Six Monthly Progress Report

February 2008 to July 2008

(Month 25 to 30)

Project Number:	FP6-2005-IST-026996
Deliverable id:	D 1.1.4
Deliverable name:	Six Monthly Progress Reports
Submission Date:	19/09/2008

Information Society Technologies

COVER AND CONTROL PAGE OF DOCUMENT	
Project Acronym:	ACGT
Project Full Name:	Advancing Clinico-Genomic Clinical Trials on Cancer: Open Grid Services for improving Medical Knowledge Discovery
Document id:	D 1.1.3
Document name:	Six Monthly Progress Reports
Document type (PU, INT, RE)	RE
Version:	1
Submission date:	19/09/2008
Editor: Organisation: Email:	Florence Pesce ERCIM Florence.pesce@ercim.org

Document type PU = public, INT = internal, RE = restricted

ABSTRACT:

This Deliverable presents the full range of project activities during the period from month 25 to month 30, including management activities, disseminations activities as well as technical and scientific activities in accordance to the DoW of the project.

KEYWORD LIST: Progress report, Workpackages activity, achievements, deliverables

MODIFICATION CONTROL			
Version	Date	Status	Author
0.0	25/07/2008	Template	R. Ronchaud / ERCIM
1.0	10/09/2008	Compilation	F. Pesce /ERCIM
2.0	16/09/2008	Modification	F.Pesce/ERCIM
3.0	18/09/2008	Review	M. Tsiknakis/FORTH
4.0	19/09/2008	Final	F. Pesce/ERCIM

List of Contributors

Alberto Anquita Sanchez, Upm (Spain)
Robert Belleman, UVA (The Netherlands)
Anca Bucur, PHILIPS (The Netherlands)
Francesca Buffa, UOXF (United Kingdom)
Johan Carlsson, UMA (Spain)
Marie-Luise Christ-Neumann, FhG (Germany)
Brecht Claerhout, CUSTODIX (Belgium)
Vasiliki Danilatou, UOC (Greece)
Christine Desmedt, IJB (Belgium)
Alberto d'Onofrio, IEO (Italy)
Nikolaus Forgo, LUH (Germany)
Norbert Graf, USAAR (Germany)
Radu Gramatovici, SIVECO (Romania)
Alexander Hoppe, USAAR (Germany)
Julien Jacques, INRIA (France)
Regine Kollek, UH (Germany)
Yannick Legré, HEALTHGRID (France)
Aran Lunzer, UHOK (Japan)
Mattias Ohlsson, LundU (Sweden)
Andreas Persidis, Biovista (Greece)
Juliusz Pukacki, PSNC (Poland)
Rémi Ronchaud, ERCIM (France)
Stefan Rüping, FhG (Germany)
Thierry Sengstag, SIB (Switzerland)
Georgios Stamatakos, ICCS (Greece)
Manolis Tsiknakis, FORTH (Greece)
Jean-Marc Van Gyseghem, FUNDP (Belgium)

Contents

1 Executive Summary

ACGT Objectives

ACGT's vision is to become a pan-European voluntary network connecting individuals and institutions to enable the sharing of data and tools and thereby creating a European Wide Web of cancer clinical research.

An initial architectural blueprint has been designed during the previous reporting period. During the current reporting period the project has focused on the (a) development of the core set of components up to a stage where they can effectively support in silico investigation and (b) set up cross-disciplinary task forces to propose guidelines concerning issues related to data sharing, for example legal, regulatory, ethical and intellectual property, and is developing enhanced standards for data protection in a web (grid) services environment. Initial prototypes have been useful in crystallizing requirements for semantics.

In addition the project is developing

- new, domain-specific ontologies, built on established theoretical foundations and taking into account current initiatives, existing standard data representation models, and reference ontologies;
- innovative and powerful data exploitation tools, for example multi-scale modelling and simulation, considering and integrating from the molecular to the systems biology level, and from the organ to the living organism level;
- standards for exposing the properties of local sources in a federated environment;
- a biomedical GRID infrastructure offering seamless mediation services for sharing data and data-processing methods and tools;
- advanced security tools including anonymisation and pseudonymisation of personal data according to European legal and ethical regulations;
- a Master Ontology on Cancer and use standard clinical and genomic ontologies and metadata for the semantic integration of heterogeneous databases;
- an ontology based Trial Builder for helping to easily set up new clinico-genomic trials, to collect clinical, research and administrative data, and to put researchers in the position to perform cross trial analysis;
- data-mining services in order to support and improve complex knowledge discovery processes;

Finally, the project has also focused with more emphasis on its dissemination activities, and is gradually engaging in dialog with several of the relevant end-user communities.

2 Project objectives and major achievements over reporting period

The requirements for the ACGT Platform, which have been documented during the previous reporting periods of the project, can be met by designing a federated environment articulating independent tools, components and resources based on open architectural standards, which are customizable and capable of dynamic reconfiguration.

An initial architectural blueprint for such an environment has been designed. A layered approach has been selected for providing different levels of abstraction and a classification of functionality into groups of homologous software entities. In this approach we consider the security services and components to be pervasive throughout ACGT so as to provide both for the user management, access rights management and enforcement, and trust bindings that are facilitated by the Grid and domain specific security requirements like pseudonymization and anonymization.

In specifying this architectural blueprint of the ACGT technological platform, architectural specifications of other relevant projects have been thoroughly studied. Of particular relevance are the Cancer Biomedical Informatics Grid (caBIG) in the US and the CancerGrid project in the UK. The infrastructure being developed uses a common set of services and service registrations for the entire clinical trial on cancer community. We are currently focusing on further development of the core components up to a stage where they can effectively support in silico investigation. Initial prototypes have been useful in crystallizing requirements for interoperability and semantics.

During the reporting period the central emphasis of all project activities were focused on achieving the major project Milestone 8 (M8) - The integrated ACGT environment for internal Piloting.

For such an initial “end-to-end” demonstration of the integrator ACGT environment, it was decided to transform the global description of the trials as given in the deliverables provided by WP2 and WP12 into scenarios highlighting the role of the various components of the ACGT environment in the clinical context. For this purpose a corresponding deliverable, i.e. D13.3 - Specification of scenarios for the first integrated demonstrator of the ACGT platform was brought forward in terms of timing.

The scenarios have been modularized in a series of *scenes*, which follow the natural steps of data handling in a clinical trial and which put the focus on the key features of the ACGT environment. The scenes retained are:

- ObTiMA, which illustrates the setup and management of a clinical trial using the ACGT trial management system.
- VO Management, which illustrates how users access ACGT resources (data and workflows) through VOs, and in particular how VO-specific resources are visible to VO-registered users and not accessible to users not belonging to the VO.

- Data Exposition[1], which illustrates the usage of pseudo/anonymization tools and the integration of databases in the system at the lowest level.
- Data Access, which illustrates the process through which local databases are mapped to the global schema, i.e. the ACGT Master Ontology, thus allowing integrated queries from the mediator to be executed.
- Integration of Services, which illustrates how newly developed services can be published and used in ACGT, emphasizing also their annotation.
- Workflow Creation and Execution, which illustrates how ACGT-connected analytical services and data access services can be combined into scientific discovery workflows, which are executed in the search of a scientific answer to research questions.
- Workflow Discovery, which illustrates how services, workflows and data sources previously made available in the context of ACGT can be reused, thus making the scientific discovery process faster and more efficient.
- Oncosimulator, which illustrates the use of a high-level scientific research tools that can be made available to clinicians as an additional resources in the treatment of patients.

In achieving the integrated demonstration of the above scenes, a range of technical developments were required and significant progress in a number of scientific/technological domains has been achieved.

These are fully documented in the work done in the various WPs of the project in subsequent sections of this report.

In summarizing the main developments and achievements, we can list the following:

a) The ACGT Master Ontology has been constantly reviewed with respect to usability (by the ACGT services, e.g. the mediator and ObTiMA) and completeness. The clinical partners are constantly asked to hand in reviews on the coherence and correctness of the representation of clinical reality. We have experienced that these activities gradually lead to minor adjustments and no structural changes were necessary over the last six months.

b) In parallel to the above we have initiated the process of submitting the ontology to the Open Biomedical Ontologies (OBO) Foundry and begun the requirements analysis and functional specification of an Ontology Submission System, which is believed to be necessary in supporting future evolution and maintenance of the ontology.

c) The issue of maintaining ACGT and ObTiMA was identified as been the most crucial point regarding the adoption of ObTiMA by clinical researchers for their clinical trials. Increased emphasis was therefore given to issues related to optimized implementation of ObTiMA. Hence, the integration of ObTiMA in the ACGT Portal, the ACGT roles and rights management and the use of the Custodix anonymisation tool (CAT) with ObTiMA were the main areas of activities in this domain. The major achievement during the reporting period has been the implementation of the first release of ObTiMA (Ontology based Trial Management System for ACGT) including
   - The Integration of ObTiMA into the ACGT grid environment,
   - Integration of the ACGT Master Ontology
   - Integration of the basic version of CRF Repository via Web Services

[1] We use the term "Data Exposition" to refer to the process through which proprietary clinical trial datasets and databases are published and made available, in a legally compliant manner, to the ACGT infrastructure for analysis.

- Initial integration of the Trial Outline Builder.

d) Integration of the Grid Layer with services/components of higher layer of ACGT architecture that are developed by other WPs has also taken a significant effort, in view of the initial integrated demonstrator. In addition to this the extension and maintenance of the ACGT computational Grid has taken parts of our efforts.

e) The first integrated version of the analysis environment was successfully demonstrated at the ACGT review in Eindhoven in May 2008. This demonstration included:
   - distributed processing of large scale data set
   - combination of various analysis tools to enact a real-world scientific workflow
   - use of meta data to select and control data analysis operators

f) The ACGT Workflow Editor Version 2.0 was developed and demonstrated in the second formal ACGT Review meeting. The version of the workflow editor featured integration with the Metadata Repository for accessing the list of the available ACGT services (R scripts, Mediator, Data Access Services) and the available metadata for each of these services. Furthermore, it allowed the graphical design of workflows by interconnecting the chosen services with basic support for the (syntactic) validation of these connections based on the data types information that is part of services' metadata. The publication of the new workflows in the metadata repository and service registry and their subsequent execution through the portal were also demonstrated.

g) Increased emphasis was put on the validation of the security architecture of the project, as well as the extension and refinement of key security services. The Custodix Anonymization Tool has been rewritten in this period to use a unified underlying data model. This has the advantage that general profiles can be created, re-used and exchanged between users. Data fields can be grouped in privacy data types and processed using a single configuration option and using a unified data model also allows the integration of other privacy tools to, e.g. analyze the privacy level of a dataset.

h) With respect to WP8 work focused on a) extension of the simulation codes of tumour growth and response to therapeutic schedules for the cases of nephroblastoma and breast cancer so that instead of a triaxial ellipsoidal shape [see deliverable D8.2], a generic shape and internal structure of the tumour can be handled and b) extension and integration of image processing tools for aided segmentation, interpolation, 3D reconstruction and registration of tumour images (e.g. MRI, CT etc.)

In parallel to these activities a range of other activities were initiated, completed or continued, such as:

- In depth analysis of the intellectual property issues in ACGT;
- In depth analysis of legal risks regarding the data security and data protection framework is in progress;
- Implementation of the ACGT post-genomic clinical trials and collection of the different samples;
- Implementation of various advanced post-genomic analyses;
- Investigation of the harmonization issues for cross-platform biological data integration and analysis;
- Integration into the ACGT Portal of the first demonstration scenario", including several services and partners.

In addition to these RTD activities the project has also focused with more emphasis on its dissemination activities, and is gradually engaging in dialog with several of the relevant end-

user communities. Significant improvement has also been made on the external ACGT website to differentiate target group messages and to complete the several contents.

Based on the experiences accumulated in building the initial integrated “end-to-end” demonstrator the project has identified some key areas where improvements are required in speeding up further coordinated development. One such area relates to the need for a stable “demonstration” platform. Hence, it was decided to separate the “development environment” from the “demo one”. All related technical and procedural decisions were taken and this is a key part of our activities for the next reporting period.

3 Workpackage progress report over the period

Workpackage 1 - Project Management

- **Partner Responsible : ERCIM**
- **Contributing partner(s):** FORTH, FhG
- **Reporting Period:** 01/02/2008 – 31/07/2008
- **Workpackage objectives and starting point of work at beginning of reporting period**

-**The Workpackage has the following major objectives:**

The objective of this Workpackage is to ensure a strong and coherent administrative and financial management of the project. It addresses the Administrative and Financial Coordination; as well as the Scientific Coordination of the project.

- Objectives during reporting period

- Submit the annual reports (Periodic Management Report and Periodic Activity Report)
- Prepare the new Implementation Plan and submit the amendment request for the next period (Month 24 to 42) including a transfer of budget between partners and integration of a new subcontractor EORTC
- Prepare the annual Review (held in Eindhoven in May 2008)
- Conclude the subcontract with EORTC

- Progress towards objectives

The ACGT Project activities have been successfully coordinated and the collaboration of the different research teams involved has been efficiently managed. The periodic scientific and technical meetings and audio-conference have provided the coordination with an appropriate yield to steer the multiple underlying activities of the ACGT work plan. The administrative and financial coordination has pursued its activities, and has provided assistance to all Partners in preparing and justifying their information for the second periodic management report. This document required substantial work from all partners and regular interaction with the European Commission to ensure the timely release of the next advance payment.

- Main Activities & Tasks worked on

The WP focused on both administrative and scientific management tasks. Significant efforts were devoted to the administrative tasks, due to the fact that the project was preparing its second annual reports (PMR and PAR) and review. Also, the scientific management activities, since a range of activities are progressing was much more demanding, requiring continuous monitoring and full functioning of the Technical Management Committee that has been previously established

- Major Achievements towards planned objectives, identify main partners Involved

The management has devoted significant efforts in making sure that this ambitious project will meet its annual objectives.
This required that (a) all partners are fully engaged in project activities, (b) responsibilities and task assignments were fully clarified and (c) continuous and effective communication and information flow does take place among all project partners.
We believe this has been achieved and maintained since the kick-off meeting of the project, essentially through the establishment of an ACGT community in which all project partners mutually support and complement each other, technically, but also personally.

- **Deviations from the project work programme, and corrective actions taken/suggested**

There were no major deviations encountered.
The delay in delivering the following deliverables is not in the critical path of the project and the management is taking care to make sure that it is also delivered as soon as possible:
D14.4 -Training Workshop for end-users on ACGT Technologies & Methodologies
D14.5- Methodology and guidelines for service integration in the ACGT Portal on the Business Process Layer
D15.4- Organisation and Report of a Project Conference

The Project Management focuses primarily on the development and implementation of the technical and scientific modules that will compose the heart of the ACGT prototype and the organisation of demonstration workshops and conference is another priority that can only be considered when all technical concerns are addressed. Yet, efforts are now concentrated on the ACGT Portal, which is a cornerstone of the system integration and the spearhead of user interaction with the ACGT demonstrator.

- **List of deliverables, including due date and actual/foreseen submission date**

During the reporting period, the WP had to prepare and deliver some critical deliverables:
D1.1.5a - PMR – due T0+24 + 45days – Submitted 04/04/2008
D1.1.5b – PAR – due T0+24 + 45days – Submitted 20/05/2008

The six monthly report, which was due in the same time as the PMR has been cancelled in accordance with the Project Officer. The Periodic Management Report (PMR) including the financial Statement has been prepared and revised regularly to comply with the underlying amendment and changes requested in the work plan, in accordance with the demands of the European Commission

- **List of milestones, including due date and actual/foreseen achievement date**

During the reporting period, the WP had no Major project milestones besides the Second annual Review which delivered a positive evaluation.

Workpackage 2 – User Needs Analysis & Specifications

- **Partner Responsible : USAAR**

- **Contributing partner(s):** Forth, UvA, Philips, IJB, SIB, LundU, UMA, UPM, FHG, Biovista, UOC, PSNC, Custodix, ICCS, USAAR, SIVECO, UOXF.BP, UHoK, IEO

-

- **Reporting Period:** 01/02/2008 – 31/07/2008

- **Workpackage objectives and starting point of work at beginning of reporting period**

-The Workpackage has the following major objectives:

1. To update deliverable D2.1 regarding guidelines for clinical trials (e.g. ICH and GCP), tools and software for the management of clinical studies and needs for clinico-genomic integration (including technological, legal issues, ethics, security, quality control, etc.).

2. To refine requirements and assessment of the relevance (from the point of view of the clinical research) of the architectures and applications that are developed.

3. To ensure the feasibility of implementing and to increase the number of clinical studies for cancer into ACGT based on specific clinicogenomic scenarios

4. To define and implement usability criteria as part of the quality process for the evaluation of developed tools and software driven by clinicians and other end-users.

5. To define criteria for a submission system for tools, software and data from an end-user perspective

6. To define criteria for the selection of tools, software and data from a clinical perspective

7. To elaborate maintenance criteria for ACGT (together with WP16)

- Objectives during reporting period

The main focus was laid on clinical aspects of the project with special emphasis on ObtiMA.

The following main points were investigated:

- User needs for clinicians and basic researchers for ObTiMA including the user friendly integration of the Master Ontology
- Clinico-genomic integration, including technological, legal and ethical issues, security and quality control within ObTiMA.
- Those specific clinico-genomic scenarios that were implemented in the clinical studies as defined in WP12 are further developed and discussed how to integrate them into the trial builder.

- Progress towards objectives

Main progress was done in optimizing ObTiMA to get it ready for the use in concrete clinico-genomic scenarios

- Main Activities & Tasks worked on

The main focus was laid on the user requirements and the functionality of the TrialBuilder. This task is leaded by USAAR (Norbert Graf). Over the entire period IFOMIS worked in optimizing the Master Ontology. The issue of integration into ObTiMA was continued by optimizing the Clinical view. Multiple meetings and discussions about technical issues with project partners (FHG [IBMT], Hokkaido University, Custodix, Ifomis) took place to enhance feedback between developers of the TrialBuilder and the users. Since February 2008 one person (Jochen Boehm) is only dealing with optimizing the usability of ObTiMA keeping a close contact with the developers of the software and the end-users.

This WP continued to elaborate on the various requirements from a clinical point of view that are necessary for the proposed ACGT platform. The main points of investigation as defined in the first two years were supplemented by defining criteria for the evaluation of developed software and tools. The corresponding deliverable 2.3 (User requirements for the evaluation of developed software and tools regarding usability criteria) was finished and submitted on the 15th of March 2008.

A main focus was laid on answering the question, what are the requirements and needs for clinicians to use ObTiMA as a clinical data management system. The issue of maintaining ACGT and ObTiMA was founded to be the most crucial point, before clinicians will use ObTiMA for their clinical trials. The integration of ObTiMA in the ACGT Portal, the ACGT roles and rights management and the Custodix anonymisation tool (CAT) for the use with ObTiMA was decided and will be evaluated by end-users.

As can be seen in the list of meetings and dissemination activities, ACGT and ObTiMA was presented to different clinical groups in different workshops and meetings to increase the number of clinical trials for cancer. Special focus was given to EORTC, SIOP and GPOH. These groups all are interested and are willing to use the ACGT infrastructure, if a guarantee is given that ACGT and ObTiMA will be maintained. Besides EORTC and SIOP the clinical partners of the University of Oxford and the Instituto Europeo di Oncologia in Milano are on board increasing the number of clinicogenomic scenarios.

The report on additional user-driven scenarios in post-genomic clinical trials on Cancer (D2.4) is under work. Because of the feedback from different clinical groups the deliverable will be postponed to month 33.

Together with WP16 the elaboration of criteria for maintenance of ACGT has been started.

During this period the state of the art review was updated on a regular basis, regarding current guidelines for clinical trials, the assessment of tools and software for the management of clinico-genomic studies and trials. The user needs for clinico-genomic integration (including technological, legal issues, ethics, security, quality control, etc.) was consolidated within the corresponding WPs.

Regarding the InSilico Oncology further progress is done regarding the workout of the scenarios and the need for clinical validation of the InSilico experiments. Anonymised DICOM data are now available at ICCS for use in the simulator. A tool for the segmentation of tumour in DICOM files is developed by Fraunhofer and used by clinical partners for submission to the InSilico scenario.

- Major Achievements towards planned objectives, identify main partners Involved

The main tasks carried out by USAAR can be summarized in:

The activities of USAAR are described in the section: 'Main Activities & Tasks worked on' in this chapter.

The main tasks carried out by IFOMIS in WP2 and WP7:

- Review of ACGT MO
- Addition of constraints and relations to the ACGT MO
- Addition of anatomical classes
- Provided mappings for the SPARQL queries
- Validation of conceptual design by means of terminology techniques
- Re-evaluation of NCI Thesaurus (caBIG, caCORE)
- Intra-project communications on ontology maintenance
- Intra-project communications on the possibility of a "service ontology"
- Preparation of documentation
- Preparation of publications
- Networking with the OBO Foundry

The ACGT Master Ontology is constantly reviewed with respect to usability (by the ACGT services, e.g. the mediator and ObTiMA) and completeness. The clinical partners are constantly asked to hand in reviews on the coherence and correctness of the representation of clinical reality. However, we experienced that these activities lead to minor adjustments now. No structural changes were necessary over the last six months.
Of course, the consistency is constantly checked while working with the owl-File, using the Pellet reasoner.

Addition of constraints and relations to the ACGT MO
This effort aims to create a rich resource of knowledge to be used by the CRF Builder of ObTiMA. The addition of constraints and axioms to the ontology has continued. This work was done in collaboration with the Fraunhofer IBMT which is developing ObTiMA. Along with this report we hand in a document demonstrating our work (**Documentation on Ontology Development February to July 2008)** and listing all changes in the ontology after the last review (s. **Preparation of documentation**).

Addition of anatomical classes
An unforeseen problem did arise quite before the reporting period: With respect to anatomy we were always very confident that we will be able to re-use the **Foundational Model of Anatomy** (FMA) one way or the other. Basically, we hoped for a re-usable, open source owl-implementation. Even though two such implementations exist, they confronted us with a severe problem. The turned out to be too large. The size of an ontology is critical in two respects: 1) The size might slow down applications exploiting the ontology considerably; 2) Reasoners can only be used to validate the coherence of an ontology up to a specific size.
Copying an owl-Implementation of the FMA in its entirety would probably result in an ontology to large to check with a reasoner and rather slow in use for both ObTiMA and the mediator.
Realizing this problem we decided to look around for alternatives. Alan Rector proposed to talk to Jay Kola who developed an anatomy ontology which is not part of the OBO Foundry and is based on ontology terms from the NCI Thesaurus (s.b.). After reviewing this ontology, which was rather small, but not build to the quality criteria formulated for ACGT we had to find an alternative.

We decided to create the anatomical classes as needed in the domain (used in the CRFs) in accordance with the FMA. This means that we added most parts of the middle layer of the FMA ontology, but restricted the leaf nodes to those needed in ObTiMA at the moment. Adding new classes will, however, be not problematic since all that the curators need to do is search the FMA and add the content.
This method provides the best solution for the problem at hand. The conceptual modelling we make use of is the best available representation of anatomy that is on the market. Furthermore, the FMA is open source and there are no restrictions for re-use.

Provided mappings for the SPARQL query
In order to support the query tools IFOMIS provided mappings for the SPARQL queries. This task was done in close collaboration with UPM and Philips.

Validation of conceptual design by means of terminology techniques
A critical aspect for the success of the ACGT MO is whether we manage to provide a correct and complete representation of the given domain. In order to validate our conceptual design we decided to collaborate with terminology experts outside ACGT to get an impression on the completeness of our representation.
In this task we co-operated with the Institut für Angewandte Informationsforschung (IAI, Institute for Applied Information Science) located at Saarland University. We were in contact with the director of the institute, Prof. J. Haller, and a PhD student (G. Grigonyte).
The AIA offered to extract a terminology from domain specific abstracts. We decided to use 200 abstracts on clinical trials, mostly in nephroblastoma and breast cancer. The abstracts where provided by our clinical partner in Homburg, namely Alexander Hoppe and Norbert Graf. The IAI provided us with a 19-page list of terms extracted automatically from the abstracts early in July. The final analysis of the ACGT MO and its accordance to the extracted terminology had to be postponed until middle of August due to our efforts in adding the anatomy branch to the ontology.
However, our first survey of the terminology led to the result that most terms are already present, but minor adjustments might be necessary.
We plan to prepare a document on conceptual design in the next months. Within that document we will give a more elaborate account of these activities.

Re-evaluation of NCI Thesaurus (caBIG, caCORE)
Since the start of ACGT the project and especially WP7 is confronted with questions whether the NCI Thesaurus would not be a better terminology resource than the newly developed ACGT MO. This situation became urgent again by the fact that the NCIT is distributed and advertised under a number of new names, respectively in a number of different systems, for instance caCore.
Given requests of colleagues we understood that it is our responsibility to re-evaluate the NCIT. Doing so we, sadly, came to the result that the grave problems already described in Deliverable 7.1 have not been corrected and thus, the assessment of the NCIT reaches the same result as before.

Intra-project communications on ontology maintenance
One of the most pressing problems with respect to the ontology is the question who we can maintain the ontology in years when the development and the funding are finished. Together with FORTH we already proposed a submission system. In June we had a working meeting with Martin Dörr formulating the submission process. IFOMIS carried out a state-of-the-art-analysis of submission systems in biomedical OTDs utilizing the list of OTDs given in D 7.1.
The results of the meeting along with the results of the state-of-the-art analysis can be found in the attached document **Meeting Notes on Ontology Development and**

Maintenance June 25-26, 2008, Saarbrücken (Including Submission Process and Implementation Process).

Intra-project communications on the possibility of a "service ontology"
Together with University of Malaga, and FORTH IFOMIS has discussed the possibility and the usability of a "service ontology," The aim of such an ontology would be to classify tools and services. It was agreed that the existence of such an ontology can foster the use of ACGT and its tools by users. IFOMIS agreed to support the development by bringing in expertise from ontology development.

Preparation of documentation
On the last review IFOMIS was encouraged to intensify its documentation efforts. Better documentation on the development of the ontology and the conceptual design was demanded by the reviewers. With this report we submit two documents:

1. **Documentation on Ontology Development February to July 2008**
2. **Meeting Notes on Ontology Development and Maintenance June 25-26, 2008, Saarbrücken (Including Submission Process and Implementation Process)**

The first documents the development of the ontology over the last months. The second gives the results of consultations with Martin Dörr (FORTH) focusing on future research and maintenance.
We plan to prepare another document describing the conceptual design methods (reality representation) utilized in the development of the ACGT MO in detail.

Preparation of publications
Over the last six month IFOMIS was extremely active with respect to publication. Besides the accepted papers given in the report, IFOMIS, together with other partners, submitted a two page abstract to a HL7 Meeting in Crete. This was accepted as a poster, but the authors decided to skip this and rather concentrate on preparing a journal article.
The IEEE Meeting in Finland spawned yet another opportunity: The chair of the ontology workshop, Tharam Dillon (Curtin University of Technology) asked us to submit a paper on the ACGT MO and ObTiMA to **4th International Workshop On Semantic Web & Web Semantics (SWWS '08), Monterrey, Mexico** (http://www.cs.rmit.edu.au/fedconf/index.html?page=swws2008cfp).
IFOMIS took the lead in preparing and submitting a paper to this event. Results of the review process are expected around August 15, 2008.
Furthermore, Tharam Dillon proposed to present ACGT in a book publication to be published 2009 focusing on new Semantic Web approaches. This, however, has to be negotiated.

Networking with the OBO Foundry
IFOMIS is keeping contact with the OBO Foundry to make the ACGT MO part of the Foundry. Barry Smith recently signalled that we could start with the submission process. This will be done late in August.

The main tasks carried out by Philips can be summarized in:

Philips continued to collect requirements for an ACGT-specific clinico-genomic electronic health record (EHR).

The main tasks carried out by UPM can be summarized in:

UPM continued to gather and interpret user requirements for querying clinical databases (SIOP and TOP) using SQL predefined queries. Natural language is used for the interpretation of concepts contained in the SIOP and TOP databases.

The main tasks carried out by UvA can be summarized in:

UvA has continued in providing the visualization environment (Vtkfly) and to support interactive visualization on a distributed (grid) architecture, to support interactive volume rendering of medical data sets, including CT, MR and ultrasound. In parallel UvA has extended Vtkfly to support simultaneous and registered visualization of medical data sets and results from in-silico tumour simulation results.

The main tasks carried out by EIO can be summarized in:

EIO mainly developed theoretical research activities, by continuing focusing on antiangiogenic therapy.

In collaboration with Prof. A. Gandolfi of IASI CNR, Rome, and with Dr. Andrea Rocca MD of the "Istituto Oncologico Romagnoli" at Cesena, in the framework of the revision work of the paper (A. d'Onofrio, A. Gandolfi, A. Rocca, cell Proliferation, in press 2008), they analyzed the influence of pharmakinetic of the anti antiogenic drugs, also in case of non mono-exponential drug concentration profile. To this aim they defined an index of deviation from the continuous infusion delivering and showed that the Hahnfeldt-Folkman mathematical model of anti-angiogenic therapy seems to indicate (coherently with the experimental results) that this index is negatively correlated with the effects of the therapy.

Concerning the interaction between chemotherapy and anti-angiogenic therapy, they developed a model where both the therapies are present. This model is also suitable to represent chemotherapeutic agents also showing a vessel-destroying action. Their simulation confirms that even in case of boli-based therapy there is a synergistic effect. (A manuscript is in preparation on this subject.)

Moreover, an important effect has been recently hypothesized in medical and medical-physics literature: the so called "pruining effect", i.e. the beneficial effect of moderate quantities of anti-angiogenic drugs in order to regularize the vessels and, as a consequence, to improve the flow of chemotherapeutic drugs. They elementary modified the Hahnfeldt-Folkman model to take into account this effect, and, from numerical simulations and theoretical analysis, they obtained positive results well agreeing with some experimental data. A more complex model is in phase of elaboration.

Finally, research on the optimisation of the drugs scheduling are also led in collaboration with USA colleagues Prof. Urszula Ledzewicz and Prof. Heinz Schaettler.

The main tasks carried out by ICCS can be summarized in:

ICCS mainly focused on the "Oncosimulator". ICCS contributed to the translation of the user needs into algorithmic and software requirements, thus accelerating the achievement of the ACGT main goals. Special attention was paid to the adaptation of the tumour growth and response development models to the particular formats of the clinical trials data used for the "Oncosimulator" validation.

The main tasks carried out by Biovista can be summarized in:

Experiments performed with Biovista lit mining tools in collaboration with University of Oxford to determine utility in their workflow. This is an ongoing effort. The question of how to maintain ObTiMA is part of the dissemination task.

The main tasks carried out by SIB can be summarized in:

The activity done was in relation to scenarios for meta-analysis on public datasets. Besides that, SIB started to find the needs of hospitals (clinicians, IT-people, and basic

researchers) for using ACGT in their daily practice. A meeting in Lausanne was carried out in July 2008 focusing primarily on this topic. SIB was involved in preparing and editing deliverable 2.3.

The main tasks carried out by Custodix can be summarized in:

The main activity done was in optimizing the Custodix Anonymisation Tool (CAT). The integration in the ACGT platform for the use within ObTiMA is on the way.

The main tasks carried out by UOXF can be summarized in:
UOXF continued to develop theoretical research activities in the context of the MCMP scenario described in WP12 and more generally methods for the development of prognostic/predictive signatures.

- **Deviations from the project work programme, and corrective actions taken/suggested**

There were no deviations from the work programme. Deliverable D2.4 will be postponed for 3 months as explained above.

- **List of deliverables, including due date and actual/foreseen submission date**

Deliverable 2.3 due at T0+24 + 45days (on the BSCW server since March 2008) – has been submitted on 13/05/08

Deliverable D2.4 - Report on additional user-driven scenarios in post-genomic clinical trials on Cancer due at T0+30 is foreseen at T0+33

- **List of milestones, including due date and actual/foreseen achievement date**

No milestones due within this reporting period.

Workpackage 3 – Architecture and Standards

- **Partner Responsible : PSNC**

- **Contributing partner(s):** FORTH, Philips, LundU, UMA, UPM, FHG, BIOVISTA, Custodix, LUH, USAAR

- **Reporting Period: 01/02/2008 – 31/07/2008**

- **Workpackage objectives and starting point of work at beginning of reporting period**

-**The Workpackage has the following major objectives:**

- To invent and define the reference grid architecture to support complex project collaboration and to provide a blueprint for grid implementations in this project and beyond
- To design the overall architecture of a grid based interoperability system for the biomedical sector and make a substantial contribution to standards

- Objectives during reporting period

The main objective of WP3 during this reporting period was to continue working on architecture of ACGT environment.

We can distinguish between two main goals of this activity. The first one is to develop the final ACGT architecture that includes all components existing in ACGT testbed, not only the ones implemented within ACGT but also third party services. It will provide complete view of the project in the context of components taking part.

The second issue of WP3 activity was to monitor ACGT development in all technical WPs to guarantee compatibility with proposed architecture, taking into account not only communication between component but also technology used for implementation.

- Progress towards objectives

All implementation work done in ACGT is consistent with proposed architecture

- Main Activities & Tasks worked on

During the reporting period, the WP3 worked on developing final architecture of ACGT that includes all components implemented within the project. The important achievement was the definition of data flow model that presents all components taking part in exchanging and managing data in the ACGT environment.

WP3 in cooperation with WP4 and WP11 designed guidelines for implementing services compliant with ACGT architecture, taking into account communication and security issues.

- Major Achievements towards planned objectives, identify main partners Involved

All technical WPs were conducting their development according to the architecture proposed.

- **Deviations from the project work programme, and corrective actions taken/suggested**

There were no serious deviations from the work programme

- **List of deliverables, including due date and actual/foreseen submission date**

D3.3 "Report on Standards' development" due at T0+24 has been submitted on 13/05/08

- **List of milestones, including due date and actual/foreseen achievement date**

No milestones due within this reporting period.

Workpackage 4 – Biomedical Grid Technology Layer

- **Partner Responsible : PSNC**

- **Contributing partner(s):** FORTH, UMA, FHG, BIOVISTA, Custodix, ICSS, SIVECO

- **Reporting Period:** 01/02/2008 – 31/07/2008

- **Workpackage objectives and starting point of work at beginning of reporting period**

-**The Workpackage has the following major objectives:**

- To provide semantic grid services that take advantage of the grid functionality, such as security, etc.
- To provide OGSI/Globus compliant interfaces to state-of-the art grid databases.
- To define and provide the information grid that is capable of secure, safe, semantically rich, and ontology committed information.
- To enable an ontology aware biomedical grid infrastructure into which all biomedical information, handled by sector applications is stored.
- To provide access capability to distributed computational resources, mainly relying on existing functionality of the grid toolkits, but taking into account the possible exploitation of the higher level semantics that will be built into the grid.

- Objectives during reporting period

During the reporting period the most important objectives were focused on integration Grid Layer with components of higher layer of ACGT architecture that is developed by other WPs.

The second issue was to take care of grid testbed for ACGT environment - extend, maintain and keep operational.

There was also deliverable to prepare and submit: D4.3. "First production Grid Layer"

- Progress towards objectives

We noted the significant progress in software integration that was demonstrated in the second formal ACGT Review meeting in Eindhoven.

- Main Activities & Tasks worked on

The most important activities of reporting period:

- Creation and maintenance of the Grid testbed (Common Grid Services)

WP4 is responsible for providing Grid infrastructure for the project. We support other partners in installation and configuration of services required to be part of the testbed (mainly Globus Toolkit)

- Tuning and improvements of Grid Services

WP4 is providing advanced grid services that need to be tuned to ACGT needs. In cooperation with WP11, installation and configuration of authorization service for ACGT grid was supported. There were many bug fixing and adjustments done in this area. Data Management Service and Resource Management Service (GRMS) were integrated with higher level tools such as Workflow Engine (WP9) or Knowledge Discovery Tools - GridR (WP6).

There is still ongoing work on more tight integration between Data Management System and Authorization System to be able to authorize access to separate files.

There were some significant improvements in GRMS to support Oncosimulator scenarios (WP8). For this scenario new important feature was implemented - support for parametric applications. Besides that integration with visualisation system was introduced. The results of this work were presented during the second formal ACGT Review meeting in Eindhoven.

- Major Achievements towards planned objectives, identify main partners Involved

All partners taking part in WP4 were involved in maintaining grid infrastructure on their resources.

- **Deviations from the project work programme, and corrective actions taken/suggested**

There were no serious deviations from the work programme

- **List of deliverables, including due date and actual/foreseen submission date**

Deliverable 4.3 due at T0+24 has been submitted on 13/05/08

- **List of milestones, including due date and actual/foreseen achievement date**

No milestones due within this reporting period.

Workpackage 5 – Distributed Data Access and Applications

- **Partner Responsible : PHILIPS**

- **Contributing partner(s):** Philips, FHG-IBMT, UPM, LundU, USAAR, Uhok

- **Reporting Period:** 01/02/2008 – 31/07/2008

- **Workpackage objectives and starting point of work at beginning of reporting period**

-**The Workpackage has the following major objectives:**

- To provide seamless and interoperable data access services to the distributed data sources, by developing a set of compatible software key modules/services based on Web Services
- To provide services for ontology-based ubiquitous interoperability within the integrated ACGT environment (developed in WP9)
- To define a generic architecture that enables distributed access to all relevant patient data across the clinical trial sites
- To investigate architectural alternatives and design solutions to enable computationally-demanding medical applications to make use of distributed (remote) resources

- Objectives during reporting period

- Implementation of data access services to various types of data.
- Implementation of tools for the creation, management and monitoring of clinical trials and biobanks.
- Requirements analysis, specification and data model for genomic data in a future clinico-genomic EHR

- Progress towards objectives

- Generic OGSA-DAI activity that delivers query results to the Gridge Data Management System (Poznan). This activity is also used by the Mediator development team.
- Generic OGSA-DAI activity that enables the compression of results of a retrieval activity to a single file
- Integration of ACGT security infrastructure into our data access services: authorization via GAS
- Development of a data access service for the BASE database (querying and CEL file retrieval)
- Upgraded the relational data access service to OGSA-DAI version 3, to estimate the effect of upgrading completely to this new version
- Coordinating role in the work needed from the Mediator, Ontology, and Data Access Services sides for the May 2008 Demonstrator

- Definition of relevant and illustrative queries (underlying database, local ontology, master ontology)
- Modifications to the Master Ontology to support these queries
- Modifications to the Mediator to support these queries
- Implementation of the first release of ObTiMA (Ontology based Trial Management System for ACGT) including
    - The Integration of ObTiMA into the ACGT grid environment,
    - Integration of the ACGT Master Ontology
    - Integration of the basic version of CRF Repository via Web Services
    - Initial integration of the Trial Outline Builder, developed by Hokkaido University.
- Demonstration of ObTiMA on the review in Eindhoven (Mail 2008)
- Preparing the Deliverable 5.4 "Conceptual specification and a first prototype for an ontology based Clinical Data Management System and for the Trial Builder"
- Preparation of a questionnaire to collect requirements and build realistic scenarios for the data model of genomic data in an EHR
- Interviews with clinicians and molecular biologists concerning requirements of genomic data in clinical practice
- Study of the HL7 Genomic Variation data model and the RIM, as a potential candidate standard for the clinico-genomic EHR data model

- Main Activities & Tasks worked on

T5.2 Implementation of the data access services

T5.4 Model definition of an ACGT-specific, integrated Clinico-Genomic EHR

T5.5 Implementation of tools for the creation, management and monitoring of clinical trials and biobanks

- Major Achievements towards planned objectives, identify main partners Involved

- Contribution to the integrated demonstrator and to the implementation of the scenarios for the ACGT review in Eindhoven (Philips, UPM)
- Integration of ACGT security infrastructure into our data access services:
    - authorization via GAS (Philips)
    - Development of a data access service for the BASE database (querying and CEL
    - file retrieval) (Philips)
    - Implementation of the first release of ObTiMA (Ontology based Trial Management System for ACGT) (FHG-IBMT)
    - Demonstration of ObTiMA during the review in Eindhoven (FHG-IBMT)
    - -Deliverable 5.4 "Conceptual specification and a first prototype for an ontology based Clinical Data Management System and for the Trial Builder" (FHG-IBMT, USAAR, Uhok)

- **Deviations from the project work programme, and corrective actions taken/suggested**

  No significant deviations from the work plan.

- **List of deliverables, including due date and actual/foreseen submission date**

  D5.4 Initial model definition of an ACGT-specific Clinico-Genomic EHR due at T0+30 foreseen in November 2008

- **List of milestones, including due date and actual/foreseen achievement date**

  No milestones due within this reporting period.

Workpackage 6 – Data Mining and Knowledge Discovery Tools

- **Partner Responsible : FHG**

- **Contributing partner(s):** UMA, SIB, INRIA, UOXF, EIO, UvA

- **Reporting Period:** 01/02/2008 – 31/07/2008

- **Workpackage objectives and starting point of work at beginning of reporting period**

  -**The Workpackage has the following major objectives:**

  The objective of this WP is to provide an integrated analysis environment for clinical data analysis and knowledge discovery. Specifically:

  - To adapt standard analysis modules for statistics, data mining and knowledge discovery to the ACGT environment.
  - To adapt advanced data mining and text mining modules to the ACGT use care.
  - To provide an innovative and user-friendly interface to the analysis tasks.

  - Objectives during reporting period

  During the reporting period, the main objective of WP6 was the implementation and demonstration of the first integrated version of the ACGT analysis environment.

  - Progress towards objectives

  The first integrated version of the analysis environment was successfully demonstrated at the ACGT review in Eindhoven in May. This demonstration included

  - distributed processing of large scale data set.
  - combination of various analysis tools to enact a real-world scientific workflow.
  - use of meta data to select and control data analysis operators.

  - Main Activities & Tasks worked on

  T6.1: Implementation of required services for knowledge discovery

  T6.2: Meta data for knowledge discovery

  T6.3: The integrated ACGT Knowledge Discovery Environment

  - Major Achievements towards planned objectives, identify main partners Involved

  Additional features were integrated into the gridified version of the R toolkit, GridR. In particular, by connecting GridR with the ACGT meta data repository it is now possible for the GridR service to download necessary information for the execution directly from the repository, instead of requiring the user to input this data. In addition, the integration of GridR with the Grid Data Management System was improved, including the use of

file-related meta data to support information about file formats and enable automatic data conversion. The main partner involved was FhG.

- A GridR demonstrator for a real-world scientific workflow was developed and deployed. This demonstrator was presented at the ACGT review in Eindhoven. Main partners: FhG, SIB.
- A concept for file-related meta data was developed. Main partners: FhG, FORTH.
- Development of a "pilot" web-service in the ACGT context. This service performs hierarcical clustering and is integrated with ACGT security (GAS) and storage (DMS) architecture. This initial service will constitute a template for additional service development within this workpackage. Main partner: UMA.
- Development of a library (magallanes) for discovery of services based on keywords and descriptions used during service registration. The library will be improved to use semantical annotations of the services. In its current version, the library could be used in the portal to improve the current service discovery. Main partner: UMA.
- Consolidation of the meta data repository. Main partner: UMA.
- Design of a demonstration scenario (MCMP) for high-performance parallel computation. Implementation of a first version of corresponding R scripts. This scenario is designed to build the basis of a future ACGT demonstrator. Main partner: UOXF.
- Initial Gridification of algorithms for graph-based identification of cancer-related pathways from published literature. Main partner: IEO.
- Implementation of the clustering tool “chavl” based on the likelihood linkage analysis in the R-package "LLAhclust". A newer version of chavl, that can simultaneously take into account variables of different type (numeric, nominal, ordinal, boolean etc.) for clustering, is now available. A demonstration of this tool with an application to real data within the context of ACGT is under preparation.

- **Deviations from the project work programme, and corrective actions taken/suggested**

  No deviations foreseen.

- **List of deliverables, including due date and actual/foreseen submission date**

  No deliverables due within this reporting period.

- **List of milestones, including due date and actual/foreseen achievement date**

  No milestones due within this reporting period.

Workpackage 7 – Ontologies and Semantic Mediation Tools

- **Partner Responsible : UPM**

- **Contributing partner(s):** UvA, Philips, IJB, SIB, LundU, UMA, UPM, FHG, BIOVISTA, UoC, PSNC, Custodix, ICCS, UHok

- **Reporting Period:** 01/02/2008 – 31/07/2008

- **Workpackage objectives and starting point of work at beginning of reporting period**

-The Workpackage has the following major objectives:

- To provide, through the Master Ontology, a formal description of the knowledge domain of the clinical trials on cancer included in ACGT.
- To develop a semantic mediation layer that integrates distributed and heterogeneous biomedical databases. This mediator is supported by the ACGT Master Ontology, which provides the necessary semantic background by modelling the domain.
- To fully exploit powerful languages, such as OWL, in order to provide mediation services across a wide range of information sources, resulting in the implementation of the ACGT semantic mediation tools and services.
- The core of the ACGT platform is formed by the semantic mediation layer. This is composed of several mediation services, and supported by the ACGT Master Ontology. The services will be provided to a number of tools developed inside the ACGT project, as well as end-users, who will get access to a query system that integrates a great number of biomedical sources concerning clinical trials on cancer
- To, ultimately, develop the mediation technologies required for achieving a vertical integration among many different levels of granularity (molecular, cellular, tissue, organ, individual and population)

- Objectives during reporting period

- To integrate the Semantic Mediator in the ACGT platform to be used seamlessly in a workflow execution together with the rest of the ACGT tools.
- To develop new tools and formats enhancing the heterogeneous database integration tasks.
- To maintain and curate the ACGT Master Ontology of Cancer.
- To deliver D7.4 - Consolidated approach for semantic mediation and integration of heterogeneous data sources for clinical trials.

- Progress towards objectives

Deliverable D7.4 has been submitted. The mapping format and new mapping tool have been successfully developed and tested. A prototype of the end user query tool has been presented. The integration with the main ACGT platform and Obtima has been carried out.

- Main Activities & Tasks worked on

The pre-defined tasks (DoW) that have had specific dedicated effort during this period have been:

- T7.4.1 Development of the mediator
- T7.4.2 Development of the end-user query interface
- T7.4.4 Integration of the ACGT master ontology in clinical data management system
- T 7.5 Design of the final mediation approach

- Major Achievements towards planned objectives, identify main partners Involved

The main activities during the reported period relate to:

- Development of ACGT Master Ontology: further specification of requirements and review (IFOMIS, FhG, UPM)
- Initial integration of ObTiMA into ACGT environment using the mediator via OGSA DAI services (FhG, UPM, IFOMIS)
- Development of the mapping format for the mapping of data sources to the ACGT Master Ontology (UPM, FORTH, IFOMIS, Philips)
- Developing of the OGSA-DAI Semantic Mediator service (UPM, Philips)
- Mapping API new version supporting new mapping format (UPM)
- Mapping tool Beta version (UPM)
- Query tool prototype (UPM)
- Mappings with TOP database for review (UPM, Philips, IFOMIS, FORTH)
- Mappings for Obtima (UPM, FhG)
- Semantic mediator optimizations, and new features (UPM)
- Support for the new mapping API (UPM)
- Output modification for storage of results in web (UPM, FhG, Philips)
- Output of metadata associated to results (UPM, FhG)
- Enhancements on the data integration algorithm (enabling of cross-constraints) (UPM)
- Preparation of the integrated demonstration for the 2nd annual review.

Specifically:

a) Review of ACGT MO: The ACGT Master Ontology is constantly reviewed with respect to usability (by the ACGT services, e.g. the mediator and ObTiMA) and completeness. The clinical partners are constantly asked to hand in reviews on the coherence and correctness of the representation of clinical reality. However, we experienced that these activities lead to minor adjustments now. No structural changes were necessary over the last six months. Of course, the consistency is constantly checked while working with the owl-File, using the Pellet reasoned. (IFOMIS)

Addition of constraints and relations to the ACGT MO: An unforeseen problem did arise quite before the reporting period: With respect to anatomy we were always very confident that we will be able to re-use the **Foundational Model of Anatomy** (FMA) one way or the other. Basically, we hoped for a re-usable, open source owl-implementation. Even though two such implementations exist, they confronted us with a severe problem. The turned out to be too large. The size of an ontology is critical in two respects: 1) The size might slow down applications exploiting the ontology considerably; 2) Reasoners can only be used to validate the coherence of an ontology up to a specific size. Copying an owl-Implementation of the FMA in its entirety would probably result in an ontology too large to check with a reasoner and rather slow in use for both ObTiMA and the mediator. (IFOMIS)

- Addition of anatomical classes: An unforeseen problem did arise quite before the reporting period: With respect to anatomy we were always very confident that we will be able to re-use the **Foundational Model of Anatomy** (FMA) one way or the other. Basically, we hoped for a re-usable, open source owl-implementation. Even though two such implementations exist, they confronted us with a severe problem. The turned out to be too large. The size of an ontology is critical in two respects: 1) The size might slow down applications exploiting the ontology considerably; 2) Reasoners can only be used to validate the coherence of an ontology up to a specific size. Copying an owl-Implementation of the FMA in its entirety would probably result in an ontology too large to check with a reasoner and rather slow in use for both ObTiMA and the mediator. Realizing this problem we decided to look around for alternatives. Alan Rector proposed to talk to Jay Kola who developed an anatomy ontology which is not part of the OBO Foundry and is based on ontology terms from the NCI Thesaurus (s.b.). After reviewing this ontology, which was rather small, but not build to the quality criteria formulated for ACGT we had to find an alternative. We decided to create the anatomical classes as needed in the domain (used in the CRFs) in accordance with the FMA. This means that we added most parts of the middle layer of the FMA ontology, but restricted the leaf nodes to those needed in ObTiMA at the moment. Adding new classes will, however, be not problematic since all that the curators need to do is search the FMA and add the content. This method provides the best solution for the problem at hand. The conceptual modelling we make use of is the best available representation of anatomy that is on the market. Furthermore, the FMA is open source and there are no restriction for re-use (IFOMIS)

- Validation of conceptual design by means of terminology techniques: A critical aspect for the success of the ACGT MO is whether we manage to provide a correct and complete representation of the given domain. In order to validate our conceptual design we decided to collaborate with terminology experts outside ACGT to get an impression on the completeness of our representation. In this task we co-operated with the Institut für Angewandte Informationsforschung (IAI, Institute for Applied Information Science) located at Saarland University. We were in contact with the director of the institute, Prof. J. Haller, and a PhD student (G. Grigonyte). The AIA offered to extract a terminology from domain specific abstracts. We decided to use 200 abstracts on clinical trials, mostly in nephroblastoma and breast cancer. The abstracts where provided by our clinical partner in Homburg, namely Alexander Hoppe and Norbert Graf. The IAI provided us with a 19-page list of terms extracted automatically from the abstracts early in July. The final analysis of the ACGT MO and its accordance to the extracted terminology had to be postponed until middle of August due to our efforts in adding the anatomy branch to the ontology. However, our first survey of the terminology led to the result that most terms are already present, but minor adjustments might be necessary. We plan to prepare a document on conceptual design in the next months. Within that document we will give a more elaborate account of these activities (IFOMIS)

b) Re-evaluation of NCI Thesaurus (caBIG, caCORE): Since the start of ACGT the project, and especially WP7 is confronted with questions whether the NCI Thesaurus would not be a better terminology resource than the newly developed ACGT MO. This situation became urgent again by the fact that the NCIT is distributed and advertised under a number of new names, respectively in a number of different systems, for instance caCore. Given requests of colleagues we understood that it is our responsibility to re-evaluate the NCIT. Doing so we, sadly, came to the result that the grave problems already described in Deliverable 7.1 have not been corrected and thus, the assessment of the NCIT reaches the same result as before. (IFOMIS)

c) Intra-project communications on ontology maintenance: One of the most pressing problems with respect to the ontology is the question who we can maintain the ontology in years when the development and the funding are finished. Together with FORTH we already proposed a submission system. In June we had a working meeting with Martin Dörr formulating the submission process. IFOMIS carried out a state-of-the-art-analysis of submission systems in biomedical OTDs utilizing the list of OTDs given in D 7.1. The results of the meeting along with the results of the state-of-the-art analysis can be found in the attached document Meeting Notes on Ontology Development and Maintenance June 25-26, 2008, Saarbrücken (Including Submission Process and Implementation Process). (IFOMIS, FORTH)

d) Intra-project communications on the possibility of a “service ontology”: Together with University of Malaga, and FORTH IFOMIS has discussed the possibility and the usability of a “service ontology,” The aim of such an ontology would be to classify tools and services. It was agreed that the existence of such an ontology can foster the use of ACGT and its tools by users. IFOMIS agreed to support the development by bringing in expertise from ontology development. (IFOMIS, UMA, FORTH)

e) Preparation of documentation: On the last review IFOMIS was encouraged to intensify its documentation efforts. Better documentation on the development of the ontology and the conceptual design was demanded by the reviewers. With this report we submit two documents

a. **Documentation on Ontology Development February to July 2008**
b. **Meeting Notes on Ontology Development and Maintenance June 25-26, 2008, Saarbrücken (Including Submission Process and Implementation Process)**

The first documents the development of the ontology over the last months. The second gives the results of consultations with Martin Dörr (FORTH) focusing on future research and maintenance. We plan to prepare another document describing the conceptual design methods (reality representation) utilized in the development of the ACGT MO in detail. (IFOMIS, FORTH)

f) Preparation of publications: Over the last six month IFOMIS was extremely active with respect to publication. Besides the accepted papers given in the report, IFOMIS, together with other partners, submitted a two page abstract to a HL7 Meeting in Crete. This was accepted as a poster, but the authors decided to skip this and rather concentrate on preparing a journal article. The IEEE Meeting in Finland spawned yet another opportunity: The chair of the ontology workshop, Tharam Dillon (Curtin University of Technology) proposed to submit a paper on the ACGT MO and ObTiMA to **4th International Workshop On Semantic Web & Web Semantics (SWWS '08), Monterrey, Mexico** (http://www.cs.rmit.edu.au/fedconf/index.html?page=swws2008cfp). IFOMIS took the lead in preparing and submitting a paper to this event. Results of the review process are expected around August 15, 2008. Furthermore, Tharam Dillon proposed to present ACGT in a book publication to be published 2009 focussing on new Semantic Web approaches. This, however, has to be negotiated. (IFOMIS)

- **Deviations from the project work programme, and corrective actions taken/suggested**

  Deliverable D7.3 was delayed due to a late decision of including additional information on the Master Ontology after taking into consideration reviewers comments during the 2nd informal review in December 2007. The final document has been already delivered. This issue motivated a minor delay in the delivery of the following deliverable D7.4.

- **List of deliverables, including due date and actual/foreseen submission date**

  D7.3 - Demonstration and report of the Ontology Mediation services - Due at month 21 has been delivered at month 25.
  D7.4 - Consolidated approach for semantic mediation and integration of heterogeneous data sources for clinical trials - Due at month 24 - has been delivered at month 26.

- **List of milestones, including due date and actual/foreseen achievement date**

  No milestones due within this reporting period.

Workpackage 8 – Technologies and Tools for In Silico Oncology

- **Partner Responsible : ICCS**

- **Contributing partner(s):** USAAR , IJB, INRIA, UvA, FHG, UHok, IEO, FORTH, PSNC
- **Reporting Period:** 01/02/2008 – 31/07/2008
- **Workpackage objectives and starting point of work at beginning of reporting period**

-The Workpackage has the following major objectives:

The objective of this WP is to develop a technologically advanced and user friendly system, the Oncosimulator, able to spatiotemporally simulate within well defined reliability limits tumour growth and tumour and normal tissue response to chemotherapy for the cases of breast cancer and nephroblastoma in the patient's individualized context. Pertinent imaging, histopathologic, molecular data in conjunction with the ACGT clinical trials will be exploited in order to validate the model both prospectively and retrospectively.

At the start of the reporting period an early version of the simulation module of the Oncosimulator was available as well as early versions of several of its technological workpackages. No integration of the modules into the single Oncosimulator had taken place.

- Objectives during reporting period

- Extension of the simulation codes of tumour growth and response to therapeutic schedules for the cases of nephroblastoma and breast cancer so that instead of a triaxial ellipsoidal shape [see deliverable D8.2], a generic shape and internal structure of the tumour can be handled.
- Use of a variable number of progenitor tumour cell stages instead of the three indicative stages considered in D8.2
- Production of a number of "nomograms" correlating individual tumour cell state transition probabilities {e.g. probability of a symmetric [stem → (stem, stem)] or asymmetric [stem → (stem, progenitor)] division, probability of a newborn cell to enter the dormant state etc.} and the percentages of the various tumour cell categories within the tumour {e.g. percentage of stem cells, percentage of progenitor cells, percentage of differentiated cells, percentage of proliferating cells, percentage of dormant cells etc.} in order to cover the critical parameter value ranges of the problems relatively densely.
- Extension and integration of image processing tools for aided segmentation, interpolation, 3D reconstruction and registration of tumour images (e.g. MRI, CT etc.)
- Internal parallelization of the simulation code in order to considerably lower the execution time needed
- Automation of the execution of different instances of the simulation code on a cluster via a portal

- Automation of the execution of different instances of the code on grid architectures via a portal
- Interactive visualization of the tumour before, during and after the application of a therapeutic scheme/schedule [both real and simulated]
- Execution and parametric exploration of the simulation code through the development of subjunctive interfaces
- Integration of the previous components in order to produce the initial version of the ACGT Oncosimulator
- Initial use of (pseudo)anonymized real medical data and actual treatment data in order to adapt, optimize and validate the simulation system.

- Progress towards objectives

During the reporting period clear progress towards all objectives has been achieved. Virtually all initially set targets have been successfully reached. Some small delays in the optimization and integration of certain technological modules that incurred due to the frequent improvements in the simulation code led to paying special attention to the code development platform. By proceeding using more adequate development platforms such as the Eclipse platform (http://www.eclipse.org/) it is expected that optimization changes in the simulation code will have a minimal effect on the optimization of the technological modules as well as on the next steps of integration (regarding both module integration and integration of the Oncosimulator into the entire ACGT platform).

- Main Activities & Tasks worked on

1. Clinical Orientation of *In Silico Oncology* – Provision of Medical Data

USAAR provided two sets of anonymized MRI nephroblastoma slices, one before and another one after treatment along with histopathological and treatment schedule data. Different tools for aided segmentation of the tumour were tested and feedback was sent to **FHG** in Darmstadt, the provider of the segmentation tools. Subsequently **USAAR** performed an optimized segmentation of the imaging data and provided the produced segmentation files to **FHG** for interpolation and three dimensional reconstructions of the tumours. The reconstructed tumour data was sent to **ICCS** to be used by the simulation module during the simulation executions and the module optimization process. Requirements for visualization of the results of the Oncosimulator were formulated by **USAAR** according to user needs. Continuous interaction of **USAAR** and **ICCS** ensured a clear clinical orientation of the whole process by constantly addressing clinical needs and requirements. In parallel **IJB** provided pseudoanonymized volume, treatment, histopathological and molecular data for ten cases of breast cancer to **ICCS.** Using the approximation of spherical tumours a number of data sets were exploited in order to optimize the simulation module.

2. The Simulation Module

Two discrete states based, four dimensional, multiscale tumour dynamics models were specially developed by the *In Silico* Oncology Group, **ICCS** in order to mimic one branch of the SIOP 2001/GPOH clinical trial concerning nephroblastoma treated with vincristine and dactinomycin and one branch of the Trial Of Principle (TOP) clinical trial concerning breast cancer treated with epirubicin respectively. Both the SIOP 2001/GPOH and the TOP trials constitute two of the “ACGT clinical trials”. A substantial part of the models can address other tumour types as well. The actual (pseudoanonymized) imaging (*with arbitrary tumour shape*), histopathological,

molecular and clinical data of the patient were exploited. Special emphasis was put on the effect of cancer stem/clonogenic, progenitor, differentiated and dead cells, the cell category transition rates and the cell category relative populations within the tumour from the treatment baseline onwards. The importance of adaptation of the cell category relative populations to the cell category transition rates for free tumour growth was revealed. A novel method which ensures adaptation of these two sets of entities at the beginning of the simulation execution was proposed and subsequently successfully applied. The method does not rely on the production of nomograms which is a great achievement in relation to the previous method that was demonstrated during the December 2007 ACGT annual review. Convergence and code checking issues were addressed. Parametric/sensitivity studies were also performed. The models' behaviour substantiates their potential to serve as the basis of a treatment optimization system following an eventually successful completion of the clinical validation and optimization process.

3. Image Processing of the Medical Data

The following three image processing procedures were undertaken by **FHG** in Darmstadt:

I. Drawing contours

Contours are drawn slice-wise as a polygon-strip

II. Converting contours to binary data

A scan-line algorithm is used to fill the contour in each slice

The result is a binary volume with same dimensions as the MRI data set

III. Resampling and interpolation of binary segmentations

Using ITK (Insight Segmentation & Registration Toolkit) a surface is placed around the binary volume. The area of surface is minimized using level sets and taking the binary volume as a constraint. The output is resampled (using a distance transform) to isotropic voxels. A zero level set is computed in order to recover the surface and to convert it into a binary volume.

In parallel **FORTH** explored the application of methods of automatic segmentation of the real clinical data.

4. The Oncosimulator Grid Execution Scenario

The integration of the Oncosimulator application with the Grid infrastructure was undertaken by **PSNC**. Integration concerned the running of application code in ACGT testbed, using GRMS for application submission and GDMS for storing input and output data. Based on the Oncosimulator requirements, PSNC worked on the development of a new feature of the Resource Management System providing the ability to submit parametric jobs.

5. Cluster Execution and Parallelization of the Oncosimulator Code

INRIA undertook the optimization of the original simulation code. For internal ACGT WP8 exploratory reasons an auxiliary job submission webpage (http://acgt.genouest.org) addressing only a small subfraction of the model parameters has been updated based on the latest optimized version of the simulation module. **INRIA** also explored the possibility to implement multithreaded internal parallelization of the Oncosimulator simulation to be executed on multicore processors.

6. Subjunctive Interfaces for the Oncosimulator

UHok designed, built and demonstrated an interface for showing the parameter settings used in a repository of pre-computed simulator results, and letting a user carry out parametric exploration by requesting visualisations of selected results and performing synchronised manipulation of those visualisations. They also achieved necessary enhancements to the parameter exploration platform (the RecipeSheet), including porting it to work within a Web browser rather than as a standalone application. They also designed and built the mechanisms for user-driven communication with a result repository and visualisation server.

7. The Oncosimulator Component Collaboration Diagram

A collaboration diagram of the various technological modules-components of the Oncosimulator was produced by **PSNC, INRIA, UvA, FHG** and **ICCS**. The diagram includes i.a. the segmentation tool, an application portlet, the Grid environment, the RecipeSheet, the visualization tools and the visualization services.

8. Interactive and Virtual Reality Visualization

Regarding the visualization of clinical data and simulation predictions undertaken by **UvA** a specific task was dedicated to the development of a software framework to support the interactive visual exploration of simulation data. The framework is now being tested in several settings, including web portals, 3rd party applications and interactive virtual reality devices. The implementation of the interactive framework for distributed visualization of Oncosimulator data and medical imaging data is well underway.

9. Initial Clinical Validation and Adaptation of the Oncosimulator

Functioning of the initial Oncosimulator platform which includes both basic science and technology modules was demonstrated during the Eindhoven ACGT annual review (May 27-28, 2008) under the coordination of **ICCS** and with the participation of **USAAR, INRIA, UHok, UoC, FHG, PSNC**. Using the real medical data referring to nephroblastoma and breast cancer in conjunction with plausible values for the model parameters (based on available literature), a reasonable prediction of the actual tumour volume shrinkage was made possible through the simulation module. Obviously as more and more sets of medical data are exploited the reliability of the model “tuning” is expected to increase. It should also be stressed that the large number of biological boundary conditions (e.g. monotonic increase of *all* tumour cell categories for an imageable freely growing tumour) dramatically limits the number of possible solutions (i.e. sets of parameter values that are able to predict real tumour shrinkage following treatment). This is very important since such limitations drastically facilitate the approach to *the* solution best representing clinical reality for each given medical data case.

10. Future Extensions of the Model (Immune Response Modelling)

During the WP8 meeting that took place in Milan in February 8, 2008 it was decided that **IEO** would start work on a future extension of the core Oncosimulator simulation module dealing with the simulation of tumour-immune system interaction and the response to immunotherapies (the “TIS module”). Work on that module will proceed in parallel with the development of the Oncosimulator. Following an eventually satisfactory clinical adaptation and validation of the Oncosimulator, the TIS module will be integrated into the Oncosimulator and theoretical studies will be carried out in order to explore the effect of various factors on the tumour-immune system interaction and the response to immunotherapies. Regarding the definition of the main issues to be

included in the TIS module, an analysis and preliminary modelling of them in the framework of the Oncosimulator setting was performed. Careful theoretical support work through mathematical models was done.

- Major Achievements towards planned objectives, identify main partners Involved

- Construction of plausible instances of a virtual tumour modelling the clinical tumour at baseline (before treatment) based on a novel strategy ensuring adaptation of the cell category relative populations to the cell category transition rates (ICCS).
- Explicit consideration of cancer stem/clonogenic, progenitor, differentiated and dead cells (ICCS)
- Exploratory simulation execution of the simulation code in order to ensure convergence and study the sensitivity of the model (ICCS)
- Provision of sets of real (pseudo)anonymized medical data before and after treatment (USAAR, IJB)
- Integration of a segmentation tool into the Oncosimulator in order to provide part of the input to the simulation module. Sets of real DICOM images can be sent along with their segmentation at diagnosis and after preoperative chemotherapy (FHG, USAAR).
- Segmentation of actual DICOM data (USAAR)
- Development of a new feature to GRMS facilitating the submission of parametric jobs based on the Oncosimulator requirements (PSNC)
- Optimization of the simulation code and development of internal multithread execution versions (INRIA)
- Design and implementation of mechanisms for building a repository of pre-computed results, and invoking visualisation services on chosen result instances and their corresponding real-world tumour data (UHok, UvA, PSNC, INRIA, FHG , USAAR)
- Demonstration of visualization services integrated with RecipeSheet (UvA, UHok)
- Visualization services successfully ported to Personal Space Station (UvA)
- Integrated Grid execution of Oncosimulator, RecipeSheet and visualization services (ICCS, UHok, UvA, INRIA, PSNC)
- Demonstration of the technologically advanced process of the adaptation of the simulation code to the real medical data (ICCS, USAAR, INRIA, UHok, UvA, FHG, PSNC)
- Proposal of numerical experiments and of their implementation on passive and/vs. active immunotherapy, effects of scheduling of therapies, effects of delays of immune proliferation (IEO)

- **Deviations from the project work programme, and corrective actions taken/suggested**

No deviations from the project work programme were noticed in the development of *most* modules. However, frequent changes to the simulation code resulted in certain delays in availability of a platform for experimenting with end-to-end operation of the Oncosimulator. One of the many problems this caused was late discovery of security constraints that prevent direct invocation of the simulator from the RecipeSheet. With no time left to resolve this before the Eindhoven annual review, we abandoned the plan to demonstrate live invocation and instead used just pre-computed results. As already mentioned by using more adequate development platforms such as the Eclipse platform it is expected that optimization changes in the simulation code will have a minimal effect on the optimization of the technological modules as well as on the next steps of integration (regarding both module integration and integration of the Oncosimulator into the entire ACGT platform).

- **List of deliverables, including due date and actual/foreseen submission date**

  D8.3 Report on the refinement and optimization of the algorithms and codes, and the initial clinical validation and adaptation of the "Oncosimulator". Due date: T0+30. Foreseen submission date: T0+31.5

- **List of milestones, including due date and actual/foreseen achievement date**

  No milestones due within this reporting period.

Workpackage 9 – The Integrated ACGT Environment

- **Partner Responsible : FORTH**

- **Contributing partner(s):** UvA, Philips, IJB, SIB, LundU, UMA, UPM, FHG, BIOVISTA, UoC, PSNC, Custodix, ICCS, UHok

- **Reporting Period:** 01/02/2008 – 31/07/2008

- **Workpackage objectives and starting point of work at beginning of reporting period**

The Workpackage has the following major objectives:

The main objectives of WP9 according to the DoW are:

- To demonstrate large scale system integration within the ACGT environment

- To implement the workflow layer for achieving composability of applications and services

- To investigate the evolution of the ACGT integrated platform proposing enhancements to all levels with respect to functionality and performance

Objectives during reporting period

During the reporting period emphasis was given to the following areas:

- Design and implementation of a web based workflow authoring tool that is integrated in the ACGT portal so that the users use a unified interface to gain access to the wealth of functionality offered by the ACGT platform.

- Implementation of the necessary infrastructure for supporting the composition of the ACGT services into scientific workflows in conformance to the ethics, legal, and security requirements imposed by WP10 and WP11.

- Prepare and submit the Deliverable 9.3 “Data and Metadata Management”

- Progress towards objectives

Deliverable 9.3 was submitted. The development of the web based ACGT Workflow Editor has been started and will be an ongoing task. Furthermore we have defined a generic architecture for integrating Grid and non-Grid based technologies at the workflow layer that will allow us to greatly expand the ACGT platform by incorporating even “third party services” in the future.

- Main Activities & Tasks worked on

A prototype implementation of the ACGT Workflow Editor was demonstrated in the second formal ACGT Review meeting in Eindhoven. The version of the workflow editor that was shown featured integration with the Metadata Repository for accessing the list of the available ACGT services (R scripts, Mediator, Data Access Services) and the available metadata for each of these services. Furthermore, it allowed the graphical design of workflows by interconnecting the chosen services with basic support for the

(syntactic) validation of these connections based on the data types information that is part of services' metadata. The publication of the new workflows in the metadata repository and service registry and their subsequent execution through the portal were also demonstrated.

For the secure integration of services at the workflow layer, an implementation of the "credential delegation" functionality is necessary so that the user identity is transparently transmitted through the workflow enactor to the services participating in the workflows. A general architectural framework has been designed and implemented by the introduction of the so called "*proxy services*" that allows such "single-sign on" and "credential delegation" scenarios in compliance with the Grid security and the ACGT specific requirements. These proxy services are integration points that permit the communication and interaction of the Grid-agnostic BPEL workflow environment with the Grid and other kind of services.

- **Major Achievements towards planned objectives, identify main partners Involved**
  - Design and implementation of a prototype version of the ACGT Workflow Editor (FORTH)
  - Integration of the Workflow Editor and the ACGT Portal (FORTH, Siveco)
  - Implementation of a REST based web service API for the execution of published workflows, services, and R scripts (FORTH)
  - Survey of the available "non-BPEL" enactors and their evaluation with respect to the level of support for Grid Security and credential delegation. The findings are documented in the ACGT Wiki at http://wiki.healthgrid.org/ACGT:Non_BPEL_Workflow_Engines (FORTH)
  - Discussions and study of the available options for achieving the "credential delegation" functionality in the BPEL workflow enactor. (FORTH, PSNC, Custodix)
  - Design and initial implementation of the Proxy Services framework for making possible the secure, authenticated, and authorized invocation of Grid ACGT Services from within BPEL Workflow Enactors. (FORTH)
  - Integration of GridR in the workflow editor and implementation of the "script as service" abstraction based on the metadata descriptions of scripts (FORTH, FHG)
  - Integration of the Semantic Mediator and the microarray specific Data Access Services (DAS) in the workflow editor (FORTH, UPM, Philips)
  - Design and initial implementation of interactive visualization services and integration in web portals (UvA)
  - Integration of the Grid Data Management Service (DMS) in the workflow editor so that the user can browse his folders and use his files as inputs to his workflows. (FORTH)
  - Implementation of the Proxy Services for Mediator, GridR, and the Microarray (BASE) DAS (FORTH)
  - Preparation of Deliverable 9.3 (FORTH, UMA, PSNC)
  - Development of realistic workflows simulating clinical-research data analysis based on microarrays (SIB)
  - Design and preparation for the integrated demonstrators of the second ACGT formal review in Eindhoven (FORTH, Philips, SIB, UMA, UPM, GHG, PSNC, Custodix, UvA)

- Demonstration of the first release of ObTiMA (Ontology based Trial Management System for ACGT) on the review in Eindhoven (FhG)

- **Deviations from the project work programme, and corrective actions taken/suggested**

  There were no serious deviations from the work programme

- **List of deliverables, including due date and actual/foreseen submission date**

  Deliverable 9.3 was prepared and made available for submission to the EC on May 2008

- **List of milestones, including due date and actual/foreseen achievement date**

  No milestones due within this reporting period.

Workpackage 10 – Ethics, Legal and QA issues

- **Partner Responsible : LUH**

- **Contributing partner(s):** IJB, UOC, LUH, Custodix, USAAR, FUNDP, UH, UOXF

- **Reporting Period:** 01/02/2008 – 31/07/2008

- **Workpackage objectives and starting point of work at beginning of reporting period**

  -**The Workpackage has the following major objectives**

  - Objectives during reporting period

  - Analysis of intellectual property rights concerning the data, the genetic material and the scientific outcome
  - Analysis of the intellectual property issues concerning computer software and licensing
  - Analysis of the GRID infrastructure and its legal implications, especially concerning intellectual property rights
  - Risk analysis regarding the data security
  - Risk analysis regarding data protection

  - Progress towards objectives

  - The analysis of legal requirements concerning data, genetic material and scientific outcome and their implications is in progress.
  - The production of contracts regarding lit. 1 will be started as soon as lit. 1 is finished.
  - The analysis of licenses used/to be used in ACGT and their legal requirements and implications is in progress.
  - The analysis of the GRID-infrastructure and its legal implications is in progress.
  - Risk analysis concerning the data security and data protection framework is in progress.
  - An empirical survey on patients´ and parents' perspectives and needs is in progress
  - Analysis of the consent of the data subject in the field of the research.

- Main Activities & Tasks worked on

- In depth analysis of the intellectual property issues in ACGT
- In depth analysis of legal risks regarding the data security and data protection framework is in progress
- Meetings with ACGT-partners (especially with WP11) took place for the analysis of risks regarding the data security and data protection framework is in progress
- WP10/11 meeting took place.
- Co-operations with the clinical ACGT-partners (IJB, UOXF, UOC, and USAAR), the German Childhood Cancer Registry, and the West German Study Group were installed and intensified.
- The questionnaire of the planned survey was pre-tested in a German hospital and translated into English, French and Greek
- The approvals for local ethics committees and institutional review boards were prepared
- Papers and a poster regarding ethical considerations on data protection proceedings were presented on conferences;
- Poster on the concept of Trusted Third Party;
- Article on the Directive 2000/31/EC and the eHealth services.

- Major Achievements towards planned objectives, identify main partners Involved

- Several articles were published/are accepted for publication (LUH).
- Presentation of ACGT during several meetings with experts in the field and professional exchange (Heraklion, Berlin, Vienna, Oxford, foreseen: Edinburgh) (LUH).
- Analysis of legislation and literature regarding the analysis of the intellectual property issues in ACGT (LUH).
- Analysis of legislation and literature regarding the analysis of legal risks regarding the data security and data protection framework is in progress (LUH).
- Cooperation with WP11 regarding the analysis concerning the data security and data protection framework (LUH, CUSTODIX).
- The design of an empirical survey on patients' and parents perspectives and needs was finalized (UH)
- The survey on parents with children affected by cancer was accepted by the local ethics committee of Hamburg on April 1, 2008-07-28 (UH)
- The survey on patients affected by breast cancer was submitted to the institutional review board of Crete University Hospital (UH);
- Several articles were published/are accepted for publication (FUND);
- Presentation of ACGT framework on professional meetings by FUNDP (Edinburgh, Luxembourg, etc) -

- **Deviations from the project work programme, and corrective actions taken/suggested**

  No deviations from the project work programme.

- **List of deliverables, including due date and actual/foreseen submission date**

  D10.5: Design of an empirical survey on patients´ perspectives and needs (due month 25) has been submitted on 13/05/08

- **List of milestones, including due date and actual/foreseen achievement date**

  No milestones due within this reporting period

Workpackage 11 – Trust and Security

- **Partner Responsible : CUSTODIX**

- **Contributing partner(s):**

- **Reporting Period:** 01/02/2008 – 31/07/2008

- **Workpackage objectives and starting point of work at beginning of reporting period**

-The Workpackage has the following major objectives:

The ACGT resources are dispersed among different organizations, requiring the possibility to establish (dynamic) trust relationships between different security domains (e.g. to enforce a uniform authorization strategy). The objective of this WP is to provide the necessary security services to the ACGT platform to reach this goal. Further, WP11 aims to create a technical environment in which processing of sensitive patient data for research purposes complies with the relevant (data protection) regulations "by default". WP11 has the supportive role of providing documentation and guidelines for the developers of the ACGT platform. Finally, WP11 has the task to continuously monitor the ACGT security and privacy requirements and revisit and evolve them based on the additional feedback that is acquired in the course of the project from the other work packages.

- Objectives during reporting period

The objectives set for this reporting period contain both continuations from the previous period as some new tasks. First of all further implementation of Security Services was set as a task, as well as integration of existing services into the security infrastructure. Experience obtained during integration of these first services was then to be used finalising the architecture and setting up security guidelines for all services.

As a second objective, management of the security and in more detail of Virtual Organisations was chosen as objective towards a fully integrated setup.

The final objective of this reporting period, further development of the CAT tool included a rewrite of the underlying data model and more general support for data types and anonymization methods.

- Progress towards objectives

In cooperation with the TMC (Technical Management Committee) and the other work packages integration of the security architecture with those services that are ready has been started. Feedback from the process has been collected and has been used to improve the security architecture. However, not enough feedback is available at this time to finalize the architecture.

Feedback from integration of services with the security architecture has also been collected for D11.5 to provide guidelines to the community targeted to the technologies that are actually used.

Integration problems have been discussed during (biweekly) online TMC sessions and a live-session in the Netherlands. The incompatibility of the workflow enactor with the security infrastructure (due to the technology used: axis 1 vs axis 2) has been solved by wrapping the workflow enactor with compatible proxy-services. During this period it was also decided to increase the number of live sessions since they are more productive than online sessions.

In order to prepare ACGT for use by end-users the discussion on user and resource management has been initiated. A major step has been taken by bringing together the different viewpoints on VO management by grid managers and end users. During a workshop organised by Custodix and several email discussions the VO management procedures have been worked out in further detail. These procedures will be transferred onto the ACGT portal during the next periods.

The Custodix Anonymization Tool has been rewritten in this period to use a unified underlying data model. This has the advantage that general profiles can be created, re-used and exchanged between users. Data fields can be grouped in privacy data types and processed using a single configuration option and using a unified data model also allows the integration of other privacy tools to, e.g. analyze the privacy level of a dataset.

Further input and anonymization modules have been added to CAT, a regular expression parser that allows CAT to support a wide range of new file formats and a MySQL database plugin.

Finally a continuous effort was made to acquire new requirements from end users for security. During a workshop in Lausanne, where delegates of the local hospital CHUV were present, Custodix was present to learn their requirements for using ACGT infrastructure within their organisation.

- Main Activities & Tasks worked on

Cfr. Progress towards objectives

- Major Achievements towards planned objectives, identify main partners Involved

- **Deviations from the project work programme, and corrective actions taken/suggested**

  Deliverables D11.4 and D11.5 have been slightly postponed in the new Implementation Plan because a number of services are not fully integrated with the ACGT platform yet. Hence, only initial feedback (insufficient) on the security architecture is available. As more services are integrated into the security architecture the required feedback becomes available to complete D11.4 and D11.5.

- **List of deliverables, including due date and actual/foreseen submission date**

  No deliverable due during the reporting period

- **List of milestones, including due date and actual/foreseen achievement date**

  No milestones due within this reporting period.

Workpackage 12 – Clinical Trials

- **Partner Responsible : IJB & FORTH – IMBB**

- **Contributing partner(s):** UHANN, UH, USAAR, Biovista, EIO, UOXF, UoC, SIB, Custodix, FUNDP.

- **Reporting Period:** 01/02/2008 – 31/07/2008

- **Workpackage objectives and starting point of work at beginning of reporting period**

-**The Workpackage has the following major objectives:**

- Initiate the development of the ACGT medical knowledge discovery infrastructure and promote post-genomic medicine according to the ethical, regulatory and technical requirements.
- Implement the ACGT post-genomic clinical trials collecting multilevel clinical information for the validation of the ACGT infrastructure.
- Collect and maintain nucleic acids, tissues and cells according to the highest operational standards for the implementation of the ACGT clinico-genomic trials and research activities.
- Implement various advanced post-genomic analyses including expression profiling, genotyping, proteome and metabolome profiling methodologies.
- Identify and address the various harmonization issues related to cross-platform and multi-centric post-genomic data collection.

- Objectives during reporting period

- Implementation of the ACGT post-genomic clinical trials and collection of the different samples;
- Implementation of various advanced post-genomic analyses;
- Investigation of the harmonization issues for cross-platform biological data integration and analysis;
- Promotion of post-genomic medicine in the context of ACGT.

- Progress towards objectives

1. Implementation of the ACGT post-genomic clinical trials and collection of the different samples:

SIOP 2001 trial: During the reported period the collection of samples and data continued. Up to now sera of 132 patients with nephroblastoma have been collected. The patient's clinical data were recorded and basic clinical data for the characterisation and statistics was selected and transferred in a separate datasheet. In the reference groups sera of 80 healthy and 69 patients with tumours other than nephroblastoma are available. Also imaging studies of 130 patients can be used. The second step of the

antigen scenario started at the beginning of the reporting period. The analysis of the patient's sera in the genetic laboratory in Homburg as well as the characterisation of the target antigens is ongoing. The list of target antigens, the scenario and the ACGT project were presented by Prof. Graf at the annual SIOP Nephroblastoma meeting in Chamonix beginning of March 2008. In addition the trial protocol and the Case report forms (CRFs) were used as prototypes to improve the web design and the database functionalities of the clinical data management system for ACGT (ObTiMA). The work on ObTiMA was carried out in a way that during the next period real data of patients of SIOP 2001/GPOH can be put into ObTiMA to test ObTiMA with SIOP 2001 data.

TOP Trial: One hundred and forty nine patients have now been included in this trial. An amendment to the trial was necessary to allow data of the patients to be shared in the context of ACGT and this amendment was approved by the Ethics Committee of IJB in the beginning of 2008. During the last months, patients who were already included in the TOP trial protocol were re-contacted to inform them with regard to the additional tests proposed in the amendment and the sharing of the data in the context of the TOP trial. Additional gene expression profiling has been carried out regarding the primary tumor biopsies of these patients.

Trials from IEO: The first clinico-genomic study focuses on surrogate markers of antiangiogenic therapy in Triple Receptor Negative Breast Cancer tumours. The collected data regarding patients included in this trial have been temporarily stored in classical databases, and in next months will be fully embedded in ACGT, and analyzed by the developed tools to test them. The second study focuses on non-small cell lung cancer (NSCLC). The goal of this study is to assess the impact of specific gene profiles on efficacy of gemcitabine and platin in untreated patients affected by this tumour. Clinical-molecular data will be analyzed in the framework of the GRID tools of the ACGT project as soon as they will be finalized.

2. Implementation of various advanced post-genomic analyses:

Given the fact that not enough data were available yet from the different clinical trials to carry post-genomic analyses, a realistic scenario (pseudoTOP) based on the structure of the TOP trial was developed. The virtual dataset simulates 198 patients with data similar to those collected in the TOP trial, e.g.: date of birth, date of recruitment in trial, tumor characteristics (size), nodal status, biochemical markers such as ER status, etc. Microarray files from a published dataset were associated to each patient in order to simulate the gene-expression aspects of the TOP study. A neo-adjuvant response status was associated to each patient according to the numerical value of a known gene signature (proliferation) computed from the microarray gene expression. The pseudoTOP dataset is thus realistic from the viewpoint of the complexity of the data structure, and provides a mean to validate the discovery process.

3. Investigation of the harmonization issues for cross-platform biological data integration and analysis:

In order investigate the various harmonization issues related to cross-platform and multi-centric post-genomic data collection and analysis, we developed a study which aims to assess the variability in gene expression microarrays, and of the prognostic and predictive profiles obtained from this technology, performed at different sites and using different array methodologies in human breast cancer samples. To this end we are comparing reproducibility of results obtained in two different ACGT partners institutions (IJB and UOXF) using two different but well established technologies for gene expression microarrays; namely, Affymetrix gene expression arrays (processed at IJB) and Illumina arrays (processed at UOXF).The annotation and statistical methods for

this comparison have been discussed in collaboration with WP13 and WP6, and are being implemented using R. This will allow executing the analysis in the grid environment using and furthering validating GridR in collaboration with WP6.

4. Promotion of post-genomic medicine in the context of ACGT:

As there is the need of a deeper and wider involvement of end-users, extensive dissemination work was carried out.

- Prof Graf approached organisations and trial leaders to join and use the ACGT platform for future trials. In addition Prof. Graf, a member of SIOP Europe, is involved in the Clinical Trials Group. There are three different working groups:

1. Protocol Guidelines Working Group
2. Clinical Trials Regulation Working Group
3. Clinical Trials Ethics Working Group

By working with the clinical trial groups that are already active in Europe, SIOPE is establishing a Clinical Trials Help Desk to provide easier access to the procedures required for running investigator-initiated trials under current European regulations and to share and build on 'best practice'. As there are several common targets between ACGT and the SIOPE platform, a discussion about opportunities of collaborative work will be launched.

Following the initial meeting between ACGT and the European Organisation for Research and Treatment of Cancer (EORTC) in December 2007, additional steps were taken aiming at officialising the collaboration and launching it in practice.

- Main Activities & Tasks worked on

See above

- Major Achievements towards planned objectives, identify main partners Involved

- Further development regarding the clinico-genomic trials, collection and sharing of data (IJB, USaar, IEO, FORTH, Philips, Custodix).
- Implementation of post-genomic analyses (SIB, USaar, IJB, IEO, UoC, FORTH, Philips, Custodix, UH, FUNDP).
- Progresses regarding the cross-platform biological data integration and analysis (IJB, FORTH, UoC, SIB).
- Promotion of post-genomic medicine (IJB, USaar, IEO, UoC, Biovista, FORTH).

- **Deviations from the project work programme, and corrective actions taken/suggested**

  None

- **List of deliverables, including due date and actual/foreseen submission date**

  D12.5 Report on the implementation of the ACGT validation trials (month 24) has been submitted on 19/05/2008
  D12.6 Review and extension of the ACGT clinical studies (T0+30) will be submitted at month 33

- **List of milestones, including due date and actual/foreseen achievement date**

  No milestones due within this reporting period

Workpackage 13 – Evaluation & Validation

- **Partner Responsible : SIB**

- **Contributing partner(s): SIB, FhG, FORTH, Philips, Siveco, UPM, UMA, LundU, UvA, INRIA, IJB, Biovista, PSNC, Custodix, ICCS, UHok, USaar, UOXF**
- **Reporting Period:** 01/02/2008 – 31/07/2008

- **Workpackage objectives and starting point of work at beginning of reporting period**

-The Workpackage has the following major objectives:

The objectives of WP13 for the reporting period are as follows:

-Formulate evaluation criteria, verification procedures and feedback report guidelines

- Coordinate local validation activities and feedback reports
- Coordinate formal usability evaluation of the ACGT platform

- Objectives during reporting period

During the reporting period the efforts in WP13 were focused on the following areas:

- Definition of a consistent set of scenes underlying the end-to-end integrated demonstrator to be shown during the review. The scenes of the demonstrator address the various technological components of the ACGT platform.
- Setup a feature-request and bug-reporting environment to inform developers of the areas in which significant improvements could be brought to the platform.
- Conduct regular testing of the platform on the basis of the end-to-end scenario designed for the review.
- Conduct usability survey of state-of-the-art tools relevant to the ACGT platform (clinical data management by clinicians, use of R in data mining, etc.) in view of the definition of the final human interface of the ACGT platform.

- Progress towards objectives

A deliverable not foreseen in the initial DoW was issued. This deliverable (D13.3) describes the various scenes to be demonstrated during the spring 2008 review of the project, keeping of a realistic clinical data-analysis scenario (the TOP trial) as guiding thread.

The feature-request and bug-reporting tool was configured and populated with an initial set of requests and bugs (http://iapetus.ics.forth.gr/ACGT_Repository/). The adequacy and usability of this tool from the viewpoint of users and developers will be assessed in the course of the reporting period.

Skype-based debugging sessions regrouping developers of the platform took place on a regular basis after the review in order to identify areas in which the platform can be

improved. Several software bugs were uncovered and fixed during these sessions. This continuous integrated-testing effort will be reconducted in the next periods.

A review of tools usability was conducted by the ACGT usability engineer. Currently the survey addresses tools as they are in use with state-of-the-art environments. Interviews were conducted with clinicians and data miners. The text resulting from these interviews is currently under discussion and will result in a new deliverable by the end of the next reporting period.

- Main Activities & Tasks worked on

See above.

- Major Achievements towards planned objectives, identify main partners Involved

- A modularized set of scenes representative of a clinical data analysis was defined, addressing all core components of the ACGT platform (SIB, FORTH, Philips, Siveco, UPM, UMA, LundU, UvA, INRIA, IJB, FhG, Biovista, PSNC, Custodix, ICCS, UHok)
- A Skype-based collaborative procedure for debugging was setup and used for the data mining aspects of the ACGT platform (SIB, FORTH, Philips, Siveco, UPM, UMA, LundU, FhG, PSNC, Custodix)
- A bug-reporting tool was setup (SIB, FORTH)
- A usability review was initiated (FhG, USaar, UOXF, SIB)

- **Deviations from the project work programme, and corrective actions taken/suggested**

The actions occurring in WP13 depend largely on the developments that take place in other WPs (notable technical WPs). Progress is in-line with the rest of the project. A rescheduling of one deliverable will be necessary to address the lack of a “user-grade” prototype of the platform.

- **List of deliverables, including due date and actual/foreseen submission date**

D13.2: Intermediate evaluation report
Due Month 30: July 2008
This deliverable is delayed due to the lack of a stable prototype of the ACGT platform usable by regular clinicians and data miners. A revised description for the contents of this deliverable will be addressed in a dedicated session during the September 2008 plenary meeting of the project.

D13.3: Specification of scenarios for the first integrated demonstrator of the ACGT platform
Due Month 27, April 2008 – has been submitted on 20/05/08
This document was delivered in due time.

- **List of milestones, including due date and actual/foreseen achievement date**

No milestones due within this reporting period.

Workpackage 14 – Training and Portal

- **Partner Responsible : SIVECO**

- **Contributing partner(s):** FORTH, INRIA, IJB, UPM, FHG, UOC, UHANN, Custodix, HealthGrid, ICCS, USAAR, FUNDP, IEO, UMA

- **Reporting Period:** 01/02/2008 – 31/07/2008

- **Workpackage objectives and starting point of work at beginning of reporting period**

-**The Workpackage has the following major objectives:**

- To develop the ACGT Portal, based on the GridSphere Portal platform that provides a grid-enabled integrated, customizable, multi-lingual, and user-friendly interface to end-users.
- To develop a uniform, grid enabled, training platform for biomedical data analysis by providing professional training tools to end-users (physicians, biologists, etc.) as to perform individual and cross-disciplinary data analysis and clinico-genomic trials design, monitoring and evaluation, thereby paving the way towards the advance of Clinico-Genomic Trials in Practice.

- Objectives during reporting period

- The integration at the interface level of the ACGT services into the ACGT Portal
- The development of online training modules and other electronic training materials to be integrated in the ACGT Portal.

- Progress towards objectives

The above objectives are the objectives of WP14 for the period until 31/07/2008. In the first 6 months of this period, we have studied and demonstrated different ways for achieving the objectives.

- Main Activities & Tasks worked on

The main activities corresponding to the reported period were:

- Integration into the ACGT Portal of the first demonstration scenario “Magnetic Pig”, including several services and partners.
- Demonstration of the first “Magnetic Pig” scenario in several workshops with a various attendance.
- Initiation of technical development of new interfaces for the ACGT services to be integrated in the ACGT Portal.
- Initiation of the development of online tutorials for different ACGT services to be exposed through the portal.

- Major Achievements towards planned objectives, identify main partners Involved

The major achievement for this period was the integration of the first ACGT demonstrator in the portal. Main partners involved were SIVECO, FORTH, FhG, Custodix, UMA, and PSNC.

- **Deviations from the project work programme, and corrective actions taken/suggested**

There were several deviations from the project work programme in what concerns the demonstration of the training modules, either online or in face-to-face workshops.

The small delay registered with these activities was determined by the need to wait for the ACGT services to reach a certain state of development, in which they are ready to be exposed and demonstrated to the ACGT users.

This delay will be covered in the next 6 months by focusing on the training related activities. A workgroup for the ACGT Portal and Training was created that has to come in the next Consortium Meeting with a plan for accelerating the delivery of demonstrations and training to ACGT users.

- **List of deliverables, including due date and actual/foreseen submission date**

D14.3 Demonstration and Report of training modules, due and submitted on Month 21, was rejected. The deliverable has to be resubmitted in Month 34.

- **List of milestones, including due date and actual/foreseen achievement date**

No milestones due within this reporting period.

Workpackage 15 - Dissemination

- **Partner Responsible : HEALTHGRID**

- **Contributing partner(s):** ERCIM FORTH, INRIA, UvA, Philips, IJB, SIB, LundU, UMA, UPM, FHG, BIOVISTA, UOC, UHANN, PSNC, Custodix, ICCS, USAAR, SIVECO, FUNDP, UH, UOXF, UHok, IEO

- **Reporting Period:** 01/02/2008 – 31/07/2008

- **Workpackage objectives and starting point of work at beginning of reporting period**

-The Workpackage has the following major objectives:

This six monthly dissemination summary outlines the WP15 work and process during the reporting period. Our WP's objective is to spread the projects' results all over the world and widely in Europe in order to inform and to attract different communities.

- Objectives during reporting period

The main objectives that had to be achieved were to go on improving the external project image using and/or developing specific dissemination tools (flyers, poster, etc).

- Progress towards objectives

Significant improvement has been made on the external ACGT website to differentiate target and to complete the several contents.

There was a general tendency of augmentation in the number of conference participation, organisation of workshops and exhibitions from ACGT collaborators.

- Main Activities & Tasks worked on

The ACGT website

The ACGT website has been revised including six different parts corresponding to each target: medical professionals, researchers, industry, patients, regulatory bodies and general public. Work is achieved concerning the design and in progress along with the collection of information for four different parts: take action, research (regulatory bodies), simulator (regulatory bodies), and dialog procedure for nephroblastoma (patient/general public).

Flyers

Flyers were produced to highlight different aspects of the multidisciplinary work carried out in ACGT.

- Oncosimulator
- Medical professionals

Poster

A general poster has been created to introduce the ACGT project during events like the EBCC-6 or the UICC 2008 in Geneva.

Newsletter

The first newsletter has been published in November 2007 and the second edition of the ACGT newsletter has been edited in spring 2008 (May). The aim of this communication tool is to introduce the important opportunities for the ACGT participants and external persons to obtain updated information concerning the project.

Conferences

ACGT participated to the EBCC-6 Conference in Berlin allowing a workshop during a half day. Details on conferences can be found in the conferences table – part 5 of this report

Publications

All project teams have been invited and encouraged to use scientific publication as an additional vector to convey ACGT information and to promote the research undertaken. The list of publications is to be found in section 5 of the present document.

- **Major Achievements towards planned objectives, identify main partners Involved**

The major activities achieved are the revised website and the attendance to the EBCC-6 in Berlin
Other important efforts have been spent on the dissemination (tools flyers, posters...) to introduce in a general manner the ACGT project:

To be successful all partners gave us some important information concerning ACGT technical aspects.

- **Deviations from the project work programme, and corrective actions taken/suggested**

The idea was to organise an ACGT conference which would gather people from many different backgrounds (from medical to technical people) on a same place and same time to discuss about and spread tools and technology. It might have however presented some risks. Therefore it has been decided to better meet professionals in their own conferences, and to be where they expect to meet the project members able to explain and introduce the advances.
Moreover, the “Editorial Board” prepared some content material for some dissemination tools, like the poster or the website. Yet, due to lack of other technical content, some dissemination vectors still lack of content and/or have been slightly delayed.

- **List of deliverables, including due date and actual/foreseen submission date**

  D15.4: Organisation and Report of a Project Conference – due at Month 24, has been submitted on 16/03/08.
  D15.5: Revised Dissemination Plan has been submitted on 13/05/08

- **List of milestones, including due date and actual/foreseen achievement date**

  No milestones due within this reporting period.

Workpackage 16 – Market Investigation & Exploitation

- **Partner Responsible : BIOVISTA**

- **Contributing partner(s):** ERCIM, PHILIPS, UPM, FHG, SIVECO, FUNDP

- **Reporting Period:** 01/02/2008 – 31/07/2008

- **Workpackage objectives and starting point of work at beginning of reporting period**

-**The Workpackage has the following major objectives:**

To identify, organize and exploit the results of the project. Supporting fo this it also has the following objectives:

- create all necessary supporting materials and resources
- plan and implement appropriate promotion actions
- build appropriate relationships with interested stakeholders

- Objectives during reporting period

Deliver version 2 of the Exploitation Plan (EP), develop exploitation materials and implement planned actions for the period.

- Progress towards objectives

- Version 2 of the EP was delivered in March 2008 in preparation for the 2nd Review meeting.
- Issue 2 of the ACGT Newsletter was released in May 2008. Work on Issue 3 began.
- Preliminary discussions regarding the development of one or more ACGT project videos

- Main Activities & Tasks worked on

Task 16.2: Exploitation Plan

- Major Achievements towards planned objectives, identify main partners Involved

Publication of ACGT Newsletter 2 (USAAR, UHANN, PSC, BIOVISTA, IEO, FORTH, FHG, HEALTHGRID)
A number of meetings have been held in Athens and Heraklion involving Biovista, FORTH and a group of professional video producers and screenplay writers. Initial parameters concerning the target audience, main message, duration, goal and main storyline of the ACGT video have been discussed. This is new and ongoing task that is expected to last until the end of the project.

New supporting materials (technical documents, user manuals, tutorials etc) have been produced and/or updated as the related software itself evolves. (BIOVISTA)

- **Deviations from the project work programme, and corrective actions taken/suggested**

No deviations occurred. Newsletter issue 3 delayed by 1 month.

- **List of deliverables, including due date and actual/foreseen submission date**

No deliverables due within this reporting period.

- **List of milestones, including due date and actual/foreseen achievement date**

No milestones due within this reporting period.

4 Consortium Management

➢ Project Meetings *(including WP technical meetings)*

Title	Place and Date	Main conclusions
Consortium Meeting Milan 2008	05.02.2008 – 07.02.2008	Consortium Meeting and Preparation for the project review
VO Management workshop	Merelbeke, Belgium, 27/3/2008	Merged different VO management viewpoints
ACGT Technical Meeting	Berlin, Germany, 14 April 2008	Organization and preparation for the next review's demonstrator. The minutes are available at https://bscw.ercim.org/bscw/bscw.cgi/d421856/ACGT_Berlin_TM_Minutes.doc
Integration Meeting	Eindhoven, 8. / 9.5. 2008	Integration meeting for the next review's demonstrator. Preparation of technical environment for review. Provided and fixed mappings.
ACGT Review Meeting	Eindhoven, Netherlands, 27-28 May 2008	Second ACGT review
WP10-WP11WPL meeting	Brussels, Belgium 09/07/2008	Work Package Leader meeting: synchronisation on joint tasks. Discussions on joint paper.
Meeting concerning genomic EHR	Crete, Greece, July 2008	Discussions at FORTH concerning the data model for genomic EHR. Interviews.
Meeting concerning use scenarios	Eindhoven, Netherlands, January 2008	Discussions about scenarios for data access services and for genomic data in EHR
Clinical Workshop at CHUV	Lausanne, Switzerland, July 2008	Discuss the use of ACGT tools and services

➢ Local meetings:

Title	Place and Date	Main conclusions
TMC tele-conference meeting	20/02/2008	Technical (security) issues discussed and solved.
TMC tele-conference meeting	12/03/2008	Technical (security) issues discussed and solved.
TMC tele-conference meeting	30/04/2008	Technical (security) issues discussed and solved.
TMC tele-conference meeting	14/05/2008	Technical (security) issues discussed and solved.
TMC tele-conference meeting	16/05/2008	Technical (security) issues discussed and solved.
TMC tele-conference meeting	20/05/2008	Technical (security) issues discussed and solved.
TMC tele-conference meeting	04/06/2008	Technical (security) issues discussed and solved.
TMC tele-conference meeting	09/07/2008	Technical (security) issues discussed and solved.
TMC tele-conference meeting	23/07/2008	Technical (security) issues discussed and solved.
ObTiMA and Trial Outline Builder	Homburg, 1st – 3rd February	Meeting with Micke Kuwahara and Jun Fujima from Hokaido University and Norbert Graf, Alexander Hoppe from UdS and Fatima Schera and Gabriele Weiler from Fraunhofer St. Ingbert to coordinate the work for the Trial Outline Builder
Ontology and ObTIMA workshop	Homburg, 15th of February	Coordination in the development of the Ontology for ObTiMA, Meeting between UdS and IFOMIS
Integration of ObTiMA into the ACGT grid environment	St Ingbert, Germany - 20th of February	Integration of ObTiMA into the ACGT grid environment by using OGSA DAI services
Workshop with I-BFM-ALL (International ALL Studyof the BFM Group)	Hannover, 5th of March	Presentation of ACGT and ObTiMA to other clinicians in search for an IT infrastructure. There is big interest in using the ACGT infrastructure for their clinicogenomic research in ALL
GPOH Strukturtagung	Hannover, 17th – 18th of April	Presentation of ObTiMA to the German Paediatric Oncologists, dissemination activity, great interest in ObTiMA, new clinico-genomic trials in the German Paediatric Oncology want to use ObTiMA for future trials (e.g. Rhabdoid tumour Registry 2008, Stem cell transplantation Registry)
Workshop with LESS (Long Effect surveillance Study)	Homburg, 23rd of April	Discussion about the use of ObTiMA for analysing cardiotoxicity in the SIOP Wilms Tumour trial of GPOH
GPOH Meeting	Berlin, 16th – 17th of May	Multiple discussions with Paediatric Oncologists and chairmen of clinical trials regarding ObTiMA for upcoming clinical trials in Paediatric Oncology in Germany; dissemination activity done by Norbert Graf
Meeting of the IT Group for Stem cell transplantation of the German Paediatric Oncology Society (GPOH)	Frankfurt, 17th of June	Discussion of ACGT and ObTiMA for the use in clinical trials regarding Stem cell transplantation in childhood in Germany
ACGT Video production meeting 1	Heraklion 26 June 2008	First meeting to explore possibility to create project video
Development of ObTiMA	2 th July 2008 - University clinics in Homburg, Germany	Web design and Layout of ObTiMA
ACGT Video production meeting 2	Athens, BIOVISTA Inc. 21 July 2008	Discussion of main parameters of video: goal, target group, scenario, etc.

5 Use and Dissemination

➢ Conferences and/or Workshops organised/foreseen by the project

Dates	Name	Participant profiles	Type	Number of Particip	ACGT Partner responsible /involved
La Petite Pierre, France	Conference of "Medizinisch Juristischer Arbeitskreis des Saarlandes"	People from legislation, clinicians, researchers	Local conference	~15	Norbert Graf, UdS
Chamonix, France, 12th – 13th of March	SIOP Nephroblastoma Conference	Clinicians, Researchers	International Conference	~100	Norbert Graf, UdS
April 10th and 11th 2008	"Personal data and anonymity: a try at giving a new approach", European Association of Health Law, Edinburgh	Lawyers, physicians	International conference – founding conference	Approximately 120	FUNDP (poster)
Berlin, Apr.14th – 19th, 2008	ACGT (Advancing Clinico-Genomic Trials) Workshop at the European Breast Cancer Conference 6 (EBCC 6)	Clinicians, Researchers	International	~50	Manolis Tsiknakis, Christine Desmedt, Thierry Sengstag, Norbert Graf, Regine Kollek, Mathias Brochhausen, Georgios Stamatakos, Francesca Buffa, Brecht Claerhout
15. April 2008	6th European Breast Cancer Conference (EBCC6), Workshop "Advancing Clinico Genomic Trials on cancer: open grid services for improving medical knowledge discovery", Berlin/Germany	Physicians, Data protection specialists, lawyers, ethicians, molecular biologists	Conference	200	LUH (presentation), UH (presentation)
Hannover, 17th – 18th of April	GPOH Strukturtagung	German Paediatric Oncologists	Meeting	N.N.	Norbert Graf, UdS
17-18 April 2008	"Genomic & Society", Amsterdam/Netherlands	Data protection specialists, lawyers, computer scientists, physicians, ethicians, molecular biologists, social scientists	International conference		UH (poster presentation)
Milano, 28th – 29th of April	SIOP Nephroblastoma Study conference				
1-3 May 2008	„Translating Ethical, Legal and Social Implications of Genomic Research", Cleveland/USA	Data protection specialists, lawyers, computer scientists, physicians, social scientists, ethicians, molecular biologists	International Conference	Approximately 300	UH (abstract accepted)
Aleppo, Syria- 4th – 7th of May	German Syrian Medical Conference				
May 6th – 8th 2008	"How to deal with legal aspects in the deployement of e-health in Europe?", 6th High Level Conference on eHealht : eHealth without frontiers (invited by the Solvenian Presidency)	General	International conference	300	FUNDP
16th – 17th of May, Berlin	GPOH Meeting Berlin	Paediatric Oncologists	Meeting	N.N.	Norbert Graf, UdS
June 2nd – 3rd 2008	"Le défi toujours plus grand de la responsabilité médicale : réponses nationales et européennes?, Conseil de l'Europe, Strasbourg, France.	Lawyers, physicians, academics	International conference	80	FUNDP (presentation)
Jyväskylä, Finland, June 17-19, 2008	21st IEEE International Symposium on Computer-Based Medical Systems	Medical Informatitions,Clincial users	International		Mathias Brochhausen (IFOMIS)

Heraklion, Crete17-20/06/2008	"FIDIS INTERDISCIPLINARY DOCTORAL CONSORTIUM JOINT EVENT WITH ACGT PROJECT" / "IDENTITY OF THE MIND, BODY AND SPIRIT",	Keynote speaker	Interdisciplinary Doctor Consortium	20+	Custodix
June 19th and 20th 2008	"Protection of personal data in the field of clinical research : a comparative approach", colloque européen organise par l''Espace Ethique Méditerranéen et le Réseau européen d'Excellence TEDDY « Ethique et Recherche Clinique en Pédiatrie en Europe ».	General	International conference	60	FUNDP (with Professor Duguet, Toulouse) (presentation)
June 27th	Nano2Life Conference	Bio/nano researchers, international	conference	Approx. 90	FORTH /Biovista
Edinburgh (UK) - June 29 – July 5	European conference on Mathematical and Theoretical Biology	Researchers	International conference	~400	A d'Onofrio
July 2008	Université européenne d'été de la santé et éthique biomédicale; Toulouse (France) and Cracovia (Poland)	General public	Summer university	50	FUNDP
July 1st	Knowledge and data Management - Univ. of Aegean	Graduate students,	Summer School	15	Biovista
July 4th	"Data protection audit in biobanks: Pre-conditions, criteria, procedures", Kiel/Germany	Data protection specialists, lawyers, computer scientists, physicians, ethicians, molecular biologists, social scientists	Workshop	about 60	UH (organization, presentation)
Lausanne, 21st of July	ACGT Workshop	Clinicians, IT people, researchers	Conference	~15	Thierry Sengstag / Norbert Graf, Anca Bucca, etc…

➢ Scientific publications

Date and Type	Details
15.04.08, Invited talk	Brochhausen Mathias (2008) The ACGT Master Ontology on Cancer: a necessary tool to cover semantics on clinical trials on cancer. ACGT (Advancing Clinico-Genomic Trials) Workshop, European Breast Cancer Conference 6 (EBCC 6), Berlin, Germany, April 15, 2008.
16.05.08, Congress talk	Brochhausen M, Brochhausen C, Kirkpatrick CJ (2008) Using Formal Ontology in Analyzing Complex Systems in Pathology - Data Integration and Standardization. 92. Jahrestagung der Deutschen Gesellschaft für Pathologie e.V., May 16, Berlin, Germany.
25-28 May; Conference; oral communication	A. Anguita, L. Martín, J. Crespo, M. Tsiknakis, *"An Ontology Based Method to Solve Query Identifier Heterogeneity in Post-Genomic Clinical Trials",* Proceedings of the 21st International Congress of the European Federation for Medical Informatics (MIE2008). May 25-28, 2008, Göteborg (Sweden). pp. 3-8.
17-19 June; Confence; oral communication	A. Anguita, D. Pérez-Rey, J. Crespo, V. Maojo, "Automatic Generation of Integration and Preprocessing Ontologies for Biomedical Sources in a Distributed Scenario", 21st International Symposium on Computer-Based Medical Systems (CBMS2008). June 17 19, 2008, Jyväskylä (Finland). pp. 336-341
18.06.08, Congress talk	Brochhausen Mathias, Weiler Gabriele, Cocos Cristian, Stenzhorn Holger, Graf Norbert, Doerr Martin, Tsiknakis Manolis (2008) The ACGT Master Ontology on Cancer - a New Terminology Source for Oncological Practice, IEEE CBMS 2008: 21st IEEE International Symposium on Computer-Based Medical Systems, Jyväskylä, Finland, June 17-19, 2008.
16.07.08, Invited talk	Brochhausen M (2008) Biomedical Ontologies: Principles and Perspectives of Exploitation – A critical review. Special Session on Personalised Medicine: Current Trends and Scientific Challenges, TEMU 2008, International Conference on Telecommunications and Mutlimedia, Ierapetra, Greece, 16.07.2008.
Conference; accepted	L. Martín, A. Anguita, A. Jiménez, J. Crespo, "*Enabling Cross Constraint Satisfaction in RDF-based Heterogeneous Database Integratio* n", 20th IEEE Int'l Conference on Tools with Artificial Intelligence (ICTAI 2008) (Accepted)
Conference; accepted	Stamatakos, G, The "Clinical Oncosimulator": a multilevel, four dimensional, clinically oriented, patient specific simulation system for cancer therapy optimization," lecture given in the European Breast Cancer Conference (EBCC-6) , Berlin, Germany, 15-19 April 2008
March 2008, paper	Stelios Sfakianakis, Norbert Graf, Alexander Hoppe, Stefan Rüping, and Dennis Wegener. Building a System for Advancing Clinico-Genomic Trials on Cancer, accepted for publication at ICSOFT 2008
International Conference "Genomic & Society", 17-18 April 2008, Amsterdam/Netherlands	Imme Petersen/Regine Kollek: "Disclosure and confidentiality in clinico-genomic research: Patients' attitudes and perspectives towards Individual Donor Feedback" (poster, awarded the prize of the audience and the jury in the poster competition)
International Conference „Translating Ethical, Legal and Social Implications of Genomic Research", 1-3 May 2008, Cleveland/USA	Imme Petersen/Regine Kollek: "Disclosure and confidentiality in clinico-genomic research. Patients' attitudes and perspectives towards individual donor feedback" (abstract)

UK e-Science 2008 All Hands Meeting, 8-11 September, Edinburgh/UK	Arning, Marian/Forgó, Nikolaus/Kruegel, Tina: "Data protection in grid-based multicentric clinical trials: killjoy or confidence-building measure?" (abstract)
International Conference "The Rights of Children in Medicine", 9-10 October 2008, Goettingen/Germany	Imme Petersen/Regine Kollek: "Facing the challenges of tissue-based research: An empirical survey on parents' attitudes and needs regarding informed consent and data protection" (abstract)
October 2008, Conference	"The need for integration of genomic information in a future EHR: an ACGT case study", A. Bucur (Philips), D. Kafetzopoulos (FORTH), V. Danilatou (FORTH), A. Persidis (Biovista), M. Tsiknakis (FORTH, L.Koumakis (FORTH), 9th International Interoperability Conference.
2008, Conference paper	Brochhausen Mathias, Weiler Gabriele, Cocos Cristian, Stenzhorn Holger, Graf Norbert, Doerr Martin, Tsiknakis Manolis (2008) The ACGT Master Ontology on Cancer - a New Terminology Source for Oncological Practice, In: Puuronen S, Pechenizkiy M, Tsymbal A, Lee DJ (eds.): Proceedings of the 21st IEEE International Symposium on Computer-Based Medical Systems, IEEE Computer Society, Los Alamitos, 324-329.
2008, Conference paper	D.D.Dionysiou, G. S.Stamatakos, D. Gintides, N. Uzunoglu, K. Kyriaki, "Critical Parameters Determining Standard Radiotherapy Treatment Outcome for Glioblastoma Multiforme: A Computer Simulation", *The Open Biomedical Engineering Journal*, accepted with minor revisions
2008, Conference paper	E. A. Kolokotroni, G. S. Stamatakos, D. Dionysiou, E. Ch. Georgiadi, C. Desmedt, N Graf, "Translating Multiscale Cancer Models into Clinical Trials: Simulating Breast Cancer Tumor Dynamics within the Framework of the "Trial of Principle" Clinical Trial and the ACGT Project," accepted to be published as an 8 page full paper in *Proceedings of the 8th IEEE International Conference on Bioinformatics and Bioengineering*, Athens, Greece, 8-10 October 2008
2008, Conference paper	E. Ch. Georgiadi, G. S. Stamatakos, N. M. Graf, E. A. Kolokotroni, D. D. Dionysiou, A. Hoppe, N. K. Uzunoglu, "Multilevel Cancer Modeling in the Clinical Environment: Simulating the Behavior of Wilms Tumor in the Context of the SIOP 2001/GPOH Clinical Trial and the ACGT Project"accepted to be published as an 8 page full paper in *Proceedings of the 8th IEEE International Conference on Bioinformatics and Bioengineering*, Athens, Greece, 8-10 October 2008
Conference; pending approval	D. Wegener, T. Sengstag, S. Sfakianakis, and S. Rüping, "*Supporting parallel R code in clinical trials: a grid-based approach* ", submitted to the International Symposium on Parallel and Distributed Processing and Applications (ISPA 2008) - Workshop on High Performance and Grid Computing in Medicine and Biology (HiPGCoMB)
May 2008, Journal publication	Arning, Marian/Kruegel, Tina/Petersen, Imme: Erbgut gut – alles gut? in: Technikfolgenabschätzung – Theorie und Praxis 2008, pp. 122-126
June 2008, journal paper	Dennis Wegener; Thierry Sengstag; Stelios Sfakianakis; Stefan Rueping; Anthony Assi. GridR: An R-based tool for scientific data analysis in grid environments, submitted in June to FGCS
June 2008, paper	Dennis Wegener, Dirk Hecker, Christine Körner, Michael May and Michael Mock. Parallelization of R-programs with GridR in a GPS-trajectory mining application, submitted in June to UKD08@ECML/PKDD 2008

June 2008, paper	Brochhausen Mathias, Weiler Gabriele, Cocos Cristian, Stenzhorn Holger, Graf Norbert, Doerr Martin, Tsiknakis Manolis (2008) "The ACGT Master Ontology on Cancer - a New Terminology Source for Oncological Practice" in Proceedings of the 21st IEEE International Symposium on Computer-Based Medical Systems, Jyväskylä, Finland, June 2008
July 2008, paper	Natalja Punko, Stefan Rüping, Stefan Wrobel, "Facilitating Clinico-Genomic Knowledge Discovery by Automatic Selection of KDD Processes", Workshop on Machine Learning in Healthcare Applications at the International Conference on Machine Learning, Helsinki, Finland
July 2008, Internet publication	Arning, Marian/Kruegel, Tina/Petersen, Imme - Tagungsrezension "Genetische Daten zwischen Ethik, Recht und personalisierter Medizin" available at: http://dests.de/wp-content/uploads/2008/07/arning_krugel_petersen_ta_ende.pdf
Poster presentation at the European Breast Cancer Conference, Berlin, April 2008	Desmedt C, Giobbie-Hurder A, Neven P, Paridaens R, Christians MR, Smeets A, Lallemand F, Gelber R, Piccart M, Sotiriou C for the BIG 1-98 Collaborative Group and International Breast Cancer Study Group (IBCSG). The Gene expression Grade Index: a potential predictor of relapse for endocrine-treated breast cancer patients in the BIG 1-98 trial.
Poster presentation at the American Society of Clinical Oncology Meeting, Chicago-Illinois 2008.	Desmedt C, Azambuja E, Larsimont D, Delaloge S, Duhem C, Rouas R, Di Leo A, D'Hondt V, Piccart M, Sotiriou C on behalf of the investigators of the TOP trial. Investigating the predictive value of topoisomerase II alpha (TOP2A) gene, mRNA and protein levels in anthracycline-treated estrogen receptor (ER) negative breast cancer patients.
Poster presentation at the American Society of Clinical Oncology Meeting, Chicago-Illinois 2008.	Symmans WF, Hatzis C, Liedtke C, Desmedt C, Valero V, Kuerer M, Hortobagyi GN, Piccart-Gebhart M, Pusztai L, Sotiriou C. Use of genomic grade index (GGI) to predict pathologic response to preoperative chemotherapy in breast cancer.
Poster presentation at the American Society of Clinical Oncology Meeting, Chicago-Illinois 2008.	Sotiriou C, Equeter C, El Ouriaghli F, Haibe-Kains B, Durbecq V, Larsimont D, Igniatiadis M, Desmedt C, Willard-Gallo K, Piccart M. Gene expression analysis of tumor infiltrating CD4+ cells reveals differences in immune function and survival benefit according to different breast cancer (BC) molecular subtypes.
April 2008, Publication	Schenk JP, Graf N, Günther P, Ley S, Göppl M, Kulozik A, Rohrschneider WK, Tröger J.: Role of MRI in the management of patients with nephroblastoma. Eur Radiol 18:683-691, 2008
May 2008, Publication	Loi S, Haibe-Kains B, Desmedt C, Wirapati P, Lallemand F, Tutt AM, Gillet C, Ellis P, Ryder K, Reid JF, Daidone MG, Pierotti MA, Berns EM, Jansen MP, Foekens JA, Delorenzi M, Bontempi G, Piccart MJ, Sotiriou C. Predicting prognosis using molecular profiling in estrogen receptor-positive breast cancer treated with tamoxifen. BMC Genomics 9:239, 2008.
May-June 2008, Publication	Zils K, Furtwänler R, Reinhard H, Alkassar M, Graf N: Consultation within SIOP 2001/GPOH as part of the competence centre for nephroblastoma. Klin Pädiatr 220:183-188, 2008
June 2008, Publication	van den Heuvel-Eibrink MM, Grundy P, Graf N, Pritchard-Jones K, Bergeron C, Patte C, Peter E, van Tinteren H, Rey A, Hutton C, Anderson JR, de Kraker J: Characteristics and survival of 750 children diagnosed with a renal tumor in the first seven months of life: A collaborative study by the SIOP/GPOH/SFOP, NWTSG, and UKCCSG Wilms tumor study groups.. Pediatr Blood & Cancer 50:1130-1134, 2008

June 2008, Publication	Wetli SC, Leuschner I, Harms D, Rufle A, Foerster A, Bihl M, Graf N, Furtwaengler R, Paulussen M, Briner J, Tornillo L, Mihatsch MJ, Zlobec I, Bruder E: KIT, PDGFRa and EGFR Analysis in Nephroblastoma. Virchow Archiv 452:637-650, 2008
July 2008, Publication	Royer-Pokora B, Weirich A, Schumacher V, Uschkereit C, Beier M, Leuschner I, Graf N, Autschbach F, Schneider D, von Harrach M: Clinical relevance of mutations in the Wilms tumor suppressor 1 gene WT1 and the cadherin-associated protein ß1 gene CTNNB1 for patients with Wilms tumors. Results of long-term surveillance of 71 patients from International Society of Pediatric Oncology Study 9/Society for Pediatric Oncology. Cancer accepted, 2008
July 2008, Publication	Haibe-Kains B, Desmedt C, Sotiriou C, Bontempi G. A comparative study of survival models for breast cancer prognostication based on microarray data: does a single gene beat them all? Bioinformatics. 2008
July 2008, Publication	Durbecq V, Ameye L, Veys I, Paesmans M, Desmedt C, Sirtaine N, Sotiriou C, Bernard-Marty C, Nogaret JM, Piccart M, Larsimont D. A significant proportion of elderly patients develop hormone-dependant "luminal-B" tumours associated with aggressive characteristics. Crit Rev Oncol Hematol 67:80-92, 2008.
Publication	A d'Onofrio, A. Gandolfi and A. Rocca "The cooperative and nonlinear dynamics of tumor-vasculature interaction suggests low-dose, time-dense antiangiogenic schedulings" in press on *Cell Proliferation*
Publication	A. d'Onofrio and P. Cerrai "A bi-parametric phenomenologic model for the tumor angiogenesis and anti-angiogenesis therapy". In press on *Mathematical and Computer Modelling* (PDF available at Elsevier Website: http://dx.doi.org/10.1016/j.mcm.2008.05.001)
Publication	Fuchs J, Kienecker K, Furtwängler R, Bürger D, Thüroff JW, Hager J, Graf N: Surgical Aspects in the treatment of patients with unilateral Wilms´ tumor – a report by the SIOP 93-01/ German Society of Pediatric Oncology and Hematology, Ann Surg accepted 2008
Publication	Furtwängler R, Schenk JP, Alkassar M, Leuschner I, Rübe C, von Schweinitz D, Gessler M, Graf N: Das Nephroblastom und andere pädiatrische Nierentumoren. Pädiat Prax 72:59-77, 2008
Publication	Georgiadi ECh, Stamatakos GS, Graf NM, Kolokotroni EA, Dionysiou DD, Hoppe A, Uzunoglu NK, Senior Member IEEE: Multilevel Cancer Modeling in the Clinical Environment: Simulating the Behavior of Wilms Tumor in the Context of the SIOP 2001/GPOH Clinical Trial and the ACGT Project. IEEE BIBE (Bioinformatics and Bioengineering Conference), Athens, Greece, 8 –10 October 2008
Publication	J. HERVEG, "Theory of risks and processing of medical data in Healthgrids in European Law", in J. HERVEG (éd.), *La protection des données médicales. Les défis du XXIe siècle - The protection of medical data. Challenges of the 21st century*, Anthémis et L.G.D.J., 2008, pp. 183-205.
Publication	J. HERVEG, « Panorama des responsabilités liées aux services et produits de la santé en ligne en droit européen », in A.-M. DUGUET, I. FILIPPI et J. HERVEG (éd.), *Evolution récente des actions en responsabilité médicale en France. Comparaison avec l'étranger* , Bordeaux, Les éditions hospitalières, 2008, p. 69-118.
Publication	Kolokotroni EA, Stamatakos GS, Dionysiou DD, Georgiadi ECh, Desmedt Ch, Graf NM: Translating Multiscale Cancer Models into Clinical Trials: Simulating Breast Cancer Tumor Dynamics within the Framework of the "Trial of Principle" Clinical Trial and the ACGT Project. IEEE BIBE (Bioinformatics and Bioengineering Conference), Athens, Greece, 8 –10 October 2008
Publication	Reinhard H, Schmidt A, Furtwängler R, Leuschner I, Rübe C, von Schweinitz D, Zoubek A, Niggli F, Graf N: Outcome of relapses of nephroblastoma in patients registered in the SIOP/GPOH trials and studies. Oncology Reports 20:463-467, 2008

Publication	Royer-Pokora B, Weirich A, Schumacher V, Uschkereit C, Beier M, Leuschner I, Graf N, Autschbach F, Schneider D, von Harrach M: Clinical relevance of mutations in the Wilms tumor suppressor 1 gene WT1 and the cadherin-associated protein ß1 gene CTNNB1 for patients with Wilms tumors. Results of long-term surveillance of 71 patients from International Society of Pediatric Oncology Study 9/Society for Pediatric Oncology. Cancer accepted, 2008
Publication	Smith B, Brochhausen M: Establishing and Harmonizing Ontologies in an Interdisciplinary Health Care and Clinical Research Environment. Blobel B, Pharow P, Nerlich M (eds.): *eHealth: Combining Health Telematics, Telemedicine, Biomedical Engineering and Bioinformatics on the Edge* . IOS Press: Amsterdam, 219-34, 2008.
Publication	Tsiknakis Manolis, Brochhausen Mathias, Nabrzyski J., Pucaski L, Potamias G., Desmedt C., Kafetzopoulos D: A semantic grid infrastructure enabling integrated access and analysis of multilevel biomedical data in support of post-genomic clinical trials on Cancer. In: IEEE Trans Inf Technol Biomed. Mar;12(2):205-17, 2008
Publication	Urszula Ledzewicz, Heinz Schaettler and Alberto d'Onofrio, "Optimal Control for Combination Therapy in Cancer". In press on *Proceedings of the 47th IEEE Conference on Decision and Control*
Publication	Zils K, Furtwänler R, Reinhard H, Alkassar M, Graf N: Consultation within SIOP 2001/GPOH as part of the competence centre for nephroblastoma. Klin Pädiatr 220:183-188, 2008
ACGT-Newsletter Volume 2	Imme Petersen/Regine Kollek: "Do patients want feedback of data from clinico-genomic research?

6 Disseminated Project Results

The project has organised a number of dissemination related activities and events. Specifically it organised dissemination related scientific sessions at:

a) The HEALTHINF 2008 conference, Madeira, Canary Islands, Portugal, 28-31 January 2008.
b) The European Breast Cancer Conference Berlin, (EBBC6, April 2008).
c) Lausanne University Hospital (CHUV) (July 2008).

During these events a range of ACGT technologies were disseminated. These include:

Description	**Details**
SW prototype	First release of ObTiMA (Ontology based Trial Management System for ACGT)
SW prototype	Data Access services to the BASE database
SW prototype	Generic OGSA-DAI activity that delivers query results to the Gridge Data Management System
SW prototype	The Custodix Anonymization tool (ACGT)
SW prototype	The ACGT MO
SW prototype	The ACGT Mediator
SW prototype	The mapping tool
SW prototype	The Ontology viewer
SW prototype	The GridR (a gridified version of the R statistical package)
SW prototype	The ACGT workflow editor, enactment environment
SW prototype	The ACGT metadata repository
SW prototype	The ACGT Oncosimulator suite

7 Person Month Status Report

PERIOD: 01/02/2008	31/07/2008	TOTALS	1-ERCIM	2-FORTH	3-INRIA	4-UVA	5-PHILIPS	6-IJB	7-SIB	8-LUNDU	9-UMA	10-UPM	11-FHG	12-BIOVISTA	13-UOC	14-LUH	15-PSNC	16-CUSTODIX	17-HEALTHGRID	18-ICCS	19-USAAR	20-SIVECO	21-FUNDP	22-UH	23-UOXF-BP	24 (CPF25)-UHOK	25 (CPF 26) -IEO
Total Eligible PM	Actual total	268,9	5,5	33	7,11	12	16,7	4,64	8,5	6,99	12	22,5	19,28	17		8,49	12	10,6	12	7,98	22,3	10	6	4,75	6,31		3,25
Total Eligible Planned PM	Plan. total	279,3	9,66	28,3	8,69	7	15,3	7,33	8,33	9,33	12	22,66	16,91	20	7,33	8	14,3	9,5	15,3	7,99	12	8	6	6,66	7		11,7
Total Non eligible PM	Actual total	44,1				3		1,66							6,64	1	9,91				4,83		0,2	2	0,36	7	7,5
Total Non eligible planned PM	Plan. total	7																								7	
Total all PM	Actual total	313	5,5	33	7,11	15	16,7	6,3	8,5	6,99	12	22,5	19,28	17	6,64	9,49	21,9	10,6	12	7,98	27,2	10	6,2	6,75	6,67	7	10,8
Total all planned PM	Plan.	286,3	9,66	28,3	8,69	7	15,3	7,33	8,33	9,33	12	22,66	16,91	20	7,33	8	14,3	9,5	15,3	7,99	12	8	6	6,66	7	7	11,7

ACGT Person-Month Status Table

CONTRACT Nº: 026996
ACRONYM: ACGT
PERIOD: 01/02/2008 31/07/2008

All Partners - Eligible Person-month per Workpackage

		TOTALS	1-ERCIM	2-FORTH	3-INRIA	4-UVA	5-PHILIPS	6-IJB	7-SIB	8-LUNDU	9-UMA	10-UPM	11-FHG	12-BIOVISTA	13-UOC	14-LUH	15-P-SNC	16-CUSTODIX	17-HEALTHGRI	18-ICCS	19-USAAR	20-SIVECO	21-FUNDP	22-UH	23-UOXF.BP	24 (CPF25)-UHOK	25 (CPF 26) - IEO
WP1 - Consortium Management acti	Act. WP total:	7,08	5,25	1,00			0,30					0,20					0,33										
Project Management	Plan. P total:	8,99	6,00	1,00			0,33					0,33	1,00				0,33										
WP2 - RTD/Innovation activities	Act. WP total:	9,75				0,50	0,20	0,33	0,50			0,50	0,35	0,20			0,73			0,13	4,30				1,01		1,00
User Needs Analysis and Specificatic	Plan. P total:	9,95				0,33	0,67	0,33	0,33			0,33	0,33	0,50	0,33		1,00			0,13	2,67	0,33		0,33	0,67		1,67
WP3 - RTD/Innovation activities	Act. WP total:	8,80		1,50			1,50					1,00	1,00				2,50	1,00		0,30							
Architecture and Standards	Plan. P total:	9,64		1,67			1,00					2,00	0,67				3,00	1,00		0,30							
WP4 - Demonstration activities	Act. WP total:	0,75															0,75										
Biomedical GRID technology Layer	Plan. P total:	2,65		0,66							0,33						1,33					0,33					
WP4 -RTD/Innovation activities	Act. WP total:	10,66		1,00	0,50						1,33		0,50	2,00			3,00			0,33		2,00					
Biomedical GRID technology Layer	Plan. P total:	9,49		0,66	0,50						1,00		2,00				4,00			0,33		1,00					
WP5 - Demonstration activities	Act. WP total:	2,00					2,00																				
Distributed Data Access, Tools and A	Plan. P total:																										
WP5 - RTD/Innovation activities	Act. WP total:	26,92		3,00			9,00	0,33	0,50	1,33		1,50	2,50	1,00			1,00			0,80	5,54				0,42		
Distributed Data Access, Tools and A	Plan. P total:	21,01		1,67	1,22		8,66	0,67		1,33	0,33	2,00	1,33	1,00	0,67					0,80	0,66				0,67		
WP6 - Demonstration activities	Act. WP total:																										
Knowledge Management and Discov	Plan. P total:																										
WP6 - RTD/Innovation activities	Act. WP total:	32,96		5,00	1,61	0,75			2,00	4,00	5,00	4,00	4,00	5,00											1,35		0,25
Knowledge Management and Discov	Plan. P total:	33,12		3,00	1,61	0,67			2,00	4,00	4,67	4,00	2,67	4,50											2,00		4,00
WP7 - Demonstration activities	Act. WP total:																										
Ontologies and Semantic Mediation `	Plan. P total:																										
WP7 - RTD/Innovation activities	Act. WP total:	34,71		3,00			1,20	0,33		1,00	0,67	11,00	4,61	3,30							9,39				0,21		
Ontologies and Semantic Mediation `	Plan. P total:	27,18		4,00			1,67	0,67	0,67	2,34	0,67	8,00	1,67	3,50	0,33						3,33				0,33		
WP8 - Demonstration activities	Act. WP total:	0,92				0,75														0,17							
Technologies and Tools for in-silico (	Plan. P total:	0,84				0,67														0,17							
WP8 - RTD/Innovation activities	Act. WP total:	22,11		4,00	4,00	6,00		0,33					3,35							3,83	0,60						
Technologies and Tools for in-silico (	Plan. P total:	15,91		2,00	3,41	3,00		0,33					0,67							3,83	0,67						2,00
WP9 - Demonstration activities	Act. WP total:	2,61		1,00							1,00	0,30	0,31														
The integrated ACGT Environment	Plan. P total:	3,49		1,33		0,33	0,66					0,67		0,50													
WP9 - RTD/Innovation activities	Act. WP total:	22,16		7,00		2,00	1,20		1,00	0,33	2,00	2,00		2,00			1,50	2,63		0,50							
The integrated ACGT Environment	Plan. P total:	20,07		6,00		1,00	0,67	0,33	0,66	0,33	3,00	1,33	0,91	2,00	0,67		1,67	1,00		0,50							
WP10 - RTD/Innovation activities	Act. WP total:	17,02						0,33								5,82		1,50			0,08		5,30	3,75	0,24		
Ethical, Legal and QA Issues	Plan. P total:	18,66						0,33							0,33	5,33		1,00			0,67		5,34	5,33	0,33		
WP11 - Demonstration activities	Act. WP total:	0,50																0,50									
Trust and Security	Plan. P total:	1,00																1,00									
WP11- RTD/Innovation activities	Act. WP total:	6,67										0,50	1,00			0,67	1,50	3,00									
Trust and Security	Plan. P total:	9,00						0,33				1,00	2,00			0,67	2,00	3,00									
WP12 - Demonstration activities	Act. WP total:																										
Clinical Trials	Plan. P total:	4,83		0,33				1,00						0,50	1,00						1,00				1,00		
WP12 - RTD/Innovation activities	Act. WP total:	12,44		3,00				2,00	1,50					0,50		0,33				0,33	0,79				1,99		2,00
Clinical Trials	Plan. P total:	15,32		2,66				2,00	1,67					1,00	2,33	0,33				0,33	1,00				1,00		3,00
WP13 - RTD/Innovation activities	Act. WP total:	8,83		0,50		1,00	0,75	0,33	2,00		0,67	0,50	0,66				0,33	1,00		0,20	0,48				0,41		
Evaluation and Validation	Plan. P total:	10,56		0,33		0,67	0,67	0,67	1,67		0,67	0,67	1,67	0,50			0,67	0,50		0,20	0,67				0,67		0,33
WP14 - Training Activities	Act. WP total:	3,15		0,50							0,33									0,08		2,00			0,24		
Training	Plan. P total:	12,27		1,00	1,50				1,00	1,00	1,00	1,33	0,67	0,50	0,67			0,33	1,00	0,60	0,67	1,00					
WP14 - RTD/Innovation activities	Act. WP total:	8,51		0,50				0,33			0,67					0,33			2,00	0,60	0,08	4,00					
Training	Plan. P total:	8,75	0,67	0,33				0,34				0,33			0,67	0,33		0,33	2,00	0,08	0,33	2,68	0,33				0,33
WP15 - RTD/Innovation activities	Act. WP total:	20,52	0,25	1,00	1,00	1,00	0,50	0,33	1,00	0,33	0,33	1,00	1,00	0,50		0,67	0,33	0,50	7,00	0,11	1,08	1,00	0,70	0,67	0,22		
Dissemination	Plan. P total:	23,19	1,66	0,33	0,45	0,33	1,00	0,33	0,33	0,33	0,33	0,67	0,66	1,00	0,33	0,67	0,33	0,67	10,33	0,12	0,33	1,33	0,33	0,67	0,33		0,33
WP16 - RTD/Innovation activities	Act. WP total:	9,82		1,00										2,50		0,67		0,50	3,00	0,60		1,00		0,33	0,22		
Market Investigation and Exploitation	Plan. P total:	13,42	1,33	1,33									0,66	4,50		0,67		0,67	2,00	0,60		1,33		0,33			
	Actual total	268,89	5,50	33,00	7,11	12,00	16,65	4,64	8,50	6,99	12,00	22,50	19,28	17,00		8,49	11,97	10,63	12,00	7,98	22,34	10,00	6,00	4,75	6,31		3,25
Total PM	Planned total	279,34	9,66	28,30	8,69	7,00	15,33	7,33	8,33	9,33	12,00	22,66	16,91	20,00	7,33	8,00	14,33	9,50	15,33	7,99	12,00	8,00	6,00	6,66	7,00		11,66

CONTRACT Nº:	026996	AC Partners - Own Staff																								
ACRONYM:	ACGT																									
PERIOD: 01/02/2008	31/07/2008	TOTALS	1-ERCIM	2-FORTH	3-INRIA	4-UVA	5-PHILIPS	6-IJB	7-SIB	8-LUNDU	9-UMA	10-UPM	11-FHG	12-BIOVISTA	13-UOC	14-LUH	15-PSNC	16-CUSTODIX	17-HEALTHGRID	18-ICCS	19-USAAR	20-SIVECO	21-FUNDP	22-UH	23-UOXF.BP	24 (CPF 25)-UHOK	25 (CPF 26) - IEO
WP1 - Consortium Management acti	Act. WP total:	0,20															0,20									
Project Management	Plan. P total:																									
WP2 - RTD/Innovation activities	Act. WP total:	6,23				0,50									0,33		0,81				1,50				0,09		3,00
User Needs Analysis and Specificati	Plan. P total:																									
WP3 - RTD/Innovation activities	Act. WP total:																									
Architecture and Standards	Plan. P total:																									
WP4 - Demonstration activities	Act. WP total:	1,00															1,00									
Biomedical GRID technology Layer	Plan. P total:																									
WP4 -RTD/Innovation activities	Act. WP total:	4,00															4,00									
Biomedical GRID technology Layer	Plan. P total:																									
WP5 - Demonstration activities	Act. WP total:																									
Distributed Data Access, Tools and /	Plan. P total:																									
WP5 - RTD/Innovation activities	Act. WP total:	7,58						0,33							0,66		1,00				0,50				0,09	5,00	
Distributed Data Access, Tools and /	Plan. P total:	5,00																								5,00	
WP6 - Demonstration activities	Act. WP total:																									
Knowledge Management and Discov	Plan. P total:																									
WP6 - RTD/Innovation activities	Act. WP total:	2,17				0,50																				0,67	1,00
Knowledge Management and Discov	Plan. P total:	0,67																								0,67	
WP7 - Demonstration activities	Act. WP total:																									
Ontologies and Semantic Mediation	Plan. P total:																									
WP7 - RTD/Innovation activities	Act. WP total:	1,09																			1,00				0,09		
Ontologies and Semantic Mediation	Plan. P total:																									
WP8 - Demonstration activities	Act. WP total:																									
Technologies and Tools for in-silico (	Plan. P total:																									
WP8 - RTD/Innovation activities	Act. WP total:	5,41				2,00															0,41					1,00	2,00
Technologies and Tools for in-silico (	Plan. P total:	0,33																								0,33	
WP9 - Demonstration activities	Act. WP total:																									
The integrated ACGT Environment	Plan. P total:																									
WP9 - RTD/Innovation activities	Act. WP total:	1,66													0,66		1,00									
The integrated ACGT Environment	Plan. P total:	0,33																								0,33	
WP10 - RTD/Innovation activities	Act. WP total:	3,31													0,33	0,50					0,19		0,20	2,00	0,09		
Ethical, Legal and QA Issues	Plan. P total:																									
WP11 - Demonstration activities	Act. WP total:																									
Trust and Security	Plan. P total:																									
WP11- RTD/Innovation activities	Act. WP total:	1,75														0,25	1,50									
Trust and Security	Plan. P total:																									
WP12 - Demonstration activities	Act. WP total:																									
Clinical Trials	Plan. P total:																									
WP12 - RTD/Innovation activities	Act. WP total:	6,12						1,00							3,33						0,54						1,25
Clinical Trials	Plan. P total:																									
WP13 - RTD/Innovation activities	Act. WP total:	0,53						0,33									0,20									
Evaluation and Validation	Plan. P total:																									
WP14 - Training Activities	Act. WP total:																									
Training	Plan. P total:																									
WP14 - RTD/Innovation activities	Act. WP total:	1,00													1,00											
Training	Plan. P total:																									
WP15 - RTD/Innovation activities	Act. WP total:	1,56													0,33	0,25	0,20				0,20					0,33	0,25
Dissemination	Plan. P total:	0,67																								0,67	
WP16 - RTD/Innovation activities	Act. WP total:	0,49																			0,49						
Market Investigation and Exploitation	Plan. P total:																									
	Actual total	44,10				3,00		1,66							6,64	1,00	9,91				4,83		0,20	2,00	0,36	7,00	7,50
Total PM	Planned total	7,00																								7,00	