind. In this respect the first version of the p-medicine architecture has been developed following a layered approach of functional requirements alongside personalized user scenarios. Some of the identified architectural elements ("components") are ObTiMA, the data warehouse, the portal, the annotation tool as an interface to annotate external databases with the HDOT ontology, the identity provider and other security tools, like CAT. All these tools are described in the updated version of D3.2. First versions of these tools are ready to use after the second year of the project. ObTiMA will collect data in a prospective trial for Wilms Tumour. Data can be uploaded to the data warehouse after de-facto anonymization and semantic annotation. The annotation tool is ready for use as a first version of the HDOT (Health Data Ontology Trunk) ontology is in place. The initial release of the data integration technology is described in D4.3. In addition an initial release of the patient view is described and evaluated (D4.4). In this process, a fundamental step is the definition of a lay language by which information primarily coded in medical jargon is then presented to patients in an easily understandable and non-technical fashion. For this purpose, we extend HDOT in a dedicated specific patient-oriented module called the Health Data Ontology Trunk for Patient Empowerment (HDOT_PEM). This was done is close cooperation with ecancer and the work on D14.2.

The general data integration method in p-medicine is defined as a three-step process, which starts with data submission to the data warehouse, followed by a data annotation step in which a metadata mapping file is created and finally a semantic mediation step in which the pushed data is stored in a new standardized and integrated form in the data warehouse as RDF triples. Deliverable (D7.2) describes deployed data warehouse components, how these components will change in the future, and what further components are yet to be developed and deployed. The currently deployed components support the immediate work of p-medicine in integrating data from many sources under a common ontology, storing it securely, and making it available to systems which enable clinical decision support. Interfaces for storing imaging data for the p-medicine project are provided. The proposed solution takes advantage of cloud storage based on OpenStack technology. The report on federated storage services is described in D8.1.3. Furthermore, the positioning of the extended Trial Outline Builder (TOB) in the initial system architecture, especially in ObTiMA, as well as its functionality are discussed with the aim of integrating legacy bioinformatics databases and analysis tools in a generic way into the TOB. Finally, Custodix provided important components of the p-medicine security architecture that have already been prototyped. This prototype is in line with the data protection and data security framework for p-medicine that is built on a clear separation of the clinical domain and the research domain.

Patient data will be used only in de-facto anonymous form. Within p-medicine de-facto anonymization will be achieved by a state-of-the-art pseudonymization of all data entering the network, the implementation of a Trusted Third Party (TTP), the work of a data protection authority within p-medicine (Center for Data Protection, CDP) and the signing of contracts by all participants ensuring the compliance with the p-medicine data protection and data security policies that will primarily exclude the use of matching tables for re-identification of patients. In this context the necessary contractual agreements to be concluded have been developed and signed by the beneficiaries. Legal and ethical issues regarding data warehouse, data mining and IP issues were analysed and the corresponding deliverable D5.2 was submitted in time. As the first version of the security and legal framework is in place the upload of data into the data warehouse is now possible. Furthermore, a Patient Identity Management System (PIMS) is developed. The release and demonstration on data anonymization tools is

[3] *http://atlas.ics.forth.gr/pMedicine/wiki/index.php/WP2#Tool_Scenarios*

described in D8.3. In addition legal and ethical rules and principles have been outlined with regard to the access to biobanks and issues relating to p-medicine tools and international GCP clinical trials. In this respect ObTiMA is enhanced to make it compliant with GCP criteria. Results are written in D 8.4. A Report on legal and ethical issues for p-medicine tools used for international GCP trials was finalized in time (D5.5). The validation of ObTiMA will be carried out together with ECRIN. The legal and ethical framework is further enhanced for biobanking (D5.3). A meeting with the International Ethical Committee took place in Homburg in December 2012. This committee will provide a white paper dealing with Ethics in personalized medicine in the VPH setting at the end of the project.

Users can get credentials to access p-medicine via the p-medicine portal using Single Sign-On (SSO). Liferay has been chosen as the portal framework for p-medicine and published on the project Wiki. The design and prototype implementation of the p-medicine portal is described in D8.1.2. Further work on DrEye (D8.2), ObTiMA (Audit trail, pseudonymization, validation of data, biobanking module, GCP compliance), Custodix Anonymization Tool (CAT) (conversion to a service) and the development of a patient identity management solution were carried out during the reporting period. A report on the validation and certification of ObTiMA and DoctorEye is given in D9.3. D9.4 describes the usage of DoctorEye for the segmentation of Wilms tumours. The biobanking access framework, and the push and sync service are being developed further and first versions will be available at the end of 2013. Integration guidelines were developed to monitor the integration process of tools, services and models in the p-medicine platform. This is supported by a hardware and software infrastructure that is set up at FORTH to ease the integration work and the monitoring and administration of the p-medicine Wiki. The integration guidelines and monitoring of tools and services is described in D8.6.1 and a description of the initial version of the p-medicine integrated platform is provided in D8.6.2.

For validating the p-medicine environment use cases were developed for the selected diseases in p-medicine (Wilms tumour, breast cancer and acute lymphoblastic leukaemia (ALL)). Parts of them are use cases for the Oncosimulator, others are use cases for decision support and others are use cases for answering research questions or using p-medicine tools and services. User scenarios for decision support are described in D13.1. For all scenarios necessary data has been defined and workflows described. Extensive interactions and discussions with the clinical partners involved in WP12 have led to the clarification of the types of multiscale data that are both exploitable by WP12 and available to the clinical institutions. Representative series of fake data sets have been created for nephroblastoma, breast cancer and ALL and sent to ICCS to partially drive the development of the corresponding Oncosimulator models. The Oncosimulator was further developed by defining the architecture and information flow diagrams and by providing high-level guidelines to the developers of the biomechanism models. Initial algorithms for the three basic simulation models corresponding to the three tumour types under consideration (nephroblastoma, breast cancer, acute lymphoblastic leukaemia) were further developed and implemented (D12.2). A report on the development of the Oncosimulator and the utilization of the biomechanism models is provided in D12.3.

For nephroblastoma, a new prospective study was written and approved by the UK Research Ethics Committee. ObTiMA will be used as the trial management system. Further tools, like a DICOM server established at PSCN will be exploited in this prospective nephroblastoma study. A report on the ALL integrated data analysis environment is available (D9.9).

Biobanking use cases for ALL and SIOP as well as the initial architecture for the biobank access framework are available. A state-of-the-art analysis of tools and frameworks for biobanking is available. The report states that very different approaches exist regarding legal and ethical provisions and guidelines for biobanking (D5.3). Different contracts are to be drawn up. An initial biobank data set has been compiled that harmonizes the terminology used by existing biomaterial repositories in the nephroblastoma and ALL use case. There was mutual agreement regarding a standardisation of the data schema for biobanking by taking the BBMRI minimal set, leukaemia-, and nephroblastoma datasets into account. This

will give a sound basis for the development of a p-medicine biobank ontology module. Initial prototypes of the components of the p-medicine biobank access framework have been elaborated on and described in D10.2.

Requirements, scenarios and the architecture for the data mining environment were further analysed and developed. The concept of data mining patterns and its intended use in p-medicine were elaborated. Initial data mining patterns were defined by the partners and have partly been implemented as initial prototypes in R. A first prototype version of the data mining web service was implemented by FhG-IAIS, providing the initial facilities for executing workflows and R scripts. Biovista designed and developed an interface through which the platform will be able to talk to any ontology. Several scenarios were developed and workflows for the integrated analysis of MRI and RNA data and for analysis of DNA and RNA data have been implemented.

The datasets used for building the clinical decision support system (CDS) are described in D13.3. This includes the description of the documents that serve as an input to the treatment recommendation module and the datasets used for data mining activities, which lead to creating models that will also be used in the CDS application.

With regard to patient empowerment instruments a methodology has been identified by *e*cancer to understand patients' needs. This ALGA questionnaire was produced. Results of the questionnaire will guide specific requirements of the patient empowerment services and the development of the Interactive Empowerment Service (IEmS). Several scenarios with focus on the patient are described in this respect. The specification of the linguistic schema is provided in D14.2.

In close cooperation with all partners in WP15 an evaluation and validation plan for tools is in place and has already achieved first results, e.g. in evaluating ObTiMA. The corresponding deliverable (D15.2) has been submitted on time. WP16, education and training, has successfully started. First flash tutorials and eLearning tools are available (D16.2).

The p-medicine website is regularly updated. A second newsletter was published and distributed. The project was demonstrated at several meetings where clinicians were also present. Scientific publications have been written. Interfacing with other projects has continued (VPH-Share, CONTRACT, INTEGRATE, TUMOR, EURECA, CHIC, MyHealthAvatar, BioMedBridges, ENCCA and others). A meeting with ECRIN, EORTC and p-medicine is scheduled for the 30th of April 2013 to discuss collaboration between the 3 projects in running clinical trials. To sustain and maintain p-medicine a legal entity called STaRC (Study, Trial and Research Center) will soon be founded. Collaboration with Thomson Reuters was initiated. They attended the last p-medicine consortium meeting in Lausanne in March 2013. p-medicine was introduced at a meeting in the greater area of Tokyo/Yokohama which was attended by politicians, industry and scientists who are exploring infrastructures like the one built by p-medicine. Further meetings will follow. A first summer school of p-medicine will take place in June 2013.

Expected final results and their potential impact and use

p-medicine will provide an environment that facilitates personalized medicine in all aspects. A legal framework guarantees the secure handling of large amounts of heterogeneous data to be stored in a data warehouse for further exploitation by p-medicine end-users. By addressing semantic interoperability, data mining, tools development based on clinically driven use cases, a validation process including quality aspects and education and teaching activities, clinicians will be able to enrol more patients in clinical trials by using p-medicine tools and services. They will be able to run VPH models and other tools for decision support. Access to biobanks will enhance post-clinical trial research. Patients will be empowered through respective tools for active participation in the health care decision process and clinical research. A self-supporting infrastructure will be maintained. The legal and ethical framework that is developed can serve as a best practice standard in personalized medicine.

For further information, please visit: http://www.p-medicine.eu

2 Project objectives for the period

p-medicine has 17 work packages all of which were supposed to start in the first year except WP16. Despite the later start of WP16 work has already been done during the first year in WP16. Therefore objectives for all work packages are listed here. Objectives for this period are written in Italic:

WP1: Project management

- *To ensure the timely and qualitative achievement of the project results through administrative coordination;*
- *To ensure the quality control of the project results and the risk management of the project as a whole;*
- *To provide the timely and efficient administrative and financial coordination of the project and the compliance with contractual commitments.*

WP2: User needs and requirements

- To define user needs and requirements for tools, methods and services for VPH research focused on clinical usage;
- To review current guidelines for the validation and certification of tools and software to make them GCP conform for usage in clinical trials and in daily clinical practice.
- *To ensure the empowerment and safety of patients in daily clinical care and to increase their participation in clinical trials*
- *To facilitate the process of bringing state-of-the-art knowledge in the decision process of treating physicians leading to personalized medicine*

WP3: IT architecture

- *To focus on the definition of a reference architecture (RA) for subsequent implementation;*
- *Integration of the different modules/services developed by the project;*
- *To provide software architecture design patterns to effectively guide and support the construction of coherent, consistent and interoperable SOA-based systems and services;*
- *To define appropriate interfaces among the modules to enable interoperability;*
- *To identify, analyse and select relevant existing standards with impact on the system;*
- *To study and analyse security-related issues in dynamic collaborative environments, which includes electronic consent management.*

WP4: Standardization, semantic Interoperability and data integration

- *To identify in a functionality-driven and user-oriented way the semantic resources needed, identify the candidates for re-use (by evaluation), and provide a common structure to unify the semantics for the project or the sub-task at hand. For this purpose the start of the development of the health data ontology trunk (HDOT) is necessary;*
- *To find technical solutions aimed at the specific needs of the project in identifying case-relevant ontologies and re-using or merging them (the research focus of WP4 is not to create new ontologies). We survey and assess existing resources in use for this objective;*
- *With respect to this, the challenge of p-medicine regarding semantic interoperability revolves around two key issues: mapping of data in pre-existent HIS and extension and optimisation of semantic resources against the background of evolving data that is pushed into the system. Initial work on D4.2 is providing the basis for achieving this semantic interoperability with regard to data in hospital information systems and clinical trial management systems as well as other relevant data sources (biobanks, data repositories, etc.);*
- *To explore possibilities to automatically search and assess existing ontologies, not only with respect to common quality criteria, but also regarding specific issues in biomedical*

semantics, like granularity. Groundwork for this objective has started by evaluating semantic resources needed and suitable for re-use;
- *We provide a patient view connected to the ontology, which will help to organize information from the data collection of p-medicine for patients in an understandable manner. With regard to semantic resources and the scientific information stored there, we consider possibilities for accessing and processing this information in patient-friendly ways.*

WP5: Legal and ethical framework
- *To guarantee that p-medicine is compliant with all legal and ethical rules applicable;*
- *To do systematic in-depth research on legal and ethical rules of sharing data and biological material on a European level with the final objective of empowering patients.*

WP6: Integration in clinical research infrastructures
- *Effective and interoperable integration of p-medicine tools in an international clinical trials infrastructure (ECRIN);*
- *Evaluation of the usability and effectiveness of p-medicine tools used in a real clinical trial as part of the ECRIN clinical trial infrastructure.*

WP7: Data warehouse
- *To develop federated data warehouse infrastructure components to store the multiple different types of medical data produced in this project;*
- *To develop storage services for large data objects;*
- *To develop mechanisms for ensuring reliability and auditability of the data;*
- *To develop and deploy suitable programmatic interfaces, to allow the different types of data to be uploaded to the warehouse via tools developed in other work packages;*
- *To develop a service integrated in the web portal to allow users to search for and view available data;*
- *To develop federated capability-based secure access mechanisms compliant with the legal and ethical framework of the project;*
- To integrate security and role-based access, based on the legal and ethical framework developed in the project;
- To integrate the disparate types of data produced and available in the project using appropriate ontological tools.

In this WP a close cooperation with VPH-Share will take place. The cooperation includes the following:
- Exchange of information on Cloud computing and storage environments with a focus on how they may support distributed medical information systems;
- Exchange of technical knowledge pertaining to the exploitation of specific Cloud technologies;
- Joint assessment of the applicability of Cloud platforms to storing, processing and exposing data in the context of medical applications;
- Exchange of prototype software and detailed technical documentation thereof, with the possibility of cross-exploitation of synergies between both projects.

WP8: p-medicine workbench
- *To develop and handle tools used in translational clinico-genomic research;*
- *To address the development of the appropriate pseudo-anonymization and pre-processing tools for nephroblastoma and breast cancer applications;*
- *To create tools that can be identified by users and used in clinic-genomic VPH studies as well as workflow integration and clinical trial management and services for interacting with the clinical patient record;*
- *To provide annotations and metadata, so that end users can easily retrieve them;*

- *To adopt available VPH standards allowing other open source tools to be easily integrated and re-used in the tools repository;*
- *To emphasise the interaction with the VPH NoE toolkit in the sense that p-medicine will utilise available tools but also share tools with the toolkit in order to be used by the wider VPH community.*

WP9: Clinical trials

- *To validate the p-medicine environment by focusing on running clinical trials;*
- *The three selected diseases are Wilms tumour, breast cancer and acute lymphoblastic leukaemia (ALL);*
- *For all trials clinical relevant use cases will be defined;*
- Data coming from these trials will be stored in the data warehouse in a secure and anonymized way according to the legal and ethical framework of p-medicine;
- *The Wilms tumour trial will be used to employ the newly developed and validated tools of p-medicine. The trial also provides data for the Oncosimulator testing a specific Wilms tumour scenario;*
- *The primary aim of the breast cancer studies will be to maximize efficacy of therapy while minimizing side effects as well as to find biomarkers useful for predicting patients' response to treatments;*
- *The leukaemia trial in p-medicine will be used to develop such a model for the prediction of MRD and disease recurrence.*

WP10: Access to biobanking

- To analyze existing open biobank frameworks which enable the sharing of biomaterial with respect to usability, GCP criteria and legal aspects. This will be done in close cooperation with WP2 (User needs and requirements) and WP5 (Legal and ethical framework). One aspect is the evaluation of potential re-usability of existing tools for p-medicine;
- *To develop an integrated biobanking infrastructure in close cooperation with BBMRI. This service framework includes a biobank annotation service, a generic wrapper tool, a meta search engine for biomaterial with the possibility to integrate biomaterial stocks into larger bio-databanks;*
- *To provide a semantic biobank query interface that allows users to search for cases and materials in various bio-repositories according to their selection criteria and to match this with corresponding case related data in the data warehouse. This tool will serve as a meta search engine for biomaterial;*
- *To integrate a mechanism for monitoring and safeguarding the patients'/donors' decisions on research that might or should be performed on their samples. This mechanism will be provided by WP14 'Collaborative Environment for Patient Empowerment';*
- *To evaluate the biobanking framework by integrating distributed biomaterial resources of the SIOP Wilms tumour trial into the p-medicine infrastructure in addition to the publicly available German-Austrian metabiobank in the cancer domain, namely the biobank Central Research Infrastructure for molecular Pathology CRIP.*

WP11: Patterns for data mining and predictive analytics

- *Transition of state-of-the-art data mining solutions to clinical practice;*
- *Building of the basic support for reusable data mining solutions;*
- *Definition of data mining patterns for several scenarios.*

WP12: VPH modelling and the integrated Oncosimulator

- *To develop three exemplary multiscale simulation models of clinical tumour response to treatment: one for nephroblastoma, one for breast cancer and one for acute lymphoblastic leukaemia (ALL) based on the principles that have been shown to be most appropriate for the clinical trial context. These three models will constitute the simulation core of the "p-medicine Oncosimulator";*

- *To clinically adapt, optimize and validate the three Oncosimulator models using the data generated by one clinical trial per tumour type. Especially with regard to the breast cancer type two complementary breast cancer trials will be considered which will be jointly viewed as the "Oncosimulator breast cancer branch clinical trial";*
- *To develop the p-medicine integrated Oncosimulator as a treatment support system;*
- *To develop a number of separate mutually compatible models focused on various biological mechanisms that determine tumour dynamics at various combinations of biocomplexity levels/scales in order to gain insight into the complex phenomenon of cancer and suggest treatment strategies by studying these mechanisms in silico;*
- *To utilize the tumour biomechanism focused models in order to explore the dynamics of the corresponding mechanisms in silico;*
- To utilize high performance computing resources such as DEISA/PRACE petascale facilities in order to increase the accuracy and the speed of numerical calculations;
- To evaluate the p-medicine Oncosimulator and the tumour mechanism focused models.

WP13: Clinical decision support

- *To develop tools able to support the clinicians to efficiently access all relevant data and infer knowledge necessary to reach the most accurate diagnosis and prescribe the most suitable treatment.*
- To support clinicians to provide personalized treatment and improve patient outcomes.
- *To proper implement and use clinical decision support systems*
- To support the clinicians to prevent or identify early in the treatment potentially serious side effects to treatments and drugs, and the patients most susceptible to develop serious side effects.

WP14: Collaborative environment for patient empowerment

- *To develop the Interactive Empowerment Service (IEmS);*
- *To provide the IEmS to:*
  - *Help the patient to understand her/his medical documentation;*
  - *Empower the patient to make informed choices;*
- *To achieve this objective the following steps need to be taken:*
  - *To analyse the p-medicine scenarios and identify use cases for IEmS;*
  - To develop and to test an interactive tool to support patients' empowerment.

WP15: Quality assurance, evaluation and validation

- *To test software components and services;*
- *To identify objectives that need to be specifically tested in each case, define the proper evaluation criteria and devise monitoring procedures that will be executed;*
- *To assess the quality of all services and tasks of the p-medicine environment and iteratively give feedback to all responsible persons;*
- To provide combined evaluations covering the whole integrated p-medicine environment;

Specifically:

- To formulate evaluation criteria, verification procedures, and feedback report guidelines;
- *To coordinate validation activities by partners and feedback reports;*
- *To evaluate the developed software tools by testing functionalities, accessibility, respect of user needs, data integration and execution times;*
- *Verification of GCP (Good Clinical Practice):*
  - ✓ *Protection of human rights as a subject in clinical trial;*
  - ✓ *Standards on how clinical trials should be conducted;*
  - ✓ *Clinical audit: performance will be regularly reviewed to ensure scheduled activities will be properly executed;*
- To do a survey about certification criteria for software components in clinical research settings and evaluation of their adherence in p-medicine environment;

- To write a final evaluation report.

WP16: Education and training

- *To impart understanding of the vocabulary and systems biology which underlie translational cancer research and understanding of IT infrastructures and their possibilities, e.g, the p-medicine environment;*
- To teach professionals when to use p-medicine tools or services, which one to use and how to make them work to their patients' benefit;
- To help patients to understand and use the IEmS (patient empowerment service).

WP17: Exploitation and dissemination

- *to coordinate the exploitation and dissemination of this project's objectives, approaches and results to target groups, new users and communities*
- *to exchange information and establish relationships with current projects and networks*
- *to promote the use of tools and methods created by p-medicine through workshops (in close cooperation with WP16), conferences and publications*

Summary of the recommendations from the previous review

The first p-medicine review meeting took place in Brussels on May 3, 2012. In the reviewers' consolidated report, the following recommendations were given resulting in the explained actions:

Recommendations concerning the period under review:
Collaboration with VPH-Share is regarded as not fully adequate. The terminologies are still different, even though concepts are very similar. p-medicine could be a use case in VPH-Share, but that is not the practice. Because of the different focus of each project, it is suggested to establish at least uniform semantics.
Actions: *Members of VPH-Share attended the p-medicine progress meeting in St. Augustin, Bonn (Germany) in August 2012 and members of p-medicine took part in the consortium meeting of VPH-Share in Madrid (Spain) in March 2013. Main areas of collaboration include security interoperability, data integration, clouds and semantics. It is agreed that p-medicine's Oncosimulator should run within the VPH-Share cloud infrastructure.*

The year 1 periodic report should be shortened and its context cumulated since it has currently over 150 pages.
Actions: *the report has been carefully edited and proof-read which minimises the possibility of redundancies. The partners have also been advised to provide short and concise summary reports. However, most p-medicine partners have frequently submitted scientific papers to conferences and journals, most of which got accepted and published. Therefore, the list of publications as well as the list of conferences are comparatively long. Moreover, a large number of deliverables was due in the second project year, which also elongates the overall report.*

Deliverables 7.1 and 13.2 are accepted, but still not completely adequate.
Actions: *Deliverable 7.1 has been enhanced with respect to the system design description and technical approaches are indicated. Deliverable 13.2 has been updated.*

Recommendations concerning future work:

1. **Exploitation and Sustainability**: more efforts should be directed to the project future exploitation and potential commercialization which will guarantee its sustainability, too. This issue has to be addressed particularly during the second year of the project. Therefore, the consortium should specify targets for exploitation.

Actions: *Contacts were established with industry during the second project year. Thomson Reuters was approached. A delegation of Thomson Reuters participated in our 5th progress meeting in Lausanne. Questions of sustainability and possible collaboration with Thomson Reuters were discussed. Thomson Reuters will provide a plan outlining the way the company can support p-medicine. In particular, the curation of data and the provision of external tools by Thomson Reuters will be subjects of collaboration as stated during that meeting. The p-medicine infrastructure itself is very interesting for the company.*
In addition to this a meeting took place in Yokohama, Japan on November 29, 2012. Norbert Graf, the coordinator of p-medicine, had the opportunity to take part in an information and exchange meeting between the Keihin Costal Area Life Innovation project of the City of Yokohama, Japan and the p-medicine project. The meeting took place at the Pacifico Yokohama Conference Center and was initiated by Professor Yuzuru Tanaka from our partner Hokkaido University (UHok). The objective was to discuss views and opinions of both projects with regard to the reinforcement of possible collaborations. More information is given in the 2nd newsletter.
The data warehouse as it is built in p-medicine will be used as a local data warehouse at the Saarland University Hospital to push data from the hospital information system into the local data warehouse to use these data in clinical trials and in research. This will be part of STaRC. A data warehouse for DICOM files will be continuously available at PSNC. ObTiMA will be used in a productive way. The first trial collecting data prospectively is IMPORT for nephroblastoma in the SIOP setting. ObTiMA will be maintained in STaRC.
During the reported period, Biovista has been engaged in meetings discussing p-medicine with collaborators, such as Novartis and Pfizer. The focus of these was mainly to lay foundations for further work in several areas, including personalized medicine challenges. These efforts done by Biovista in establishing new contacts in the personalized medicine field and raising awareness to p-medicine is seen as a starting point with the goal for collaboration with biotechnology and pharmaceutical companies.

2. **Architecture**: the project is grounded on the same architectural basis as VPH-Share. The execution level for both projects can be unified; the functional architecture could stay different according to different goals. Ensure that at least data sets are compatible, so interoperability may be possible.
   Actions: *Both projects have agreed that the Oncosimulator, developed within p-medicine, will also run within the cloud infrastructure of VPH-Share. This task is currently elaborated.*

3. **Collaboration** with other related initiatives and projects (e.g. ENCCA and INTEGRATE) needs to be intensified. Also, initiatives in US, such as "the big data initiative" by NFS may be of importance and relevance.
   Much closer cooperation between p-medicine and INTEGRATE is suggested. This includes the possibility of organizing common meetings, workshops and seminars, as well as reviewing the work the alternative project work by clinicians from another one.
   Actions: *Members of the p-medicine consortium regularly attended meetings of different other projects including INTEGRATE, TUMOR, CONTRACT, EURECA and BioMedBridges. In addition, a deep evaluation of the RICORDO project took place. In the future all these projects will work closely together with p-medicine. p-medicine is represented in the board of the VPH-Institute by USAAR. During our regular consortium progress meetings, we invite guest speakers from different projects to give keynote lectures. In p-medicine's upcoming summer school VPH projects are invited to participate via the website of the VPH Institute. Initiatives in US are addressed via the TUMOR project and Thomson Reuters, who sent one representative from US to the last p-medicine progress meeting in Lausanne.* A meeting with ECRIN, EORTC and p-medicine is scheduled in Paris for the 30th of April 2013 to discuss collaboration between the 3 projects for running clinical trials in Europe.

4. The project should care for scalability, performance and context awareness.
   Actions: *This will be continuously done. Feedback loops are set up between different stakeholders to achieve this goal. A new working document for the tools to be developed was initiated. The content of this document is put in the p-medicine Wiki (http://atlas.ics.forth.gr/pMedicine/wiki/index.php/WP2#Tool_Scenarios) for regular updates.*

5. **Usability**: Architecture and design of user interfaces and service logic need to be simple and clear for use of non-technical persons like physicians, nurses and patients. Interfaces need to be prototyped and validated as much as possible to foster wider acceptance of the results.
   Actions: *This is and will be done continuously in a process in which stakeholders, including physicians, will evaluate the developed tools. The ALGA questionnaire, providing data from patients for the IEmS, is running as an app and patients have so far been satisfied with this tool.*

6. **Critical path**: The main contribution is the medical aspect. The project needs to be focused on the "red line" connecting: Biodata (Biomarkers) - Semantics - Data Mining/Simulation - Medical App. - Personal Trials
   Actions: *Tools which reflect such critical paths will be developed, like the pathway scenario tool, or other decision supporting tools. This is also guaranteed by the clinicians involved, who are the drivers in the project, as they need these kinds of tools.*

7. **Medical issues**: There are some reservations about how realistic the development and clinical application of the Oncosimulator is. Apart from scientific constraints (unavailability of retrospective data needed for further data validation, insufficient data from peripheral blood microarray studies in solid tumours), financial constraints may apply which make this part of the project unrealistic.
   Hence, alternative scenarios and solutions should be sought, i.e. based on the statistical predictive approach taken in the INTEGRATE project. For the same reason it is recommended to make the preliminary data available confirming the possibility of creation the solid tumour, e.g. nephroblastoma, biology profile based on peripheral blood microarrays.
   Actions: *The level at which the clinical adaptation and validation of the Oncosimulator can be achieved varies considerably depending on the type of tumour addressed. For the case of leukemia (ALL) whole genome data has recently been made available in addition to blood cell counts, treatment schedules and other data. Furthermore, classifiers which can in principle distinguish between good and bad responders, e.g. to prednisone, are available and in use. This appears to be a pretty good situation. We have already started working on the genetic data. For the solid tumours, however, this is more difficult as imaging data are involved as well. To overcome these problems in a first step we only ask simple questions, such as "Does the tumour response to a given treatment, yes or no?" We do not ask how much. There will always be a validation with the real data to optimize the Oncosimulator. A close collaboration with INTEGRATE in this issue will be reinforced.*

8. The patients' empowerment seems to be an excellent idea which may help them to orient better in the nature of their disease and available therapeutic choices. It is of utmost importance, however, that any advice and/or consultation is given to patients through their primary treating physicians.
   Actions: *This will be guaranteed by all tools developed.*

9. A useful feature to consider would be Patients and/or Parents Forum development which would go in line with an idea of patients' empowerment. Creation of such communication platform should be seriously taken into account.

Actions: *Within p-medicine, it has been decided that such a communication and consultation tool for patients be developed.*

Work progress and achievements during the period

2.1 Work Package 1: Project Management

Regarding Work Package 1 reference is made to Section 1 “Project Management” following the individual work package descriptions.

2.2 Work Package 2: User Needs and Requirements

The work of this WP within this reporting period started with an update to the deliverables D2.1 to include technical requirements for clinical decision making and to D2.2 to include the scenario of biobanking. Based on the latter deliverable, the deliverable D2.6 was created highlighting use-cases and requirements updated based on user feedback. In the following Content and discussions were also produced for the deliverables D2.4 and D2.5.

Main objectives of this WP

The main objectives of the work package are:

- Elaborate on the user needs and requirements for the proposed technological and clinical research infrastructure to develop an environment capable to run tools for clinical decision support and VPH by different end user groups (e.g. clinicians) to drive common clinical practise to personalized medicine, providing the project’s clinical perspective and taking into account the state of the art in research and in practice in the addressed healthcare domains;
- Address the needs to develop a seamless, secure and consistent integration of clinical care data provided by hospital information systems and clinical trials as well as clinical and basic research data, taking into account the technological requirements from the clinical application standpoint to build an environment to facilitate VPH research. As user needs and requirements might change during the project, the respective specifications will be updated.

The active task in the work package in the reporting period concerned are:

- Task 2.5: Requirements for tools and services supporting patient empowerment (M1-M36)

Additional work has been done in the following tasks:

- Task 2.1: State-of-the-art review (M1-M8)
- Task 2.2: Scenario based user needs and requirements analysis (M1-M9)
- Task 2.4: Enhancing VPH models for clinical decision support (1-12)

Summary of progress achieved towards objectives

The deliverables D2.1 and D2.2 were both updated to make the current state as well as the needs and requirements clearer in the given areas. Deliverable D2.6 was written based on D2.2 to highlight changes to the use-cases and requirements based on user feedback. Provision of content and data as well as discussions took place in the process of creating the deliverables D2.4 and D2.5.

Summary of details for each task

Task 2.1, State-of-the-art review: Philips started off from the existing clinical scenarios as basis and translated the clinical needs found in them into technical requirements towards clinical decision making and the result was added to D2.1.

Task 2.2, Scenario based user needs and requirements analysis: UOXF refined the existing use cases and scenarios for the three different roles contributed by their institution (i.e. data manager, data entry and eCRF developers).
USAAR integrated these changes updating D2.2 together with adding use cases and data structures for biobanking contributed by Fraunhofer IBMT.
Subsequently, USAAR asked the different partners involved in the work package to provide updates to their respective use-case based on the feedback received from the different user groups. USAAR collected all partners' results and updates and combined them into deliverable D2.6 "Regular update of the user needs and requirements based on evaluation and validation". The update also embraces the recommendations to make the system easy to sustain after the project and to interface better with other research initiatives, like VPH Share. A working document to be used alongside D2.6 has been prepared. This document named "Tools for p-medicine scenarios and responsibilities for their building" has been uploaded to the p-medicine Wiki for easier access to the partners concerned. The purpose of this document is to monitor the progress of tool development and integration and to regularly outline and edit use cases and scenarios.

Task 2.4, Enhancing VPH models for clinical decision support: UOXF provided a literature review of existing tools as well as contributed to the discussion for the creation of D2.4. USAAR as well provided content and suggestions for this deliverable.

Task 2.5, Requirements for tools and services supporting patient empowerment: UOXF provided a literature review of existing tools and took part in the discussion towards creating D2.5. UOXF, together with SIB and FhG IAIS, also participated in the testing of ObTiMA which resulted in feedback for the use-case update.
CAU edited the dataset of the ALL-BFM 2000 study to allow anonymization of all personal data on demand as well as to use it for different scientific investigations.

eCancer collaborated further with FORTH to identify and fulfill any additional requirements as they are identified towards the IEmS.

FhG IAIS Identified some usage problems of the first tool prototypes that should be improved in the next version (and then tested again by prospective end-users) and provided a summary of the performed tests.

Summary of significant results

Deliverable D2.2 was carefully updated, also with regards to the question of sustainability of the p-medicine results. A working document complementing D2.6 has been initiated, in which the development of tools will be closely documented and monitored. The user needs and requirements were revised in an iterative process. A spiral process of requirement analysis, elicitation and validation is adopted. In the p-medicine wiki a special site was set up to support this process: http://atlas.ics.forth.gr/pMedicine/wiki/index.php/WP2#Tool_Scenarios. This iterative process of refining scenarios and tools guided the activity in all other work packages.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

There were no deviations from Annex I.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP2			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	38.00	4.50	7.62
3 – FORTH	5.00	0.00	0.00
4 – UCL	3.00	0.00	0.00
5 – FhG	2.50	0.00	0.50
7 – CUSTODIX	2.00	0.00	0.42
8 – Philips	7.00	2.00	1.00
9 – UDUS	8.00	0.00	1.36
11 – UPM	2.00	0.00	0.00
12 – CAU	2.40	1.50	1.12
14 – ecancer	6.00	1.00	1.00
15 – UOXF	4.00	1.33	2.17
16 – BIOVISTA	7.00	0.00	0.00
17 – SIB	7.00	0.00	0.00
Total	**93.40**	**10.33**	**15.19**

UOXF: spending is higher than planned as some activities were moved from period 1 to period 2.

2.3 Work Package 3: IT Architecture

Main objectives of this WP

WP3 focuses on the definition of a reference architecture (RA) for subsequent implementation and on the integration of the different modules/services developed by the project. The RA specification will provide software architecture design patterns to effectively guide and support the construction of coherent, consistent and interoperable SOA-based systems and services. Particular emphasis will be given to the definition of appropriate interfaces among the modules to enable interoperability. In addition, the relevant existing standards with impact on the system will be identified, analysed, and selected. Special emphasis will be devoted to the study and analysis of security related issues in dynamic collaborative environments, which includes electronic consent management.

The active tasks in the work package planned in the reporting period concerned are:

- Task 3.2: Reference Architecture Definition (M3-M36)
  - Subtask 3.2.2: Refinement of the p-medicine reference (M8-M36)
- Task 3.3: Open consultation process (M3-M18)
- Task 3.4: Security in dynamic collaborative environments (M6-M42)

Summary of progress achieved towards objectives

The activity in WP3 was devoted to further develop the architecture of the system built for the p-medicine project. In deliverable D3.4 we defined the security architecture in collaboration with WP5. Moreover, a first step was made in defining and deploying the delegations infrastructure for REST services.

A security gateway has been deployed and is being integrated with the Ontoloy Annotator and the Biobank Access Framework. This security gateway is responsible for the integration with the p-medicine security infrastructure. Through this gateway, websites can be integrated into the p-medicine security infrastructure.
We also analyzed the applicable standards in the field of data management and cloud computing, paying particular attention to security issues.

Summary of details for each task

Task 3.2, **Reference Architecture Definition**: The information view of the architecture is refined and elaborated based on the selected scenarios.

Subtask T3.2.2, Refinement of the p-medicine reference, was initiated and refinements to the architecture were performed. More concretely, progress has been achieved with regard to the data workflow within the semantic layer and the architecture of the components involved in the annotation of databases was refined. Annotations storage is handled by the Ontology Annotator, and this tool submits indexes of the available annotations to the Data Warehouse. We further described the reference architecture requirements concerning the data annotation process. In particular we added details about the interaction between the annotator tool developed by UPM in WP4 and the ontology annotator tool developed by USSAR-IFOMIS in WP4. Work on storage services according to architecture guidelines defined for the project. Detailed descriptions of the components of the storage infrastructure have been provided. We clarified the newly required functionalities and their provision as components of trial outline builder (TOB). By considering the bio markers obtained by analysis of biological and genomic data of patients as extended diagnostic events, the original TOB architecture can still work as a basis of the extended TOB.

Task 3.3, Open consultation process: There was continuation of the activities concerning exploiting of the standards of cloud data management solutions. We evaluated and selected candidate technologies for the development of the semantic mediation layer. In this reporting period this process involved the analysis of an API for the management of OWL documents. Two different APIs will be employed: OWLAPI (http://owlapi.sourceforge.net/) and the ARQ querying engine for Jena (http://jena.apache.org/documentation/query/index.html).

The deliverable D3.3 (“Annual report on the Open Consultation Process and Architectural Refinements”) has been prepared.

Task 3.4, **Security in dynamic collaboration environments**: The security architecture (in collaboration with WP5) was further defined (deliverable 3.4). The experience gained in setting up the security architecture and integrating ObTiMA and p-medicine portal has been used to describe in deliverable D3.4 how services can be integrated with the authentication components of the p-medicine security framework.

Delegation has been integrated into Liferay. A delegation demonstration portlet has been developed. A first step was also made in defining and deploying the delegations infrastructure for REST services.

The security gateway has been deployed. Integration is a work in progress.

We integrated a Shibboleth-based authentification into the data mining services of WP11. In addition, we adapted the data mining services in order to use the secure cloud services. An approach was implemented to integrate Taverna workflows, which were developed for non-security-enabled environments, into the p-medicine environment.

Summary of significant results

The second version of the p-medicine architecture (including delegation for REST services) is ready according to schedule. A security gateway has been deployed and is being integrated with the Ontology Annotator and the Biobank Access Framework. Work has

started on extending the gateway with support for REST. A first version (with limited functionality) of a Secure Token Provider as described in deliverable 3.4 was setup. Delegation has been integrated into Liferay and a delegation demonstration portlet has also been developed. Security functionality was integrated into the data mining services (in collaboration with Task 11.1)
Architecture design, third-party technologies and APIs selection were completed. Definition and design of reference architecture for the p-medicine environment focusing on the semantic layer architecture has been finalized. The architecture of the components involved in the p-medicine semantic layer was refined. In cooperation with WP4 we described the functionality, data exchange requirements and workflow of the ontology aggregator tool, in particular in conjunction with the annotator tool and the portal.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

There were no deviations from Annex I.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP3			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	4.00	1.40	0.84
3 – FORTH	26.00	9.00	7.50
4 – UCL	8.00	1.50	1.23
5 – FhG	12.00	3.50	7.00
7 – CUSTODIX	14.00	4.00	3.26
8 – Philips	8.00	2.00	2.00
11 - UPM	6.00	2.00	2.10
16 – BIOVISTA	1.00	1.00	0.00
18 – UHok	2.00	0.80	0.80
20 – PSNC	7.00	2.00	1.36
Total	**88.00**	**27.20**	**26.09**

2.4 Work Package 4: Standardisation, Semantic Interoperability and Data Integration

Main objectives of this WP

The main objectives of the work package are:
- To identify in a functionality-driven and user-oriented way the semantic resources needed, identify the candidates for re-use (by evaluation), and provide a common structure to unify

the semantics for the project or the sub-task at hand. For this purpose the start of the development of the health data ontology trunk (HDOT) is necessary.
- To find technical solutions aimed at the specific needs of the project in identifying case-relevant ontologies and re-using or merging them (the research focus of WP4 is not to create new ontologies). We survey and assess existing resources in use for this objective.
- With respect to this, the challenge of p-medicine regarding semantic interoperability revolves around two key issues: mapping of data in pre-existent HIS and extension and optimisation of semantic resources against the background of evolving data that is pushed into the system. Initial work on D4.2 is providing the basis for achieving this semantic interoperability with regard to data in hospital information systems and clinical trial management systems as well as other relevant data sources (biobanks, data repositories, etc.)
- To explore possibilities to automatically search and assess existing ontologies, not only with respect to common quality criteria, but also regarding specific issues in biomedical semantics, like granularity. Groundwork for this objective has started by evaluating semantic resources needed and suitable for re-use.
- We provide a patient view connected to the ontology, which will help to organize information from the data collection of p-medicine for patients in an understandable manner. With regard to semantic resources and the scientific information stored there we consider possibilities for accessing and processing this information in patient friendly ways.

The active tasks of the work package planned in the reporting period concerned are:
- Task 4.2: Semantic data integration and resource annotation tools (M3-M24)
- Task 4.4: Developing and testing patient views to represent data to the patient in an understandable way (M12-M32)
- Task 4.5: Developing, prototyping and testing a strategy for ad hoc aggregation of semantic resources (M12-M48)

Additional work has been done in the following task:
- Task 4.1: Creation and collection of semantic resources for p-medicine (M3-M12)

Summary of progress achieved towards objectives

In task 4.1 the initial integration of HDOT in ObTiMA has been finalized by FhG-IBMT. We further extended HDOT with a patient empowerment molule, a biobank module, a pathological formation module, and a more general disease module. We now have a library of modules as extensions to HDOT ready for download.

In task 4.2 HDOT was included in the Ontology annotator by UPM. Many improvements achieved. The tool was improved by adding numerous features including a more efficient HDOT representation.FORTH has started the review of relevant resource annotation methodologies and interesting pertinent efforts such as RICORDO.
We also analysed the data integration strategy of other European projects like VPH-Share in order to optimize ways of collaboration in semantic standardisation.

In task 4.4 IFOMIS have established a patient language schema in close cooperation with WP 14 and related it to the heath data ontology trunk (HDOT). We have extended HDOT further and specified methods to provide information represented in p-medicine's ontological framework in a patient friendly way by generting patient views of the ontology. Initial identification of testing methods was performed and a patient empowerment extension for HDOT constructed.
Furthermore IFOMIS established a use case for the ontology aggregator tool (oat) and specified a workflow for it. For this we analysed possible co-operation with other tools such as the annotator service and the Interactive Empowerment Service (IemS).

In task 4.5 the design of a strategy for aggregating semantic resources was initiated by IFOMIS in co-operation with UPM and IFOMIS started its implementation with the construction of core components of the ontology aggregator tool (OAT).

Summary of details for each task

Task 4.1, Creation and collection of semantic resources for p-medicine: Discussions between IFOMIS and FhG-IBMT about the structure of HDOT and the integration of HDOT into ObTiMA took place. Initial integration of HDOT in ObTiMA has been finalized. We added new extensions to HDOT, i.e. several new modules to cover the domain of the project in more detail and provide necessary standardized concepts both for ObTIMA and the ontology annotator tool developed in Task 4.2. so that we are able to cover clincal trials data specified in WP9.

Task 4.2, Semantic data integration and resource annotation, was devoted during this reporting period to the development of the Ontology Annotator for creating mappings between HDOT and external databases. Work realized has led to the inclusion of the first version of HDOT in the tool and its representation in a usable manner. New features have also been added such as hints and instructions for users to easily access the tool, and performance related fixes that allow the tool to be used in a wider array of machines. Further work has focused on improving end-user experience by adding new features, reworking the HDOT representation to make it more efficient and intuitive. In addition, a first version of the Data Translation service was achieved, and tests with real data were performed. The RDFizers from UCL were integrated with our tool set, and deliverable D4.3 was produced. Finally, integration with the p-medicine portal and with the security infrastructure was completed.
Task 4.2 focuses on the construction of technologies to properly use the semantic infrastructure of WP4 for integrating heterogeneous data repositories and resources. The annotation of different data resources and the need of the supporting technical infrastructure is the subject of the RICORDO project. FORTH has started the review of this initiative in relation to the work of WP8 in order to evaluate the proposed methodology and tools.
We identified differences and similarities between our approach and that of other European projects such as VPH-Share so that we can best find areas of co-operation.

Task 4.4, **Developing and testing patient views to represent data to the patient in an understandable way**: IFOMIS, together with WP14 partners, specified a linguistic patient language schema with patient profile terms at its core and we carried out mappings of patient language terms to integrate them in the overall semantic framework of p-medicine provoided by HDOT. Furthermore we extended HDOT by a patient empowerment module as a crucial step to provide patient friendly views of HDOT so that we can present information encoded in the project's semantic frame in a patient friendly way.

Task 4.5, Developing, prototyping and testing a strategy for ad hoc aggregation of semantic resources: IFOMIS, in close cooperation with UPM, initiated the design of the strategy for automatic aggregation of semantic resources. During this period an analysis of the ontologies available at Bioportal, the Ontology Look-Up Service, Ontobee and other semantic resources was performed, studying possibilities for using the information contained in them for the pursued aggregation process. UPM examined the integration of the interface with the Ontology Annotator, defining specific plans for this sub-task. IFOMIS designed a work flow for the aggregator tool and specified the necessary componets and the expected data exchange requirements with other tools and services in collaboration with WP3. IFOMIS implemented the core components and started a testing phase and software development cycles.

In collaboration with WP2 IFOMIS developed a use case based on the possible failure of the ontology annotator tool (OAT) to provide a desired annotation value. The relevant mapping cannot be executed because HDOT or its modules do not contain an adequate class to map the desired annotation value to. Instead of introducing new HDOT-classes ad hoc we developed a method to quickly search existing semantic resources like BioPortal or Ontobee and we specified a way to extract relevant information from these resources to semi-automatically extend HDOT or its modules with desired classes and related terms.

Summary of significant results

One of the most important achievements was the inclusion of an initial version of HDOT in the Ontology Annotator tool and the development of methods for its proper representation. Further significant results were the integration with the portal and the security infrastructure, the optimization of the OA, the improvement of the overall user experience, the production of deliverable D4.3 and the initial design of the Ontology Aggregator strategy and interface. The initial integration of HDOT in ObTiMA has been finalized. We performed an initial specification of use case, workflow and service architecture of the ontology aggregator tool and implementation of core components. We also designed a patient empowerment module for HDOT together with a patient view of the ontology to represent information in a patient friendly way and initially defined testing methods. Moreover, we also designed a biobank module and a pathological formation module for HDOT. We released deliverable D4.4.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

There were no deviations from Annex I.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP4			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	48.00	17.70	14.11
3 – FORTH	15.00	7.00	5.00
5 – FhG	6.00	0.00	0.00
8 – Philips	8.00	3.00	0.00
11 – UPM	42.00	14.00	17.08
Total	**119.00**	**41.70**	**36.19**

2.5 Work Package 5: Legal and Ethical Framework

Main objectives of this WP

WP5 has two main objectives:

On the one hand it will guarantee that p-medicine is compliant with all legal and ethical rules applicable. On the other hand WP5 does systematic in-depth research on legal and ethical rules of sharing data and biological material on a European level with the final objective of empowering patients.

The active tasks of the work package planned in the reporting period concerned are:
- Task 5.2: Specific analysis of data warehouse and data mining (including Intellectual Property Issues) (M12-M24)
- Task 5.3: Legal and ethical issues regarding access to biobanks (M12-M36)
- Task 5.4: Legal and ethical issues regarding patient empowerment (M24-M48)
- Task 5.5: Legal and ethical issues regarding international clinical trials (M1-M18)

Summary of progress achieved towards objectives

The legal and ethical frameworks for the p-medicine data warehouse and the p-medicine meta-biobank have been set up in close collaboration with WP10 and WP14.

Summary of details for each task

A data protection and data security framework for p-medicine has been set up in task 5.1, Initial analysis of the data protection and data security framework and setting up of this framework (M1-M12), and the following tasks are building on that framework to give a fine grained structure in the whole architecture of the project involving data sharing and protection.

Task 5.2, Specific analysis of data warehouse and data mining (including Intellectual Property Issues): we analysed the legal and ethical issues regarding data warehousing, data mining and intellectual property in the project. Various EU and international laws and regulations, as well as ethical guidelines that form the preconditions for the establishment of a data warehouse that integrates health-related sensitive data were considered. These were all aimed at protecting the data of trial participants and complying with legal obligations as applicable to the project. In addition to data protection and security standards set for the project, a privacy preserving data mining technique was incorporated into the data warehouse architecture as developed by FhG-IAIS. Furthermore, a fine grained guideline for the use of the data warehouse was established. Issues related to intellectual property inherent in the use of background and foreground property were equally analysed in line with the EC Grant Agreement and the Consortium Agreement. It was opined in the end that a more favourable approach for the project in view of its complex nature will be joint ownership of foreground.

Task 5.3, Legal and ethical issues regarding access to biobanks: the legal framework for the p-medicine metabiobank (p-BioSPRE) has been developed in cooperation with WP14. This metabiobank can be used by biobank operators to provide data about their stored samples, and by researchers for the search of suitable biomaterial and related data once established. An analysis of the legal and ethical rules to be considered for biobanking with emphasis on informed consent and data protection law has been done with special consideration of the issues of transnational sharing of samples and relating (personal) data. Relevant legislation and a multitude of guidelines concerned with the quality and safety of biobanking have been examined for their relevance in p-medicine. The contractual framework for the data transfer to the p-medicine metabiobank has been drafted and guidelines for the safe use of the p-medicine metabiobank have been developed. This is aimed at regulating the smooth and safe cooperation of all participants - the metabiobank operator, the biobank operators and the researchers accessing the metabiobank, to search for suitable samples for their research.

Task 5.4, Legal and ethical issues regarding patient empowerment: an analysis of the legal implications of the patient empowerment tools and strategies in the project has begun.

Task 5.5, Legal and ethical issues regarding international clinical trials: this task was carried out in conjunction with UDUS as the team leader, where an analysis of the legal and ethical issues surrounding Good Clinical Practice in international clinical trials in relation to p-medicine tools was carried out. Having identified the applicable regulations relating to the tools, their validation will be followed by UDUS in WP6.

Summary of significant results

In task 5.2, we performed an in depths analysis of the legal and ethical issues regarding data warehousing and mining, set up guidelines for the use of the p-medicine data warehouse and provided an outline of the legal situation regarding intellectual property on background and foreground in the p-medicine project.
In task 5.3, we developed the legal and ethical framework of the p-medicine metabiobank (p-BioSPRE) as well as guidelines for the use of the metabiobank. We also set up a draft for the Biobank Data Transfer Agreement between the p-medicine metabiobank operator and participating biobank operators.
In task 5.5, we outlined the ethical and legal requirements in clinical trials in relation to p-medicine tools.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

There were no deviations from Annex I.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP5			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	6.00	1.00	0.03
5 – FhG	3.00	3.00	2.90
6 – LUH	52.00	13.00	18.95
7 – CUSTODIX	12.00	3.50	5.00
9 – UDUS	3.00	2.00	3.22
Total	**76.00**	**22.50**	**30.10**

UDUS: For the second project period, UDUS has doubled the amount of person months compared to their original plan. This is more than indicated in planned PM. But this is agreed with UDUS' administration and will be included in the overall financial plan. The legal and ethical analysis conducted for the deliverable D5.3 (Report on legal and ethical issues regarding access to biobanks) required more resources than planned. This was due to the fact that not only regulations had to be analyzed, but also a multitude of guidelines and standard procedures. In addition, the developed requirements were applied to p-medicine

use cases for biobanking as well as p-medicine tools that are used for biobank data management. This additional analysis was done to ensure the practicability and legal usability of the developed p-medicine tools.

2.6 Work Package 6: Integration in Clinical Research Infrastructures

Main objectives of this WP

Based on the approach of developed requirements and specifications for the collaboration of the p-medicine environment with other research infrastructure initiatives (WP2), the main objectives of the work package are:

- Effective and interoperable integration of p-medicine tools in an international clinical trials infrastructure (ECRIN)
- Evaluation of the usability and effectiveness of p-medicine tools used in a real clinical trial as part of the ECRIN clinical trial infrastructure.

The active tasks of the work package planned in the reporting period concerned are:
- Task 6.1: Basic principles for the use of p-medicine tools in a clinical trials infrastructure (M1-M18)
- Task 6.2: Evaluation of p-medicine tools within the ECRIN clinical trials infrastructure (M12-M36)

Summary of progress achieved towards objectives

A scenario based approach was used. Use cases, scenarios and the specifications for user needs, were developed with the focus on the integration of the p-medicine tools into the heterogeneous data management environment of ECRIN using applicable use cases for employing p-medicine tools in international clinical trials (Deliverable 6.1). These developed use cases specify the involvement of a reference radiologist in clinical trials for second/third opinion, the design of CRFs with semantically assistance (ontology based), patient empowerment in clinical trials to access own data, ObTiMA as clinical data management system in ECRIN trials. Use cases for breast cancer were considered. To ease integration, the process of validation simulation for computerized systems integration that uses the ECRIN GCP standard for data centres was developed and conveyed by a validation workshop.

Summary of details for each task

Task 6.1, Basic principles for the use of p-medicine tools in a clinical trials infrastructure: Requirements clusters were developed for the following main categories: interoperability requirements, technical requirements, business requirements and legal & ethical requirements.
What is more, the ECRIN Integration Scenario was specified for scenario interfaces for ObTiMA, DoctorEye, Patient empowerment and Portal (problems and challenge, user needs, etc.). The developed use cases cover the involvement of reference radiologists in clinical trials, the design of CRF with semantically assistance, patient empowerment in clinical trials, and ObTiMA as CDMS. We also identified ECRIN pilot centres for the integration (ECRIN standard for GCP trial centres) and performed a validation simulation of computerized systems used in clinical trials. We held a validation workshop with p-medicine developers at the University of Duesseldorf on April 4, 2012.
Deliverable D6.1 “Report on use cases, scenarios, user needs, tools, interoperability issues for the ECRIN community” was submitted.

Task 6.2, Evaluation of p-medicine tools within the ECRIN clinical trials infrastructure: We are currently developing the usability evaluation process for p-medicine. For this purpose, together with WT6.1, several preparatory documents were developed (use cases, p-medicine tools and interface descriptions, validation documents). A usability evaluation plan will also be created.

Summary of significant results

An integration scenario for the use of p-medicine tools in ECRIN was specified for ObTiMA, DoctorEye, Patient empowerment and Portal and the corresponding use cases describe the involvement of a reference radiologist in clinical trial, the design of CRF with semantically assistance, the use of patient empowerment in clinical trials, and the use of ObTiMA as data management system in ECRIN clinical trials.
Validation simulation is a tool to prepare developers for the requirements of GCP validation of p-medicine tools used in clinical trials.
The preparation of the usability evaluation of p-medicine tools in ECRIN was achieved.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

There were no deviations from Annex I.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP6			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	8.00	3.00	0.00
7 – CUSTODIX	2.00	1.00	0.29
9 – UDUS	24.00	9.00	13.69
12 – CAU	3.70	1.50	1.25
13 – IEO	3.00	1.00	0.44
Total	**40.70**	**15.50**	**15.67**

2.7 Work Package 7: Data Warehouse

Main objectives of this WP

The main objectives of the work package are:
- To develop federated data warehouse infrastructure components to store the multiple different types of medical data produced in this project;
- To develop storage services for large data objects;
- To develop mechanisms for ensuring reliability and auditability of the data;

- To develop and deploy suitable programmatic interfaces, to allow the different types of data to be uploaded to the warehouse via tools developed in other work packages;
- To develop a service integrated in the web portal to allow users to search for and view available data;
- To develop federated capability-based secure access mechanisms compliant with the legal and ethical framework of the project.
- To integrate security and role based access, based on the legal and ethical framework developed in the project.
- To integrate the disparate types of data produced and available in the project using appropriate ontological tools.

The active tasks of the work package planned in the reporting period concerned are:
- Task 7.1: Development of imaging data store component (M6-M24)
- Task 7.2: Development of structured data store component (M12-M30)
- Task 7.3: Development of file based data store component (M18-M36)
- Task 7.4: Auditability of biomedical storage services (M24-M48)
- Task 7.5: Interface and infrastructure development (M12-M48)
- Task 7.6: Integration with security and legal/ethical framework (M24-M40)
- Task 7.7: Integration with ontology tools (M24-M40)
- Task 7.8: Integration and use of the Cloud Computing Technologies and Services developed (M1-M48)

Summary of progress achieved towards objectives

In Task 7.1, PSNC have provided the imaging service for the project, and integrated it with security framework of p-medicine. The solution is based on open source software called dcm4chee.
In Task 7.2, UCL have deployed a local test triplestore, PSNC have deployed a central triplestore for storage of structured data, and UHok have discussed interfacing TOB with ObTiMA DB.
In Task 7.5, UCL have specified and implemented much of the programmatic interface, and implemented a Liferay portlet supporting simple SPARQL querying of the structured data store, with browsable table-based presentation of results. UHok have specified the federation architecture of components in TOB.
In Task 7.6 Custodix have started work on integration with security architecture.
In Task 7.7 UPM started analysing the integration of the ontology-based services with the Data Warehouse. Discussions were carried out to define the interfaces of different tools with the Data Warehouse.

Summary of details for each task

Task 7.1, Development of imaging data store component: PSNC have continued their work on imaging service for the project. The solution is based on an open-source product called dcm4chee. They have worked on the integration of a dcm4chee DICOM server with cloud technology (OpenStack Swift). The other issue was to analyse the compliance of the selected solution with the security recommendations of the project. They have also implemented security mechanisms proposed for the project within imaging service.

Task 7.2, Development of structured data store component: UCL have deployed locally an OWLIM-based triplestore for development and for testing our infrastructure independently of that provided by PSNC. PSNC have deployed a central triplestore for storage of all structured data. UHok have discussed the interface between TOB and ObTiMA DB with FhG-IAIS.

Task 7.3, Development of file based data store component: This task is dedicated to developing file based data store components. PSNC were working on a cloud based

infrastructure for storing files in the p-medicine environment. The implementation is based on OpenStack Swift solution with production storage services as a background infrastructure.

Task 7.5, Interface and infrastructure: in detail, UCL have:

- updated D7.1 to include a more detailed specification of the RESTful programmatic interface
- implemented enough of this interface to allow upload of a file and extraction of structured data from CSV and Microsoft Access files.
- integrated the programmatic interface with Custodix' AAI components
- integrated the programmatic interface with PSNC's filestore component
- integrated the programmatic interface with PSNC's structure data store component
- deployed the programmatic interface on PSNC servers
- implemented the Liferay portlet for SPARQL querying of the data warehouse, ready for deployment on the p-medicine portal

UHok have specified the federation architecture of components in TOB including those components working as biological and genomic analysis tools.

Task 7.6, Integration with security and legal/ethical framework: Custodix, UCL and PSNC have started the initial integration of the data warehouse with the p-medicine security framework.

Task 7.7, Integration with ontology tools: UPM started analysing the integration of the ontology-based services with the Data Warehouse. More specifically, discussions were carried out to define the interface that allows the Ontology Annotator to feed the Data Warehouse with user-generated database annotations. The interface of the Data Translation service with the Data Warehouse was also partly agreed, although more details need to be settled.

Summary of significant results

PSNC have provided the prototype infrastructure for storing imaging data and file based data for the project including integration with security infrastructure of p-medicine
UCL have fully specified the programmatic interface, and implemented 70% of it, deployed it on PSNCs servers, and integrated with AAI, filestore and structured data store components.
Initial details of the interfaces of ontology tools with the Data Warehouse have been established.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

Deliverable 7.2 "Demonstration of different data store components" was slightly delayed.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Deliverable 7.2 slightly delayed in submission due to delay in internal review. The deliverable has now been submitted. This will have no further impact on resources or planning.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP7			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	4.00	0.00	0.00
3 – FORTH	10.00	2.00	2.00
4 – UCL	68.00	23.50	22.62
5 – FhG	6.00	2.00	2.00
7 – CUSTODIX	8.00	0.00	0.88
11 – UPM	10.00	2.00	0.25
18 – UHok	1.00	0.30	0.30
20 – PSNC	40.00	15.00	15.76
Total	**147.00**	**44.80**	**43.81**

UPM's planned 2 PM of Task 7.5 will be achieved in upcoming periods.

2.8 Work Package 8: p-medicine Workbench

Main objectives of this WP

WP8 deals with the development and handling of tools used in translational clinicogenomic research. It addresses the development of the appropriate pseudo-anonymisation and preprocessing tools for nephroblastoma and breast cancer applications and creates tools that can be identified by users and used in clinic-genomic VPH studies as well as workflow integration and clinical trial management and services for interacting with the clinical patient record. To this end, the tools will have annotations and metadata, so that end users can easily retrieve them, while available VPH standards will be adopted allowing other open source tools to be easily integrated and re-used in the tools repository. Strong emphasis will be given in interacting with the VPH NoE toolkit in the sense that the WP will utilise available tools but also share tools with the toolkit in order to be used by the wider VPH community.

The tasks active in this work package in the reporting period concerned are:

- Task 8.1: The p-medicine sharing, collaborating, and orchestrating environment (M1-M48)
  - Subtask 8.1.1: Requirements and specifications for the interaction of the p-medicine workbench with the VPH Toolkit (M1-M48)
  - Subtask 8.1.2: The p-medicine portal (M12-M40)
  - Subtask 8.1.3: Integration of federated storage services for biomedical objects (M3-M48)
- Task 8.2: Specific image analysis tools development for nephroblastoma and breast cancer applications (M8-M42)
- Task 8.3: Data de-identification and pseudonymisation tools (M8-M48)
- Task 8.4: Further development of new services for ObTiMA clinical trial management (M8-M40)
- Task 8.5: Push- and sync-services to retrieve data from Clinical Information Systems (M8-M40)
  - Subtask 8.5.1: Push service to select and upload data from clinical information systems to p-medicine data warehouse (M8-M40)
  - Subtask 8.5.2: Sync service to facilitate the conduction of clinical trials through HIS connectivity (M8-M40)
- Task 8.6: The Integrated p-medicine platform (M3-M48)

Summary of progress achieved towards objectives

The integration of the VPH-Toolkit registry of tools into the p-medicine workbench has started along with the implementation of the presentation layer of the p-medicine workbench as a "portlet" in the p-medicine portal.
The deliverables D8.6.1 “Integration guidelines and monitoring of tools and services” and D8.6.2 “Initial version of the p-medicine integrated platform” have been prepared.
The work in the tools area (visualization, anonymization, literature mining) and new services for ObTiMA was continued.
The prototype of the cloud storage system based on OpenStack solution was deployed and extended with support for security mechanisms of the p-medicine environment.
We were able to finalize an initial production version of ObTiMA (beta) as main data collection tools of the next SIOP nephroblastoma clinical trial.

Summary of details for each task

Task 8.1, **The p-medicine sharing, collaborating, and orchestrating environment**: Input of the p-medicine tools to be integrated into the p-medicine workbench has been gathered and a prototype implementation was built. The RICORDO methodology was tested and considered for adoption. In the end we decided to follow a similar semantic annotation strategy for the p-medicine and other tools but to not re-use the RICORDO middleware and components because the ontologies used are different and their focus is more specific to the VPH computational models. The p-medicine Ontology Annotator has been initially integrated into the portal. Work on the integration of ObTiMA in the p-medicine portal continues.

Subtask 8.1.1, Requirements and specifications for the interaction of the p-medicine workbench with the VPH Toolkit: Integration of the VPH-Toolkit registry of tools in the p-medicine workbench started. The design of the best integration policy is under development since the VPH Toolkit does not offer (at least publicly) any programmatic interface to its contents.

Subtask 8.1.2, The p-medicine portal: Implementation of the presentation layer of the p-medicine workbench as a "portlet" in the p-medicine portal started. We have also performed the implementation of a Liferay portlet for a SPARQL query of structured data store components of the data warehouse.

Subtask 8.1.3, Data de-identification and pseudonymisation tools: we continued the work on the integration of OpenStack Swift cloud technology with the production environment of NDS (National Data Storage). The capacity of storage was extended with new storage resources, based on NFS or Samba protocols. We also worked on integration of storage services with the p-medicine security framework. We have added the support for SAML protocol (integration of assertion libraries with OpenStack), and the communication with the p-medicine Identity Provider.

Task 8.2, Specific image analysis tools development for nephroblastoma and breast cancer applications: FORTH have been focusing on developing/customizing methods for tumor segmentation (nephroblastoma) as well as a Contrast-Enhanced MRI (CE MRI) toolkit for pharmacokinetic modeling and biomarker extraction. These advances are incorporated in the DrEye platform and are reported in detail in D8.2 “Release of tools for multi-modal cancer image analysis and annotation”. The functionality for including an Angiomap-based enhancement classification algorithm that automatically categorizes the enhancement of each voxel in the three types has been implemented in the DrEye platform while preliminary results for an analysis on infiltrative ductal carcinoma pre- and post-chemotherapy have been reported in various publications. ICCS provided the detailed specifications for the foreseen image analysis tools.

Task 8.3, Data de-identification and pseudonymisation tools: The pseudonymisation services (CATS, PIMS) have been deployed. Furthermore, Custodix PESF (Privacy

Enhanced Storage Framework) has been adapted to fit ObTiMA as additional security measure (PESF has a proven track record for securing clinical study data entry sites) for running ObTiMA with live data. UCL collaborated with Custodix in designing a user-friendly and secure data import workflow and a specified interface of pseudonymisation service with the data warehouse.

Task 8.4, Further development of new services for ObTiMA clinical trial management: the TOB (Trial Outline Builder) can be extended to cope with various visualizations and analysis tools without changing its basic architecture and its relationship to ObTiMA. We have developed the heat map component for the visualization and selection of patient gene expression, and made it work as a diagnostic event in TOB to federate with other components. We have also extended the functionality concerning CRF creation and deployment (e.g., cascaded sections and questions, adding CRFs to running trials, etc.) and implemented an extended audit functionality. We have achieved usability improvements focusing on the handling of users, organizations and patients within the system as well as an improvement of stability and performance. An industry-style infrastructure was established for building and deploying ObTiMA as well as for reporting bugs and documentation. We worked together with WP9 in Task 9.3 to establish and prioritize the concrete development goals necessary in order to head towards GCP conformance. Finally, we wrote deliverable D8.4 (“Provision of new modules for clinical trial management”) describing the latest developments of ObTiMA.

Task 8.5, Push- and sync-services to retrieve data from Clinical Information Systems: we defined both the organizational, legal and technical needs and structures to retrieve data from a Clinical Information System with the Saarland University Hospital as pilot provider of such a system.

Subtask 8.5.1, Push service to select and upload data from clinical information systems to p-medicine data warehouse: FORTH has gathered the requirements for the “push services” and started the implementation of the upload tools as intermediate “buffers” of files prior to their submission to the data warehouse (through the Custodix Trusted Third Party).

Task 8.6, **The Integrated p-medicine platform**: The Deliverable 8.6.2 (Initial version of the p-medicine integrated platform) has been prepared by FORTH with contributions from the rest of the WP8 partners. The Integration Manager coordinates the relevant discussions and regular teleconferences for the realization of the integrated p-medicine platform. The TOB architecture was extended to deal with various visualization and analysis tools. Visualization also allows directly selecting visualized objects or areas to filter out the other records in different visualizations. Generic wrappers have been developed which allow us to wrap any legacy tools developed in R or Octave into components with standard interoperable interface, and to use them in the extended TOB. Biovista is developing a user graphical interface for the literature data mining RESTful service (task 11.1). The goal of this new frontend is to allow the backend service to easily integrate with the p-medicine platform, as it will digest the XML encoded service results and produce a user friendly representation. The integration of this service with the p-medicine workbench has been started.

Summary of significant results

Input of the p-medicine tools to be integrated into the p-medicine workbench was gathered and a prototype implementation was built. Implementation of the presentation layer of the p-medicine workbench as a "portlet" in the p-medicine portal has started.
The prototype of the cloud storage system based on OpenStack solution was deployed and extended with support for security mechanisms of p-medicine environment.
The Liferay portlet for SPARQL query of data warehouse is ready for deployment on the p-medicine portal.
Sensitive data fields in ObTiMA are encrypted in the browsers before being uploaded to the ObTiMA server.

The specifications regarding the three branches of the Oncosimulator have been finalized.
The TOB (Trial Outline Builder) architecture is extended to introduce graphical body maps and geographical maps to work as visual coordinates in the parallel coordinate system, which allows analysts to graphical choose organs or geographical areas to select tumour sites or patient birthplaces respectively.
An initial production version of ObTiMA has been finalized and installed on a secure server at the Saarland University Hospital. It is currently being (beta) tested before being rolled in the next few months as main data collection tools of the next SIOP nephroblastoma clinical trial.
The implementation of the upload tools as intermediate "buffers" of files prior to their submission to the Data Warehouse has started.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

There were no deviations from Annex I.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP8			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	10.00	4.00	3.58
3 – FORTH	52.00	15.00	12.00
4 – UCL	18.00	3.00	2.56
5 – FhG	34.00	4.00	5.66
7 – CUSTODIX	18.00	6.00	6.50
10 – ICCS	13.00	2.50	1.50
15 – UOXF	4.00	1.00	0.00
16 – BIOVISTA	5.00	5.00	9.81
18 – UHok	16.00	4.00	4.00
20 – PSNC	20.00	2.00	7.31
Total	**190.00**	**46.50**	**52.92**

UOXF: underspending reason is that some activities were moved and will be done in period 3-4.

2.9 Work Package 9: Clinical Trials

Main objectives of this WP

The main objectives of the work package are:
- To validate the p-medicine environment by focusing on running clinical trials;
- The three selected diseases are Wilms Tumour, Breast Cancer and Acute Lymphoblastic Leukaemia (ALL);
- For all trials clinical relevant use cases will be defined;

- Data coming from these trials will be stored in the data warehouse in a secure and anonymized way according to the legal and ethical framework of p-medicine;
- The Wilms tumour trial will be used to employ the newly developed and validated tools of p-medicine. The trial also provides data for the Oncosimulator testing a specific Wilms Tumour scenario;
- The primary aim of breast cancer studies will be to maximize efficacy of therapy while minimizing side effects. And also to find biomarkers useful for predicting patients' response to treatments;
- The leukaemia trial in p-medicine will be used to develop such a model for the prediction of MRD and disease recurrence.

The active tasks of the work package planned in the reporting period concerned are:
- Task 9.1: Support of regulatory and international aspects of the clinical trials (M1-M24)
- Task 9.2: Clinical trials (M1-M48)
    - Subtask 9.2.1: SIOP Wilms Tumour (M1-M48)
    - Subtask 9.2.2: Breast Cancer phase II trial (Bevacizumab trial-1) (M1-M48)
    - Subtask 9.2.3: Breat Cancer phase II trial (Bevacizumab trial-2) (M1-M48)
    - Subtask 9.2.4: Breast Cancer (Circulating tumour cells (CTCs) trial) (M1-M48)
    - Subtask 9.2.5: Breast Cancer Stem cell models (M1-M48)
    - Subtask 9.2.6: Acute lymphoblastic Leukaemia (ALL) (M1-M48)
- Task 9.3: Certification of tools for the use in GCP conform clinical trials (ObTiMA, DoctorEye, …) (M1-M48)

Summary of progress achieved towards objectives

Preliminary work was initiated on interpreting the ALL-BFM 2000 data received from CAU. This, together with information extracted from literature mining using semantic NLP techniques, will be used to perform the relevant prediction runs by Biovista's platform. UOXF provided an on-going contribution of details regarding fields and attributes for data collected in Oxford. CAU has been sharing data sets with IAIS and Philips. Support on using and interpreting the data is provided. ICCS is collecting a significant number of real patient datasets for the case of acute lymphoblastic leukemia. At UDUS, the application of regulations and guidance for several of the software applications developed in p-medicine were evaluated in detail: clinical trial data management systems (CDMS) in trials with medicinal products, with special consideration of the ObTiMA clinical trial management system, eSource (electronic source data) data collection, as well as studies with secondary use of data, DoctorEye, Oncosimulator and clinical decision support in clinical trials, and clinical trials involving biobank data. Moreover, UDUS contributed validation requirements to USAAR. Validation training was held at UDUS (Duesseldorf) in April 2012.
At UCL**,** further consultation and discussion with all partners has taken place at national and international meetings to ensure a balanced viewpoint is obtained to take forward. The SIOP Wilms study is provisionally ethically approved for the use of retrospective and new clinical data within the p-medicine environment. The use of test data has successfully demonstrated routes for data transfer and access to p-medicine. USAAR constructed a pathological formation module for HDOT called HDOT_pfm to cover necessary concepts for the annotation process on the general level of three diseases and added a dedicated module for enabling the annotation of a data schema used in the Bevacizumab trial provided by UOXF.
Breast cancer trials with metronomic and antiangiogenic chemotherapy ongoing at European Institute of Oncology (IEO) within the framework of p-medicine are:

1. Phase II study of metronomic oral Vinorelbine (Navelbine®) plus Bevacizumab (Avastin®) as first line treatment for metastatic breast cancer patients
2. A phase II study of metronomic oral chemotherapy with cyclophosphamide plus capecitabine and vinorelbine in metastatic breast cancer patients (VEX trial)
3. A phase II study of cisplatin plus cyclophosphamide for patients with previously treated, advanced, triple receptor negative breast cancer.

In these studies 63 patients were treated until now. For each of these patients IEO collected clinical and laboratory data and also had data regarding imaging, in specific time-points. The enrolment of the phase II randomized Bevacizumab breast cancer trial ended on 20th October of 2011. In this study 66 patients were enrolled. The final report will be available at the end of the study.

Summary of details for each task

Task 9.1, Support of regulatory and international aspects of clinical trials: UDUS will accompany the clinical trials with advice about regulatory and international aspects of the trials. ECRIN consultation will address ethics, monitoring, data management and biostatistics. In particular, UDUS performed the following actions:

- Analysis of guidelines specifying various aspects of clinical trials: (1) the information to be submitted to the competent authorities and to the ethics committees, (2) requirements on safety monitoring and the reporting of adverse reactions, (3) requirements regarding Good Clinical Practice, including the documentation, of the clinical trials (e.g. Trial Master File), (4) specific requirements regarding the products and the clinical trials, (5) inspections of competent authorities and the applicable procedures and (6) requirements relating to the quality, safety and efficacy of products.
- Because in p-medicine developed software will have direct implications on patient safety, the developed software must be validated according to GCP (System Validation) and according to medical device laws. Clinical trials on medical devices are regulated by EN ISO 14155:2011 "Clinical investigation of medical devices for human subjects - Good Clinical Practice" and in Europe by EU Directive 2007/47/EG. Discussion about when software is regarded as medical device.
- Consideration of guidance on information security, electronic source data and data privacy and their impact on p-medicine software and data processing (ISO 27001: Information Security and in Europe, EU Directive 95/46/EC, GCP Inspectors Group's Reflection paper on expectations for electronic source documents used in clinical trials, GMP Annex 11 and in the US HIPAA Health Insurance Portability and Accountability Act of 1996)
- Consideration of regulations about advanced therapies in cancer research and innovative products and areas covering requirements for biomarkers, genetic tests and use of tissues, is in development.

Regulatory aspects of sharing clinical and biology information were discussed with other representatives of the work package from USAAR. USAAR analysed the ACGT Master Ontology and identified standardized concepts ready for re-use to cover data integration needs of the Wilms Tumor trial; they also analysed the data schemata used for the collection of ALL and breast cancer trial data and started the development of HDOT extensions (dedicated modules) to cover the required concepts and terms so that they can be integrated into the overall semantic framework of the project. Biovista supported the regulatory and international aspects of the clinical trials, certification of tools for the use of GCP-conform clinical trials. UOXF continued their efforts to better develop the Obtima software.

In the period from M19 to M24, Biovista put emphasis on collecting, organizing and evaluating data from the Acute Lymphoblastic Leukemia (ALL) ALL-BFM 2000 study (received from CAU) with the scope of utilizing it for the predictive experiments. This data involves clinico-genomic data from over 5000 ALL patients, including medical history (family incidence of cancer or previous cancer occurrence), blood blast counts and other haematological indices, immunophenotyping, relevant cytogenetic analysis, response to pharmacological treatment (prednisone), minimal residual disease (MRD) analysis, etc. UXOF reviewed and discussed document D9.1 with authors.

IEO produced "Regulatory and research related issues concerning personalised medical trials in p-medicine", in which various aspects regarding clinical trial regulation were analysed. The analysis focused on different kinds of clinical trials (with particular attention to phase 0 trials). USAAR performed an analysis of the data collection schemata that used the trials for Breast Cancer, ALL and Wilms Tumor in order to achieve semantic metadata

standardisation and developed ontological modules for the project's Health Data Ontology Trunk (HDOT) to enable data annotations when the data is pushed into the data warehouse.

UDUS reviewed the ethical and legal framework of the ACGT project (ACGT ethical and legal requirements report) and the privacy framework of the TRANSFoRm project. The impact of data protection regulations on the use of p-medicine tools were examined, with focus on the use of eSource data (Electronic Source Data). A register of European and international laws, directives, legal ordinance, guidelines and instructions that have an impact on clinical trials conduct in p-medicine were developed (Del. 9.1). The application of these regulations and guidance for p-medicine tools was evaluated based on the results of a survey conducted in p-medicine specifying the types of clinical trials tools that will be used in GCP trials. This register will be the basis for the advisory support of p-medicine trials.
Deliverable D9.1 lists a multitude of applicable regulations that play a role for p-medicine clinical trials. The application of these regulations and guidance for several of the software applications developed in p-medicine were evaluated: clinical trial data management system, DoctorEye, Oncosimulator and clinical decision support in clinical trials, and clinical trials involving biobank data. For most p-medicine tools multiple guidelines and regulations apply. The developed register of clinical trial laws and guidance was used as source for the development of D5.5 and D6.1. It is a source for advice to the p-medicine clinical trial groups and to software developers concerning system validation.
A rationalised process for parent/patient consent for use of clinical and imaging data and ‘omics analysis of tissue samples in childhood renal tumours has been ethically approved in one member state (UK). This has been discussed within the framework of CONTRACT (Consent in a Trial & Care Environment), an EU funded project where several aspects were presented to legal experts in the field at a meeting in Brussels for consideration. However, from these consultations it is clear that the design of a universally acceptable consent process is not easy to achieve across Europe at this time. There are significant differences in national legal frameworks that are currently seen as an impediment to EU wide collaborative research on shared pseudonymised tissue samples linked to clinical data.

Task 9.2, Clinical trials: Extensive interactions and discussions with the clinical partners involved in WP12 have led to the clarification of the types of multiscale data that are both exploitable by WP12 and available by the clinical institutions. Representative series of fake data sets have been created for the Breast Cancer Oxford trial and Acute Lymphoblastic Leukaemia and sent to ICCS, in order to partially drive the development of the corresponding Oncosimulator models.
Acute lymphoblastic Leukaemia (ALL): Data sets for the different scenarios were defined, associated data dictionaries including variable lists were generated, the generated data sets and clinical protocols including consent forms were provided to LUH for legal evaluation, followed by a discussion of legal aspects with LUH and the preparation of data sets for exporting. UXOF hosted a meeting with IEO representatives to define the collaboration on breast cancer trials and studies. UXOF visited IEO to compare protocols, trial design and data management. In particular, the Avastin study protocol was discussed in fine detail. For the latter, a detailed list of fields and attributes was compiled and we circulated this list for all users, as this data will be used in the Oncosimulator, data mining, Obtima development and ontology. We perfomed a demonstration of the open source clinical trial software, OpenClinica, in use at UOXF, as IEO is potentially interested in using it for our future collaborative trials.
A tight collaboration of ICCS with CAU has led to the provision of a significant number of the foreseen datasets for the case of acute lymphoblastic leukemia model. The clinical data of about 4000 patients were edited by CAU in the discussed way and shared with the partners, with information and support on using and interpreting the data provided by CAU.
ICCS interacted with USAAR with regards to the expected antigen scenario data and performed related exploratory studies. ICCS interacted with IEO and UOXF in order to accelerate the provision of the foreseen data. Moreover, ICCS interacted with the clinical partners of p-medicine, in order to identify the constraints in the sets of clinical data that

constitute a clinical case exploitable by Oncosimulator. UOXF preprocessed collected data in collaboration with WP11.

At the moment IEO is evaluating different systems that should be used in order to collect the data, but nothing has been defined about the proper system to be used. The most important problems when choosing a new electronic system is the possibility to have a certified system. To enhance the process of sample accessibility UCL will be setting up an EU wide contact group to establish precise rules that govern the availability of tissue EU wide. This will be done within the context of an international collaborative project designed to add statistical significance to current and new molecular characterisations. At present, centres with established collaborations in Germany and UCL are receiving and analysing tissues for this process and a short protocol detailing the scope of the work to be undertaken is under preparation.

Subtask 9.2.1, SIOP Wilms Tumour: We organized a meeting in London attended by around 30 participants in the current SIOP WT 2001 trial. We also discussed the trial at the SIOP WT trial management meeting in Lyon. It was concluded that a prospective clinical study was required.
Moreover, we wrote a new prospective feasibility clinical study to run 24 months prior to opening a randomized trial. This study has been developed and submitted for ethical approval. The UK Research Ethics Committee has given provisional approval for this study to continue. Data generated along with clinical data will be consented for use in p-medicine. Parent/patient consent forms specifically mention the use of such data in p-medicine.
UCL has led on the development of a prospective clinical study called IMPORT (Improving Outcomes in Renal Tumours of Childhood) that will evaluate genomic and imaging biomarkers in the context of a continuation of the risk stratification and standard treatment arms of the SIOP-RTSG 2001 protocol. This updated protocol includes updated patient/parent information and consent processes for sample collection for genetic analysis ('-omics') and personalized data sharing through p-medicine. This is the preliminary work to enable the next randomised trial for analysis and imaging of WT to be instigated across Europe. The IMPORT study also aims to establish centralized review and standardised radiology protocols to facilitate the integration of DICOM files and clinical data collected through the ObTIMA framework. The prospective sampling and collection of imaging and all clinical data will feed into p-medicine and help develop a more accurate approach to risk stratification and biomarker discovery.

Subtask 9.2.2: Breast Cancer phase II trial (Bevacizumab trial -1): This trial is concluded with 66 patients enrolled and 2 patients still ongoing.

Subtask 9.2.4: Breast Cancer (Circulating tumour cells (CTCs) trial): The first part and the second part of the study are concluded. The third part of the study aimed at assessing HER-2 receptor conversion rate on CTCs in patients with advanced breast cancer intensively treated with chemotherapy during the course of their disease, with or without an anti Her2neu targeted treatment. Seventy-nine patients were enrolled. Only one patient presented HER 2 overexpression on CTCs and he was treated with trastuzumab for 3 cycles before progression disease. The concordance of HER-2 status between CTCs and the primary tumour was concluded and the results were published.[4]

Subtask 9.2.5: Breast Cancer Stem cell models: The Study will consist of 3 phases:
Phase I: Murine breast cancer SCs will be exposed to drugs in order to assess target genes' modification before and after exposure. In order to prepare BSCs and BCSCs we used for each experiment 80 wild type mice for the preparation of BSCs and 5 to 6 animals that have developed Breast Cancer. The difference in numbers (80 out of 5 to 6) between the normal

[4] *Munzone E et al. Clinical Breast Cancer, Vol. 10, No. 5, 392-397, 2010.*

mice and tumour are due to the effect that breast cancer tumours contain more stem cells than the normal tissue.
Phase II: After purification of the SCs from the different mouse models, we will inject single SCs into the mice and we'll treat the animal with different chemotherapeutics and biological agents. Once and if the tumour will grow as an effect of resistance to treatment, serial transplantation will be performed in order to assess if treatment failure is related to stem cell or to progenitors growth.
For each experiment we need at least 10 mice treated and 10 mice for control (non-treated). This number correlates with one type of treatment.
Phase III: the same experimental approach of phase II will be adhered to with transplantation in immunodeficient mice of human SC obtained from primary tumour and lymph node metastases.
During the first year of research IEO also tested the TIC (tumor initiating cells) frequency in vivo by extreme limiting dilution assay (ELDA) upon cell isolation with the modified protocol.
IEO is currently testing several parameters that are needed to set up our RNAi screening in the MMTV-NeuT model.

Subtask 9.2.6*, *Acute lymphoblastic Leukaemia (ALL): In CAU's meetings with Philips and FhG, the provided data description from CAU was used to discuss the variables from the data collected in the ALL-BFM 2000 study. It was defined how the data of the ALL-BFM 2000 study have to be edited and anonymised that they can be used by IAIS for data mining and by Philips for decision support.
The useful variables for data mining and decision support were selected. All personal patient information was identified and excluded or anonymised. The clinical data for about 4000 patients were already edited and are ready to share. The data for the other scenarios will be ready soon.

Task 9.3, Certification of tools for the use in GCP conform clinical trials (ObTiMA, DoctorEye, …): UCL has provided Wilms tumour 'test data' for the development and validation of tools being developed in p-medicine. Work was undertaken regarding the certification of tools for the use in GCP conform clinical trials (ObTiMA, DoctorEye):
UOXF contributed to discussion and provided feedback. We discussed with the legal team the DCE MRI data from the shared clinical trial; the data has the potential to be made anonymous if genetic, i.e., the RNA data from a tumour would not be identifying a patient. UOXF also reviewed and discussed (mainly with IFOMIS) in detail how to define individual data items from our retrospective study for use in ontology, then sharing in data mining and data warehouse settings. We generated a set of fake data with typical values using definitions discussed above, to provide working data to the colleagues in WP11 and WP12.
USAAR collaborated with the respective partners (mainly UDUS and FORTH) in producing the content for the deliverable D9.3 ("Report on the validation and certification of ObTiMA and DoctorEye"). Collaboration with the respective partners (FORTH) was initiated in order to produce the content for the deliverable D9.4 ("Report on the segmentation of Wilms tumours using DoctorEye"). UCL collected prospective IMPORT data on forms specifically designed for the ObTiMA framework and will begin entering new patient data, including DICOM files. This will help drive the development of a framework to be used by p-medicine. Norbert Graf will lead the establishment of the framework for information entry in ObTiMA. The process of data entry from the GPOH SIOP into ObTIMA is on-going.

Summary of significant results

The most important results from the work carried out in this reporting period are highlighted as follows:

- Collection of clinico-genomic data from CAU corresponding to the ALL-BFM 2000 study
- Evaluation of the reported data/parameters with respect to relevance and usage in the predictive setting, and depending on the query of interest; i.e. prediction of response to therapy or patient stratification in ALL trials.

- Finalizing of preparatory work in order to enrich the predictive platform with the relevant clinico-genomic parameters (in parallel with the work carried out in WP11 and WP13)
- In view of the growing amount of bibliographic information published in the cancer field and particularly in ALL, BIOVISTA has performed extensive literature reading in this setting. Significant focus was given to the identification of possible biomarkers, e.g. other cell-surface markers. Moreover, micro RNA (miRNA) profiling, DNA methylation patterns, and others are emerging as important events in the prognosis of ALL, therefore, BIOVISTA could suggest that additional fields could be of use for constructing the experiments. They consider that this knowledge will not only provide significant insight in the later stages of the project, where data interpretation is required, but will also help organizing and running future experiments in ALL.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

The conclusions from SIOP meetings in London and Lyon were that, whilst the total volume of residual viable blastemal cells in a Wilms tumour is associated with relapse risk, that further work was needed to understand where a threshold could be set that would be suitable for incorporation into risk stratification for clinical use. Therefore it was agreed that we needed a further period of registration of new patients (approx. 24 months) with associated high quality prospective data and sample collection, to include DICOM files and tissue samples, in order to be in a position to undertake these analyses. This work is being done as part of the SIOP WT trial going forward.

It was agreed that a new protocol will be written that will not be a clinical trial but a prospective clinical study, continuing the current treatment arms of the SIOP WT 2001 trial, duration: 24 months. The registration process will include obtaining consent from patients/parents for data collection (clinical, imaging, pathology) and access to biological samples and international data sharing through p-medicine. Kathy Pritchard-Jones, a partner of p-medicine from UCL, is leading on writing the protocol and obtaining the necessary permissions in the UK.

There have been some delays in getting ObTIMA available to international partners and these are being effectively addressed.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

In the case of Acute Lymphoblastic Leukaemia (ALL), it was legally asserted that germline genomic SNP profiles could be made available to the project but the problem of anonymization will prevent this.

Corrective actions

Data collection is occurring in UK with adapted consent and we will expect to have access to ObTIMA in year 3.

Statement on the use of the resources

Planned versus actual efforts in WP9			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	14.00	4.75	5.67
4 – UCL	40.00	12.00	4.32
7 – CUSTODIX	3.00	1.50	0.00
9 – UDUS	3.00	1.25	0.22

10 – ICCS	4.00	1.00	1.50
12 – CAU	33.40	9.00	9.68
13 – IEO	24.00	6.00	24.35
15 – UOXF	10.00	2.50	2.89
16 – BIOVISTA	10.00	7.00	3.80
Total	**141.40**	**45.00**	**52.43**

For CAU, the total person months in WP9 has been reduced from 36 to 33.4 in order to allow the financing of adequate biostatistical data management software. The reduction was taken into account in the revised planning which corresponds to the actual person months for this reporting period. For the work on WP9, Martin Stanulla and Martin Zimmermann contributed their own efforts to compensate for the reduced funding of personnel.
The discrepancy in person months at IEO is due to the fact that the work on clinical trials (drafting of protocols, following patients, collecting data...) was much more extensive than originally expected.

2.10 Work Package 10: Access to Biobanks

Main objectives of this WP

The main objectives of the work package are:
- To analyse existing open biobank frameworks which enable the sharing of biomaterial in respect to usability, GCP criteria and legal aspects. This will be done in close cooperation with WP2 (User needs and requirements) and WP5 (Legal and ethical framework). One aspect is the evaluation of potential re-usability of existing tools for p-medicine.
- To develop an integrated biobanking infrastructure in close cooperation with BBMRI. This service framework includes e.g. a biobank annotation service, a generic wrapper tool and a meta search engine for biomaterial.
- To provide a semantic biobank query interface that allows users to search for materials in various bio-repositories according to their selection criteria. This tool shall serve as a meta search engine for biomaterial.
- To integrate a mechanism for monitoring and safeguarding the patients'/donors' decisions on research that might or shall be performed on their samples. This mechanism will be provided by WP14 (Collaborative Environment for Patient Empowerment).
- To evaluate the biobanking framework by integrating distributed biomaterial resources of the SIOP Wilms Tumour Trial into the p-medicine infrastructure in addition to the publicly available German-Austrian meta biobank in the cancer domain namely the biobank Central Research Infrastructure for molecular Pathology CRIP.

The active tasks of the work package planned in the reporting period concerned are:
- Task 10.2: Development of a generic wrapper service for biomaterial repositories (M10-M36)
- Task 10.3: Provision of a meta search engine for biomaterial (M12-M38)

Summary of progress achieved towards objectives

In task 10.2 a first prototype of the ObTiMA Trial Biomaterial Manager has been implemented. The Deliverable D10.2 "Initial prototypes of the components of the p-medicine biobank access framework" has been prepared and submitted to the EC. Furthermore, the semantic standardisation requirements for the information needs in biobanks have been analysed. In particular the annotations have been investigated that are necessary to cover an electronic case report form for biobanks so that this information can be integrated in the overall semantic framework of the project provided by the Health Data Ontology Trunk (HDOT).

In task 10.3 a first prototype of the p-BioSPRE metabiobank was implemented.

Summary of details for each task

Task 10.2, Development of a generic wrapper service for biomaterial repositories: Several meetings with users from USAAR and CAU took place to discuss the user requirements for the biobank access framework and the realisation. A first prototype of the ObTiMA Trial Biomaterial Manager has been implemented. Implementation of the first prototype of the p-Biobank Wrappers took place. The Deliverable D10.2 "Initial prototypes of the components of the p-medicine biobank access framework" was prepared and submitted to the EC. Biobank integration requires harmonization of formats and nomenclatures used to describe the human biomaterial and the related patient case. For this purpose, in co-operation with WP4, an extension for the semantic framework of the project has been designed to cover biobank specific information needs. This extension consists of a module for HDOT called HDOT_bsds which is ready for use as an owl.-file.

Task 10.3: Provision of a meta-search engine for biomaterial: the interface was designed to extract biobank data from the databases in Kiel and Berlin to upload them to the p-BioSPRE metabiobank. The first prototype of the p-BioSPRE metabiobank was implemented.

Summary of significant results

A first prototype of the ObTiMA Trial Biomaterial Manager is available. Deliverable D10.2 "Initial prototypes of the components of the p-medicine biobank access framework" has been prepared and submitted to the EC.
In co-operation with WP4 a biobank module for the Health Data Ontology Trunk has been constructed, which can be used to perform standardised annotations of biobank specific information within the project.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

There were no deviations from Annex I.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP10			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	10.00	2.75	2.63
3 – FORTH	2.00	0.70	0.00
5 – FhG	32.00	8.00	13.00
6 – LUH	12.00	0.00	0.00
13 – IEO	3.00	1.00	0.38
Total	**59.00**	**11.45**	**16.01**

2.11 Work Package 11: Patterns for Data Mining and Predictive Analysis

Main objectives of this WP

The main objectives of the work package are:
- transition of state-of-the-art data mining solutions to clinical practice
- build basic support for reusable data mining solutions
- definition of data mining patterns for several scenarios

The active tasks of the work package planned in the reporting period concerned are:
- Task 11.1: Data Mining Patterns (M1-M36)
- Task 11.2: Large-Scale Data Mining (M12-M36)
- Task 11.3: Privacy-preserving Data Mining (M18-M42)
- Task 11.5: Predictive literature mining (M6-M40)
- Task 11.6: Integration of VPH, system biology and bioinformatics approach in the data mining of clinical trials (CT) (M6-M48)

Work has started early in the following task:
- Task 11.4: Data Mining for Collaborative Research Environments (M24-M48)

Summary of progress achieved towards objectives

In task 11.1, an architecture was developed and tools were implemented for data mining
For task 11.2, we succeeded with the integration of solutions for large scale data analysis into the Trial Outline Builder and the rule discovery learner. In Task 11.3, development of an approach for privacy-preserving publication of rule models, such as the decision support models of task 11.4, took place. Task 11.4 included the implementation of software for generating decision support models in the Jess language for interaction with the p-medicine CDS tool and the planning/elaboration of scenarios. In task 11.5, we augmented the capabilities of the literature mining tool and in task 11.6, we gathered and prepared data sets.

Summary of details for each task

Task 11.1, Data Mining Patterns: FhG-IAIS integrated the p-medicine data mining toolkit into the p-medicine security infrastructure by implementing Shibboleth-based authentication and access to the secure cloud storage services from the Taverna data mining environment. FhG-IAIS also set up and coordinated an integrated demonstrator based on data mining for decision support applications. The demonstrator will be shown at the 2013 annual Review. UHOK developed generic wrappers which allow to wrap any legacy analysis and/or visualization tools developed in R or Octave into components with standard interoperable interface, and to use them in the extended TOB.

Task 11.2, Large-scale Data Mining: FhG IAIS implemented a distributed algorithm for rule learning. This learning approach will be used in the Task 11.4 for the data mining of clinical trials for decision support. The implementation has been shown to effectively reduce the runtime of the model generation for scenarios of mining the ALL data set. By considering the bio markers obtained by analysis of biological and genomic data of patients as extended diagnostic events, UHok have naturally extended the TOB architecture for the integration of large scale data analysis into the original TOB architecture.

Task 11.3, Privacy-preserving Data Mining: FhG IAIS developed a privacy-preserving rule discovery algorithm. The algorithm can be applied to privacy-sensitive data and prevents the leakage of sensitive information when the rules that the algorithm generates, are published. The algorithm is based on the principles of t-closeness. The usage scenario of the algorithm

is based on the p-medicine scenarios and architecture, in particular the decision support scenario.

Task 11.4, Data Mining for Collaborative Research Environments: FhG-IAIS implemented software for generating decision support rules based on data mining of clinical trial data. The data mining approach of Subgroup Discovery is used to learn relevant rules from data. Rules are then automatically converted into decision support models the Jess scripting language, which is executed by the p-medicine decision support tool. A demonstrator based on the ALL BFM study has been implemented. Philips elaborated the scenarios and derived requirements for the prediction of adverse events based on available trial data. Philips also prioritized these scenarios and selected adverse events relevant for the clinical domains in p-medicine and analysed the available data sets and data needs. UOXF developed several scenarios and implemented workflows for integrated analysis of MRI and RNA data, and for analysis of DNA and RNA data. Matlab and R are used at the moment. Workflows are transferred to Taverna using the R shell and are tested. One workflow will be shown at the annual review.

Task 11.5, Predictive Literature Mining: Biovista's primary aim has been to augment the RESTful service's literature mining capabilities. Towards this goal, Biovista has added new biomedical and clinical categories to its LBD predictive technology, including attributes of relevant animal models. An important step in literature mining is the precise identification of relations between biomedical and clinical terms in free text. An issue pertinent to this task is the presence of false positives among the extracted relations. For this purpose it has been considered necessary to initiate a linguistic approach towards the resolution of false versus true positives. This technology is expected to aid in the analysis of clinical data. Biovista extended the functionality of the service, in order to support a more varied set of input parameters. The graphical Web application interface, currently in development for task 8.6, is planned to expose the new parameters through its input form.

Task 11.6, Integration of VPH, System Biology and Bioinformatics Approach in the Data Mining of Clinical Trials (CT): UOXF have gathered data from public databases to prepare the work of this task. This included data from cancer cell lines and hypoxia experiments. Scripts were written to gather data in automatic fashion. A review of models of hypoxia, proliferation, tumour growth and angiogenesis is in progress.

Summary of significant results

A security-enabled data mining framework was implemented as well as a demonstrator for data mining of decision support rules from the ALL clinical trial data. We also developed scenarios, gathered data, and implemented workflows for analysis of systems biology data. There was significant improvement of the Trial Outline Builder and the Literature Mining Service.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

Because of the earlier availability of data for clinical decision support tasks, task 11.4 has been started ahead of plan in this reporting period. In addition, for technical reasons the decision support scenario based on the ALL data was selected as the primary scenario for the overall integrated p-medicine demonstrator, such that an earlier involvement of this task was necessary.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

No negative effect on the overall goals of this WP, and on the scheduling of the other work packages, will result of this modification.

Corrective actions

The work in tasks 11.2 and 11.3 has been reduced compared to the original planning in this reporting period in order to balance out the increased effort in Task 11.4. This will be balanced out in the next reporting period, such that at the end of project year 3 Task 11.2 – 11.4 again proceed according to the original plan.

Statement on the use of the resources

Planned versus actual efforts in WP11			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	2.00	0.75	0.00
5 – FhG	38.50	7.00	10.10
7 – CUSTODIX	2.00	1.00	0.00
8 – Philips	10.00	2.00	5.00
15 – UOXF	22.00	5.50	5.99
16 – BIOVISTA	36.00	10.00	19.63
18 – UHok	4.00	1.60	1.60
Total	**114.50**	**27.85**	**52.32**

For Biovista, the additional PMs in this work package have been required in order to support the integration of novel data sources in the literature mining platform which was not foreseen in the original planning. Initial experiments have indicated the need to enrich pure literature sources with other data types such as expression data, pathway analytics, etc. the bulk of the additional work has been dedicated to this activity.

2.12 Work Package 12: VPH Modelling and the Integrated Oncosimulator

Main objectives of this WP

The goal of this work package is to develop an integrated multiscale Oncosimulator able to simulate the response of clinical tumours to several treatment schemes and/or schedules in the patient individualized context, as well as a number of mutually compatible detailed models of specific tumour biomechanisms aiming at enhancing our understanding of the natural phenomenon of cancer.
The main objectives of the work package are:

- To develop three exemplary multiscale simulation models of clinical tumour response to treatment: one for nephroblastoma, one for breast cancer and one for acute lymphoblastic leukaemia (ALL) based on the principles that have been shown to be most appropriate for the clinical trial context. These three models will constitute the simulation core of the “p-medicine Oncosimulator”.
- To clinically adapt, optimize and validate the three Oncosimulator models using the data generated by one clinical trial per tumour type. Especially for the breast cancer type two complementary breast cancer trials will be considered which will be jointly viewed as the “Oncosimulator breast cancer branch clinical trial”.
- To develop the p-medicine integrated Oncosimulator as a treatment support system
- To develop a number of separate mutually compatible models focused on various biological mechanisms that determine tumour dynamics at various combinations of biocomplexity levels/scales in order to gain insight into the complex phenomenon of cancer and suggest treatment strategies by studying these mechanisms in silico

- To utilize the tumour biomechanism focused models in order to explore the dynamics of the corresponding mechanisms in silico
- To utilize high performance computing resources such as DEISA/PRACE petascale facilities in order to increase the accuracy and the speed of numerical calculations
- To evaluate the p-medicine Oncosimulator and the tumour mechanism focused models.

The active tasks of the work package planned in the reporting period concerned are:
- Task 12.1: Development of the three p-medicine Oncosimulator models (M1-M42)
- Task 12.2: Clinical adaptation, optimization and partial validation of the Oncosimulator models (M12-M48)
- Task 12.3: Development of the p-medicine Oncosimulator as a treatment support system (M18-M48)
- Task 12.4: Development of the tumour biomechanism focused models (M1-M42)
- Task 12.5: In silico studies using the tumour biomechanism focused models (M12-M48)

Summary of progress achieved towards objectives

ICCS has refined existing simulation codes for all three branches of the Oncosimulator, performed pertinent sensitivity analyses and developed a systems biology-based model for cell cycle regulation in ALL cells.
Sets of real and fake data for the various tumour types under consideration are being collected (USAAR, CAU, UOXF, IEO, ICCS). Interaction of ICCS with the clinical partners regarding the final provision of the actual multiscale data to be used for the validation continues.
Moreover, ICCS has performed initial adaptation studies. PSNC has worked on prototype implementation of optimization procedures in the nephroblastoma branch of the Oncosimulator application and has performed work on Cactus framework with CaKernel technology as a tool for running the Oncosimulator application in parallel environment using GPU architecture. ICCS has provided the nephroblastoma code for parallelization and has interacted with PSNC for the development of a supercomputing platform for the execution of the Oncosimulator. UHok has considered the invocation of the Oncosimulator from TOB environment. FORTH has implemented plugins of cancer VPH models in the DrEye platform.
ICCS has ensured the timely coordination of the development of the special molecular and cellular cancer biomechanism models by UCL and IEO.
UCL developed a molecular level model to study protein molecules. A highly automated molecular simulation/free energy calculation workflow tool has been built. A high throughput calculation is achieved by distributing the simulations and analyses to various computational resources, including local clusters and national and international supercomputers.
IEO worked on the refinement of the immuno-oncological add-on to the Oncosimulator (models of tumour-immune system interplay, model of spatiotemporal interplay between tumour and cytotoxic T lymphocytes). IEO also worked on various special molecular biomechanism models: a spatiotemporal and population based model of p53 and its effects on proliferation and differentiation of tumour stem cells, a model of the pharmacodynamics of nutlin, a model of the proliferation of stem cells based cellular populations and the effect of nutlin on their dynamics and the wave-pinning and the phase models of the p53 regulated stem cell polarity in breast cancer.
UOXF completed first workflow integrating avastin trial genomic and imaging data, and contributed to the development of the biomechanism models of tumour angiogenesis.
In silico simulations for the models described in task 12.4 have been performed by IEO and UCL. UOXF worked on avastin trial genomic and MRI data. ICCS has coordinated the timely performance of *in silico* studies for the specific biochemical and molecular biomechanism models.

Summary of details for each task

Task 12.1, Development of the three p-medicine Oncosimulator models: Refinements and sensitivity analyses of the simulation code of the three multiscale models corresponding

to the three tumour types to be addressed (nephroblastoma, breast cancer, acute lymphoblastic leukaemia) have been performed by ICCS. More specifically:

Nephrobrastoma: Refinements of the simulation code.

Breast cancer: Thorough sensitivity analyses of the continuum approach to the simulation of angiogenesis and the effect of anti-angiogenic treatment in combination with chemotherapy. Bevacizumab monotherapy is considered.
Initial steps towards the coupling of the continuum angiogenesis-based model with the ISOG discrete model for the case of combination treatment (bevacizumab and vinorelbin) have been undertaken.

Leukemia: Refinement of the cellular and supercellular discrete-entity discrete-event model for non-solid tumors ("non spatial model"). Development of a systems biology-based model of the sub-cellular biochemical dynamics of the cell cycle in pre-B ALL cells. A central feature of the model was the prediction of a delayed, although undisturbed, passage to S-phase even when the hyper-phosphorylated form of retinoblastoma protein predominates, as is the case in pre-B ALL cells.
Details can be found in the submitted deliverable D12.3 ("Report on the development of the Oncosimulator and the utilization of the biomechanism models").

Task 12.2, Clinical adaptation, optimization and partial validation of the Oncosimulator models: Sets of real and fake data for the various tumour types under consideration are being collected (USAAR, CAU, UOXF, IEO, ICCS) and ICCS has performed initial clinical adaptation studies.
For the case of Acute Lymphoblastic Leukemia branch of the Oncosimulator, the flow of data from CAU to ICCS is as planned and part of the data sets have already been used by ICCS in order to train several versions of the ALL model. The useful variables from the data collected in the ALL-BFM 2000 study have been edited by CAU. The clinical data for about 4000 patients have been shared. Information on the data, the usability, the medical significance and support on interpreting the modelled results is provided by CAU.
In view of the expected provision by USAAR of real antigen data for the nephroblastoma case, exploratory scenarios of their utilization have been formulated and studied by ICCS.
The interaction of ICCS with UOXF and IEO regarding the final provision of the actual multiscale data to be used for the validation is continuing. UOXF continues extensive discussions regarding legal issues about the sharing of Avastin trial data (PI shared with a pharmaceutical company).

Task 12.3, Development of the p-medicine Oncosimulator as a treatment support system: PSNC has worked on prototype implementation of optimization procedures in the Oncosimulator application and has performed work on the Cactus computational framework with CaKernel technology, as a tool for running the Oncosimulator application in parallel environment using GPU architecture. Internal data structures have been changed for memory management procedure optimization. Improvements in the CaKernel framework have been performed in order to permit adaptation. ICCS has provided the nephroblastoma code to PSNC for acceleration and parallelization using the Cactus framework in conjunction with GPU units. Interaction with PSNC regarding the development of the supercomputing platform for the execution of the Oncosimulator has taken place. This has been the first towards the development of the Oncosimulator as a treatment support system. UHok has considered the invocation of the Oncosimulator from the TOB environment. FORTH has implemented plugins of cancer VPH models in the DrEye platform in order to allow the clinician to run the models seamlessly from a DICOM viewer (DrEye in this case). This is an important functionality that will facilitate clinical use and adaptation of the models.

Task 12.4: Development of the tumour biomechanism focused models: UCL developed a molecular level model to study protein molecules. The model is based on molecular dynamics simulation and free energy calculation methods. A highly automated molecular simulation/free energy calculation workflow tool has been built. A high throughput calculation

is achieved by distributing the simulations and analyses to various computational resources, including local clusters and national and international supercomputers. Moreover, UCL has applied the molecular modelling method to three proteins: EGFR, JAK2 and KRAS. The former two are tyrosine kinases which initiate signal cascades, and the latter serves as a hub in multiple signal transduction pathways. Various lengths of simulations have been performed, ranging from hundreds of nanoseconds to tens of microseconds. IEO worked on the refinement of the immuno-oncological add-on to the Oncosimulator (models of tumour-immune system interplay, model of spatiotemporal interplay between tumour and cytotoxic T lymphocytes). IEO also worked on the biomechanism models of the angiogenesis and the p-53 related polarization of stem cells. The multiscale model of chemotherapy of a vascularized tumour (with or without a parallel or sequential antiangiogenic therapy scheme) has been finalized. The models describing the spatiotemporal dynamics of the effect of p53 on the polarity of stem cells and the apoptosis of proliferating cells, as well as the interplay of the p53 network with the p53 targeting drug Nutlin have been finalized. An individual cell- model of stem cell-based cellular proliferation has been developed, both in absence and in presence of therapies. A stochastic model of the effects of p53 on stem cell differentiation has been finalized. A stochastic model of stem cell symmetric/asymmetric division, significantly extending the description of PTEN role in determining cellular polarization is under development. UOXF completed the first workflow integrating avastin trial genomic and imaging data, and contributed to the development of the biomechanism models of tumour angiogenesis, blood flow, and immune response. The workflows focus specifically on hypoxia and angiogensis signature gene analysis and the investigation of effects of CNA on miRNA target expression and control. Workflow testing using Copy Number Abberation information in combination with mRNA expression, miRNA expression and clinical factors has been completed. ICCS coordinated the timely development of the specific biochemical and molecular biomechanism models.

Task 12.5, In silico studies using the tumour biomechanism focused models: IEO tested via in silico simulations the models described in task 12.4. UCL performed a benchmark and partial validation of the molecular level model by applying the model to well-studied molecules. Numerical validation of the models, and prediction of the molecular properties were completed for two of the above three molecular systems described in task 12.4, and the analyses for the third one is in progress. UOXF worked on avastin trial genomic and MRI data. ICCS coordinated the timely performance of in silico studies for the specific biochemical and molecular biomechanism models.

Summary of significant results

We have performed code refinements and sensitivity analyses for the three basic simulation models corresponding to the three tumour types under consideration (nephroblastoma, breast cancer, acute lymphoblastic leukaemia). Initial clinical adaptation studies were undertaken. We have used ALL datasets to train several versions of the ALL model.
We have begun with the initial steps towards the combination of the continuum angiogenesis-based model with the ISOG discrete model of breast cancer clinical tumour growth. We developed a systems biology-based model of the regulation of the cell cycle in ALL cells by several proteins. We also improved a version of the Oncosimulator nephroblastoma application that is exploiting the Cactus with CaKernel computational framework.
What is more, we refined the immuno-oncological add-on to the Oncosimulator (tumour-immune system interplay, tumour-cytotoxic T lymphocytes interplay) and finalized the following models: effect of p53 on the polarity of stem cells and the apoptosis of proliferating cells; interplay of p53 network with the p53 targeting drug nutlin; chemotherapy of vascularized tumor with or without antiangiogenic therapy; stem cell-based cellular proliferation; stem cell symmetric/asymmetric division. We also refined the molecular level model to study protein systems and developed a highly automated workflow tool.

We completed the first workflows for specific processing of avastin trial MRI and RNA data to be fed into the models. We completed workflow testing using Copy Number Abberation information in combination with mRNA expression, miRNA expression and clinical factors.
Initial plugins of cancer VPH models in the DrEye platform were implemented.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

Delays in the provision of multiscale data by IEO and UOXF might cause delays in the implementation of the remaining clinical adaptation and validation work. As many efforts are taking place at the moment to receive the required data in time, a negative impact cannot be foreseen at the moment.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

The delays in the provision of multiscale data were due to a number of legal and administrative limitations at IEO and UOXF respectively. At the moment this does not influence other tasks and planning.

Corrective actions

In case that part of the data is not finally provided within the next three months, special emphasis will be put on multiscale data available in literature.

Statement on the use of the resources

Planned versus actual efforts in WP12			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	7.00	1.50	0.00
3 – FORTH	10.00	3.00	2.81
4 – UCL	32.00	4.00	13.91
10 – ICCS	64.00	18.00	22.59
12 – CAU	3.00	0.50	0.71
13 – IEO	20.00	5.00	17.24
15 – UOXF	16.00	4.00	6.56
18 – UHok	3.00	0.60	0.60
20 – PSNC	15.00	4.00	4.70
Total	**170.00**	**40.60**	**69.12**

UOXF's overspending was due to activities moved from period 1 (when there was an under spending) to period 2.
For IEO, the various and complex tasks for this WP, ranging form theoretical methods to numerical simulations and requiring the elaboration of novel mathematical algorithms (such as hybrid systems and spatiotemporal bounded noises), implied a work effort by Dr. d'Onofrio that was remarkably larger than the one initially scheduled for this WP.

2.13 Work Package 13: Clinical Decision Support

Main objectives of this WP

The main objective of WP13 is to develop tools able to support the clinicians to efficiently access all relevant data and infer knowledge necessary to reach the most accurate diagnosis and prescribe the most suitable treatment. By making use of the latest medical evidence, the CDS solutions developed in this work package aim to support clinicians to provide personalized treatment and improve patient outcomes.
A second objective of this WP is to support the clinicians to prevent or identify early in the treatment potentially serious side effects to treatments and drugs, and the patients most susceptible to develop serious side effects.
This WP starts with the elaboration of relevant CDS user scenarios in the context of p-medicine, based on the clinical scenarios developed in WP2. Further on the scenarios will be prioritized and those considered most relevant will be the basis of the use case development and requirements analysis and for the development of CDS functionality.
The scenarios will focus on the user needs and provide input of what type of information is needed to manage, what decision support services we aim to build, etc. On top of that, of course we need to look at ways to extract and combine the relevant information and to make it targeted to a specific patient.
Further, the work package will develop relevant CDS tools that will be integrated in the P-Medicine environment.

The active tasks of the work package planned in the reporting period concerned are:
- Task 13.1: Requirements analysis and scenario definition for CDS (M6-M24)
- Task 13.2: Decision support based on Data mining of Clinical Trial (CT) data (M12-M48)
- Task 13.4: Annotation of the data sets to be used in the CDS tools (M12-M36)
- Task 13.5: Building a CDS system (M12-M48)
- Task 13.6: Decision support tool interface (M1-M48)
- Task 13.7: Running the predictive platform (M1-M48)

Summary of progress achieved towards objectives

In task 13.1, Philips refined the scenarios for decision support, extracted requirements and prioritized the development. They also selected data sets from the Leukaemia data set of partner CAU as well as data mining scenarios. FORTH contributed to development of clinical decision support tools with a particular focus on patient empowerment. FORTH also held regular meetings with the IEO to discuss their needs in this area. In task 13.2, a data mining approach to generate decision support models has been implemented by FhG in software for generating decision support rules based on data mining of clinical trial data. The data mining approach of Subgroup Discovery is used to learn relevant rules from data. Rules are then automatically converted into decision support models using the Jess scripting language, which is executed by the p-medicine decision support tool. A demonstrator based on the ALL BFM study has been implemented. Philips worked on a model repository to facilitate the easy store and share of models. Philips also evaluated the datasets that will be used for the tool development. In task 13.5, Philips looked into the scenarios previously defined for the CDS system. They focused on the implementation of patient stratification and looked into some related methods and technologies relevant for making the treatment recommendation and the knowledge necessary for decision making accessible by the clinicians. Moreover, they worked towards building a methodology for semi-automatic translation of free-text protocols to be used as the evidence-based recommendation source in the CDS. In task 13.6, Philips came up with a first interface design of the CDS. The interface is designed in a way that brings together all the information in use during the care process, including diagnosis and stratification, treatment advice and their evidences, adverse events and their management, along with follow-up actions in a single tabular screen. ICCS continued the provision of feedback regarding the specifications of the Oncosimulator niche. Specifications for the

Oncosimulator were assessed and described as a decision support tool. In order to prepare a predictive platform for the experiments to be carried out in the context of the clinical trials in p-medicine, Biovista has initiated methods to optimize/enhance prediction, by exploiting and integrating modern NLP technologies, and has initiated preliminary work towards integrating patient data (ALL-BFM 2000 study).

Summary of details for each task

Task 13.1, Requirements analysis and scenario definition for CDS: Philips refined the scenarios for decision support, extracted requirements and prioritized the development. They also selected data sets from the Leukaemia data set of partner CAU as well as data mining scenarios. FORTH contributed to development of clinical decision support tools with a particular focus on patient empowerment. FORTH also held regular meetings with the IEO to discuss their needs in this area.

Task 13.2, Decision support based on Data mining of Clinical Trial (CT) data: FhG implemented software for generating decision support rules based on data mining of clinical trial data. The data mining approach of Subgroup Discovery is used to learn relevant rules from data. Rules are then automatically converted into decision support models the Jess scripting language, which is executed by the p-medicine decision support tool. A demonstrator based on the ALL BFM study has been implemented.

Task 13.4, Annotation of the data sets to be used in the CDS tools: Philips evaluated the datasets that will be used for the tool development. They selected initial data mining approaches, in particular subgroup discovery and planned the integration of learning phase of CDS models from clinical trial data in the p-medicine infrastructure. UOXF has been working on the curation of data from Avastin trial.

Task 13.5, Building a CDS system: As a part of the diagnosis functionality in the CDS, stratification based on St.Gallen model was implemented, As a source of treatment recommendation Philips is working on incorporating the free-text evidence-based treatment protocols in the CDS by semi-automatically translating them into a computer-understandable format which can then be executed by connection to EMR data. Philips performed a literature review about the technologies and representation models for clinical narrative text, and inspected the protocol documents from ALL and nephroblastoma in order to find the specific aspects of such complex documents in terms of linguistic properties both semantic and syntactic as well as domain-specific phrases, references and document structure.
Philips devised a first version multi-dimensional modeling approach to semi-automatic protocol text translation. Philips derived the modeling primitives in some of the recognized representational aspects as well as finding the common modeling primitives between the reviewed representation languages.
Fhg has been working on predictive models to be integrated into the CDS. A prototype which is capable to store and execute clinical models that are developed based on medical findings resulted out of data mining was implemented by Philips.Using the repository models could be shared and used by different entities (e.g. hospitals, research institutes) regardless their location.

Task 13.6, Decision support tool interface: A user interface suitable for bringing the care process information together was introduced. For each phase of patient care including selection of patient, stratification based on various models, treatment recommendation and follow up a tab section was designed. Philips landscaped the Java user interface technologies. Popular Java (and JavaScript) user interface frameworks were studied including pros and cons, usage scenarios in order to evaluate what are the possibilities to build easy-to-use yet good looking user interface that could be used for a clinical decision support. For each technology a small prototype was implemented to demonstrate the

findings. What is more, ICCS continued to provide feedback regarding the specifications of the Oncosimulator niche for all its branches.

Task 13.7, Running the predictive platform: BIOVISTA has been running the predictive platform. This task involves the performing of the predictive experiments in the context of the three cancer trials. For these purposes, Biovista aims to use its predictive platform to focus on adverse event prediction, biomarker identification and patient stratification. The software-generated and ranked output consisting of multidimensional profiles of biological concepts (e.g genes, proteins, diseases, drugs) will be filtered out by biologists and assessed in terms of relevance depending on each query, i.e. prediction of adverse events, identification of possible biomarkers and stratification strategies for future clinical trials. Optimization of the output/results will be achieved by performing multiple runs of experiments and fine-tuning of the platform. To achieve the later, we have initiated processes to enrich the predictive platform with multi-level data, and use these alongside bibliographic information extraction (e.g. PubMed).

Summary of significant results

We identified relevant areas for research in the field of CDS, identified the user needs that CDS will address, described the research direction, analysed the available datasets and the data needs of the applications. A first interface design for the CDS was developed.
The predictive platform has been run and the Oncosimulator was described as a decision support tool.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

There were no deviations from Annex I.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP13			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	6.00	1.50	0.03
3 – FORTH	12.00	4.00	3.46
4 – UCL	4.00	0.50	0.00
5 – FhG	6.00	2.00	2.00
8 – Philips	51.00	15.00	14.10
10 – ICCS	3.00	0.70	1.30
13 – IEO	18.00	4.00	2.30
14 – ecancer	10.00	4.50	4.50
15 – UOXF	7.00	1.75	0.00
16 – BIOVISTA	18.00	4.00	9.45

17 – SIB	8.00	1.00	1.00
Total	**143.00**	**38.95**	**38.14**

For Biovista, the original PM allocation for this WP was based on the status of the Literature Mining platform at time of the project start. The necessity to add new data sources (see WP11 explanation) plus the earlier access to the ALL data (provided by partner CAU) has resulted in a concomitant increase in the experimentation work covered in this WP, this effort being front loaded so that there is time to absorb the findings in the final version of the delivered services.

2.14 Work Package 14: Collaborative Environment for Patient Empowerment Tools

Main objectives of this WP

The main objectives of the work package are:

- To help the patient to understand her/his medical documentation
- To empower the patient to make informed choices.

In order to achieve these objectives, the following steps need to be taken:

- To analyse the p-medicine scenarios and identify use cases for IEmS
- To develop and to test an interactive tool to support patients' empowerment

The active tasks of the work package planned in the reporting period concerned are:

- Task 14.1 Assess patients' involvement demands (M1-M15)
- Task 14.2 Establish the linguistic nature of individual/institution communication (M3-M21)
- Task 14.3 Tool to monitor and implement donors' decisions on research to be performed on their samples (M1-M24)
- Task 14.4 Development of IEmS (M12-M30)

Summary of progress achieved towards objectives

We completed and submitted report for D14.1, identifying the way in which patients would like to be involved in the tools created by p-medicine. The ALGA-C questionnaire was finalized and algorithms to extract information from them were also finalized. Moreover, we established the linguistic and semantic implications of patient profiles.
A linguistic schema document was completed in collaboration with the ontology team to enable the creation of a patient ontology. The need for a PHR system was identified and we started the design/analysis based on the required functionality. We established the core of a patient language schema and related this schema to the overall semantic framework within p-medicine provided by the Health Data Ontology Trunk (HDOT).
The data basis for the tool to monitor the sample donor's consent has been agreed with partners (cf. 3.) and a module for the p-BioSPRE search tool was designed accordingly (cf. D10.2). A project (Encore) with similar targets was identified and p-medicine will explore possible collaboration.
The IEmS platform was designed based on the requirements and implementation started.

Summary of details for each task

T14.1, Assess patients' involvement demands: The ALGA questionnaire was developed and test centres were contacted about running trails in English, German, Japanese, French, Spanish and Italian. The implementation of the ALGA-C questionnaire started. The protocol entitled "Patient empowerment" was approved by the EC on 02 April 2012. To better understand patient needs and requirements concerning patient empowerment patient profiles are designed in order to enable the provision of relevant data by the patients (and others). In

order to collect this information we need to ask patients for information in an easily understandable but at the same time unambiguous fashion. We contributed to the clear formulation of necessary concepts and associated terms and expressions (at this stage only in English).

T14.2, Establish the linguistic nature of individual/institution communication: A review on the candidate PHR systems was performed. Moreover, open source PHR systems were installed and tested (Tolven, OpenMRS) to identify their applicability in the p-medicine patient empowerment platform. We do not expect patients to be familiar with medical expert language and expect medical professionals to provide important information to patients in a way that is most beneficial to the overall success of their medical treatment. Thus, on the one hand we have to deal with medical expert terms mainly used amongst medical professionals and on the other hand we expressions used amongst lay persons or in doctor-patient-communication. In a first step we designed a linguistic patient language schema in which we specified crucial concepts for patient empowerment and related layperson expressions, expert terms, concepts and ontological classes to each other in a kind of mapping process.
We identified cases in which the transition from expert to lay person terms can be easily achieved because there are widely understood synonymous expressions for one and the same concept or ontology class. However, we found a few cases, too, in which no such method was conceivable. In those cases a medical expert term cannot just be substituted by another widely understood expression but must be explained and elaborated in an extended description of the intended concept referred to. We established that one way to achieve such a concretization of an intended concept referred to by medical expert language is the provision of relevant parts of the overall semantic framework in p-medicine with HDOT.

T14.3, Tool to monitor and implement donor's decisions on research to be performed on their samples: Since the biobanking use case partners (USAAR and CAU) both confirmed at the consortium meeting in St. Augustin (August 2012) that retrospective test data on patients' informed consent will not be available throughout the p-medicine project phase, it was decided with the Coordinator and WP5 that the tool to monitor the sample donor's consent should be based upon and complement the recently published web-based Consent Generator (https://cdp.custodix.com/index.php/ic-generator) of the FP7 project CONTRACT (http://www.contract-fp7.eu/site/). This Consent Generator has been analysed and the first version of a module for the p-BioSPRE search tool, displaying the categories of consent indicated by the Generator, has been developed and implemented as described in D 10.2. Moreover, a project (Encore) with similar targets was identified and possible collaboration is explored.

T14.4, Development of IEmS: The IEmS architecture was established. Implementation of the IEmS has started and regular communication with FORTH (the developer of the IEmS) is taking place to ensure their needs are met for the development of the IEmS.

Summary of significant results

Documents were produced and submitted for D14.1 and D14.2.
The ALGA questionnaire was translated into English, German, Japanese, French, Spanish and Italian and trials are being instigated to test the ALGA questionnaires in different languages and cultures.
The first patient was enrolled on May 2012 and at the moment we have enrolled 52 patients. After the interim analysis (first 25 patients) the protocol was amended to increase the sample size to evaluate the usability of the questionnaire and the support instruments. The data will be analysed in the next months
In close co-operation with WP4 we designed a patient language schema and established a patient language module for the health data ontology trunk (HDOT) called HDOT_pem in order to enable patient friendly views of the p-medicine ontology and semantic framework.

This module can be used for the standardisation of patient empowerment specific information within the project.
The first version of a Tool to monitor and implement donors' decisions on research to be performed on their samples has been integrated into p-medicine's biobank access framework p-BioSPRE.
Requirement for IEmS were finalized. Analysis and design of the IEms was performed, the implementation plan was established and implementation phase has started.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

In accordance with the coordinator, the deliverable D14.3 "Deployment of Donor's decision tool", scheduled for M24 (January 31, 2013) was postponed for two months. The deliverable will be submitted before the 2nd Review.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Since our task could be clarified with partners no earlier than August/September 2012, we have not been able to discuss our work with WP 5 in detail and agree upon the text of D 14.3 on schedule. The postponement of D14.3 will impact neither other tasks nor available resources and planning.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP14			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	8.00	0.75	0.94
3 – FORTH	0.00	0.00	5.00
4 – UCL	4.00	1.00	0.00
5 – FhG	6.00	2.50	3.00
7 – CUSTODIX	2.00	1.00	0.27
8 – Philips	6.00	2.00	0.00
13 – IEO	12.00	3.00	1.32
14 – ecancer	28.00	14.00	13.96
Total	**66.00**	**24.25**	**24.49**

FORTH: even though FORTH is not directly involved in WP14, FORTH is the developer of IEmS and, therefore, has been involved in the organization of regular Skype and teleconference meetings as well as in a WP14 meeting in Milan to discuss its implementation.

2.15 Work Package 15: Quality Assurance, Evaluation and Validation

Main objectives of this WP

The main objectives of the work package are:

- test software components and services
- Identify objectives that need to be specifically tested in each case, define the proper evaluation criteria and devise monitoring procedures that will be executed
- Assess the quality of all services and tasks of the p-medicine environment and iteratively gives feedback to all responsible persons
- Provide combined evaluations covering the whole integrated p-medicine environment

Specifically:
- Formulate evaluation criteria, verification procedures, and feedback report guidelines
- Coordinate validation activities by partners and feedback reports
- Evaluate the developed software tools by testing functionalities, accessibility, and respect of user needs, data integration and execution times
- Verification of GCP (Good Clinical Practice):
    - protection of human rights as a subject in clinical trial
    - standards on how clinical trials should be conducted
    - clinical audit: performance will be regularly reviewed to ensure scheduled activities will be properly executed
- Survey of certification criteria for software components in clinical research settings and evaluation of their adherence in p-medicine environment
- Write a final evaluation report

The active tasks of the work package planned in the reporting period concerned are:
- Task 15.2: Coordinate evaluation activities by partners (M6-M18)
- Task 15.3: Joint evaluation activities (M12-M48)
- Task 15.4: Criteria for and implementation of the certification (M1-M48)

Summary of progress achieved towards objectives

The user needs and requirements gave the basis for the p-medicine environment used by the various user groups (bioinformaticians, biostatisticians, data managers, clinicians and patients). We identified and described them in context scenarios in WP2 (D2.2).
In WP15 (D15.1) we summarized these user needs and requirements to be carefully read by the different developer groups concerning the workflow environment, the clinical and VPH tools. The document aims to support the developers for better understanding of the various tasks the end-users have to conduct with the software but it does not substitute to read the whole context scenarios in D2.2.
In task 15.2, the 1st usability testing activity has been completed mainly with the contribution of FhG-IAIS, SIB, UPM, ecancer and UOXF. D15.02 “First evaluation workshop round submitted”. In WP15 (D15.2) we started the first usability tests with the first prototype of the ontology based trial management application (ObTiMA). Two external volunteers tested the first available functionalities with the task concerning entering fictional patient data. The interaction of the system and user's “thinking aloud” were recorded and evaluated in form of use scenarios. After evaluation by the volunteers the developers received the use scenarios with the results and developed a new enhanced prototype.
In task 15.3, ObTiMA and the Ontology Annotator have been evaluated. We also started the study of the whole environment under development. Thanks to the “Report on the validation and certification of ObTiMA and DoctorEye” (D09.03, WP9) the dialogue between partners started toward certification. Criteria for GCP and certification are under review, guidelines will be extracted from D9.01 and D9.03 and sent to participants for feedback about intended guidelines compliants prototypes development.
In task 15.4, detailed descriptions of the developed tools for quality assessment were produced. In addition, a test version of the Ontology Annotator (under development by UPM) tool was set up for quality control process. The ontology annotator was tested by a member of p-medicine and will be integrated in D15.4. Detailed descriptions of the developed tools for quality assessment were produced (UPM). In addition, a test version of the Ontology Annotator tool was set up for quality control process. The process has involved the group

from SIB evaluating the Ontology Annotator and generating a list of issues which were tackled by UPM group. Another usability test (UOXF) was accomplished with an improved prototype of ObTiMA by a member of p-medicine without the participatory observation of the usability engineer. It will be described in D15.4.

Summary of details for each task

Task 15.2: Coordinate evaluation activities by partners: Early usability test of the first prototype of ObTiMA have taken place with the first evaluation results. The ACGT project experience and the first annual review were really fruitful in terms of "lesson learned" and suggested the optimal direction in selecting the evaluation activities; they highlighted the importance of usability and to run usability evaluation as soon as tools become available. In this frame, establishing an iterative evaluation process is extremely important for two main reasons: first, the feedback reports list issues and suggest possible improvements, modifications, and additional functionalities to be implemented by developers and second, users will benefit a new and improved tool version and they will continue in the learning process. An evaluation workshop has been held to bring together the groups implementing tools and services with the testing groups to hold usability evaluation sessions and discuss found issues. In deliverable 15.02 we provided a comprehensive overview of key demonstration results based on the correct assessment of the user requirements.
Notably, USAAR worked together with SIB, UOXF and Fraunhofer IAIS on establishing evaluation criteria for ObTiMA. To achieve the above, USAAR visited Fraunhofer IAIS to give an in-depth workshop into ObTiMA followed by a return visit to USAAR to evaluate ObTiMA with several trial persons. First prototype of ObTiMA was tested by two external volunteers, a clinician and a study nurse

Task 15.3, Joint evaluation activities: based on the documentation provided by D09.03, WP15 participants started the dialogue on requirements and criteria for achieve the aim of certification. A detailed analysis compliant with the "tool descriptions" for WP15 has been created for the tools under development (e.g. UPM did for Ontology Annotator tool). This description will be updated periodically. In addition, a test version of the Ontology Annotator has been set up allowing the Quality Committee of the project to assess its quality in a regular basis.

Task 15.4, Criteria for and implementation of the certification: the 1st portal prototype was developed, several tools and functions are already available. ObTiMA and Data Mining work-flows have been demonstrated during the 1st annual review. This achievement was the first fundamental step in centralized evaluation.
A detailed analysis compliant with the "tool descriptions" for WP15 has been created for the Ontology Annotator tool (the tool in development by the UPM at this moment). This description will be updated periodically. In addition, a test version of the Ontology Annotator has been set up allowing the Quality Committee of the project to assess its quality in a regular basis. The Quality Committee has performed regular evaluations of the tool for all the released versions. The evaluations described the weaknesses of the tool and the features to include for improving the quality. These issues were appropriately taken care by UPM.
The improved prototype of ObTiMA was tested by a member of p-medicine, a data manager (UOXF). The first prototype of the ontology annotator was tested by a bioinformatician (SIB). Contribution to evaluation, discussion and participated to meetings and provided feedback by UOXF.

Summary of significant results

An evaluation workshop has been held to bring together the groups implementing tools and services with the testing groups to hold usability evaluation sessions of ObTiMA and discuss found issues and a comprehensive overview of key demonstration results have been

reported in D15.02. Identified usage problems of the first prototypes were improved in the next prototype and tested again by prospective end-users. ObTiMA and Data Mining work-flows have been demonstrated during the 1st annual review this achievement was the first fundamental step in centralized evaluation. The Ontology Annotator is also undergoing the expected and required quality process.
WP15 participants contributed to the discussion for formulation of evaluation criteria and started the dialogue on requirements and criteria for achieve the aim of certification.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

There were no deviations from Annex I.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP15			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	8.00	2.09	0.16
4 – UCL	4.00	0.50	0.00
5 – FhG	8.00	2.00	2.40
11 – UPM	4.00	1.00	1.00
14 – ecancer	10.00	2.00	0.00
15 – UOXF	3.00	0.75	0.00
16 – BIOVISTA	3.00	0.00	0.00
17 – SIB	42.00	13.00	10.50
Total	**82.00**	**21.34**	**14.06**

USAAR used less person months than initially planned since the partner's contribution was partially covered by other sources.
UOXF's overspending was due to activities moved from period 1 (when there was an under spending) to period 2.

2.16 Work Package 16: Education and Training

Main objectives of this WP

The main objectives of the work package are:

- To impart understanding of the vocabulary and systems biology which underlie translational cancer research and understanding of IT infrastructures and their possibilities, e.g, the p-medicine environment
- To teach professionals when to use p-medicine tools or services, which one to use and how to make them work for their patients' benefit
- To help patients to understand and use the IEmS (patient empowerment service)

The active task of the work package planned in the reporting period concerned is:

- Task 16.1 Development of Flash Tutorials and eLearning tools for the p-medicine environment, tools and services (M12-M48)

Summary of progress achieved towards objectives

In discussion with project members, the required elearning tools have been developed and a schedule of production has been drawn up. The first elearning tools have been produced and submitted (D16.2) to give an idea of the format the final tools with take. We developed the Learning Management System with a focus on user follow up and reflection to enhance long term learning. ICCS explored the specifics of the future production of flash tutorials for the Oncosimulator. The initial help system for the Ontology Annotator was developed. In addition, video tutorials of the ontology annotators and detailed manuals of the same tool were produced.

Summary of details for each task

T16.1, Development of Flash Tutorials and eLearning tools for the p-medicine environment, tools and services: We explored the future contribution of ICCS on the flash tutorial for the Oncosimulator. We also designed the helping system in the Ontology Annotator tool. This tool aims at external users (typically, database administrators) who are not expected to have deep knowledge in ontologies and database mappings. The Ontology Annotator tool pretends to offer an easy approach to database mapping by providing a simple interface to perform this task. Design of the flash tutorials that will be implemented in the future was initiated during this period, and some basic help system was also implemented in the tool (providing hints and tooltips). Moreover, a detailed manual describing each element of the Ontology Annotator was developed and uploaded to the internal project wiki. The manual can be accessed from http://atlas.ics.forth.gr/pMedicine/wiki/index.php/Ontology_Annotator. Furthermore, several video tutorials were created in collaboration with SIB. These video tutorials provide step-by-step explanations of the tool features.

Summary of significant results

The first demonstration eLearning tools was produced. We explored the specifics for a flash tutorial on the Oncosimulator. We initiated the design and preparation of flash tutorials for the Ontology Annotator. Basic help features were implemented as well as a tool manual and video tutorials.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

Due to the need to develop user manuals and video tutorials, more PM were needed than were originally planned.
Overall, this will not affect the overall budget or delivery of the WP deliverables.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP16			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	6.00	1.00	0.00
3 – FORTH	5.00	1.00	0.00
4 – UCL	4.00	0.50	0.30
10 – ICCS	4.00	1.00	0.40
11 – UPM	6.00	0.50	1.25
13 – IEO	12.00	4.00	0.85
14 – ecancer	34.00	8.50	11.16
16 – BIOVISTA	4.00	0.00	0.00
Total	**75.00**	**16.50**	**13.96**

UPM: 1.25 PM were performed while only 0,5MM were planned. The excess was due to the need to develop the manuals and video tutorials.
***ecancer*:** Additional PMs were used above what was planned to reflect the extra input needed.

2.17 Work Package 17: Exploitation and Dissemination

Main objectives of this WP

The main objective of WP17 consists in the dissemination and exploitation of the project's results.

The tasks active in this work package in the reporting period concerned are:

- Task 17.1: Website (M1-M48)
- Task 17.2: Newsletter (M12-M48)
- Task 17.4: Conferences, exhibitions, workshops (M14-M48)
- Task 17.5: Scientific & technical papers publications (M12-M48)
- Task 17.6: Interfacing with other projects (M12-M48)
- Task 17.7: Exploitation, Intellectual property rights (M1-M48)
- Task 17.9: Analysis of existing Research Infrastructures for sustainability of p-medicine (M1-M48)

Summary of progress achieved towards objectives

During its 2nd year, the p-medicine project was promoted at a number of international conferences and workshops. Furthermore, a large number of scientific papers have been published in peer-reviewed journals. Most of these papers are joint efforts of two or more consortium members and follow an interdisciplinary approach. The second Summer School in Computational Oncology is currently being organized by p-medicine. ICCS co-organised the 5th IARWISOCI workshop (TUMOR project workshop). In the field of interfacing, p-medicine partners have established or intensified collaboration with a considerable number of related projects such as RICORDO, TUMOR, ENCCA, INTEGRATE or VPH-Share. With regards to exploitation and IPR Biovista strives for a patent application of their LBD platform. ICCS participated in initial discussions concerning at this stage the research level exploitation of the Oncosimulator. What is more, a first version of a plan for the the dissemination of foreground including a plan for sustainability of p-medicine was issued by Biovista, Eurice and USAAR. This plan was made available on the collaborative internal website. Biovista has established close collaborations with pharmaceutical companies,

patient advocacy groups (PAGs) and regulatory bodies, with an overall aim to increase awareness in the drug repositioning and personalized medicine fields, and engage these in potential collaboration with the project.
The second p-medicine newsletter was published.

Summary of details for each task

Task 17.1: Website: Thanks to the input of various p-medicine partners, the project website has been updated continuously during the reporting period. Eurice has initiated a stakeholder mapping which will help to analyse user needs and requirements more thoroughly. The contents of the website will then be adapted according to the results of the stakeholder mapping and the website is currently being overhauled.

Task 17.2: Newsletter: The second p-medicine newsletter was due in M24. Great effort was dedicated by Eurice to collect contributions from partners to the individual sections of the newsletter and to layout the newsletter in an adequate and appealing way. We were very pleased to have received contributions from Prof. Feng Dong, the coordinator of the p-medicine partner project MyHealthAvatar, which has started on March 1, 2013 and from Norman Powell from the project management office of VPH-Share, who elaborated on the continuous cooperation between the two projects and on the fruitful joint meeting which took place in St. Augustin, Germany on August 31, 2012. p-medicine members involved in providing content for the newsletter were USAAR, Eurice, ICCS, Biovista and UHok. We also received contributions from Anca Bucur in her role as coordinator of the EURECA project and of Dr Georgios Stamatkos in his role as coordinator of the about to start CHIC project. The newsletter is available for download at http://p-medicine.eu/news/newsletter/. Interested readers may subscribe to the newsletter to receive future issues. The newsletter was also expressly distributed to related projects, such as CONTRACT, EURECA, INTEGRATE, VPH-Share, and TUMOR. In addition, it was sent to contacts of the VPH Institute, VPH-NoE, ENCCA, SIOP Europe, EORTC, ECRIN, and BBMRI to guarantee a wide distribution and make people aware of the subscription function. The newsletter is also featured on the ecancer homepage.

Task 17.4, Conferences, exhibitions, workshops: To raise awareness about the project and to stimulate scientific exchange, members of the p-medicine consortium presented their work within the project at various international conferences such as the World of Health IT Conference in Copenhagen in May 2012, the eHealth Conference in Saarbruecken and the PerMediCon in Cologne (both held in June). USAAR promoted p-medicine's semantic data integration approach at the 5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation - The TUMOR Project Workshop, which took place in Athens, Greece, 22-23 October 2012 and which was co-organised by ICCS. Having been selected to be an IEEE (Institute of Electrical and Electronics Engineers) technically co-sponsored event, it has met the high standards of IEEE-EMBS (Engineering in Medicine and Biology Society). Particular attention has been paid to the peer review procedure undergone by the submitted manuscripts. Furthermore, following a strict evaluation procedure, all full conference papers, as well as specific introductory material presented in the workshop are already available through the IEEE Xplore Digital Library at http://ieeexplore.ieee.org/xpl/tocresult.jsp?isnumber=6397169. In parallel to the IEEE-EMBS Xplore channel publication, the open access version of the proceedings is available through the workshop website (http://www.5th-iarwisoci.iccs.ntua.gr). Partners from FORTH, USAAR and Philips co-organised the 12th IEEE International Conference on BioInformatics and BioEngineering (BIBE) which tookplace from November 11-13 in Cyprus. Biovista organized a Panel Discussion and lunch (Oct 2012, Washington DC) on the role of DR in rare and orphan diseases. Specific cases of targeted therapies developed by Biovista for single patients were discussed at length. A meeting between Prof. Norbert Graf and Yokohama City Government was organized by UHok on 29 Norvember 2012 in Yokohama, Japan. Yokohama City is now conducting the Keihin Coastal Area Life Innovation project, and became interested in p-

medicine project. The content and outcome of the Yokohama meeting is described in detail in the second issue of the p-medicine newsletter.

A number of publications, joint and individual, were accepted for presentation at international conferences later in 2012. The abstract for presenting the p-medicine project as a whole was submitted to the VPH 2012 conference taking place from September 18th -20th in London, UK. Together with other p-medicine partners, FhG-IBMT prepared an abstract for submission to the ESBB 2012 conference in Granada, Spain. A publication was submitted by UPM, together with other partners, to the special session of the EMBS 2013 conference. Another UPM publication was submitted to the MEDINFO2013 congress, citing the p-medicine project in the acknowledgements.

Following a successful first Summer School in Computational Oncology in Heraklion, Crete in 2011, the 2nd Summer School in Computational Oncology will take place from June 23-28, 2013 at the renowned Leibniz Center for Informatics at Schloss Dagstuhl in Wadern, Germany. The summer school is incorporated in an international network of different EU projects including p-medicine and other initiatives all dealing with the topics “Virtual Physiological Human”, “Modelling/Oncosimulation” and “personalised medicine”. It will be organised by Universität des Saarlandes (USAAR), Germany, in cooperation with FORTH and Eurice. Eurice has set up a website reflecting the p-medicine corporate identity for information and participant registration (www.computationaloncology.org) and, with the help of the p-medicine partners, promoted the event through a variety of channels. Like the first, the second summer school will target both clinicians/medical students and engineers/basic scientists/engineering students who wish to learn the principles of computational oncology from pioneers in the field.

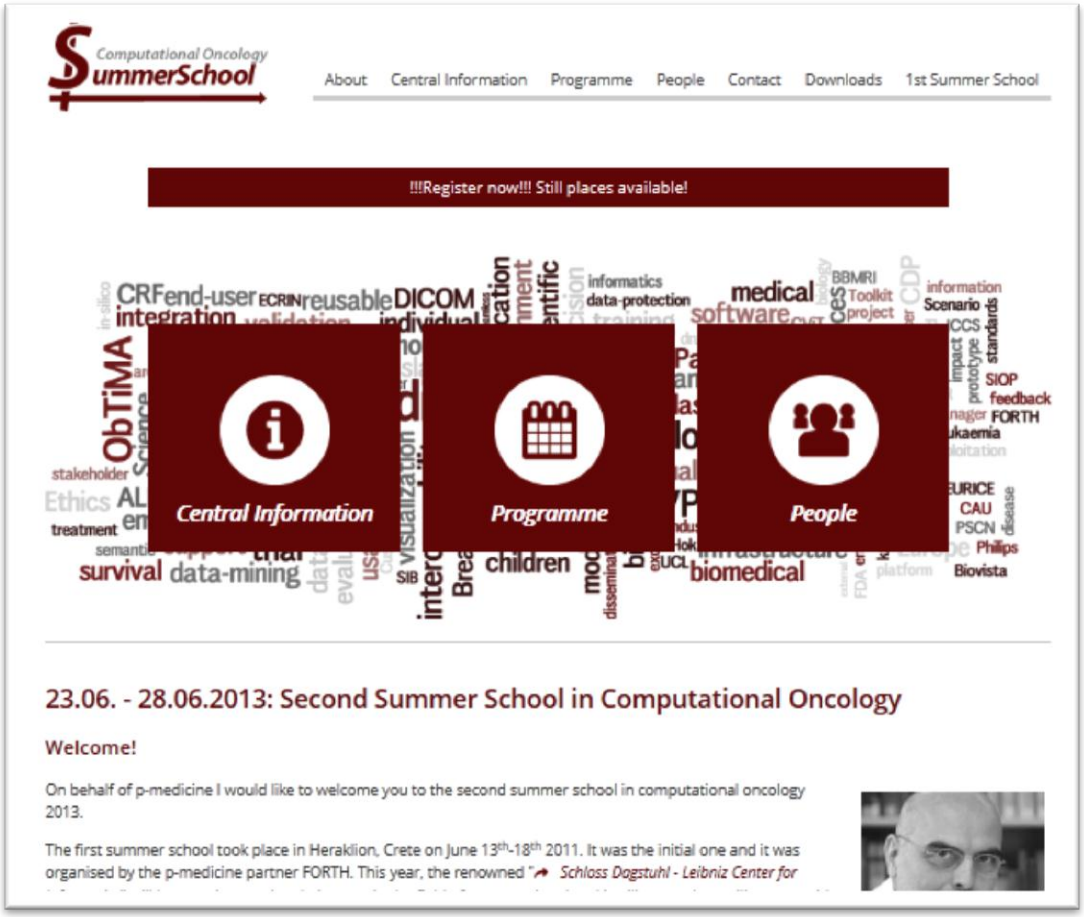

Figure 1: The p-medicine Summer School website: www. computationaloncology.org

A complete list of conferences and workshops is available at the end of the Management part of this report.

Task 17.5, Scientific & technical papers publications: There is a number of 44 publications in peer-reviewed journals for the last reporting period. Of these 44 publications, 43 have already been accepted and/or published, whereas only 1 is still in the planning or submission stage. The journals cover the IT as well as the clinical sector. What is more, 15 of the publications are joint efforts of two or more members of the p-medicine consortium. These joint papers highlight the interdisciplinary bridging of the gap between the IT and the clinical sector.
Apart from papers in scientific journals, p-medicine partners have contributed to scientific textbooks and edited volumes.

A complete list of all publications is available at the end of the Management section of this report.

Task 17.6, Interfacing with other projects: The foundation for a fruitful cooperation with the related FP7 project VPH-Share has already been laid in the first few months of the p-medicine project. As both VPH-Share and p-medicine share the common topic of cloud computing, the project's cooperation is expressly requested by the European Commission. Another successful joint meeting was held at the 4th p-medicine progress meeting in St. Augustin in August 2012. The meeting was used to intensify the on-going collaboration and define new areas of common work and research. p-medicine partners subsequently attended the VPH-Share progress meeting in Madrid in March 2013.

CAU participates in the FP7 project ENCCA. Together with their partners in the ENCCA project, researchers of CAU are generating data on the biology of childhood ALL, which may then be integrated into the p-medicine models. Childhood leukemia scenarios will gain more complex and realistic features. On 19 September 2012, USAAR also met with ENCCA in London in the context of task 11.3.

From 7-11 May the 3rd VPH study group on VPH Toolkit took place at Universitat Pompeu Fabra (UPF) www.upf.edu (Roc Boronat 138 - E08018) in Barcelona, Spain. The workshop was organized by UPF and Marco Viceconti from Sheffield, UK. Partners from p-medicine took part in it. The purpose of this one-week study group is to bring together scientists and clinicians from different projects to explore new collaborations, to come up with new ideas, to see other researchers' solutions and to make new friends. Among other things, the workshop facilitated further discussions about an intensified collaboration between the two projects p-medicine and INTEGRATE, another FP7 project (coordinated by p-medicine partner Philips), which aims to develop innovative infrastructure components and tools for data and knowledge sharing in biomedical research. The collaboration between p-medicine and INTEGRATE was intensified during a consortium meeting of INTEGRATE in Brussels from June 26-27, 2012. At this meeting, partners from the p-medicine consortium were invited to present the project in more detail.

UCL attended the first EUDAT Conference in Barcelona in October 2012 to learn about and give input to the data infrastructure they are developing. ICCS has initiated discussions with RICORDO regarding the standardized description of the Oncosimulator models. ICCS has also contributed to discussions regarding the multiscale simulation know-how interaction between TUMOR and p-medicine. ecancer met with Eurocanplatform to discuss working together and to coordinate the content of their 2014 summer school giving the opportunity for p-med to present oncologists from the leading European cancer institutes.

Collaboration between BioMedBridges and p-medicine has been initiated by UDUS, since BioMedBridges' use case for personalized medicine deals with very similar topics: hospital data, leukemia, drug response, genetic data and so on. Partners from UDUS presented the p-medicine project at the BioMedBridges Workshop at FIMM, Helsinki, in January 2013. Subsequently, Norbert Graf took part in BioMedBridge's 1st Annual General Meeting to further discuss potential areas of collaboration. It is envisaged that cooperation between the two projects contributes substantially to the sustainability of p-medicine.

To further collaborate with topic-related projects, p-medicine has become a member of Biomed Town (www.biomedtown.org), a community with free access to all those who have a professional or educational interest in biomedical research and technology. The p-medicine building on Biomed Town (www.biomedtown.org/biomed_town/pmedicine) has been provided with RSS feeds from the p-medicine official website and a variety of public documents containing detailed information about the project. Moreover, in p-medicine's upcoming summer school VPH projects are explicitly invited to participate.

To foster the cooperation with initiatives and programmes outside Europe, USAAR and Eurice held a dissemination meeting with the Medical School of the University of Namibia/Ministry of Health to discuss potential areas of collaboration and synergies with medical research initiatives and clinical studies performed in Namibia. Added value of p-medicine to relevant clinical trials supported by EDCTP programs.

Task 17.7, Exploitation, Intellectual property rights, sustainability:
Starting in the p-medicine predecessor project ACGT, the idea of a 'Study Trial and Research Centre (STaRC)' has evolved. STaRC (Study Trial and Research Center) as an entity to sustain the p-medicine infrastructure is further under discussion. Most important is the question about the kind of legal entity we need to set up STaRC. All stakeholders of p-medicine are in compliance with the endeavour of creating such an entity. To develop a business plan for STaRC, discussions with Industry (Thomson Reuters) and European infrastructures (ECRIN, EORTC) have started. Most important for STaRC will be ObTiMA. This data management tool for clinical trials was demonstrated in the second period of p-medicine to GPOH, ENCCA, ECRIN and other potential stakeholders showing the need for sustainability of ObTiMA after p-medicine. It is the intention of STaRC to guarantee this. As mentioned before a meeting with EORTC and ECRIN is scheduled for the 30th of April this year to discuss this topic within European infrastructures. Despite the fact that ObTiMA is developed in a GCP compliant way the question of how to fulfil the medical device regulation is still an open one. This was intensively discussed with Fraunhofer and their lawyers as Fraunhofer is one of the most important developers of ObTiMA. The last meeting regarding this topic took place at USAAR on 25 March 2013. During the third year of p-medicine STaRC will be founded as a legal entity. In addition to the discussion about STaRC itself the relation to CDP (Centre for data protection) is a further issue, as this legal entity needs to be sustained and needs a business plan in addition.

In addition to this, **individual partners** have further developed their individual exploitation strategies as follows:
ICCS participated in initial discussions concerning the research level exploitation of the Oncosimulator. Among other scenarios the interaction of p-medicine with activities funded by the European Commission outside the ICT research directorate has been explored preliminarily.
Biovista's Literature Based Discovery (LBD) platform has been successfully used for the repositioning of drugs in oncology indications and preliminary efforts by Biovista for a relevant patent application are under way.
During the reported period, Biovista has been engaged in meetings discussing ongoing projects with collaborators, such as Novartis and Pfizer. The focus of these meetings is naturally a successful completion of the collaboration and, once that is achieved, laying the foundations for further work in more than one area, including personalized medicine challenges. More importantly, Biovista has made efforts in establishing new contacts in the personalized medicine field while trying to raise awareness of the concept of p-medicine and pursuing the potential for collaboration with biotechnology and pharmaceutical companies.
A presentation by Dr Aris Persidis was held at the World Drug Repositioning Congress of a talk entitled "Very large scale systematic drug repositioning as a business and technology driver". The talk focused on how repositioning may confer competitive advantage on IP, patient (payer) differentiation, and innovation in target biology and covered its application to neurology and rare diseases.

PUDF

The relevant deliverable *D17.6* entitled *"Plan for the dissemination of foreground including a plan for sustainability of p-medicine"* corresponds to a live document which outlines the dissemination activities in the p-medicine environment. A first version of the document was successfully prepared by Biovista, Eurice and USAAR and was uploaded to the collaborative site on the 15 April 2012. This document focuses on the following three main sections: a) exploitation activities, b) dissemination of foreground and c) plan for the sustainability of p-medicine, and is intended to include all activities carried out during the first reporting period of the p-medicine project and to inform about planned activities during the course of the project. Updates of the report will be provided once a year (M24, M36, M48). The first update is currently under construction and will be ready in time for the 2nd Review.

Task 17.9, Analysis of existing Research Infrastructures for sustainability of p-medicine:

ECRIN: use cases, scenarios and the specifications for user needs, were developed with the focus on the integration of the p-medicine tools (ObTiMA, DoctorEye, patient empowerment, portal…) into the heterogeneous data management environment of ECRIN using applicable use cases for employing p-medicine tools in international clinical trials (Deliverable 6.1).
Requirements clusters were developed for the following main categories: interoperability requirements, technical requirements, business requirements and legal & ethical requirements. A validation workshop was held together with p-medicine developers at the University of Duesseldorf on April 4, 2012. In addition, the usability evaluation process for p-medicine is currently under development. For this purpose, together with WT6.1, several preparatory documents were developed (use cases, p-medicine tools and interface descriptions, validation documents). A usability evaluation plan will also be created.

BioMedBridges: collaboration between BioMedBridges and p-medicine has been initiated by UDUS. Partners from UDUS presented the p-medicine project at the BioMedBridges Workshop at FIMM, Helsinki, in January 2013. Subsequently, Norbert Graf took part in BioMedBridge's 1st Annual General Meeting to further discuss potential areas of collaboration. It is envisaged that cooperation between the two projects contributes substantially to the sustainability of p-medicine, as there is the possibility that p-medicine use the Data Bridges developed in BioMedBridges to connect its infrastructure with BBMRI Biobanks and/or the ECRIN study register. This collaboration also works the other way round, with p-medicine as the provider of various structures such as data protection, privacy policies or standards and tools such as ObTiMA for BioMedBridges.

In developing the biomaterial tool for ObTiMA a close collaboration took place with BBMRI. The basic data set used in the infrastructure of BBMRI is also included in the data set of the ObTiMA biomaterial tool. This allows an easy exchange of information between both projects.

Summary of significant results

p-medicine was promoted at international workshops and research results were frequently published in international scientific journals. The second Summer School in Computational Oncology will be hosted by p-medicine. With regard to interfacing, p-medicine has intensified the collaboration with VPH-Share and INTEGRATE and has established contact with many other projects in the VPH domain. The linking of a research infrastructure between p-medicine and ENCAA will allow the integration of research activities in the field of pediatric leukemia. Exploitation activities were pursued, including companies like Thomson Reuters, Novartis and Pfizer.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

There were no deviations from Annex I.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP17			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	11.00	2.46	3.21
2 – Eurice	18.00	3.67	5.60
3 – FORTH	4.00	1.00	0.69
4 – UCL	3.00	0.50	3.62
5 – FhG	4.00	0.60	0.90
6 – LUH	4.00	1.00	0.00
7 – CUSTODIX	4.00	1.00	0.14
8 – Philips	4.00	1.00	0.20
9 – UDUS	14.00	3.00	0.02
10 – ICCS	4.00	1.00	1.60
11 – UPM	4.00	0.70	0.70
12 – CAU	4.00	1.00	0.17
13 – IEO	3.00	1.00	0.08
14 – ecancer	4.00	0.50	0.50
15 – UOXF	1.00	0.25	0.00
16 – BIOVISTA	13.00	6.00	4.94
17 – SIB	2.00	0.50	0.50
18 – UHok	2.00	0.50	0.50
20 – PSNC	4.00	1.00	0.00
Total	**107.00**	**26.68**	**23.37**

3 Deliverables and milestones tables

3.1 Deliverables

Table 1. Deliverables									
No.	**Deliverable name**	**WP no.**	**Lead participant**	**Nature**	**Dissemination level**	**Due delivery date from Annex I**	**Delivered Yes/No**	**Actual / Forecast delivery date**	**Comments**
D2.6.1	Regular update of the user needs and requirements based on evaluation and validation	2	1-USAAR	R	PU	31.01.2013	YES	30.01.2013	A working document has been written alongside this deliverable which will monitor the project's progress even more closely.
D3.3.1	Annual report on the Open Consultation Process and Architectural Refinements	3	3-FORTH	R	PU	31.01.2013	YES	30.01.2013	
D3.4	Service Integration Guidelines	3	4-UCL	R	PU	31.07.2013	YES	31.07.2013	
D4.3	Initial release of data integration technology	4	11-UPM	P	RE	31.01.2013	YES	30.01.2013	
D4.4	Initial release of the patient view and its evaluation	4	1-USAAR	P	PU	31.01.2013	YES	28.01.2013	
D5.2	Report on legan and ethical issues regarding data warehouse, data mining and IP	5	6-LUH	R	PU	31.07.2013	YES	31.07.2013	

Table 1. Deliverables

No.	Deliverable name	WP no.	Lead participant	Nature	Dissemination level	Due delivery date from Annex I	Delivered Yes/No	Actual / Forecast delivery date	Comments
	issues								
D5.3	Report on legal and ethical issues regarding access to biobanks	5	6-LUH	R	PU	31.01.2013	YES	01.02.2013	
D5.5	Report on legal and ethical issues for p-medicine tools used for international GCP trials	5	9-UDUS	R	PU	31.07.2012	YES	31.07.2012	
D6.1	Report on use cases, scenarios, user needs, tools, interoperability issues for the ECRIN community	6	9-UDUS	R	PU	31.07.2012	YES	08.08.2012	
D7.2	Demonstration of different data store components	7	4-UCL	R	RE	31.01.2013	YES	07.02.2013	A delay at the review stage of the deliverable occurred, so the deliverable was handed in later than foreseen.
D8.1.2	Design and Prototype implementation of the p-medicine portal	8	5-FhG	P	PU	31.07.2012	YES	30.07.2012	
D8.1.3	Report on federated storage services	8	20-PSNC	P	RE	31.07.2012	YES	08.08.2012	
D8.2	Release of tools for multi-modal cancer	8	3-FORTH	O	RE	31.01.2013	YES	11.03.2013	The slight delay in this deliverables is due to a) the (Christmas) holiday

Table 1. Deliverables									
No.	**Deliverable name**	**WP no.**	**Lead participant**	**Nature**	**Dissemination level**	**Due delivery date from Annex I**	**Delivered Yes/No**	**Actual / Forecast delivery date**	**Comments**
	image analysis and annotation								break, which has unavoidably brought slow feedback from involved partners, b) the VPH call deadline on the 15th of January, which has extended this problem. Last but not least, D8.6.2 is one of the harder deliverables dealing with the project's integration. To hand in a thorough and elaborate deliverable, therefore, the deadline has been extended in accordance with the coordinator.
D8.3	Release/Demonstration on data anonymisation tools	8	7-CUSTODIX	O	RE	31.01.2013	YES	31.01.2013	
D8.4	Provision of new modules for clinical trial management	8	1-USAAR	O	RE	31.01.2013	YES	04.02.2013	
D8.6.1	Integration guidelines and monitoring of tools and services	8	3-FORTH	O	PU	31.05.2012	YES	31.05.2012	
D8.6.2	Initial version of the p-medicine integrated platform	8	3-FORTH	O	PU	31.01.2013	YES	15.03.2013	See explanation for D8.2.
D9.3	Report on the validation and certification of ObTiMA and	9	1-USAAR	R	PU	31.07.2012	YES	08.08.2012	

Table 1. Deliverables									
No.	**Deliverable name**	**WP no.**	**Lead participant**	**Nature**	**Dissemination level**	**Due delivery date from Annex I**	**Delivered Yes/No**	**Actual / Forecast delivery date**	**Comments**
	DoctorEye								
D9.9	Report on the ALL integrated data analysis environment	9	12-CAU	R	PU	31.01.2013	YES	04.02.2013	
D10.2	Initial prototype of the components of the p-medicine biobank access framework	10	5-FhG	P	RE	31.01.2013	YES	31.01.2013	
D11.2	Initial version of data mining tools in the p-medicine architecture	11	5-FhG	O	RE	31.01.2013	YES	26.03.2013	Due to a change in staff, the Deliverable was delayed. The demonstrator tool was intensively discussed with other p-medicine partners and changes were frequent. Therefore, and in accordance with the coordinator, the deadline for the deliverable has been extended.
D12.2	Algorithms and initial versions of the Oncosimulator and the biomechanism models	12	10-ICCS	R	RE	31.07.2012	YES	04.08.2012	
D12.3	Report on the development of the Oncosimulator and the utilization of the biomechanism models	12	10-ICCS	R	PU	31.01.2013	YES	19.02.2013	Due to a large number of assignments which are all due at the same time, the deadline for D12.3 has been extended in accordance with the coordinator.

Table 1. Deliverables									
No.	**Deliverable name**	**WP no.**	**Lead participant**	**Nature**	**Dissemination level**	**Due delivery date from Annex I**	**Delivered Yes/No**	**Actual / Forecast delivery date**	**Comments**
D13.3	Selection and annotation of the CDS training and evaluation datasets	13	8-Philips	O	PU	31.05.2012	YES	15.10.2012	Due to problems obtaining relevant datasets and protocols for futher evaluation, the deliverable was considerably delayed.
D13.4	Prototype of a clinical Decision Support System (first implementation)	13	8-Philips	P	RE	31.01.2013	YES	08.04.2013	The deliverable includes the work of Fraunhofer on data mining for CDS, with Philip's contribution of developing a model-based CDS environment. Due to delayed contributions from various partners, the deliverable was also delayed.
D14.1	Specification of patient involvement demands in the p-medicine scenarios	14	14-ecancer	R	PU	30.04.2012	YES	08.05.2012	
D14.2	Specification of linguistic schema	14	14-ecancer	R	PU	31.07.2012	YES	31.07.2012	
D14.3	Deployment of Donor's Decision tool	14	5-FhG	O	RE	31.01.2013	NO		When defining this task, we had anticipated that within the consortium retrospective data on layered consent would be available. At the consortium meeting in St. Augustin, the Coordinator confirmed that retrospective data underpinning D14.3 will definitely not be available throughout the p-medicine project. Instead, and for future research, we agreed to develop and deploy a tool for the management of multi-layered consent forms complementing the

Table 1. Deliverables									
No.	**Deliverable name**	**WP no.**	**Lead participant**	**Nature**	**Dissemination level**	**Due delivery date from Annex I**	**Delivered Yes/No**	**Actual / Forecast delivery date**	**Comments**
									recently published web-based Consent Generator[5] of the FP7 project CONTRACT.[6] Our tool is integrated in the p-medicine biobank access framework, allowing future biobank users to view the consent that has been given for specific cases and samples, and plan their research accordingly. We deem this a viable approach consistent with EU funded research, enforcing patients' decisions on research that might or must not be performed on their samples, as intended by task 14.3. So far, we have made use of access to the Consent Generator kindly provided by WP5 and Custodix, have developed our tool and implemented an initial version as already described in D10.2. However, since our task could be clarified no earlier than August/ September last year, we have not yet been able to discuss our work with WP5 in detail and agree upon the text of D14.3.
D15.2	First evaluation workshops round	15	17-SIB	R	PU	31.07.2012	YES	31.07.2012	
D16.2	First demonstration of developed flash	16	14-ecancer	D	PU	31.01.2013	YES	31.01.2013	

[5] *https://cdp.custodix.com/index.php/ic-generator*
[6] *http://www.contract-fp7.eu/site/*

Table 1. Deliverables									
No.	**Deliverable name**	**WP no.**	**Lead participant**	**Nature**	**Dissemination level**	**Due delivery date from Annex I**	**Delivered Yes/No**	**Actual / Forecast delivery date**	**Comments**
	tutorials and eLearning tools								
D17.2.1	Newsletter 2	17	2-EURICE	O	PU	31.01.2013	YES	18.03.2013	Due to the massive workload of most contributors, the newsletter had to be issued with some delay.
D17.6	Plan for the Use and Dissemination of Foreground (update)	17	16-BIOVISTA	R	PU	31.01.2013	NO		This deliverable is currently under construction and will be ready in time for the 2nd Review.
D17.7	Report on lessons learned with FDA (update)	17	16-BIOVISTA	R	PU	31.01.2013	YES	15.03.2013	This is the first regular update (M24) of deliverable D17.7.

3.2 Milestones

Table 2. Milestones							
Milestone no.	**Milestone name**	**WP no.**	**Lead beneficiary**	**Delivery date from Annex I dd/mm/yyyy**	**Achieved Yes/No**	**Actual/ Forecast achievement data dd/mm/yyyy**	**Comments**
MS4	General Assembly Meeting III	1	2 – Eurice	31.07.2012	Yes	29. – 31.08.2012	4th Progress Meeting, Fraunhofer Institutszentrum, St. Augustin, Germany
MS5	General Assembly Meeting IV	1	2 – Eurice	31.01.2013	Yes	06.-08.03.2013	5th Progress Meeting, Swiss Institute of Bioinformatics, Lausanne, Switzerland
MS15	Initial release of the data integration technology	4	11 -	31.01.2013	Yes	30.01.2013	Data integration technology available (D4.3)
MS19	Finalisation of requirements and specifications of tools and interoperability for ECRIN infrastructure	6	9 – UDUS	31.07.2012	Yes	08.08.2012	Report was published (D6.1)
MS21	Initial data warehouse component deployment	7	4 – UCL	31.03.2012	Yes	31.03.2012	The programmatic interface to the data warehouse has been fully specified.
MS22	Initial interface integration	7	4 – UCL	31.01.2013	Yes	31.01.2013	Initial interface is available.
MS28	Initial version of tools and requirements for the p-medicine workbench	8	3 – FORTH	31.07.2012	Yes	31.07.2012 / 08.08.2012	Initial version is available (D8.1.2, D8.1.3)

Table 2. Milestones							
Milestone no.	**Milestone name**	**WP no.**	**Lead beneficiary**	**Delivery date from Annex I dd/mm/yyyy**	**Achieved Yes/No**	**Actual/ Forecast achievement data dd/mm/yyyy**	**Comments**
MS31	Integrated database for running the VPH models for nephroblastoma, breast cancer and ALL	9	10 – ICCS	31.01.2013	Yes	31.01.2013	Integrated database is available
MS37	Completion of the initial version of the p-medicine Oncosimulator and the biomechanism models	12	10 – ICCS	31.12.2012	Yes	31.01.2013	The initial version of the p-medicine Oncosimulator and the biomechanism models is available. For further details, see deliverable D12.3
MS40	New user requirement based on the evaluation and validation	13	5 – FhG	31.01.2013	Yes		The corresponding report is available and will be integrated in deliverable D13.4, which will be ready well before the 2nd Review.
MS44	First evaluation workshops round	15	17 – SIB	31.07.2012	Yes	31.07.2012	Report available (D15.2)
MS47	First demonstration of developed flash tutorials and eLearning tools	16	14 – ecancer	31.01.2013	Yes	31.01.2013	Report available (D16.2)

4 Project management

Consortium management tasks and achievements

The consortium management is covered by WP1 and includes
- Task 1.1: Decision making management
- Task 1.2: Administrative coordination
- Task 1.3: Reporting procedures
- Task 1.4: Financial management.

The following achievements were made during the second year of the project's duration:

The **3rd Progress Meeting (MS3)** was held on 19-21 March 2012. It was hosted by the p-medicine partners at Poznan Supercomputing and Networking Center (PSNC) in Poznan, Poland. The purpose of the meeting was, among other things, to discuss important technical and clinical issues, the general progress of the project and to find satisfying and prompt solutions to problems that have occurred. Members of the p-medicine EAB were also present. The project management team was happy to report that the foundations for NDAs with the EAB/IEC were laid and that the NDAs regarding the cooperation with VPH-Share were signed by all partners.
What is more, a detailed agenda of the 1st Review Meeting of the p-medicine project was developed collaboratively within the consortium during the meeting. Much attention was paid to the balance of the clinical and technical aspects of the p-medicine project as well as to the fact that end users of the p-medicine tools have to be integrated into the project as early as possible.

The **1st Review Meeting** took place on 3rd May 2012 in Brussels. The coordinator Prof. Norbert Graf gave an overview of the progress achieved in the first year of the project, before members of the p-medicine consortium presented concisely various aspects of p-medicine such as clinical trial data, quality management, the legal and security framework, architecture and workbench, etc. Moreover, the p-medicine data warehouse, the Oncosimulator including complete workflows, the p-medicine portal, ObTiMA and other tools and applications were demonstrated to the reviewers. The reviewers see the project on track and consider the goals of the 1st year achieved. They complimented the p-medicine partners on their high level of cooperation within the consortium but recommend that cooperation with external projects such as ENCCA or VPH-Share be intensified. As stated in the WP17 report above, interfacing with these and other related projects has been well under way during this reporting period and a joint meeting of VPH-Share and p-medicine partners was held during the 4th Progress Meeting in St. Augustin. p-medicine is further advised to define potential markets for exploitation of the project outcome and to investigate follow-up activities in Europe and overseas.

A **4th Progress Meeting (MS4)** was held on 29-30 August 2012 at FhG-IAIS in St. Augustin, Germany, where the work done so far was presented and the work anticipated for the upcoming months was discussed. To intensify the on-going collaboration and define new areas of common work and research, a large number of partners from VPH-Share joined us for a whole day on August 31 for a fruitful joint meeting of both projects.

The **first meeting of the p-medicine International Ethical Committee** took place on 13 December 2012 at the Saarland University Hospital in Homburg, Germany. The committee was represented by Prof Dr Wolfram Henn (Saarland University) and Prof Dr Roberto W. Andorno (University of Zurich). The p-medicine project was described in detail and areas of potential IEC work were discussed. The IEC agreed to provide a white paper at the end of the project, dealing with ethics in personalized medicine in the VPH setting.

A **5th Progress Meeting (MS5)** was held on 6-8 March 2013 at SIB in Lausanne, Switzerland. Apart from an overview of the work done so far in all the work packages, an approach was formulated on how to integrate the p-medicine tools in the p-medicine architecture most effectively. The discussion resulted in a working document accompanying deliverable D2.6. This working document defines workflows and use cases, data requirements and responsibilities. It will be continuously updated by the p-medicine partners to ensure maximum quality control. Moreover, with regard to the upcoming 2nd Review Meeting, an agenda was developed collaboratively during the meeting in Lausanne.

Task 1.3, Reporting procedures: A second internal progress report was prepared by Eurice in close cooperation with all the team leaders and WP leaders. The internal report is used to monitor the overall progress of the project, discover potential and actual problems and find adequate solutions. For the (internal) reporting period in question (M13-M18), no significant problems had occurred. The report was distributed among the consortium members in October 2012 and a copy was e-mailed to the project officer at the European Commission.

The **2nd Review Meeting** will be held on 25 April 2013 at the European Commission DG CNECT headquarters in Brussels.

Task 1.4, Financial Management: The **first periodic payment** was received by the coordinator and timely and duly distributed to the partners according to the table below:

n°	Abbrev.	Total costs after amendment	Total funding after amendment	1st pre-financing acc. to original budget	claimable pre-financing acc.to new budget	difference pre-financing paid/claimable	Accepted funding year 1	1st periodic payment	Total received so far
1	**USAAR**	1,921,360,00	1,554,160,00	506,156,06	543,956,06	37,800,00	218,793,00	256,593,00	762,749,06
2	**Eurice**	701,948,00	701,948,00	228,598,33	245,681,83	17,083,50	125,441,00	142,524,50	371,122,83
3	**FORTH**	1,292,532,00	1,005,247,00	338,685,94	351,836,49	13,150,55	189,177,00	202,327,55	541,013,49
4	**UCL**	1,473,864,00	1,121,741,00	367,963,09	392,609,40	24,646,31	253,806,00	278,452,31	646,415,40
5	**FhG**	2,016,153,00	1,530,712,00	535,749,26	535,749,26	0,00	328,018,00	328,018,00	863,767,26
6	**LUH**	759,114,00	582,851,00	203,997,87	203,997,87	0,00	125,163,00	125,163,00	329,160,87
7	**Custodix**	813,400,00	624,625,00	212,476,28	218,618,78	6,142,50	88,249,00	94,391,50	306,867,78
8	**Philips**	1,697,214,00	887,920,00	310,772,04	310,772,04	0,00	130,749,00	130,749,00	441,521,04
9	**UDUS**	632,468,00	526,311,00	184,208,87	184,208,87	0,00	91,456,00	91,456,00	275,664,87
10	**ICCS**	859,400,00	674,200,00	235,970,03	235,970,03	0,00	85,934,00	85,934,00	321,904,03
11	**UPM**	647,320,00	506,790,00	177,376,52	177,376,52	0,00	120,582,00	120,582,00	297,958,52
12	**CAU**	438,400,00	340,000,00	119,000,01	119,000,01	0,00	22,116,00	22,116,00	141,116,01
	Third Party						1,887,00	1,887,00	1,887,00
13	**IEO**	727,022,00	430,118,00	150,541,32	150,541,32	0,00	54,409,00	54,409,00	204,950,32
14	**ecancer**	1,007,600,00	858,480,00	300,468,04	300,468,04	0,00	206,582,00	206,582,00	507,050,04
15	**UOXF**	771,180,00	583,980,00	201,033,02	204,393,02	3,360,00	61,341,00	64,701,00	265,734,02
16	**Biovista**	662,324,00	393,001,00	137,550,37	137,550,37	0,00	115,729,00	115,729,00	253,279,37
17	**SIB**	661,080,00	501,920,00	175,672,02	175,672,02	0,00	99,760,00	99,760,00	275,432,02
18	**Uhok**	320,808,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
19	**IBM**	0,00	0,00	228,725,73	0,00	-228,725,73	0,00		
20	**PSNC**	663,508,00	505,903,00	50,523,21	177,066,07	126,542,86	105,910,00	232,452,86	338,362,86
		18,066,695,00	**13,329,907,00**	**4,665,468,01**	**4,665,468,00**	**-0,01**	**2,425,102,00**	**2,653,827,72**	**7,145,956,79**

The € 228.725,73 of the total pre-financing payable to IBM based on their share in the original total funding were not paid to IBM due to its non-accession to the Grant Agreement. The money has been divided among those partners taking over IBM's work. Together with the first periodic payment, IBM's share of the total pre-financing was distributed to those partners who have taken over work from IBM according to the revised work plan.

Changes in the consortium

There have been no changes within the Consortium during the reporting period.

List of project meetings, dates and venues

Title	Date	Venue	Local organizer
Internal Meeting with Fraunhofer Institute for Algorithms and Scientific Computing SCAI	10 February 2012	FhG-SCAI, Bonn, Germany	FhG
Portal authentication (SSO), authorization, user management, pseudonymisation and ObTiMA meeting	14-15 February 2012	Dept. of Pediatric Oncology, Homburg, Germany	USAAR
Patient Empowerment Meeting	27 Feburary 2012	UCL, London, UK	UCL
Education and Dissemination meeting	29 Feburary 2012	Tenovus, Cardiff, UK	ecancer
Clinical Decision Support and Data Mining on Leukemia Data	29 Feb. – 01 March 2012	Medical University, Hannover, Germany	FhG-IAIS
Local meeting USAAR and FhG-IBMT	02 March 2012	Dept. of Pediatric Oncology, Homburg, Germany	USAAR, FhG-IBMT
Anonymization of Oxford data meeting & Data warehouse security meeting	12-13 March 2012	Oxford, UK	UOXF
GPOH Meeting	15 March 2012	Court Yard, Hannover, Germany	LUH
3rd Progress Meeting	19-21 March 2012	Poznan Supercomputing and Networking Center (PSNC), Poznan, Poland	PSNC
ObTiMA Validation Simulation	04 April 2012	University of Duesseldorf, Germany	UDUS
IEmS/Education platform meeting	10 April 2012	IEO, Milan, Italy	IEO
OECI Education and Patient Empowerment meeting	25 April 2012	Bari, Italy	ecancer/OECI
General rehearsal for the First Annual Review	26 April 2012	Saarland University Hospital, Homburg, Germany	USAAR-HOM
1st Review Meeting	03 May 2012	Avenue de Beaulieu, Brussels, Belgium	European Commission
ObTiMA meeting	04 May 2012	Custodix, Sint-Martens-Latem, Belgium	CUSTODIX
3rd VPH study group on VPH Toolkit	07 May 2012	University Pompeu Fabra – UPF, Barcelona, Spain	UPF
SIOP-RTSG meeting	11 June 2012	Grand Hotel Gianicolo, Rome, Italy	
European Association of Personalised Medicine meeting	12 June 2012	European Parliament, Brussels, Belgium	ecancer/ European Association of Personalized Medicine
USAAR/FhG-IBMT ObTiMA developer meeting	24 June 2012	Saarland University Hospital, Homburg, Germany	USAAR, FhG-IBMT
Meeting with INTEGRATE	26 June 2012	Institute Jules Bordet, Brussels, Belgium	
2nd meeting on decision support and data mining on leukemia data	05-06 July 2012	Pediatric Hospital, Kiel, Germany	CAU
Ontology status and planning update	06 July 2012	Saarland University Hospital, Homburg, Germany	USAAR
Discussions with oncology	21 July 2012	Graz, Austria	USAAR-IFOMIS

experts			
USAAR/FhG-IBMT ObTiMA developer meeting	08 August 2012	Fraunhofer IBMT, St. Ingbert, Germany	FhG-IBMT
Dissemination meeting with Medical School/University of Namibia and Ministry of Health	19-26 August 2012	UNAM, Windhoek, Namibia	USAAR, Eurice
4th Progress Meeting	29-31 August 2012	Fraunhofer Institute, Schloss Birlinghoven, St. Augustin, Germany	FhG-IAIS
Hackathon PESF Integration ObTiMA	11-12 September 2012	Custodix, Sint-Martens-Latem, Belgium	CUSTODIX
ENCCA – WP11, Task 11.3	19 September 2012	University College London, UK	UCL
p-medicine/ TUMOR/ RICORDO – semantic interoperability	20 September 2012	Institute of Engineering and Technology, London, UK	
European Medical Association – Education platform	21 September 2012	Euripean Medical Association	ecancer
WP14 Skype meeting	27 September 2012	Skype	
Hackathon data warehouse security integration	08-10 October 2012	Custodix, Sint-Martens-Latem, Belgium	Custodix
Panel Discussion and Lunch (topic: role of DR in rare and orphan diseases and its potential for personalized medicine)	18 October 2012	Washington DC	Biovista
Review of the nephroblastoma trial and the involvement of p-medicine	18-19 October 2012	CRUK, London, UK	
ObTiMA Meeting	31 October 2012	Fraunhofer IBMT, St. Ingbert, Germany	FhG-IBMT
TOB Meeting	30 November 2012	Wing International, Yokohama Kannai, Japan	
ObTiMA Meeting	12 December 2012	Fraunhofer IBMT, St. Ingbert, Germany	FhG-IBMT
International Ethical Committee Meeting	13 December 2012	Saarland University Hospital, Homburg, Germany	USAAR
ALGA trial set-up meeting	16 December 2012	Jules Bordet Institute, Paris, France	ecancer
LUH / CUSTODIX meeting	09-10 January 2013	Brussels, Belgium	CUSTODIX
ENCCA Consortium Meeting	16-18 January 2013	Brussels, Belgium	LUH
ObTiMA workshop	23 January 2013	Fraunhofer IBMT, St. Ingbert, Germany	FhG-IBMT
EMA Advisory Board Meeting	30 January 2013		LUH

Related documentation is available in the project management tool.

Cooperation with other projects/programmes

For cooperation with other projects/programmes reference is made to task 17.6 “Interfacing with other projects” described in the WP17 report.

Project planning and status

In general, the project’s work plan was implemented as foreseen.

Minor deviations from the original work plan occurred in the following work packages.

Work has started early in the following task:

WP11: Task 11.4 (M24-M48)
Because data for clinical decision support tasks was available earlier than expected, task 11.4 could be started ahead of plan in this reporting period. Moreover, for technical reasons the decision support scenario based on the ALL data was selected as the primary scenario for the overall integrated p-medicine demonstrator, such that an earlier involvement of this task was necessary.

Additional work has been done in the following tasks:

WP2: Task 2.1 (M1-M8), Task 2.2 (M1-M9) and Task 2.4 (M1-M12)
The deliverables for these tasks were updated (D2.1, D2.2 and D2.4) in order to clarify the current status as well as the needs and requirements for further work.

WP4: Task 4.1 (M3-M12)
The initial integration of HDOT in ObTiMA was finalized by FhG-IBMT. HDOT was further extended with a patient empowerment molule, a biobank module, a pathological formation module, and a more general disease module.

Content has been added in the following tasks to improve the work to be performed:

WP9: Clinical trials
As a result of the SIOP meetings in London and Lyon, it was decided that a further period of registration of new patients (approx. 24 months) is needed with associated high quality prospective data and sample collection, to include DICOM files and tissue samples.

Shift of person months:

Reference is made to the respective section in the reports on the work packages.

All these deviations do not have any negative impact on other tasks and do not influence the resources originally planned. They will, in general, add value to the work carried out in p-medicine.

Impact of possible deviations from the planned milestones and deliverables

In the second year of the project, deliverables and milestones have mostly been submitted or achieved as foreseen in Annex I.
Problems have occurred with regard to Deliverable D13.3, which was due on 01 June 2012. Since a number of relevant datasets and protocols were not made available to the partners involved in the deliverable on time, work was delayed and only a pre-final version of the deliverable could be handed in. Due to delayed partner contributions, deliverable D13.4 (due 31 January 2013) will also be delayed. However, the deliverable will be ready in time for the 2nd Review.
Deliverable 14.3 has also been delayed. When defining the task 14.3 upon application for p-medicine, it was anticipated that, within the consortium, retrospective data on layered consent would be available. At the consortium meeting in St. Augustin, the Coordinator confirmed that this will not be the case for the time being. For the ALL use case, we have the more detailed information that different categories of consent indeed have been and are being collected, but only documented in writing and not in an electronic format. Hence retrospective data underpinning D 14.3 will definitely not be available throughout the p-medicine project. Since a new approach could be clarified no earlier than August/September last year, WP14 have not yet been able to discuss their work with WP5 in detail and agree upon the text of D14.3. In addition, categories of consent anticipated for the SIOP biobanking scenario should also be included in this discussion with WP5, in order to provide a consistent

solution for p-medicine. Hence, the deliverable has been delayed, but will be finished and submitted to the European Commission before the second Review Meeting.

Further explanations about the new approach for D14.3 as well as on other delayed deliverables can be found in the deliverables list in section 4.

Any changes to the legal status of any of the beneficiaries

There were no changes to the legal status of any of the beneficiaries.

Development of the Project website

More information on the features of the website is available in Deliverable D17.1 (Internal and external p-medicine website).

Statement on the use of the resources

Planned versus actual efforts in WP1			
Partner	**Planned PM Total**	**Planned PM Period 2**	**Actual PM Period 2**
1 – USAAR	12.00	3.00	1.72
2 – Eurice	38.00	9.52	9.90
3 – FORTH	5.00	1.00	0.00
Total	**55.00**	**13.52**	**11.62**

Dissemination activities and publications

As an overview of the dissemination of foreground, a list of dissemination activities (divided into workshops/conferences and press) as well as a list of publications produced in the current reporting period are provided below.

Workshops and conferences

Title	Type	Main leader/Participants	Event	Venue	Date
GPOH Meeting	Workshop	USAAR-HOM	GPOH Meeting	Hannover, Germany	15-16 March 2012
eHealth Week 2012	Conference	LUH	eHealth Week 2012	Copenhagen, Denmark	09 May 2012
3rd VPH Study Group on VPH Toolkit	Workshop	USAAR-HOM, ICCS	3rd VPH Study Group on VPH Toolkit	Barcelona, Spain	07-11 May 2012
Personalised medicine symposium	Symposium	ecancer	Personalised medicine symposium	Copenhagen, Denmark	4 June 2012
Personalized medicine: from data sharing and integration via VPH models to personalized medicine	Conference, posters, flyers	USAAR-HOM	eHealth conference 2012	Saarbruecken, Germany	05 June 2012
A mathematical approach to data evaluation with focus on prediction of minimal residual disease in pediatric ALL	Conference, presentation	CAU	25. Jahrestagung der Kind-Philipp-Stiftung für Leukämieforschung	Wilsede, Germany	07 June 2012
Survivors and Chronic Cancer Patients conference	Conference, poster	ecancer	Survivor and Chronic Cancer Patients Conference	Sicily, Italy	8 June 2012
SIOP-RTSG Meeting	Workshop, Conference	USAAR-HOM	Annual Meeting of the SIOP Renal Tumor Study Group	Rome, Italy	11-12 June 2012
Von Datenaustausch und Integration über VPH Modelle zur Personalisierten Medizin	Conference	USAAR-HOM and FhG-IBMT	PerMediCon 2012	Cologne, Germany	19 June 2012
JANET conference	Conference	UOXF	JANET Conference 2012	London, UK	21 June 2012
p-medicine: from data sharing and integration via VPH models to personalized medicine	Conference	FhG-IBMT and USAAR-HOM	PerMediCon 2012	Cologne, Germany	25 June 2012

Title	Type	Main leader/Participants	Event	Venue	Date
Beyond omics Revolutions: integrative knowledge management for empowered healthcare and research	Conference		Beyond omics Revolutions 2012	Barcelona, Spain	03-05 July 2012
3rd US-Turkey Adcanced Institute on Global Healthcare Grand Challenges	Conference		3rd US-Turkey Advanced Institute on Global Healthcare Grand Challenges	Antalya, Turkey	09-15 July 2012
Visualizing Clinical Trial Data Using Pluggable Components.	Conference	UHok	16th International Conference on Information Visualization	Montpellier, France	10-13 July 2012
Computerized Clinical Guidelines: Current Status & Principles for Future Research.	Conference	FORTH	Medical Informatics Europe (MIE) 2012	Pisa, Italy	26-29 August 2012
A software prototype for the assessment of tumor treatment response using diffusion and perfusion MR imaging	Conference	FORTH	Engineering in Medicine and Biology Society (EMBC 2012)	San Diego, California, USA	28 August 2012
An architecture for integrating cancer model repositories.	Conference	FORTH, ICCS, UOXF, USAAR	Engineering in Medicine and Biology Society (EMBC 2012)	San Diego, California, USA	28 August 2012
Very large scale systematic drug repositioning as a business and technology driver	Conference	BIOVISTA	World Drug Repositioning Congress	London, UK	10-13 September 2012
In Silico Oncology: a Novel and Explicit Numerical Treatment of the Neumann Boundary Conditions Imposed by the Skull on a Multiscale Diffusion-Reaction Model of Glioblastoma Growth. Clinical Validation Aspects.	Conference	ICCS	VPH 2012	London, UK	18-20 September 2012
VPH2012	Conference	UOXF	VPH2012	London, UK	18-20 September 2012
Decoding Clinical Trials to Improve Treatment of ME/CFS	Conference	BIOVISTA	CFIDS conference	Banbury Center, Cold Spring Harbor, NY, USA	30 Sept. – 5 Oct. 2012

Title	Type	Main leader/Participants	Event	Venue	Date
European Health Forum	Conference	LUH	European Health Forum	Bad Gastein, Austria	04 October 2012
World Congress for Paediatric Oncology	Conference	USAAR, UCL	44th Congress of the International Society of Paediatric Oncology	Barbican Centre, London, UK	05-08 October 2012
Ontology Evolution, Assisting Query Migration.	Conference	FORTH	31st International Conference on Conceptual Modeling	Florence, Italy	15-18 October 2012
Collaboration between Research Initiatives and Infrastructures for Personalized Medical Research: an Underestimated Challenge	Conference	UDUS	eChallenges 2012	Lisbon, Portugal	17-19 October 2012
A Scenario-Driven Approach to Enable Collaboration Among Research Infrastructures and Initiatives	Conference	UDUS	eChallenges 2012	Lisbon, Portugal	17-19 October 2012
Modeling the interplay between pathological angiogenesis and solid tumor growth: The anti-angiogenic treatment effect	Conference, Workshop	ICCS	5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation	Royal Olympic Hotel, Athens, Greece	22-23 October 2012
Hybrid model for tumor spheroids with intratumoral oxygen supply heterogeneity	Conference, Workshop	FORTH	5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation	Royal Olympic Hotel, Athens, Greece	22-23 October 2012
The Continuous Mathematics Based Glioblastoma Oncosimulator: Application of an explicit three dimensional numerical treatment of the skull-glioblastoma Neumann boundary condition on real anatomical data	Conference, Workshop	ICCS	5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation	Royal Olympic Hotel, Athens, Greece	22-23 October 2012
Modeling nephroblastoma treatment response cases with In-Silico scenarios	Conference, Workshop	ICCS, USAAR	5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation	Royal Olympic Hotel, Athens, Greece	22-23 October 2012

Title	Type	Main leader/Participants	Event	Venue	Date
The Health Data Ontology Trunk (HDOT). Towards an ontological representation of cancer-related knowledge	Conference, Workshop	USAAR	5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation	Royal Olympic Hotel, Athens, Greece	22-23 October 2012
Scientific workflows to support in silico modeling in cancer research	Conference, Workshop	FORTH	5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation	Royal Olympic Hotel, Athens, Greece	22-23 October 2012
Towards patient personalization of an Acute Lymphoblastic Leukemia Model during the oral administration of prednisone in children: Initiating the ALL Oncosimulator	Conference, Workshop	ICCS	5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation	Royal Olympic Hotel, Athens, Greece	22-23 October 2012
Clinical Evaluation of DoctorEye Platform in Nephroblastoma	Conference, Workshop	USAAR, ICCS, FORTH	5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation	Royal Olympic Hotel, Athens, Greece	22-23 October 2012
CRI sequencing conference	Conference	UOXF	CRI sequencing Conference	Cambridge, UK	02-04 November 2012
p-BioSPRE – An ICT and Contractual Framework for Transnational Biomaterial Sharing and Access	Conference, Poster	FhG	Granada Biobanking Conference	Granada Conference and Exhibition Centre	07-09 November 2012
IEmS: A collaborative Environment for Patient Empowerment.	Conference	FORTH, IEO, ecancer	12th International Conference on BioInformatics and BioEngineering (BIBE)	Golden Bay Beach Hotel, Larnaca, Cyprus	11-13 November 2012
A technical infrastructure to support personalized medicine.	Conference	FORTH, USAAR	12th International Conference on BioInformatics and BioEngineering (BIBE)	Golden Bay Beach Hotel, Larnaca, Cyprus	11-13 November 2012
An innovative mathematical analysis of routine MRI scans in patients with glioblastoma using DoctorEye	Conference	USAAR, FORTH, ICCS	12th International Conference on BioInformatics and BioEngineering (BIBE)	Golden Bay Beach Hotel, Larnaca, Cyprus	11-13 November 2012

Title	Type	Main leader/Participants	Event	Venue	Date
EMA Workshop on clinical trial data and transparency	Workshop	LUH	EMA Workshop on clinical trial data and transparency	London, UK	22 November 2012
Panel Discussion	Conference	LUH	Nordic Conference on Legal Informatics	Stockholm, Sweden	22 November 2012
Online Education Conference	Conference	Ecancer	Online Education Conference	Berlin, Germany	29 November 2012
Partnering for Cures – Innovator Presentations Session	Conference	Biovista	Partnering for Cures Conference 2012	New York, USA	28-30 November 2012
54th Annual Meeting of the Japanese Society of Pediatric Hematology and Oncology (JSPHO2012)	Conference		54th Annual Meeting of the Japanese Society of Pediatric Hematology and Oncology (JSPHO2012)	PACIFICO, Yokohama, Japan	30 Nov. – 02 Dec. 2012
World Drug Repositioning Congress	Conference	Biovista	World Drug Repositioning Congress	Washington DC, USA	04 December 2012
Cooperation between p-medicine and BioMedBridges Use Case 8	Workshop	UDUS	BioMedBridges Workshop	FIMM, Helsinki, Finland	17 January 2013

Publications

Title	Contact person	Involved Institutions	Reference	Category	Publication date	Co-Authors	Status
Characterization of primary Wilms tumor cultures as an in vitro model	Jenny Wegert	USAAR	10.1002/gcc.20936 (Genes, Chromosomes, Cancer 51:1)	Peer-reviewed journal article	January 2012	S. Bausewein, S. Roth, Norbert Graf, E. Geissinger, M. Gessler	Published
Knowledge engineering for health: A new discipline required to bridge the "ICT gap" between research and healthcare	Tim Beck	USAAR	10.1002/humu.22066 (Human Mutation 33:5)	Peer-reviewed journal article	May 2012	S. Gollapudi, S. Brunak, Norbert Graf, U.H. Lemke, D. Dash, I. Buchan, C. Diaz, F. Sanz, A.J. Brookes	Published
Characterization of the chromosomal translocation t(10;17) (q23; p13) in clear cell sarcoma of kidney	E. O'Meara	USAAR	10.1002/path.3985 (The Journal of Pathology)	Peer-reviewed journal article	May 2012	D. Stack, C.-H. Lee, A.J. Garvin, T. Morris, P. Argani, J. Han, J. Karlsson, D. Gisselson, I. Leuschner, M. Gessler, N. Graf, J. Fletcher, M. O'Sullivan	Published
A Detailed Numerical Treatment of the Boundary Conditions Imposed by the Skull on a Diffusion-Reaction Model of Glioma Tumor Growth. Clinical Validation Aspects	Stavroula Giliati	ICCS	10.1016/j.amc.2012.02.036, (Applied Mathematics and Computation 218:17)	Peer-reviewed journal article	01 May 2012	Georgios Stamatakos	Published

Nanoinformatics: developing new computing applications for nanomedicine	Victor Maoja	UPM, USAAR	10.1007/s00607-012-0191-2 (Computing in Science and Engineering 94:6)	Peer-reviewed journal article	June 2012	M Fritts, F Martin-Sanchez, D De la Iglesia, RE Cachau, M Garcia-Remesal, J Crespo, JA Mitchell, A Anguita, N Baker, JM Barreiro, SE Benitez, G De la Calle, JC Facelli, P Ghazal, A GeissbuhlerF Gonzalez-Nilo, N Graf, P Grangeat, I Hermosilla, R Hussein, J Kern, S Koch, Y Legre, V Lopez-Alonso, G Lopez-Campos, L Milanesi, V Moustakis, C Munteanu, P Otero, A Pazos, D Perez-Rey, G Potamias, F Sanz, C Kulikowski	Published
Visualizing Clinical Trial Data Using Pluggable Components.	Jonas Sjöbergh	UHok	10.1109/IV.2012.56 (Proceedings of the 16th International Conference on Information Visualization)	Conference Proceedings	July 2012	Micke Kuwahara, Yuzuru Tanaka	Published
Multicenter study identified molecular blood-born protein signatures for Wilms tumor.	J. Schmitt	USAAR	10.1002/ijc.26419 (International Journal of Cancer 131:3)	Peer-reviewed journal article	01 August 2012	S. Heisel, A. Keller, P. Leidinger, N. Ludwig, N. Habel, R. Furtwängler, N. Nourkami-Tutdibi, J. Wegert, P. Grundy, M. Gessler, N. Graf, H.P. Lenhof, E. Meese	Published
Treatment independent miRNA signature in blood of Wilms tumor patients.	J. Schmitt	USAAR	10.1186/1471-2164-13-379 (BMC Genomics 13:1)	Peer-reviewed journal article	07 August 2012	Backes, C., Nourkami-Tutdibi, N., Leidinger, P., Deutscher, S., Beier, M., Gessler, M., Graf, N., Lenhof, H.-P., Keller, A. & Meese, E.	Published

Computerized Clinical Guidelines: Current Status & Principles for Future Research.	Haridimos Kondylakis	FORTH		Conference Proceedings	26-29 August 2012	Manolis Tsiknakis	Published
A software prototype for the assessment of tumor treatment response using diffusion and perfusion MR imaging	Vangelis Sakkalis	FORTH	10.1109/EMBC.2012.6345950 (Proceedings of the Engineering in Medicine and Biology Society (EMBC 2012)	Conference Proceedings	28 August 2012	Manikis, G.C., Papanikolaou, N., Karatzanis, I., Marias, K	Published
IMENSE: An e-infrastructure environment for patient specific multiscale data integration, modelling and clinical treatment	Stefan Zasada	USAAR, UCL	10.1016/j.jocs.2011.07.001 (Journal of Computational Science 3:5)	Peer-reviewed journal article	01 September 2012	T. Wang, A Haidar, E. Liu, N. Graf, G. Clapworthy, M. Steven, P. Coveney	Published
Ontology Evolution, Assisting Query Migration.	Haridimos Kondylakis	FORTH	31st International Conference on Conceptual Modeling	Conference Proceedings	15-18 October 2012	D. Plexousakis	Published
Towards In Silico Oncology: Adapting a Four Dimensional Nephroblastoma Treatment Model to a Clinical Trial Case Based on Multi-Method Sensitivity Analysis	E. Georgiadi	ICCS, USAAR	10.1016/j.compbiomed.2012.08.008 (Computers in Biology and Medicine 42:11)	Peer-reviewed journal article	01 November 2012	Dimitra Dionysiou, Norbert Graf, Georgios Stamatakos	Published
IEmS: A collaborative Environment for Patient Empowerment.	Haridimos Kondylakis	FORTH, IEO, ecancer	IEEE 12th International Conference on Bioinformatics and BioEngineering (BIBE)	Conference Proceedings	11-13 November 2012	Manolis Tsiknakis, Kostas Marias, L. Koumakis, Gabriella Pravettoni, Alessandra Gorini, Ketti Mazzocco	Published
A technical infrastructure to support personalized medicine.	Stelios Sfakianakis	FORTH, USAAR	IEEE 12th International Conference on Bioinformatics and BioEngineering (BIBE)	Conference Proceedings	11-13 November 2012	Manolis Tsiknakis, Kostas Marias, Norbert Graf	Published
An innovative mathematical analysis of routine MRI scans in patients with glioblastoma using DoctorEye	Jonathan Zepp	USAAR, FORTH, ICCS	10.1109/BIBE.2012.6399773 (Proceeding of the 2012 IEEE 12th International Conference on Bioinformatics & Bioengineering (BIBE)	Conference Proceedings	2012	Norbert Graf, Holger Stenzhorn, Wolfgang Reith, Ioannis Karatzanis, Georgios C.Manikis, Vangelis Sakkalis, Konstantinos Marias,Georgios Stamatakos	Published

Glucose utilization via glycogen phosphorylase sustains proliferation and prevents premature senescence in cancer cells.	E Favaro	UOXF	10.1016/j.cmet.2012 (Cell Metabolism 16: 6)	Peer-reviewed journal article	05 December 2012	Favaro E, Bensaad K, Chong MG, Tennant DA, Ferguson DJ, Snell C, Steers G, Turley H, Li JL, Günther UL, Buffa FM, McIntyre A, Harris AL.	Published
Collaboration between Research Initiatives and Infrastructures for Personalized Medical Research: an Underestimated Challenge	Wolfgang Kuchinke	UDUS	eChallenges e-2012 Conference Proceedings	Conference Proceedings	2012	Wolfgang Kuchinke, Toeresin Karakoyun, Christian Ohmann	Published
A Scenario-Driven Approach to Enable Collaboration Among Research Infrastructures and Initiatives	Toeresin Karakoyun	UDUS	eChallenges e-2012 Conference Proceedings	Conference Proceedings	2012	Wolfgang Kuchinke, Christian Ohmann, Hans Jakob Auer	Published
Modeling the interplay between pathological angiogenesis and solid tumor growth: The anti-angiogenic treatment effect	Katerina D. Argyri	ICCS	Proceedings of the 2012 5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation - The TUMOR Project Workshop (IARWISOCI)	Conference Proceedings	2012	Georgios Stamatakos, Dimitra Dionysiou	Published
Hybrid model for tumor spheroids with intratumoral oxygen supply heterogeneity	Georgios Tzedakis	FORTH	Proceedings of the 2012 5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation - The TUMOR Project Workshop (IARWISOCI)	Conference Proceedings	2012	Eleftheria Tzamali, Vangelis Sakkalis, Alexandros Roniotis, Kostas Marias	Published
The Continuous Mathematics Based Glioblastoma Oncosimulator: Application of an explicit three dimensional numerical treatment of the skull-glioblastoma Neumann boundary condition on real anatomical data	Stavroula Giliati	ICCS	Proceedings of the 2012 5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation - The TUMOR Project Workshop (IARWISOCI)	Conference Proceedings	2012	Georgios Stamatakos	Published

Modeling nephroblastoma treatment response cases with In-Silico scenarios	Eleni Georgiadi	ICCS, USAAR	Proceedings of the 2012 5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation - The TUMOR Project Workshop (IARWISOCI)	Conference Proceedings	2012	Dimitra Dionysiou, Norbert Graf, Georgios Stamatakos	Published
The Health Data Ontology Trunk (HDOT). Towards an ontological representation of cancer-related knowledge	Emilio Sanfilippo	USAAR	Proceedings of the 2012 5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation - The TUMOR Project Workshop (IARWISOCI)	Conference Proceedings	2012	Ulf Schwarz, Luc Schneider	Published
Scientific workflows to support in silico modeling in cancer research	Stelios Sfakianakis	FORTH	Proceedings of the 2012 5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation - The TUMOR Project Workshop (IARWISOCI)	Conference Proceedings	2012	Vangelis Sakkalis, Kostas Marias	Published
Towards patient personalization of an Acute Lymphoblastic Leukemia Model during the oral administration of prednisone in children: Initiating the ALL Oncosimulator	Eleftherios N. Ouzounoglou	ICCS	Proceedings of the 2012 5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation - The TUMOR Project Workshop (IARWISOCI)	Conference Proceedings	2012	Dimitra D. Dionysiou, Martin Stanulla, Georgios S. Stamatakos	Published
Clinical Evaluation of DoctorEye Platform in Nephroblastoma	Ruslan David	USAAR, ICCS, FORTH	Proceedings of the 2012 5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation - The TUMOR Project Workshop (IARWISOCI)	Conference Proceedings	2012	N.Graf, I.Karatzanis, H.Stenzhorn, G.Manikis, V.Sakkalis,G.Stamatakos, K.Marias	Published

Smart recommendation services in support of patient empowerment and personalized medicine.	Haridimos Kondylakis	FORTH, ecancer	Multimedia Services in Intelligent Environments - Recommendation Services	Edited Volume	2012	L. Koumakis, M. Tsiknakis, K. Marias, E. Genitsaridi , G. Pravettoni, A. Gorini, K. Mazzocco	Published
A framework for multi-modal imaging biomarker extraction with application to brain MRI	Kostas Marias	FORTH, USAAR	10.1007/978-1-4614-2107-8_6 (Data Mining for Biomarker Discovery) Source: Springer Optimization and Its Applications, Springer New York/Vienna, Ed. by P.M. Pardalos, et al., Vol. 65, pp. 91-116, 2012, ISBN 978-1-4614-2106-1	Chapter in an Anthology	2012	Vangelis Sakkalis, Norbert Graf	Published
In Silico Oncology: a Novel and Explicit Numerical Treatment of the Neumann Boundary Conditions Imposed by the Skull on a Multiscale Diffusion-Reaction Model of Glioblastoma Growth. Clinical Validation Aspects.	Georgios Stamatakos	ICCS	Proceedings of the VPH2012 Integrative Approaches to Computational Biomedicine	Conference Proceedings	2012	Stavroula Giliati	Published
An architecture for integrating cancer model repositories.	Stelios Sfakianakis	FORTH, ICCS, UOXF, USAAR	10.1109/EMBC.2012.6347514 (Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society)	Conference Proceedings	2012	Vangelis Sakkalis, Kostas Marias, Georgios Stamatakos, Steve McKeever, Thomas S Deisboeck, Norbert Graf	Published
Multiscale Modeling for Image Analysis of Brain Tumor Studies.	Stefan Bauer	ICCS	10.1109/TBME.2011.2163406 (IEEE Transactions on Biomedical Engineering 59: 1)	Peer-reviewed article	2012	Christian May, Dimitra D. Dionysiou, Georgios S. Stamatakos, Philippe Büchler, Mauricio Reyes	Published

From depression to neurodegeneration and heart failure: re-examining the potential of MAO inhibitors	SN Deftereos	Biovista	Expert Reviews in Clinical Pharmacology 5: 4	Peer-reviewed article	2012	Dodou E, Andronis C, Persidis A.	Published
Unchain the code: how to ease quality control in research, tips or requirements?	Antonio F. DiNarzo	SIB	Biohelikon Computational Biology 1: 1	Peer-reviewed article	2012	Simona Rossi	Published
Mechanism of Drug Efficacy within the Epidermal Growth Factor Receptor Revealed by Microsecond Molecular Dynamics Simulation	S. Wan	UCL	10.1158/1535-7163.MCT-12-0644-T (Molecular Cancer Therapeutics 11: 11)	Peer-reviewed article	2012	Peter Coveney	Published
Regulation of JAK2 Activation by Janus Homology 2: Evidence from Molecular Dynamics Simulations	S. Wan	UCL	10.1021/ci300308g (Journal of Chemical Information and Modeling 52: 11)	Peer-reviewed article	2012	Peter Coveney	Published
From base pair to bedside: molecular simulation and the translation of genomics to personalized medicine	D.W. Wright	UCL	10.1002/wsbm.1186 (Wiley Interdisciplinary Reviews: Systems Biology and Medicine 4: 6)	Peer-reviewed article	2012	S. Wan, N. Shublaq, S. J. Zasada, P. V. Coveney	Published
Top-Down Multiscale Simulation of Tumor Response to Treatment in the Context of In Silico Oncology.The Notion of Oncosimulator	Georgios Stamatakos	ICCS	New Challenges for Cancer Systems Biomedicine, Edition: 2012, Publisher: Springer, Editors: A. d'Onofrio, P. Cerrai, A. Gandolfi	Book Chapter	2012		Published
Mining scientific and clinical databases to identify novel uses for existing Drugs	C. Andronis	Biovista	Drug Repositioning: Bringing New Life to Shelved Assets and Existing Drugs (eds M. J. Barratt and D. E. Frail), John Wiley & Sons, Inc.	Book Chapter	2012	A. Sharma, S. Deftereos, V.Virvilis, O.Konstanti, Andreas Persidis, Aris Persidis	Published

Business development Strategies in the Repositioning Industry	A. Persidis	Biovista	Drug Repositioning: Bringing New Life to Shelved Assets and Existing Drugs (eds M. J. Barratt and D. E. Frail), John Wiley & Sons, Inc.	Book Chapter	2012	Elizabeth T. Starck	Published
Proceedings of the 2012 5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation – The TUMOR Project Workshop (IARWISOCI) [OPEN ACCESS VERSION and IEEE Xplore version]	Georgios Stamatakos	ICCS		Edited conference proceedings	2012	Dimitra Dionysiou	Published
miRNA Profiles as a Predictor of Chemoresponsiveness in Blastemal Wilms' Tumour	Jenny A. Watson	USAAR	10.1371/journal.pone.0053417 (PLoS ONE 8:1)	Peer-reviewed journal article	2013	Kenneth Bryan, Richard Williams, Sergey Popov, Gordan Vujanic, Aurore Coulomb, Liliane Boccon-Gibod, Norbert Graf, Kathy Pritchard-Jones, Maureen O'Sullivan	Published
Navigating legal constraints in clinical data warehousing: a case study in personalized medicine.	Benjamin Jefferys	UCL, USAAR, LUH, Custodix	10.1098/rsfs.2012.0088 (Interface Focus 3)	Peer-reviewed journal article	2013	Nwankwo Iheanyi, Neri Elias, Chang David CW, Sharmardin Lev, Hänold Stefanie, Graf Norbert, Forgó Nikolaus, Coveney Peter	Will be published in April 2013
Integrative approaches to computational biomedicine	Peter Coveney	UCL, USAAR	10.1098/rsfs.2013.0003 (Interface Focus 3)	Peer-reviewed journal article	2013	Vanessa Diaz-Zuccarini, Graf N, Peter Hunter, Peter Kohl, Jesper Tegner, Marco Viceconti	Will be published in April 2013
Towards an environment for data mining based analysis processes in bioinformatics & personalized medicine	Dennis Wegener	SIB, UOXF, FhG	Journal for Network Modeling Analysis in Health Informatics and Bioinformatics	Peer-reviewed journal article	2013		Accepted for publication in Jan. 2013

Personal Health Record Systems Evaluation through the Lenses of EU Research Projects - A systematic review of the currently available PHR systems and their comparative evaluation based on PHR system requirements and visions from currently running EU-funded research projects.	Lefteris Koumakis	FORTH	Elsevier - Computers in Biology and Medicine, special issue "The state of the personal health record".	Peer-reviewed journal article	2013		Planned

5 Explanation of the use of the resources

5.1 Budget Overview

Cost Budget Follow-up Table									
Contract n°	270089	Project acronym							
PARTICIP.	TYPE of EXPENDITURE (as defined by participants)	BUDGET	ACTUAL COSTS (EUR)					Percentage spent	Remaining Budget (EUR)
			Period 1	Period 2	Period 3	Period 4	Total	Total/ Budget	
			M1-M12	M13-M24	M25-M36	M25-M48			
USAAR	**Total Person-month**	**193,00**	28,45	40,54	0,00	0,00	68,99	36%	**124,01**
	Personnel	**965,000,00**	149,096,00	248,392,00			**397,488,00**	41%	**567,512,00**
	Other direct costs	**232,100,00**	21,349,00	28,435,00			**49,784,00**	21%	**182,316,00**
	Subcontracting	**6,000,00**	0,00	0,00			**0,00**	0%	**6,000,00**
	Adjustments						**0,00**	0%	
	Indirect costs	**718,260,00**	102,265,00	166,094,00			**268,359,00**	37%	**449,901,00**
	Total Costs	**1,921,360,00**	**272,710,00**	**442,921,00**	**0,00**	**0,00**	**715,631,00**	37%	**1,205,729,00**
EURICE	**Total Person-month**	**56,00**	14,34	15,50	0,00	0,00	**29,84**	53%	**26,16**
	Personnel	**363,440,00**	65,697,00	79,144,00			**144,841,00**	40%	**218,599,00**
	Other direct costs	**29,584,00**	3,902,00	9,021,00			**12,923,00**	44%	**16,661,00**
	Subcontracting	**0,00**	0,00	0,00			**0,00**	0%	**0,00**
	Adjustments			-14,075,00			**-14,075,00**	#DIV/0!	
	Indirect costs	**308,924,00**	55,842,00	67,154,00			**122,996,00**	40%	**185,928,00**
	Total Costs	**701,948,00**	**125,441,00**	**141,244,00**	**0,00**	**0,00**	**266,685,00**	38%	**435,263,00**
FORTH	**Total Person-month**	**146,00**	43,77	38,46	0,00	0,00	82,23	56%	**63,77**
	Personnel	**606,484,00**	114,630,00	90,446,00			**205,076,00**	34%	**401,408,00**
	Other direct costs	**67,500,00**	21,999,00	21,401,00			**43,400,00**	64%	**24,100,00**
	Subcontracting	**6,000,00**	0,00				**0,00**	0%	**6,000,00**
	Adjustments			-6,298,00			**-6,298,00**	#DIV/0!	
	Indirect costs	**612,548,00**	108,899,00	78,688,00			**187,587,00**	31%	**424,961,00**
	Total Costs	**1,292,532,00**	**245,528,00**	**184,237,00**	**0,00**	**0,00**	**429,765,00**	33%	**862,767,00**
UCL	**Total Person-month**	**188,00**	30,42	48,56	0,00	0,00	**78,98**	42%	**109,02**
	Personnel	**788,011,00**	152,818,00	220,867,00			**373,685,00**	47%	**414,326,00**
	Other direct costs	**125,654,00**	58,688,00	18,380,00			**77,068,00**	61%	**48,586,00**
	Subcontracting	**12,000,00**	0,00	0,00			**0,00**	0%	**12,000,00**
	Adjustments			-17,724,00			**-17,724,00**	#DIV/0!	
	Indirect costs	**548,199,00**	126,903,00	143,547,00			**270,450,00**	49%	**277,749,00**
	Total Costs	**1,473,864,00**	**338,409,00**	**365,070,00**	**0,00**	**0,00**	**703,479,00**	48%	**770,385,00**
FhG	**Total Person-month**	**158,00**	42,72	49,46	0,00	0,00	92,18	58%	**65,82**
	Personnel	**1,017,361,00**	232,174,00	309,185,00			**541,359,00**	53%	**476,002,00**
	Other direct costs	**74,500,00**	19,382,00	15,527,00			**34,909,00**	47%	**39,591,00**
	Subcontracting	**14,000,00**	0,00	0,00			**0,00**	0%	**14,000,00**
	Adjustments			1,430,00			**1,430,00**	#DIV/0!	
	Indirect costs	**910,292,00**	185,579,00	255,740,00			**441,319,00**	48%	**468,973,00**
	Total Costs	**2,016,153,00**	**437,135,00**	**581,882,00**	**0,00**	**0,00**	**1,019,017,00**	51%	**997,136,00**
LUH	**Total Person-month**	**68,00**	17,77	18,95	0,00	0,00	**36,72**	54%	**31,28**
	Personnel	**440,572,00**	98,855,00	71,627,00			**170,482,00**	39%	**270,090,00**
	Other direct costs	**32,000,00**	5,448,00	6,005,00			**11,453,00**	36%	**20,547,00**
	Subcontracting	**3,000,00**	0,00	0,00			**0,00**	0%	**3,000,00**
	Adjustments						**0,00**	0%	
	Indirect costs	**283,544,00**	62,581,00	46,579,00			**109,160,00**	38%	**174,384,00**
	Total Costs	**759,114,00**	**166,884,00**	124,211,00	**0,00**	**0,00**	**291,095,00**	38%	**468,019,00**
Custodix	**Total Person-month**	**67,00**	14,26	16,76	0,00	0,00	31,02	46%	**35,98**
	Personnel	**522,600,00**	77,221,00	91,193,00			**168,414,00**	32%	**354,186,00**
	Other direct costs	**25,500,00**	4,992,00	3,422,00			**8,414,00**	33%	**17,086,00**
	Subcontracting	**4,000,00**	0,00	0,00			**0,00**	0%	**4,000,00**
	Adjustments			-273,00			**-273,00**	#DIV/0!	
	Indirect costs	**261,300,00**	35,413,00	53,585,00			**88,998,00**	34%	**172,302,00**
	Total Costs	**813,400,00**	**117,626,00**	**147,927,00**	**0,00**	**0,00**	**265,553,00**	33%	**547,847,00**
Philips	**Total Person-month**	**94,00**	18,00	22,30	0,00	0,00	**40,30**	43%	**53,70**
	Personnel	**887,548,00**	79,940,00	106,147,00			**186,087,00**	21%	**701,461,00**
	Other direct costs	**29,500,00**	0,00	0,00			**0,00**	0%	**29,500,00**
	Subcontracting	**8,000,00**	0,00	0,00			**0,00**	0%	**8,000,00**
	Adjustments			2,580,00			**2,580,00**	#DIV/0!	
	Indirect costs	**772,166,00**	181,559,00	206,655,00			**388,214,00**	50%	**383,952,00**
	Total Costs	**1,697,214,00**	**261,499,00**	**315,382,00**	**0,00**	**0,00**	**576,881,00**	34%	**1,120,333,00**

UDUS	**Total Person-month**	**52,00**	13,93	18,51	0,00	0,00	32,44	62%	**19,56**
	Personnel	**285,168,00**	74,656,00	100,602,00			**175,258,00**	61%	**109,910,00**
	Other direct costs	**107,000,00**	1,504,00	5,946,00			**7,450,00**	7%	**99,550,00**
	Subcontracting	**5,000,00**	0,00				**0,00**	0%	**5,000,00**
	Adjustments			942,00			**942,00**	#DIV/0!	
	Indirect costs	**235,301,00**	45,695,00	63,928,00			**109,623,00**	47%	**125,678,00**
	Total Costs	**632,468,00**	**121,855,00**	**171,418,00**	**0,00**	**0,00**	**293,273,00**	46%	**339,195,00**
ICCS	**Total Person-month**	**92,00**	9,17	28,89	0,00	0,00	**38,06**	41%	**53,94**
	Personnel	**460,000,00**	62,636,00	179,291,00			**241,927,00**	53%	**218,073,00**
	Other direct costs	**74,000,00**	8,671,00	6,130,00			**14,801,00**	20%	**59,199,00**
	Subcontracting	**5,000,00**	0,00	0,00			**0,00**	0%	**5,000,00**
	Adjustments						**0,00**	0%	
	Indirect costs	**320,400,00**	42,784,00	111,251,00			**154,035,00**	48%	**166,365,00**
	Total Costs	**859,400,00**	**114,091,00**	**296,672,00**	**0,00**	**0,00**	**410,763,00**	48%	**448,637,00**
UPM	**Total Person-month**	**74,00**	17,80	22,38	0,00	0,00	40,18	54%	**33,82**
	Personnel	**319,162,00**	82,656,00	88,849,00			**171,505,00**	54%	**147,657,00**
	Other direct costs	**38,000,00**	9,021,00	3,795,00			**12,816,00**	34%	**25,184,00**
	Subcontracting	**8,000,00**	0,00	0,00			**0,00**	0%	**8,000,00**
	Adjustments						**0,00**	0%	
	Indirect costs	**282,159,00**	69,100,00	61,945,00			**131,045,00**	46%	**151,114,00**
	Total Costs	**647,320,00**	**160,777,00**	**154,589,00**	**0,00**	**0,00**	**315,366,00**	49%	**331,954,00**
CAU	**Total Person-month**	**50,00**	4,19	12,93	0,00	0,00	**17,12**	34%	**32,88**
	Personnel	**250,000,00**	18,430,00	65,182,00			**83,612,00**	33%	**166,388,00**
	Other direct costs	**24,000,00**	1,573,00	0,00			**1,573,00**	7%	**22,427,00**
	Subcontracting	**0,00**	0,00	0,00			**0,00**	0%	**0,00**
	Adjustments						**0,00**	0%	
	Indirect costs	**164,400,00**	12,001,00	39,109			**51,110,20**	31%	**113,289,80**
	Total Costs	**438,400,00**	**32,004,00**	**104,291,20**	**0,00**	**0,00**	**136,295,20**	31%	**302,104,80**
Third Party - Uniklinikum	**Total Person-month**	**0,00**	0,00	0,00	0,00	0,00	**0,00**	0%	**0,00**
	Personnel	**0,00**	0,00	0,00			**0,00**	0%	**0,00**
	Other direct costs	**0,00**	0,00	5,449,00			**5,449,00**	#DIV/0!	**-5,449,00**
	Subcontracting	**0,00**	0,00	0,00			**0,00**	0%	**0,00**
	Adjustments						**0,00**	0%	
	Indirect costs	**0,00**	0,00	3,269			**3,269,00**	#DIV/0!	**-3,269,00**
	Total Costs	**0,00**	**0,00**	**8,718,00**	**0,00**	**0,00**	**8,718,00**	#DIV/0!	**-8,718,00**
IEO	**Total Person-month**	**95,00**	27,51	46,96	0,00	0,00	74,47	78%	**20,53**
	Personnel	**581,685,00**	85,145,00	152,324,00			**237,469,00**	41%	**344,216,00**
	Other direct costs	**20,000,00**	2,006,00	1,734,00			**3,740,00**	19%	**16,260,00**
	Subcontracting	**5,000,00**	0,00	0,00			**0,00**	0%	**5,000,00**
	Adjustments						**0,00**	0%	
	Indirect costs	**120,337,00**	17,429,00	30,811,00			**48,240,00**	40%	**72,097,00**
	Total Costs	**727,022,00**	**104,580,00**	**184,869,00**	**0,00**	**0,00**	**289,449,00**	40%	**437,573,00**
ecancer	**Total Person-month**	**92,00**	26,60	31,12	0,00	0,00	**57,72**	63%	**34,28**
	Personnel	**460,000,00**	119,152,00	127,917,00			**247,069,00**	54%	**212,931,00**
	Other direct costs	**163,500,00**	37,568,00	21,664,00			**59,232,00**	36%	**104,268,00**
	Subcontracting	**10,000,00**	0,00	0,00			**0,00**	0%	**10,000,00**
	Adjustments						**0,00**	0%	
	Indirect costs	**374,100,00**	94,031,00	41,428,00			**135,459,00**	36%	**238,641,00**
	Total Costs	**1,007,600,00**	**250,751,00**	**191,009,00**	**0,00**	**0,00**	**441,760,00**	44%	**565,840,00**
UOXF	**Total Person-month**	**67,00**	10,87	17,61	0,00	0,00	28,48	43%	**38,52**
	Personnel	**402,000,00**	45,194,00	77,265,00			**122,459,00**	30%	**279,541,00**
	Other direct costs	**77,800,00**	5,924,00	5,935,00			**11,859,00**	15%	**65,941,00**
	Subcontracting	**3,500,00**	0,00				**0,00**	0%	**3,500,00**
	Adjustments						**0,00**	0%	
	Indirect costs	**287,880,00**	30,670,00	49,920,00			**80,590,00**	28%	**207,290,00**
	Total Costs	**771,180,00**	**81,788,00**	**133,120,00**	**0,00**	**0,00**	**214,908,00**	28%	**556,272,00**

BIOVISTA	**Total Person-month**	**97,00**	35,00	47,63	0,00	0,00	**82,63**	85%	**14,37**
	Personnel	**398,088,00**	93,511,00	126,154,00			**219,665,00**	55%	**178,423,00**
	Other direct costs	**101,000,00**	35,676,00	21,852,00			**57,528,00**	57%	**43,472,00**
	Subcontracting	**4,000,00**	0,00	0,00			**0,00**	0%	**4,000,00**
	Adjustments			6,855,00			**6,855,00**	#DIV/0!	
	Indirect costs	**159,236,00**	14,016,00	21,446,00			**35,462,00**	22%	**123,774,00**
	Total Costs	**662,324,00**	**143,203,00**	**176,307,00**	**0,00**	**0,00**	**319,510,00**	48%	**342,814,00**
SIB	**Total Person-month**	**59,00**	12,00	12,00	0,00	0,00	24,00	41%	**35,00**
	Personnel	**395,300,00**	75,627,00	78,273,00			**153,900,00**	39%	**241,400,00**
	Other direct costs	**16,000,00**	5,983,00	2,054,00			**8,037,00**	50%	**7,963,00**
	Subcontracting	**3,000,00**	0,00	0,00			**0,00**	0%	**3,000,00**
	Adjustments						**0,00**	0%	
	Indirect costs	**246,780,00**	48,965,00	48,195,00			**97,160,00**	39%	**149,620,00**
	Total Costs	**661,080,00**	**130,575,00**	**128,522,00**	**0,00**	**0,00**	**259,097,00**	39%	**401,983,00**
UHok	**Total Person-month**	**28,00**	5,90	7,80	0,00	0,00	**13,70**	49%	**14,30**
	Personnel	**123,340,00**	22,333,00	29,325,00			**51,658,00**	42%	**71,682,00**
	Other direct costs	**144,000,00**	14,086,00	2,723,00			**16,809,00**	12%	**127,191,00**
	Subcontracting	**0,00**	0,00	0,00			**0,00**	0%	**0,00**
	Adjustments						**0,00**	0%	
	Indirect costs	**53,468,00**	7,283,00	6,409,00			**13,692,00**	26%	**39,776,00**
	Total Costs	**320,808,00**	**43,702,00**	**38,457,00**	**0,00**	**0,00**	**82,159,00**	26%	**238,649,00**
PSNC	**Total Person-month**	**86,00**	19,18	29,13	0,00	0,00	48,31	56%	**37,69**
	Personnel	**380,120,00**	78,568,00	113,078,00			**191,646,00**	50%	**188,474,00**
	Other direct costs	**34,573,00**	9,691,00	6,804,00			**16,495,00**	48%	**18,078,00**
	Subcontracting	**0,00**	0,00	0,00			**0,00**	0%	**0,00**
	Adjustments						**0,00**	0%	
	Indirect costs	**248,816,00**	52,955,00	71,929,00			**124,884,00**	50%	**123,932,00**
	Total Costs	**663,508,00**	**141,214,00**	**191,811,00**	**0,00**	**0,00**	**333,025,00**	50%	**330,483,00**
Total	**Total Person-month**	**1,762,00**	391,88	525,49	0,00	0,00	917,37	52%	**844,63**
	Personnel	**9,645,879,00**	1,728,339,00	2,355,261,00	0,00	0,00	4,083,600,00	42%	**5,562,279,00**
	Other direct costs	**1,416,211,00**	267,463,00	186,277,00	0,00	0,00	448,291,00	32%	**967,920,00**
	Subcontracting	**96,500,00**	0,00	0,00	0,00	0,00	0,00	0%	**96,500,00**
	Adjustments	0,00	0,00	-26,563,00	0,00	0,00	-26,563,00	#DIV/0!	
	Indirect costs	**6,908,110,00**	1,293,970,00	1,567,682,20	0,00	0,00	2,858,383,20	41%	**4,049,726,80**
	Total Costs	**18,066,695,00**	**3,289,772,00**	**4,082,657,20**	**0,00**	**0,00**	**7,363,711,20**	41%	**10,702,983,80**

5.2 Budget Explanations

The Explanation of the Use of the Resources as directly provided via NEF is attached in the following.

5.3 Planned versus actual efforts

Planned versus actual efforts are included in each work package report. An overview of the planned efforts compared to the actual efforts is provided in a separate Excel table submitted with the report.

The following changes have occurred:

FORTH

Work Package	PM according to DoW	New distribution of PM
WP1	5.00	6.00
WP2	5.00	8.00
WP3	26.00	40.00
WP4	15.00	28.00
WP7	10.00	15.00
WP8	52.00	76.00
WP10	2.00	3.00
WP12	10.00	16.00
WP13	12.00	6.00
WP14	0.00	36.00
WP16	5.00	7.00
WP17	4.00	6.00
Total	**146.00**	**222.00**

Originally, FORTH was not directly involved in WP14. However, FORTH is the developer of IEmS and has been involved in the organization of regular Skype and teleconference meetings as well as in a WP14 meeting in Milan to discuss its implementation. Therefore, 5 PMs had to be added to WP14.
The reason for the increase of PMs without subsequent change of the budget is that FORTH had planned the budget on higher salary, experienced post-docs at an average rate given by our central administration. Eventually, no appropriate senior post-docs could be hired and instead a larger number of less experienced Engineers (Graduates) was hired for the project at lower rates. The result was an increase in the number of actual PMs for FORTH.

FhG-IAIS

Work Package	PM according to DoW	New distribution of PM
WP2	2.00	2.50
WP3	9.00	9.00
WP5	3.00	3.00
WP7	6.00	6.00
WP11	41.00	38.50
WP13	6.00	6.00
WP15	6.00	8.00
WP17	3.00	3.00
Total	**76.00**	**76.00**

FhG-IAIS noticed during the first phase of the project that they need to spend more effort on the requirements engineering and management of requirements and thus want to increase the priority of this kind of work. Decreasing the number of person month for WP11 will not affect the work initially planned in the DoW.

CAU

Work Package	PM according to DoW	New distribution of PM
WP2	3.00	2.40
WP6	4.00	3.70
WP9	36.00	33.40
WP12	3.00	3.00
WP17	4.00	4.00
Total	**50.00**	**46.50**

The total person months in WP9 had been reduced from 36 to 33.4 in order to allow the financing of adequate biostatistical data management software.
When setting up the budget for p-medicine the calculations of personnel costs were made on different assumptions. In October 2011, CAU found a qualified employee to carry out the work as proposed in the DoW. To compensate this lack of personnel during the first half year, Martin Stanulla and Martin Zimmermann have contributed their own efforts. Accordingly, the work has been done as planned in the DoW but they have not been paid by the project. On the basis of the money not paid for personnel in the first half year, CAU proposes to optimize its cost distribution and use such money to compensate the need for technical equipment. To provide an adequate IT infrastructure for CAU's new employee, Ms. Antje Torge, two new computers with different operating systems plus mathematical software required will amount to approx. 6.000€. In addition, an update and adaptation of the data management software Scopeland for biobanking and diagnostics is foreseen to facilitate an international virtual biobank scenario, in cooperation with FhG-IBMT at Potsdam. In a first approach to generate a use case for such a scenario, it was decided at a Berlin meeting with FhG-IBMT, CAU and representatives of the Department of Pediatric Hematology and Oncology at Charité Berlin to aim at integration of existing biobank data systems of a frontline and corresponding secondline clinical trial group on treatment of childhood acute lymphoblastic leukemia in Germany as an initial step for developing an unified international virtual biobank for this disease. Therefore, already existing laboratory software at CAU will have to be adapted in order to allow optimal integration of biobanks at CAU (frontline trial group) and at the Department of Pediatric Hematology and Oncology at Charité Berlin (secondline trial group). Partial financing of this prerequisite through the project will amount to approx. 10.000€.
The shift of costs will give CAU the possibility to create optimal conditions for its work in p-medicine.

BIOVISTA

Due to their relatively large increase in PM in work packages 11 and 13, Biovista expects that the total number of person months will be increased by the end of the project. This increase should leave the budget unaffected. A table showing the redistribution of Biovista's person months in each work package will be provided in the next report.

6 Financial Statements

6.1 Forms C and Summary Financial Statement

Forms C are submitted via the NEF tool in parallel. In the following, a copy of the summary financial report as available in the NEF tool is attached, together with copies of the Forms C of all beneficiaries.

6.2 Certificates

Beneficiary	Organisation short name	Certificate on the Financial Statements provided? Yes/No	Comments
1	USAAR	Yes	
2	Eurice	No	
3	FORTH	No	
4	UCL	Yes	
5	FhG	Yes	The CFL is being prepared and will be handed in shortly.
6	LUH	No	
7	Custodix	No	
8	Philips	No	
9	UDUS	No	
10	ICCS	No	
11	UPM	No	
12	CAU	No	
13	IEO	No	
14	ecancer	No	
15	SIB	No	
16	Biovista	No	
17	SIB	No	
18	UHok	No	
19	PSNC	No	

7 Annexes

7.1 p-medicine PM Effort Calculation

Provided separately in Excel format.