



Six Monthly Progress Reports 2

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ABSTRACT:

This Deliverable presents the full range of project activities during the period from month 12 to month 18, including management activities, disseminations activities as well as technical and scientific activities in accordance to the DoW of the project.

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1 **Executive Summary**

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 the reporting period

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.

In principle, the requirements for the ACGT Platform, which have been documented during the first year of activities of the project, can be met by designing a federated environment articulating independent tools, components and resources based on open architectural standards, which is customizable and capable of dynamic reconfiguration.

An initial architectural blueprint 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 the initial architecture 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 United Kingdom.

We have adopted a scenario-based development process. A range of scenarios, i.e. the tasks users want to perform, structured and described as a sequence of activities that require access to heterogeneous data, use of various tools for data analysis and invocation of appropriate tools for visualizing and interpreting the results, have been defined by the ACGT consortium.

These scenarios cover the most important functional goals of the infrastructure. In practice the following fields are covered:

- Administrative scenarios related to the setup and maintenance of the infrastructure, such as integration of databases
- Administrative scenarios related to the management of users and institutions in the context of virtual organizations
- Technological scenarios, validating the integration of data analysis tools per-se (e.g. R) and their integration with clinical data.
- Clinical-oriented scenarios, validating the analysis tools as used by clinicians and biomedical researchers in realistic context.
- Meta-analysis scenarios, validating the use of ACGT as clinical-research validation tool.

The project has conceived an overall architecture for an integrating biomedical sciences platform. 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 the development of the core set of components up to a stage where they can effectively support in silico investigation. Initial prototypes have been useful in crystallizing requirements for semantics.

The ACGT Consortium chose ontologies as the main knowledge representation (KR) tool in order to represent the relevant parts of medical knowledge gathered along the years by

cancer researchers and clinicians involved with the theory and practice of oncology. The ACGT-MO (Master Ontology) is presented as an .owl file and is written in OWL-DL. It was built, and is being maintained / curated, using the Protégé-OWL free open-source ontology editor.

The process that gave rise to the present state of the representation of clinical reality was rather convoluted and highly elaborated, requiring multiple recurring steps and a multifaceted approach. First, actual Case Report Forms (CRF) from ACGT trials were collected and analyzed with respect to the universals (classes) more-or-less explicitly present in the information gathered. In parallel, basic aspects of cancer pathology and cancer management were studied by our researchers.

The ACGT *Data Access Architecture* is comprised by a set of key services, namely the ACGT-DAS (Data Access Service), the ACGT-SM (Semantic Mediator), and the ACGT-MO, and some additional dedicated tools. While the first two services provide the means to resolve syntactic and semantic heterogeneities when accessing heterogeneous databases, the latter acts as a core resource supporting the data integration process.

The Semantic Mediation process is realized by a set of tools that support the database integration process. The core component is the ACGT-SM, in charge of exposing the global schema, processing queries and retrieving integrated results. Its functionality is offered as a Web Service to other components—i.e. Knowledge Discovery Tools, the Workflow editor, other specific end users tool, etc. Additional components that are used for overcoming several issues in the data integration process are the Mapping Tool, the Data Cleaning module—for retrieved instances—, and the Query Preprocessing Module—for literal homogenization in queries. The project, during the reporting period, has focused on their detailed specification and initial implementation.

A case study, based on the integration of two clinical trial databases—i.e. the SIOP and the TOP databases, filled with test data (actual patient data were avoided due to privacy issues)—and a corresponding DICOM image database was performed. The sources were successfully integrated, and the schemas—i.e. the views representing the underlying databases, produced after the integration process— were validated by domain experts.

The project also recognises that the sharing of multilevel data outside the walls of a hospital or a research organisation generates complex ethical and legal issues. As a result we have devoted significant efforts to the study and analysis of the ethical and legal issues related to cross-institutional sharing of post-genomic data sets. In addition we have defined every aspect, both technical and procedural, of the required security framework. It is worth mentioning at this stage that security and privacy are active areas of research, and technologies are emerging that are fully utilised in ensuring the highest possible level of security of the ACGT platform. Based on such an approach we concluded that trust and security has been addressed at multiple levels; these include (a) infrastructure, (b) application access, (c) data protection, (d) access control, which would be policy-governed, and (e) privacy-enhancing technology, such as de-identification.

During the reporting period the project has concentrated on the implementation of a range of demonstrators, stemming from the user defined scenarios, together with these core set of components will enable us to both begin evaluation and gather additional and more concrete requirements from our users. These will allow us to improve and refine the facilities of the ACGT infrastructure and services.

Initial demonstrations were (partly) integrated and demonstrated during the first annual review of the project. Following the review, the project has begun to study in more depth the aspects of semantics and metadata, which are necessary in achieving the required degree of interoperability. Specifically the project focuses on the specification of

- standards and models for exposing web services (semantics), scientific services, and the properties of data sources, datasets, scientific objects, and data elements;

- an easy to use workflow environment, so that biomedical researchers can easily design their “discovery workflows” and execute them securely on the grid.

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.

3 Workpackage progress report over the period

Workpackage 1 - Project Management

- **Partner Responsible : ERCIM**
- **Contributing partner(s): FORTH, FhG**
- **Reporting Period: 01/02/2007 – 31/07/2007**
- **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. This activity can be subdivided in two main parts:

- (i) Administrative and Financial Coordination;
- (ii) Scientific Coordination.

- Progress towards objectives

Both lines of management were, we believe, successful in making sure that project activities develop unobstructed. The periodic scientific and technical meetings and audio-conference organised allow a tight steering of the project activities. In the meantime, the financial coordination has pursued its activities with the objective to provide all information and justification concerning the First periodic management report, including the financial statement, in order to ensure the release of the second advance payment to fuel the second work plan activities.

- 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 for its 1st PAR and annual 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 (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.

It is our belief that this has been successfully achieved.

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

There were no major deviations encountered. The delay in one Deliverable (D12.3) 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.

• **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. Namely the periodic Management Report, as well as the first Periodic Activity Report (PAR). The six monthly report, which was due in the same time as the PMR has been cancelled in accordance with the Project Officer. The PAR due for T0+12 was prepared and submitted to the EC at T0+14 (50 days after its formal delivery time).

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

During the reporting period, the WP had no Major project milestones.

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:** 01/02/2007 – 31/07/2007
- **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 ensure the feasibility of implementing and to increase the number of clinical studies for cancer into ACGT based on specific clinico-genomic scenarios
3. 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.

- Objectives during reporting period

The main focus was laid on clinical aspects of the project. The state of art review in clinical trial software was a main objective, which was necessary to develop an integrated environment for cancer research on the Grid.

Main points were investigated:

- User needs for clinicians and basic researchers for the TrialBuilder including the user friendly integration of the Master Ontology
- Clinico-genomic integration, including technological, legal and ethical issues, security and quality control within the TrialBuilder.
- 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 developing requirements and functionality of the trial builder to get a tool for clinicians that will help to increase the number of clinical trials in ACGT.

- 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). A draft version 1.5 of deliverable D2.2 for review is finished in time and available via the BSCW Server. Most input for this deliverable besides USAAR was given by FHG [IBMT].

Over the entire period IFOMIS stayed in contact with Saarland University Hospital and FHG [IMBT] in order to discuss ontology related questions regarding the development of the Trial Builder. Major progress is done regarding the Clinical view and the maintenance of the Master Ontology. Part of the solution to this task is given in the functionality of the TrialBuilder. 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.

To increase the number of clinical trials for cancer into ACGT based on specific clinicogenomic scenarios the ACGT project was explained to the International Society of Paediatric Oncology (SIOP) and to the German Society of Paediatric Oncology (GPOH). It can be expected that new GPOH trials will use the TrialBuilder as soon as there is a functioning prototype. The same will be pushed in SIOP starting with the next SIOP nephroblastoma trial. 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. At the ECCO meeting in Barcelona, Spain in September 2007 and at the SIOP meeting in Mumbai, India in November 2007 active participation of WP2 (Norbert Graf) will promote ACGT to a greater and especially clinical auditorium. 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.

Review of the Custodix anonymisation tool (CAT) regarding User needs

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

Philips started collection of requirements for an ACGT-specific clinico-genomic electronic health record (EHR).

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

Gathering and interpretation of user requirements for querying clinical databases (SIOP and TOP) using SQL predefined queries. (UPM)

Gathering of user interpretation of concepts contained in the SIOP and TOP databases, using natural language. (UPM)

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

UvA has further extended Vtkfly, the UvA visualization environment, to support interactive visualization on a distributed (grid) architecture.

UvA has extended Vtkfly to support interactive volume rendering of medical data sets, including CT, MR and ultrasound.

UvA has extended Vtkfly to support simultaneous and registered visualization of medical data sets and results from in-silico tumour simulation results.

UvA has applied Vtkfly in a prototypical "augmented reality" (AR) application for the overlaid visualization of medical data over a patient using a handheld "see-through display".

Together with Cognitive Psychology dept. of Twente University, the Netherlands; performed a Visual Perception study using the Personal Space Station in an interactive visualization experiment: Studying Virtual Anatomy. May 11 to 25, 2007. (UVA)

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

In the framework of WP2, we mainly developed theoretical research activities.

In particular, in view of the collaboration with the Oxford University, we started focusing on the biophysics of anti-angiogenic anti-tumour drugs.

In collaboration with Prof. P. Cerrai of Pisa University, we applied the theory of biological cooperation in order to better characterize the Hahnfeldt-Panigrahy-Llatky-Folkman model of angiogenesis and anti-angiogenesis therapy [1].

Then, in collaboration with Prof. A. Gandolfi of IASI CNR, Rome, we developed a new biophysical family of models [2] stressing the role of the vessel density in driving both the tumour growth and the growth of the intra-tumour blood vessels. The theoretical analysis and simulations of this family seems to indicate its biological soundness. In particular, we focused in finding, under continuous infusion therapy, the theoretical minimal drug delivery guaranteeing the tumour eradication. Furthermore, we investigated the role of biological delays between the dynamics of vessels density and its effects on the tumour dynamics. We obtained that, if these delays exceeds some realistic threshold values, there may be, in some cases, impossibility of eradicate the disease via the therapy.

Another biological meaningful delay we investigated is that between the drug consumption by the endothelial cells and their death [3]. We had started this research before ACGT project, by proposing a model where this delay was exponentially distributed, but, in the framework of ACGT WP2, we extended it by considering a generic and more biologically realistic distribution. We obtained the biologically sound and novel result that if the above average delay is greater than the average time of tumour-stimulated vessel growth, the eradication via anti-angiogenesis therapy seems to be impossible; and any case the non instantaneous death increases significantly the minimal dose delivery of the eradication.

As a follow-up of this research, in the framework of both WP2 and WP8, we started developing a new model for dugs having both chemotherapeutic and anti-angiogenic effects. The preliminary results obtained up to now, summarized in the concluding remarks of paper [3], and are the following:

- In the absence of delays and of resistance to chemotherapy, the presence of direct cytotoxic action on tumor cells reduces the minimal dose required to eradicate the umor. This is an obvious consequence of the synergy between the direct chemotherapeutic effect and the anti-angiogenic action.
- Introducing the non instantaneous death but not the resistance, one obtains that the minimal dose for eradication must be increased.
- In the presence of the resistance to chemotherapy, the subpopulation of tumor cells that are sensitive to the therapy gets extinct. However, if the dose of the drug is appropriate, the anti-angiogenic action may induce the remission of the disease.

However, this research is in progress, further results will be illustrated in [4]

Finally, in the biomedical manuscript [5] we simulated and developed some bio-physical models of anti-angiogenic therapies in order to better understand the mechanisms of their action, which seems to be more effective in case of continuous infusion delivery. In particular, we investigated the role of drug elimination rate and of dose fractionation

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 main tasks carried out by SIB can be summarized in:

The activity done was in relation with a scenario for meta-analysis that they are currently building up with UMA (Federico Garcia), based on public datasets, and following a discussion with Francesca Buffa from Oxford.

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

The main activity done was gathering requirements for hospital side de-identification tools. This had lead to the definition of function specifications for the Custodix Anonymisation Tool (CAT).

- Major Achievements towards planned objectives, identify main partners Involved

A draft version 1.5 of deliverable 2.2 is available on the BSCW server.

- **Deviations from the project work programme, and corrective actions taken/suggested**
There were no deviations from the work programme
- **List of deliverables, including due date and actual/foreseen submission date**
Deliverable 2.2 with due date of month 18 is put on the BSCW server for review
- **List of milestones, including due date and actual/foreseen achievement date**
Milestone 2.1 was achieved at month 6.
No further milestones

Workpackage 3 – Architecture and Standards

- **Partner Responsible : PSNC**
- **Contributing partner(s):** PSNC, FORTH, UVA, PHILIPS, LundU, UMA, UPM, FHG, BIOVISTA, CUSTODIX, ICCS, USAAR, FUNDP, UH, UHOK
- **Reporting Period:** 01/02/2007 – 31/07/2007
- **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 blue print 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 for WP3 in this period was to make sure that the architecture of ACGT environment evolves in the right direction according to needs and requirements of the whole project, including all workpackages.

Besides, the WP3 representatives took part in initial meetings of other workpackages to familiarize with work in all areas of the project
 - **Progress towards objectives**

This work has been achieved with no delays, or any technical problems. The document describing the architecture is continuously being changed and adopted to the current needs.
 - **Main Activities & Tasks worked on**

Analysing end user requirements and mapping them on the architecture.
 - **Major Achievements towards planned objectives, identify main partners Involved**

The architecture evolves in the right direction. This work is being done with FORTH., and especially WP9.
- **Deviations from the project work programme, and corrective actions taken/suggested**

No deviations.

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

No deliverables were foreseen for this period.

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

No milestones were foreseen for this period

Workpackage 4 – Biomedical Grid Technology Layer

- **Partner Responsible** : PSNC
- **Contributing partner(s)**: FORTH, UMA, FHG, CUSTODIX, SIVECO, UHOK, INRIA
- **Reporting Period**: 01/02/2007 – 31/07/2007
- **Workpackage objectives and starting point of work at beginning of reporting period**

-The Workpackage has the following major objectives:

- To provide grid services that take advantage of the grid functionality, such as security, etc.
- To provide 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 in WP7
- To extend existing toolkits with decentralised VO management tools and workflow systems based on widely adopted standards, such as BPEL.

- Objectives during reporting period

The main objective for WP4 in this period was to setup and run the ACGT Grid testbed.

- Progress towards objectives

In this period we fully provided the Grid infrastructure. Main tasks since then included maintenance, support and monitoring the ACGT Grid infrastructure. In addition to this we have added some new features to the Gridge toolkit in the areas of grid security, resource management, and data management.

- Main Activities & Tasks worked on

Grid Security Services:

- Implementation of new security policy for ACGT inside GAS
- New GUI client for GAS
- Deployment of portal client for GAS
- Deployment of improved Globus authorization layer
- Implementation and deployment of new authorization plug-in for SW-GRAM
- Support for Custodix responsible for security architecture

Resource Management Service

- Implementation of multi-credential support for GRMS
- Work on implementation of JSDL support for GRMS
- Work on parametric jobs support for GRMS
- Support for Fraunhofer Institute IAIS in development of client for GRMS

Data Management Service

- Implementation of new logical identifier structure for DMS
- Work on new authorization methods for file access in DMS

- Major Achievements towards planned objectives, identify main partners Involved

As stated above. Most work has been done by PSNC. Extensive collaboration of PSNC with all the other partners was needed.

Grid tesbed participation declaration:

- PSNC
- Fraunhofer AIS
- Custodix NV
- FORTH
- UPM
- Fraunhofer IBMT
- University of Malaga

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

No deviations. All as planned.

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

No deliverables were foreseen for this period.

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

No milestones were foreseen for this period.

Workpackage 5 – Distributed Data Access and Applications

- **Partner Responsible : PHILIPS**
- **Contributing partner(s)**: Philips, FHG-IBMT, UPM, LundU, USAAR, Uhok
- **Reporting Period**: 01/02/2007 – 31/07/2007
- **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.
 - **Progress towards objectives**
 - Development of data access services (Philips):
 - Implemented SPARQL-enabled OGSA-DAI data access service for querying relational databases (using 3rd party SPARQL-SQL transformation code).
 - Study of the DICOM protocol to uncover its peculiarities.
 - Implemented SPARQL to DICOM query transformation code, with corresponding DICOM results to SPARQL results transformation code.
 - Development of query functionality for image data access service: OGSA-DAI based image retrieval from a DICOM server to a destination of choice (FTP-based), generic OGSA-DAI activities that allow querying of a DICOM server
 - OGSA-DAI framework experiments.
 - Performance tests of the data access service for DICOM when used by multiple clients.
 - Created framework for running validation and performance tests, and analysing their results.

- Ran extensive tests on the data access services for relational and image (DICOM) data sources. Improved code accordingly.
 - Found and reported various bugs in third party code.
 - Documented the use of data access services on ACGT wiki
- Joint WP5/WP7 demonstration of the Semantic Mediator and of the Data Access Services at the ACGT review (Poznan, April 2007) (Philips, UPM).
- Design and development of an interface between the WP7 Semantic Mediator and the WP5 Data Access Services (Philips, UPM).
- Presentation and coordination of discussions about the use and proposed implementation of the data access services, at the consortium meeting in Malaga (Philips).
- Presentations at the technical meeting in Madrid (Philips):
- Experiences with SPARQL as a common query language
 - Validation tests and performance measurements of the data access services
- Development of the prototype of the Clinical Data Management System to show the principle of implementation of the embedded Trial Builder and usage of ACGT Master ontology and demonstrator for the ACGT Review in Poznan (April, 2007) (FHG-IBMT).
- Discussions concerning clinical requirements and functionality for the development of an ontology-based CRF-generator (several meetings) (USAAR, FHG-IBMT)
- Development of the concepts for implementation of the Treatment plans and the Master protocols of trial. Design discussions and early implementation of a Trial Outline Builder (FHG-IBMT, Uhok).
- Several updates of the BASE application (2.2.0, 2.2.1, 2.2.2, 2.2.3, 2.3.0, 2.3.1, 2.3.2) (LundU).

- Main Activities & Tasks worked on

T5.2 Implementation of the data access services

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

→ Prototypes of Data Access Services to relational and image (DICOM) databases (Philips)

→ Integrated demonstrator of the Semantic Mediator and the Data Access Services (UPM, Philips)

→ Development of the prototype of the Clinical Data Management System to show the principle of implementation of the embedded Trial Builder and usage of ACGT Master ontology (FHG-IBMT)

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

No deviations from plan
- **List of deliverables, including due date and actual/foreseen submission date**

D5.2 Demonstration and report of heterogeneous data access services
(October 2007/ October 2007)
D5.3 Initial specification of a generic Clinico-Genomic EHR
(November 2007/ November 2007)
- **List of milestones, including due date and actual/foreseen achievement date**

MWP5.2 Grid services for heterogeneous data access (month 21) Part of Major Project Milestone M7

Workpackage 6 – Data Mining and Knowledge Discovery Tools

- **Partner Responsible : FHG**
- **Contributing partner(s)**: UMA, UvA, SIB, IEO, Biovista, FhG
- **Reporting Period**: 01/02/2007 – 31/07/2007
- **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

The following objectives were set for this reporting period

1. Demonstration of initial Grid-based data analysis services at the first ACGT review
2. Development of a metadata repository, and corresponding access services (ongoing)
3. Design and implementation of knowledge discovery services in the ACGT architecture, in particular services for data analysis using the R environment, literature mining services, and analysis services for clinico-genomic data (ongoing)

- Progress towards objectives

(Involved partners given in parenthesis)

1. Two demonstrators for knowledge discovery services in Grid architecture have been presented at the ACGT review, one based on the Taverna environment, and one presenting the integration of Grid-services into the R statistical environment. (FORTH, FHG, SIB)

2. A first version of the metadata schema has been developed, and been deployed in form of a relational database system. Current work is focusing on implementing ACGT-compatible services for querying and manipulating the metadata repository, and extending the current schema to the requirements posed by the integration of R scripts. (UMA, FHG)

3. Several knowledge discovery services have been implemented. As the overall ACGT architecture is currently still in development, the status of these services can be characterized as early development and testing versions. In particular, the following services have been worked on:

- Taverna-based workflow for integrated clinic-genomic knowledge discovery (FORTH)

- GridR (an implementation of R inside a Grid environment), a GridR webservice, and related functionality (e.g. data access) (FHG)
- Literature Mining webservices, including development of a service for the generation of concept types; tools for the graph-based identification of cancer-related pathways from published literature (BIOVISTA, IEO)
- An R package for Gene Set Enrichment Analysis (SIB)
- Extension of the Vtkfly visualization environment, to support interactive visualization on a distributed (grid) architecture, to support interactive volume rendering of medical data sets, including CT, MR and ultrasound, and to support simultaneous and registered visualization of medical data sets and results from in-silico tumour simulation results. (UvA)
- Development and integration of the ONTODATACLEAN data pre-processing tool in the Semantic Mediator. (UPM)

- **Main Activities & Tasks worked on**

In addition to the activities listed in the previous paragraph, a WP6 meeting was held in Madrid on July 4th. (local organization by UPM). Several subtasks and minor milestones have been identified at this meeting.

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

See Section “progress towards objectives”

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

None, However as several open questions with respect to the final ACGT architecture exist, the work programme may have to be adapted in the future. Close cooperation with other work packages to define the final architecture is currently being performed inside the technical management committee.

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

Upcoming deliverables are:

D6.2 Demonstration and report of data mining and discovery tools and services (month 21)

D6.3 Demonstration and report of a repository of knowledge-discovery-related metadata (month 24)

Until now, no delays in producing the deliverables are foreseen.

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

Upcoming milestones are:

MWP6.1 Demonstration and report of data mining and discovery tools and services (month 21), part of major project milestone M7

Until now, no delays in producing the deliverables are foreseen.

Workpackage 7 – Ontologies and Semantic Mediation Tools

- **Partner Responsible : UPM**
- **Contributing partner(s):** IFOMIS, Fraunhofer, PHILIPS, BioVista, LundU
- **Reporting Period:** 01/02/2007 – 31/07/2007
- **Workpackage objectives and starting point of work at beginning of reporting period**

-The Workpackage has the following major objectives:

→ 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 provide, through the Master Ontology, a formal description of the domain of knowledge of the clinical trials included in ACGT.

→ To achieve a vertical integration among many different levels of granularity (molecular, cellular, tissue, organ, individual and population).

- Objectives during reporting period

→ Delivery of the ACGT Master Ontology on Cancer

→ Design and development of the Semantic Mediator

→ Design and development of satellite tools

- Progress towards objectives

→ The first version of the ACGT Master Ontology has been delivered

→ The first version of the ACGT Semantic Mediator, developed for demonstration, was tested and evaluated. New decisions regarding design were taken (i.e. migration of query language from RDQL to SPARQL)

→ A new mapping format is under discussion, and the mapping tool is being developed

Main Activities & Tasks worked on

- Development of the first Demonstrator of the ACGT Semantic Mediator (UPM)
- Migration of the Semantic Mediator from RDQL to SPARQL (UPM)
- Development of the mapping tool (UPM)
- Study and specification of query transformation requirements.
Design and development of a query transformation service (UPM)
- Study of optimization of query translation techniques (UPM)
- Assistance to several meetings (Germany, Poznan, Bucharest and Madrid) (UPM)
- Participation in several audio-conferences (MB & technical) (UPM)
- Writing of several publications (UPM, PHILIPS) detailed in part 5 “scientific publications”
 - Preparation of the Deliverable 7.2: “Initial Version of the ACGT Master Ontology” (Milestone 5) (IFOMIS)
 - Analysis of the issue of maintenance and extension of the ontology (IFOMIS)
 - Analysis ontology-related questions concerning the Trial Builder (IFOMIS)
 - Review and refinement of the ACGT Master Ontology (IFOMIS)
 - Review of new trends in ontology development (IFOMIS)
 - Development of concepts for ontology based creation of CRFs (presentation on Review meeting in Poznan) and development of a very simple first prototype of the Trial Builder to demonstrate the principle of integrating the Master ontology into the process of CRF design (presentation in Madrid) (FRAUNHOFER)
 - A conference publication: “Ontology Based Data Management Systems for post-genomic clinical Trials within the Context of a European Grid Infrastructure for Cancer Research” (Authors: Gabriele Weiler, Mathias Brochhausen, Norbert Graf, Alexander Hoppe, Fatima Schera, and Stephan Kiefer) for the 29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society at August 23-26, 2007 in Lyon, France (see <http://www.embc07.ulster.ac.uk/>) (FRAUNHOFER)
 - Participation in technical meeting (incl. presentation and demonstration of the prototype) in Madrid (Spain) - July, 2007 (FRAUNHOFER)
 - Multiple meetings and discussions about technical issues with project partners, such as IFOMIS and FORTH (FRAUNHOFER)
 - Development of Biovista ontology search engine as a web service. This task is ongoing. Prototype expected by end of RP4 (BioVista)
 - Work on adapting the BASE application for ontologies (mostly CVs) (LundU)
 - Research and development of a proper mapping format (FORTH)
 - Research for the development of the mapping tool (FORTH)
 - Participation in several audio-conferences (FORTH)
 - Preparation and organization of the technical meeting with IFOMIS concerning ontology-related questions (FORTH)
 - Analysis of the issue of ontology maintenance and extension together with IFOMIS (FORTH)
 - Review and refinement of the ACGT Master Ontology (together with IFOMIS) (FORTH)
 - Participation in technical meeting in Madrid - July 2007 (FORTH)
 - Preparatory work for linking the metadata repository with an ontology of services (UMA)
 - Started classification of services and data types (UMA)

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

- Integration with WP5 database wrappers was successfully achieved and demonstrated (UPM, PHILIPS)

- An initial version of the ACGT Master Ontology on Cancer was achieved, proving its viability (IFOMIS)

- An initial version of the Semantic Mediator was achieved and demonstrated (UPM)

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

- The different query languages initially employed by the semantic mediator and the WP5 database wrappers (RDQL in the former, and SPARQL in the latter) caused important design and performance issues. A decision to migrate the Semantic Mediator to SPARQL was taking, successfully solving the mentioned problems

- The lack of expressiveness in SPARQL (no aggregation functions) was found to be a possible issue for users in the future. A study of viable techniques to add this functionality has been initiated

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

- Delivery of the ACGT Master Ontology (D7.2)

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

- Delivery of the Initial ACGT master ontology for cancer trials (major project milestone M5)

Workpackage 8 – Technologies and Tools for In Silico Oncology

- **Partner Responsible : ICCS**
- **Contributing partner(s):** ICCS, USAAR, IJB, FORTH, INRIA, UvA, , FHG-IGD, IEO, UHOK.
- **All involved partners contributed as planned in terms of person effort.**
- **Reporting Period:** 01/02/2007 – 31/07/2007
- **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 the “Oncosimulator”, a technologically advanced and user friendly system able to spatiotemporally simulate within well defined reliability limits tumour growth and tumour and to a lesser extent normal tissue response to chemotherapy, for the cases of breast cancer and nephroblastoma (Wilm’s tumour), in the patient’s individualized context. The constituent simulation models are based on the novel, essentially “top-down” modelling approach developed by the In Silico Oncology Group, ICCS, National Technical University of Athens.

Pertinent clinical, imaging, histopathologic and molecular data in conjunction with the ACGT clinical trials will be exploited in order to validate the model both prospectively and retrospectively. More specifically, the in silico oncology trial will be based on the two clinical trials (nephroblastoma SIOP 2001/GPOH, University of Saarland, and breast cancer TOP trial, Institute Jules Bordet) following their considerable enhancement in terms of data collection.

- Objectives during reporting period

- An initial version of the computer codes simulating tumour growth and tumour response to chemotherapy will be produced
- Initial versions of the basic image processing, virtual reality and interactive graphics systems will be developed
- The data storage needs and trafficking policies will be clarified in view of the use of the database for the “Oncosimulator”.
- An initial version of the grid execution platform for the “Oncosimulator” will be developed

- Progress towards objectives

- An initial version of the computer codes simulating tumour growth and tumour response to chemotherapy has been produced
- Initial versions of the basic image processing, virtual reality and interactive graphics systems have been developed

- The data storage needs and trafficking policies have been clarified in view of the use of the database for the “Oncosimulator”.
- An initial version of the grid execution platform for the “Oncosimulator” has been developed

- Main Activities & Tasks worked on

T8.1 In silico model of breast cancer tumour growth and response to therapy

This task for the reporting period has been dedicated to the continuation of the development and validation of a 4D simulation model of breast cancer tumour growth and tumour response to chemotherapeutic schemes. 4D simulation of breast tumour growth and response to chemotherapeutic schemes are primarily based on the generic Monte Carlo technique in conjunction with cellular automata theory and differential equations. Fundamental biological phenomena that are simulated include metabolism, cell cycling, cell survival following irradiation/chemotherapy, mechanical deformations, etc. Numerical and clinical testing of the simulation codes will be performed and optimized versions will emerge.

T8.2 In silico model of nephroblastoma tumour growth and response to therapy

This task for the reporting period has been dedicated to the continuation of the development and validation of a 4D simulation model analogous to the one described in T8.1 for the case of nephroblastoma (Wilm’s tumour). Initial anonymized DICOM Data have been provided.

T8.3 In silico oncology data storage

The data storage needs and trafficking policies have been clarified in view of the use of the database for the “Oncosimulator”.

T8.4 Image processing

Initial algorithms for segmentation, 3D reconstruction and registration have been adapted for the needs of the in silico oncology validation and optimization process.

T8.5 Code acceleration and parallel execution

An initial version of the grid execution platform for the “Oncosimulator” has been developed

T8.6 Visualization of clinical data and simulation predictions

This task is dedicated to the development of a software framework to support the interactive visual exploration of simulation data. An initial prototype of the software framework has been constructed and tested for the visualization of simulation results. Based on these tests, the specification has been refined and construction of a second prototype is now well underway. An interactive graphics device designed to use virtual reality techniques to enable intuitive interactive visual exploration of simulation data has been constructed. The software framework is modified to support this device.

- Major Achievements towards planned objectives, identify main partners Involved

- Initial version of the computer codes simulating tumour growth and tumour response to chemotherapy

- Initial versions of the basic image processing, virtual reality and interactive graphics systems
- Clarification of data storage needs and trafficking policies.
- Initial version of the grid execution platform.

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

No remarkable deviations from the planned activities have occurred.

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

According to the current overall ACGT planning, no deliverables have been planned for this period.

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

According to the current overall ACGT planning, no milestones have been planned for this period.

Workpackage 9 – The Integrated ACGT Environment

- **Partner Responsible : FORTH**
- **Contributing partner(s)**: UvA, SIB, UPM, UMA, FHG, BIOVISTA, ICCS, PSNC
- **Reporting Period**: 01/02/2007 – 31/07/2007
- **Workpackage objectives and starting point of work at beginning of reporting period**

-The Workpackage has the following major objectives:

- 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

- Investigate the integration requirements in ACGT and provide guidance for the creation of new services that will be interoperable, properly annotated, and semantically discoverable
- Finalize and submit the Deliverable 9.1 “Integration Requirements and Guidelines”
- Initial implementation of relatively simple workflows that provide proof of concept and experience based on the early versions of some of the ACGT services
- Make the proper decisions with respect to the specific workflow tools and standards that will be supported in ACGT
- In collaboration with WP6 work on the realization of a repository for services and workflows metadata and the accompanied services and facilities

- Progress towards objectives

- The Deliverable 9.1 was completed and submitted on time for review
- The integration of ACGT services and their composition into scientific workflows was tested and demonstrated using the Taverna Workbench workflow environment.
- An initial version of a metadata repository and its relevant access interfaces have been studied in relevance to the requirements of the workflow environment
- The choice of BPEL as a standard workflow language has been made and evaluations of the available open source tools have been started

- Main Activities & Tasks worked on

→ Implementation of a workflow enactor for the Taverna Workbench environment so that the execution of the workflows is performed on an ACGT Grid node.

This permitted the separation of the design of the workflow from its execution and the sharing of workflows between the users through the ACGT Portal

→ Implementation of Taverna compliant workflows that provide evidence for the composability of literature mining services (provided by BIOVISTA), web service interface to the R environment (provided by FhG), Association Rule Mining and Clustering services (provided by FORTH).

→ Participation on the ongoing discussions of the ACGT requirements for the metadata and the related issues of their definition, management, maintenance, etc.

- Major Achievements towards planned objectives, identify main partners Involved

→ Deliverable D9.1 prepared and submitted (FhG)

→ Integrated demonstrator: Semantic Mediator and Data Access Wrappers, using a case study based on the integration of SIOP and DICOM database. (UPM)

→ Integrated demonstration of the interactive visualization of a "live" in-silico simulation that was executing on a grid at the first annual review in Poznan (UvA, PSNC, ICCS)

→ Integration of literature mining services in Taverna compliant workflows (BIOVISTA, FORTH)

→ Integration of ACGT services and their composition into scientific workflows was demonstrated at the first annual review in Poznan. This work was a prototype implementation of a real world scenario for an integrated clinico-genomic knowledge discovery task. (FORTH)

→ Integration checks and integration of the portal site with the credential management service running at Custodix. This will allow credential forwarding between services and temporary storage of credentials. (CUSTODIX)

→ For authorization PSNC and CUSTODIX have worked together integrating the new GAS version and plugins on the Custodix grid node in preparation for setting up GAS for the whole project.

→ Development of a Web Service, Repo-persistence, providing remote access to the metadata repository. (UMA)

→ Deployment of two different instances of Repo-persistence: a production (more stable) and a development (more up-to-date) reference instances. (UMA)

→ Installation and maintenance of the ACGT Code Repository and the issue and bug tracking systems in collaboration with WP13 (FORTH, SIB)

→ Development of an alternative, SPARQL compliant, access interface to the metadata repository (FORTH)

→ Initial definition of an OWL-DL service and data type ontology based on the schema and the content of the metadata repository (FORTH)

→ Survey and initial evaluation of open source BPEL compliant workflow engines and installation and experimentation with Apache ODE (FORTH)

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

None

- **List of deliverables, including due date and actual/foreseen submission date**
Deliverable 9.1 with due date of month12 was uploaded in the BSCW server at the end of March.
- **List of milestones, including due date and actual/foreseen achievement date**

Workpackage 10 – Ethics, Legal and QA issues

- **Partner Responsible** : LUH
- **Contributing partner(s)**: FORTH, IJB, UOC, Custodix, USAAR, FUNDP, UH, UOXF, IEO
- **Reporting Period**: 01/02/2007 – 31/07/2007
- **Workpackage objectives and starting point of work at beginning of reporting period**

-The Workpackage has the following major objectives:

Ethical and legal requirements of ACGT

- Objectives during reporting period

1. Analysis of legal requirements for the establishment of an ACGT Data Protection Board
2. Establishment of an ACGT Data Protection Board
3. Production of contracts regarding data protection, data security and ethical issues
4. Empirical survey on patients' perspectives and needs

- Progress towards objectives

- The analysis of legal requirements for the establishment of an ACGT Data Protection Board is in progress.
- The establishment of an ACGT Data Protection Board will be started as soon as lit. 1 is finished.
- The production of an information leaflet for the physicians.
- The production of contracts regarding data protection, data security and ethical issues are in progress.
- An empirical survey on patients' perspectives and needs is in progress

- Main Activities & Tasks worked on

- Analysis of the Belgium non-profit-organisation
- Analysis of international model contracts with regard to data protection and Compliance
- Integration of the ethical and legal requirements in the Trial Builder in cooperation with the Fraunhofer Institute
- Cooperation and meeting with Custodix regarding the usability of CAT-software.
- WP-10 meeting
- An article in one of the main English medical law journals is turned in for publication
- Preparation of the design of an empirical survey on patients' perspectives and needs.

- Adjustment of the patient consent form, providing comments on and input to the consent documents and on the discussion on legal issues for trials in the UK
- **Major Achievements towards planned objectives, identify main partners Involved**
 - Analysis of the Belgium non-profit-organisation (FUNDP)
 - Redaction of the statutes for the non-profit-organisation (FUNDP)
 - The production of an information leaflet for the physicians (FUNDP);
 - Analysis of international model contracts with regard to data protection and compliance (LUH)
 - An article in one of the main English medical law journals is turned in for publication (LUH)
 - Summer University in Toulouse (France) and Madrid (Spain) in July 2007 (FUNDP);
 - Articles in law journals in 2007 and foreseen next year (FUNDP)
 - Analysis of literature pertinent to the perspectives, attitudes and needs of patients in large clinico-genomic trials. (UH)
 - Integration of the ethical and legal requirements in the Trail Builder (USAAR)
 - Cooperation and meeting regarding the usability of CAT-software (Custodix, USAAR)
 - Adjustment of the patient consent form (UOXF)
- **Deviations from the project work programme, and corrective actions taken/suggested**

No deviations
- **List of deliverables, including due date and actual/foreseen submission date**
 - D10.3: Establishment of the ACGT Data Protection Board (due/foreseen month 20) in progress
 - D10.4: Production of contracts regarding data protection, data security and ethical issues (due/foreseen month 24) in progress
 - D10.5: Design of an empirical survey on patients' perspectives and needs (due/foreseen month 25)
- **List of milestones, including due date and actual/foreseen achievement date**
- MWP10.2: Establishment of the ACGT Data Protection Board (due/foreseen month 20).

Workpackage 11 – Trust and Security

- **Partner Responsible : CUSTODIX**
- **Contributing partner(s)**: IJB, UPM, Fraunhofer, LUH, PNSC, FUNDP, UH
- **Reporting Period**: 01/02/2007 – 31/07/2007
- **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

During this reporting period, WP11 has been working towards the M20 milestone: “implementation of the core security services including the Pseudonymisation tool”. Effort has been concentrating on three major subjects, part of task “T11.2.1 Setup of the initial GLOBUS/GRIDGE based security infrastructure” and “T11.3 Implementation of the ACGT Pseudonymization Library and Tools”:

- [T11.3] the Custodix Anonymisation Tool (CAT)
- [T11.2.1] the GRIDGE Authorization Service (GAS)
- [T11.2.1] GRID Authentication (MyProxy / WebSphere)

- Progress towards objectives

Custodix Anonymisation Tool (CAT)

T11.3 concentrates on developing a tool which allows participating clinical centres to de-identify their exported patient data. It consists of a library of de-identification and pseudonymisation functions for use by developers, a command-line-tool and GUI for end-users. The GUI is designed according to the workbench paradigm: it allows privacy experts to design a generic data protection profile which then can be applied (through wizards) to various sources of data by clinicians wanting to share and export data.

Progress made:

- Definition of the configuration format describing data protection operations
- Implementation of the basic framework code for running the data protection function engine on multiple input-formats according to different de-identification profiles
- GUI
- Implementation of support for DICOM and CSV (Comma Separated Value) files
- Implementation of basic library functionality

Basic functionality of CAT can be considered implemented at 70% (target for initial version: M20).

Main partners involved: Custodix

GRIDGE Authorization Service (GAS)

GAS is the central authorization component within the ACGT GRID platform. During this reporting period, the existing GAS base component has been further developed, i.e. effort has been spent on:

- adding new functionality according to the ACGT requirements
- porting (Solaris 10 x86 version), subsequent debugging and stability testing on the ACGT framework
- deployment of the administration portlet of GAS service
- implementation of a new GUI client for GAS
- implementation of new authorization plug-ins
 - GRAM, Gridmap file - new functionality, deployment in ACGT environment
 - WS-GRAM - new authorization plug-in for WS-GRAM (but it can also be used in other WSRF services), deployment and testing
 - gridFTP plugin - implementation - now in testing phase

Main partners involved: PNSC (development), Custodix (deployment, testing)

GRID Authentication (MyProxy / WebSphere)

MyProxy is a credential management system that makes delegation possible within GRID infrastructures. During this reporting period MyProxy has been deployed and modified to suit the needs of ACGT (e.g. made sure that MyProxy could be deployed with minimal system privileges, etc.). MyProxy was integrated with the ACGT Portal and ACGT Public Key Infrastructure (mainly with the OCSP service).

Main partners involved: Custodix, SIVECO

- Main Activities & Tasks worked on

Cf. above

- Major Achievements towards planned objectives, identify main partners Involved

Cf. above

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

There have been no noteworthy deviations from the project programme. However, the different components scheduled for the M20 milestone will have a varying degree of completion (e.g. regarding user-friendliness and integration).

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

No WP11 deliverables were foreseen (or finalised) in this reporting period.

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

No WP11 milestones were foreseen in this reporting period.

Workpackage 12 – Clinical Trials

- **Partner Responsible : FORTH - IJB**
- **Contributing partner(s)**: University of Hannover, University of Hamburg, University of Saarland, Biovista, European Institute of Oncology, University of Oxford, University of Crete, Swiss Bioinformatics Institute, Custodix, University of Namur, and University of Lund.
- **Reporting Period**: 01/02/2007 – 31/07/2007
- **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.

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

- Progress towards objectives

→ The selection of the clinical trials has already been done during the 1st year of this project. Two clinical trials, which were already ongoing were initially selected, namely the TOP trial on breast cancer and SIOP trial on nephroblastoma. Regarding the TOP trial (coordinated by Institut Jules Bordet), an amendment to the protocol and to the informed consent has now been finalized so that the University Hospital of Heraklion could join this trial in the context of ACGT. Nevertheless, multi-level data which has already been collected in the context of this trial can be made available to the ACGT consortium through procedures in agreement with the ethical and legal requirements (work done in collaboration with WP10 and 11).

Regarding the SIOP trial (coordinated by the University of Saarland), the protocol and informed consents have already been amended to the ACGT requirements and serum samples and clinical data are being collected. For both trials, the Information System that will be used for data collection and management is being adapted.

Additionally, the European Institute of Oncology has now selected two trials for which the clinical and molecular biology data will be analyzed in the framework of the GRID tools of the ACGT project: one trial in non-small cell lung cancer (NSCLC) and the other one in prostate cancer. The goal of the NSCLC study is to assess the impact of specific gene profiles on efficacy of gemcitabine and platin in previously untreated patients affected by this specific kind of tumour. The prostate trial is a Phase I-II randomized study of oral sunitinib malate in combination with sequential versus concurrent metronomic oral cyclophosphamide in patients with hormone refractory prostate cancer.

The primary objectives are the following:

- 1/ to determine the toxicity and safety of sunitinib malate administered alone and with concurrent oral metronomic cyclophosphamide;
- 2/ to gain insight into the mechanisms of action of sunitinib in order to evaluate the effects of sunitinib alone on tumor physiology and systemic response;
- 3/ to determine the activity of the combination of sunitinib plus oral metronomic cyclophosphamide in terms of time to disease progression (TTP) in patients with HRPC and to compare the activity of two different strategies of administration of this combination.

→ The investigation of the requirements for cross-platform biological data exchange and analysis has been analysed in close collaboration between different partners (University of Saarland, University of Oxford, University of Crete, Swiss Bioinformatics Institute, and University of Lund). The state of the art for the main “omics” technologies, together with the main issues have been discussed in the deliverable D12.3.

Following this initial effort, a study project has been launched in April 2007 between these partners to identify the requirements for cross-platform data exchange, integration and analysis regarding the gene expression profiling data specifically. To this end, data from tumors which were both profiled on the Illumina platform (University of Oxford) and the Affymetrix platform (Institut Jules Bordet) are being compared and analysed.

- Main Activities & Tasks worked on

T12.1.1 - Further review of the technical, legal and bioethical requirements in particular related to biospecimen collection and management.

T12.1.2 - Establishment of local bio-banks for the collection and maintenance of biospecimens required for the implementation of ACGT clinical trials.

T12.1.3 - Adoption and operation of clinico-genomic data management systems in order to facilitate the collection and sharing of information defined in the CRFs.

T12.1.4 - Collection of post-genomic analysis and genotype data

T12.1.5 - Multi-centric post-genomic analysis data integration. Definition of common procedures and protocols and adoption of controls and standards in order to facilitate multi-centric integration.

- Major Achievements towards planned objectives, identify main partners Involved

T12.1.1 - This has been done in collaboration with the WP10 and 11. For example a joint meeting was also organized with the legal and ethical WP of the European TRANSBIG project, which is a sister network of the Breast International Group, in order to share experiences mainly regarding anonymization and pseudonymization issues.

T12.1.2 - Local bio-banks have been established for the different trials.

T12.1.3 - This is being done in collaboration with other WPs, especially WP2, which is coordinating the Ontology based Trial Management System of ACGT and will be described in D2.2. Technical issues are being discussed with the other technical WPs.

T12.1.4 Data are being collected for the different trials.

T12.1.5 Multi-centric post-genomic analysis biological data integration has been critically evaluated in D12.3. Common procedures and protocols and adoption of controls and standards in order to facilitate multi-centric integration are now being defined for gene expression data.

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

Since the amendment of the TOP trial needed to include items, in addition to ACGT, which still needed to be discussed among the different clinical investigators, this amendment was slightly delayed.

Given the numerous protocols, regulations, recommendations and projects regarding bio-banking, it appeared that D12.2 was a much more demanding task than initially planned. Therefore it has been agreed during the 1st annual review that D12.2 would be an overview of the existing initiatives & recommendations and that in ACGT we would rather aim at keeping pace with these different initiatives, than to develop its own guidelines and recommendations.

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

- D12.2 - Bio-bank protocols and regulations (initially due on month 9/ Based on the discussions and decision taken during the first annual review, this deliverable will be delivered during the next reporting period)

- D12.3 - Report on requirements for cross platform data exchange (due on month 12/ delivered during this reporting period)

- D12.4 Report on the definition and status of implementation of the ACGT validation trial (due on month 12/ delivered during this reporting period)

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

No milestones have been planned for this period.

Workpackage 13 – Evaluation & Validation

- **Partner Responsible : SIB**
- **Contributing partner(s)**: FORTH, UvA, Philips, IJB, SIB, UMA, FhG, Biovista, PSNC, Custodix, ICCS, UoS, UOXF.BP, IEO
- **Reporting Period**: 01/02/2007 – 31/07/2007
- **Workpackage objectives and starting point of work at beginning of reporting period**

-The Workpackage has the following major objectives:

The aim of WP13 is to formulate evaluation criteria; verification procedure and feedback report guidelines, to coordinate local validation activities and feedback reports and to write a final evaluation report

- Objectives during reporting period

- Establish a first series of practical evaluation and validation (E+V) scenarios compatible with the design of the first ACGT architecture. List explicit associated steps of scenarios to allow a detailed evaluation of the functionality of the infrastructure.
- Identify a subset of the validation scenarios as a priority guideline for the development of the first integrated ACGT demonstrator.
- Collect and refine test data for the validation scenarios (continuous process).
- Collect procedures for software QA from technical partners (continuous process).
- Identify software management tools used in other open-source projects.
- Setup a software management environment to support high-quality code development in ACGT.

- Progress towards objectives

- A selection of the ACGT scenarios listed in D2.1 has been modularized into “mini-scenarios” anticipated to be suitable for practical testing the initial ACGT infrastructure (SIB). Individual steps of those mini-scenarios form explicit criteria for the evaluation of the ACGT environment.
- SIB, IJB, UoS, UOXF.BP contributed to and reviewed (from an end-user perspective) the selection of mini-scenarios targeted to the testing of the first demonstrator.
- The ACGT-wide software management environment now nearly complete, FORTH being the main contributor:
 - Installation and maintenance of the ACGT code repository with version control and issue tracking,

- Design and implementation of a validation test suite for the ACGT services and the provision of the necessary infrastructure for hosting the testing environment (testing as external user was conducted by SIB)

→ An organizational structure for evaluation workshops has been proposed (SIB).

→ A series of publicly available datasets required for testing have been collected and are currently being curated to provide realistic testing conditions (SIB with contributions of UMA).

→ Several technical partners advanced enough in the development of the code to be delivered to ACGT have released an initial version of the associated QC procedures: ICCS, UvA, PSNC for the Oncosimulator, UPM for the Mediator, Custodix for the Anonymization tools, FORTH for the Workflow Designer.

→ UvA is setting up a local software management and verification environment adapted to visualization modules.

→ ICCS contributed to WP13 as planned, mainly concerning the development of the testing and validation procedures for the "Oncosimulator". More specifically it provided concrete methods for testing the simulation computer codes in terms of logic, stability, convergence, independence of the use of particular pseudorandom number generator seeds and other numerical aspects

- Main Activities & Tasks worked on

See Section "Progress towards objective"

- Major Achievements towards planned objectives, identify main partners Involved

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

Ambiguities remaining on the flow of clinical data in the ACGT environment have put several initially foreseen validation scenarios into question. A review of the implications of the anonymization procedures on the design of the ACGT architecture led to a round of discussion at the MB/TMC level and a new consensus on the data flow, from hospital databases through the anonymization tools to the data access layer and the higher levels of the ACGT infrastructure was achieved.

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

D13.1 "Evaluation criteria and verification procedures of the ACGT platform", due on Month 18, July 2007 is close to completion. A delay of a few weeks was caused by the data flow design ambiguity mentioned above.

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

Deliverable D13.1 is part of Milestone M7

Workpackage 14 – Training and Portal

- **Partner Responsible : SIVCO**
- **Contributing partner(s):** FORTH, INRIA, IJB, UPM, FHG, UOC, UHANN, Custodix, HealthGrid, ICCS, USAAR, FUNDP, IEO
- **Reporting Period:** 01/02/2007 – 31/07/2007
- **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 third 6 months period of the WP14 was concerned with the development of the *ACGT* Portal to provide a grid-enabled integrated, customisable, multi-lingual, and user-friendly interface to end-users.

- Progress towards objectives

The work for the development of the portal was continued from the previous period in three directions:

- a. User-friendly presentation of the content
- b. Integration of the portal in the grid architecture
- c. Integration of the *ACGT* services in the portal

- Main Activities & Tasks worked on

T14.1 - Consolidation of Requirements analysis for *ACGT* portal

Within this activity it was continued the work done in the previous stages for adapting the presentation of the portal to specific users. It was established the distribution of the content in Data, Services and Workflows categories and it was studied the relevance of these categories of content for each type of user.

T14.2 Development of the *ACGT* portal

There were two major activities followed in the development of the portal. First it was the implementation of the structure of the portal based on the initial functional document and to the consolidation of the user requirements received from the other partners. The second activity was the development of specific portlets for browsing and uploading services and workflows.

- Major Achievements towards planned objectives, identify main partners Involved

The main achievement of this reporting period was the increased collaboration with other WPs and partners for specific objectives:

- a. Collaboration with Healthgrid and Biovista for the dissemination and exploitation dimension of the portal.
- b. Collaboration with Custodix for the security features of the portal
- c. Collaboration with UMA for the implementation of the browse and register functions of the Service Repository

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

There were no deviations from the project work programme for this WP.

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

There were no WP 14 deliverables due during this 6 months reporting period.

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

This WP does not include its own milestones, but is involved in the Major Project milestone M7 which is due to Month 20.

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**: 01/02/2007 – 31/07/2007
- **Workpackage objectives and starting point of work at beginning of reporting period**

WP15 is designed to disseminate the project's results widely in Europe and in the world, in order to inform relevant scientific communities and attract new users groups

- Objectives during reporting period

The main objective that had to be achieved was to go on improving the dissemination tools already existing and think about others like information sheets that shall be understandable from the scientist or healthcare professional to the patient who is just curious to know more about the project.

- Progress towards objectives

→ Partners gave most of the information on the wiki (used as internal website) to complete the several contents for the external website, the information sheets and the posters.

→ All these contributions have been allowing the composition of effective communication tools.

- Main Activities & Tasks

The ACGT website

The ACGT website has been going through several revisions in order to allow easier and customized access to the different following communities: patients, doctors and clinicians, as well as researchers. Work is in progress along with the collection of information for all the web site sections.

-The Information sheets:

Information sheets are being produced to highlight different aspects of the multi-disciplinary work carried out in ACGT. In particular:

*legal and ethical aspects

*cancers (BRCA and nephroblastoma)

Additional information sheets are being prepared. They will be focusing on "the clinical trials", "the scenarios", "the grid infrastructure" and "the tools".

-Posters and flyers:

Specific posters are being prepared to showcase and emphasise some technical aspects of the ACGT work programme, and in particular:

***the oncosimulator** (with collaboration of Georgios Stamatakos, WP8)

***an integrated analysis platform for post-genomic clinical trials** (with collaboration of Thierry Sengstag, WP13)

The newsletter

The newsletter template was defined during the last period. The first newsletter and the newsletter system have been respectively produced and implemented to allow fast dissemination of ACGT information across the different project activities. This newsletter will allow ACGT participants and web site visitors to get instant updated information on the latest progress and achievements of the project.

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

Several tasks and activities were launched during this period. Particular efforts have been spent on the collection of information concerning the multiple subjects addressed by the posters, flyers and newsletter. Collaboration to gather information was done essentially with WP10 (legal and ethical) with WP2 (about nephroblastoma and breast cancers) and WP8, concerning the oncosimulator.

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

The "Editorial Board" prepared some content material for some dissemination tools, like the info sheets, the posters or the website, overall regarding the legal and ethical aspects. Yet, due to a lack of other technical content, and delay in further definition of some web sections, some dissemination vectors have been slightly delayed. In this regard, the "Editorial Board" meetings will be scheduled within the next few months in order to accelerate their final delivery.

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

D.15.3 - First Dissemination Report, delivered in September 07 (is currently in internal process)

D.15.6 - Design of the ACGT newsletter, delivered on the 5th of July (is currently in process)

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

No milestones for this reporting period.

Workpackage 16 – Market Investigation & Exploitation

- **Partner Responsible : BIOVISTA**
- **Contributing partner(s)** : PHILIPS, UPM, FHG, SIVECO, FUNDP
- **Reporting Period**: 01/02/2007 – 31/07/2007
- **Workpackage objectives and starting point of work at beginning of reporting period**

-The Workpackage has the following major objectives:

The overall objective of this work package is to consider and where appropriate implement the exploitable results of the project. During the 1st year of the project we completed the Initial Exploitation Plan (IEP) that will guide all exploitation related activities for the remainder of the project.

The starting point of work for the reporting period was the IEP itself which identifies the major stakeholder groups being addressed by ACGT as well as the 2 Initiatives we have decided to pursue. The existence of the project web site is also considered a major instrument through which some of the exploitation related goals are being pursued.

- Objectives during reporting period

During this reporting period the major objectives were to execute the tasks identified in the Initial Exploitation Plan. This foresaw the preparation of various exploitation materials and work that will support the two initiatives identified in the Plan. More specifically the following objectives were set:

- OBJ1: Create exploitation materials addressing the various stakeholder groups.
- OBJ2: Preparatory work for the ACGT Competition
- OBJ3: Create content for the site

- Progress towards objectives

→ OBJ1: Completed. Specific addressees are currently being identified so that the exploitation materials are sent to them before the end of the following reporting period.

→ OBJ2: In progress. A meeting to design the ACGT competition and begin preparatory activities will take place during the 4th reporting period.

→ OBJ3: In progress. Material is constantly being generated and released..

- Main Activities & Tasks worked on

- Preparation of exploitation materials
- Identification of specific organizations in the main stakeholder groups
- Preliminary design of the ACGT Competition

- Major Achievements towards planned objectives, identify main partners Involved

Per the Initial Exploitation plan the following achievements were reached:

Preparation of exploitation materials including

- * Introductory letter templates for the identified stakeholder groups
- * Sample code completed
- * Initial content for the FAQ list of the web site
- * Introductory documentation for the web site

In addition ACGT was linked with the submitted FP7 proposal “Virtual Physiological Human” NoE, following an invitation by the responsible of the proposal to our Project Manager.

All partners with resources allocated to this WP have been involved. Details are reported in the individual partner person-month activity reports.

In addition Custodix started working on an exploitation model for their CAT tool (Custodix Anonymisation Tool) beyond ACGT.

- They have been considering if they should use it as promotional only (i.e. free), try to exploit only attached services (modifications & consultancy on data protection)

- They are also looking at the possibilities of dual licensing (a free license for non-commercial use, and make people pay if they commercially exploit the results obtained)

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

The Initial exploitation plan foresees the organization of an ACGT Competition that aims to promote awareness and encourage the development of ACGT-compliant applications. A meeting to discuss and begin organizing this was foreseen in May in Bucharest. However due to last minute urgent commitments a number of important decision-makers from participating partners were not present. As a result only very preliminary issues were discussed and resolved. This discussion is now scheduled for the next consortium meeting. This delay while not desirable is not considered too detrimental to the overall plan since the underlying infrastructure that will allow the organizing of the competition is still being put in place.

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

No deliverables are foreseen for the reporting period

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

Following the completion of Year 1 of the project WP16 delivered the “ACGT Initial Exploitation Plan” in time for the first review. The initial plan foresaw an annual update schedule to reflect any changes in the plan and record progress to date. The next milestone is therefore the delivery of V2 of the Exploitation document in January 2008.

4 Consortium Management

➤ Project Meetings (including WP technical meetings)

Title	Place and Date	Main conclusions
WP5 Technical Meeting	St. Augustin (Germany) 5-6 March 2007	
MB	Poznan, 20-22 April 2007	Usability of the CAT-software
MB	Poznan, 23-24 April 2007	Review: preparatory meeting
Annual Review Meeting	Poznan, 20 – 25 April 2007	
Review meeting	Poznan, April 20-24, 2007	
Technical Meeting	20/04/07 - 24/04/07	one day concertation workshop on security/privacy
WP5 Technical Meeting	Bucarest, Romania, may 2007	Coordination of work
WP 10/11	Brussels, 3 May 2007	
WP10/WP11-Meeting	Brussels, 15 May 2007	
ACGT Tech Meeting	Bucharest May 20-22, 2007	See relevant Meeting Minutes
TMC meeting	Bucarest, May 21-22, 2007	- The structure of the ACGT Data Protection Board was discussed.
Technical Meeting	Bucarest, Romania 21st-22nd May 07	Coordination of work passed with success
TMC meeting	Madrid, July 2-3, 2007	aspects in healthcare projects based on Grid infrastructures,
Management Board Meeting	Madrid, 2 - 3 July 2007	
WP5 Technical Meeting	Madrid, Spain - 2-3 July 2007	
WP6 technical meeting	Madrid, July 2-3	See relevant Meeting Minutes
Technical Meeting	Madrid, Spain	The team was participating to the meeting and contributed a lot to the exchange of ideas.
Technical Meeting	Madrid, Spain - 2-3 July 07	An Editorial Board meeting is necessary to get a better task repartition and planning among the partners, notably regarding the communication tools contents.
Editorial Board	Waiting for a common agreement	Was planned in August, but had to be re-scheduled later by the end of 2007.
WP6 meeting	Madrid, July 4, 2007	Report to EU

Custodix/USAAR	Gent, 31 July 2007	- A consent-leaflet will be produced, to support local physicians in charge of getting the consent forms.
ACGT PMB meetings	Conference Calls	See relevant Meeting Minutes

➤ **Local meetings:**

Title	Place and Date	Main conclusions
Local USAAR Meeting	Homburg, 8 February 2007	Integration of the Master Ontology in the TrialBuilder and the need for a Clinical View of the Master Ontology
Local Meeting USAAR, Fraunhofer (IBMT) and Custodix	Homburg, 1-2 March 2007	Data Transfer of clinical data and DICOM data within ACGT
Meeting USAAR with UHok	Homburg, 27 April – 1 May	Defining how to use the Intelligent Pad Technology for the TrialBuilder
Meeting USAAR with Fraunhofer (IBMT) and UHok	St. Ingbert, 10 May 2007	How a Clinical Viewer for the Ontology has to look
Co-meeting with the legal workpackage of the EU-funded TRANSBIG project.	Brussels, 15 May 2007	Possible collaboration between ACGT and TRANSBIG regarding anonymization and pseudonimization issues.
Local USAAR Meeting with Fraunhofer (IBMT)	Homburg, 18 June 2007	Deliverable 2.2 was discussed
Meeting USAAR with ICCS	Athens, 28 July 2007	Discussion about WP8 and data transfer
Meeting Custodix with USAAR	Gent, 31 July 2007	Discussion of the Custodix Anonymisation Tool (CAT)

5 Use and Dissemination

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

Planned/actual Dates	Name	Participant profiles	Type	Number of Particip	ACGT Partner responsible /involved
1 – 3 February 2007	SIOP Nephroblastoma Committee meeting in London, UK	Paediatric Oncologists, molecular biologists	Meeting	50	USAAR Participants: Norbert Graf, Alexander Hoppe --> Introduction of ACGT to SIOP and promotion to run the next SIOP Wilms trial within ACGT --> Talk about ACGT and the TrialBuilder
12 February 2007	"Biobanking goes Europe" at the Telematikplattform für medizinische Forschungsnetze e.V. in Berlin	Members of the TMF	Workshop	25	LUH (participation)
22 - 25 April 2007	First formal ACGT review, Poznan, Poland. Demonstration of interactive visualization of "live" in-silico simulation results executing over distributed systems.	ACGT MB, Reviewers	Review meeting	30	all WPL
24 – 27 April 2007	"Does HealthGRID Present Specific Risks With Regard To Data Protection?" - HealthGrid 2007 Conference in Geneva	General public	Conference	200	FUNDP (Presentation)
24 April 2007	"Data base at the crossway of two legislations" - Agoria ICT eHealth: Legislation & eHealth, Brussels	Professionals	Conference	100	FUNDP (Presentation)
25.04.2007	Bio-Med Grid Workshop (organized by PSNC and ACGT)	Medical doctors, bioinformatitians	Workshop	50	PSNC, all partners presented their results
26 April 2007	Presentation of the paper: Stefan Ruping, Stelios Sfakianakis, Manolis Tsiknakis "Extending Workflow Management for Knowledge Discovery in Clinico-Genomic Data" - In HealthGrid 2007 at Geneva	Software engineers, Grid developers	European level	70	FORTH
26 April 2007	Presentation of the paper: Stefan Ruping, Stelios Sfakianakis, Manolis Tsiknakis "Extending Workflow Management for Knowledge Discovery in Clinico-Genomic Data" - In HealthGrid 2007 at Geneva	Software engineers, Grid developers	European level	70	FORTH
3 May 2007	Workshop on security/privacy issues for bio-medical applications based on GRID middleware, Brussels	Member of EU-funden project in the ICT for health area	Workshop	20	LUH/Custodix (Participation)
15 May 2006	Meeting with the TRANSBIG (Translating molecular knowledge into early breast cancer management: building on the Breast International Group (BIG) network for improved treatment tailoring) ethical and legal group and WP10 of ACGT, Brussels	WP-10	Workshop	20	UH/Crid/Custodix/LUH (Participation and presentation)
15 – 16 May 2007	in Bruxelles, Belgium	Paediatric oncologists, molecular biologists, lawyers	Meeting	15	USAAR Participant: Alexander Hoppe
16 – 17 May 2007	CTO Meeting (Clinical Trial Ontology meeting) NIH Bethesda, USA	Clinicians, Ontologists,	Meeting	100	USAAR Participants : Norbert Graf, Cristian Cocos
19 May 2007	Presentation: „Datenschutz und die Forschung am menschlichen Gen“, Hannover	General Public	Exhibition	100	LUH (presentation)
22 - 23 May 2007	The handheld "see-through display" was demonstrated at ICT Delta Congress, Jaarbeurs, Utrecht, The Netherlands.		Congress	???	UVA
30 May 2007	Oral presentation and discussion at the meeting of the EU-funded EUROCAN project.	Clinical and laboratory researchers	EU	40	6 (IJB)

1 June 2007	Les bases de données à la croisée de la protection de la vie privée et de la société de l'information - JuriTIC, Namur (Belgium)	Professionals	Workshop	50	FUNDP (Presentation)
25 - 27 June 2007	Visual Interactive Effective Worlds (VIEW) workshop, Lorentz Center, Leiden, the Netherlands		Workshop	50	UVA Participant : R.G Belleman
26 June 2007	Working group meeting of the Telematikplattform für medizinische Forschungsnetze e.V. on biomaterial banks	Members of the TMF	Workshop	25	LUH (participation)
26 June 2007	Presentation of the paper : "Data protection issues with regard to research in genetic data" at the 2nd Workshop on Personalisation for E-Health, held on the 11th international conference on User Modelling 2007, Corfu	Professionals	Conference	25	LUH (presentation)
28 June 2007	Presentation on legal aspects of Information Security in medical scenarios, Bratislava	Professionals	Conference	50	LUH (presentation)
4 – 13 July 2007	Université européenne d'été de la santé et éthique biomédicale.- Toulouse (France) and Madrid (Spain)	General public	Summer university	50	FUNDP (Presentation)
11 July 2007	Meeting with GPOH (Society of German Paediatric Oncology and Haematology) subgroup for clinical trials	Informaticians, Clinicians	Meeting	7	USAAR Participants : Norbert Graf, Alexander Hoppe --> Talk about ACGT and presentation of parts of the TrialBuilder
9 – 13 July 2007	Ontology of Biomedical Investigation (OBI) Workshop, NHI Bethesda	Ontologists	Meeting	100	USAAR [IFOMIS] Participant : Cristian Cocos
23 July 2007	Presentation of the paper: Manolis Tsiknakis, Stelios Sfakianakis, George Potamias, Giorgos Zacharioudakis, Dimitris Kafetzopoulos "A semantic grid infrastructure enabling integrated access and knowledge discovery from multilevel data in post-genomic clinical trials" - In the 15th International Conference on Conceptual Structures (ICCS 2007) at Sheffield	Software engineers, bioinformaticians	International level	50	FORTH
27 - 28 July 2007	Details concerning the simulation of nephroblastoma response to chemotherapy	USAAR, ICCS, FORTH	Meeting	10	ICCS, USAAR, FORTH
23 September 2007	Oral presentation and discussion at the Breast International Group meeting.	Breast cancer clinicians and researchers	From all over the world	300	6 (IJB),
4 October 07	ACGT Workshop	ACGT partners	Session (from 4 to 7pm)	Not defined info yet	HealthGrid

➤ **Scientific publications**

Date and Type	Details
Proceedings of the 15th International Workshops on Conceptual Structures (ICCS 2007) Beijing, China 27 - 30 May 2007	Manolis Tsiknakis, Stelios Sfakianakis, George Potamias, Giorgos Zacharioudakis, Dimitris Kafetzopoulos "A semantic grid infrastructure enabling integrated access and knowledge discovery from multilevel data in post-genomic clinical trials" in Akhgar, Babak (Ed.) , ISBN: 978-1-84628-990-3
10-15 June 2007, Statistics / data analysis workshop	ACGT Poster presented, title "ACGT: An integrated analysis platform for post-genomic trials"
Proceedings of the 13th annual conference of the Advanced School for Computing and Imaging (ASCI07), June 13 to 15, 2007, Heijen, the Netherlands.	M. Scarpa and R.G. Belleman. <i>An interaction framework for VR and AR applications</i> ,
Proceedings of the 4th pHealth Conference 2007. Porto Carras, Chalkidiki, Greece, June 20-22, 2007	Anguita A, Martín L, Crespo J, Tsiknakis M, Maojo V. "Solving semantic heterogeneities and integration between clinical and image databases in post-genomic clinical trials".
KDD-2007 Workshop on Data Mining Standards, Services and Platforms, 12. Aug. 2007, San Jose, USA.	Dennis Wegener, Michael May, "Extensibility of Grid-Enabled Data Mining Platforms: A Case Study",
29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society in conjunction with the biennial Conference of the French Society of Biological and Medical Engineering (SFGBM), August 23-26, 2007	Stamatakis GS, Dionysiou DD, Graf N, Sofra NA, Desmedt C, Hoppe A, Uzunoglu NK, Tsiknakis M: "The "Oncosimulator": a multilevel, clinically oriented simulation system of tumor growth and response to therapeutic schemes. Towards clinical evaluation of in silico oncology."
29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society in conjunction with the biennial Conference of the French Society of Biological and Medical Engineering (SFGBM), August 23-26, 2007	Weiler G, Brochhausen M, Graf N, Hoppe A, Schera F, Kiefer S: <i>Ontology Based Data Management Systems for post-genomic clinical Trials within an European Grid Infrastructure for Cancer Research.</i>
Proceedings . of the ECCO 2007 Conference, Barcelona, September 2007 - Spain.	Norbert Graf, Christine Desmedt, Alexander Hoppe, Manolis Tsiknakis, Dimitra Dionysiou , Georgios Stamatakis , <i>Clinical requirements of "In Silico Oncology" as part of the integrated project ACGT (Advancing Clinico-Genomic Trials on Cancer)</i> ,
Proceedings of the First International Workshop on Conceptual Modelling for Life Sciences Applications (CMLSA 2007), Auckland, New Zealand 5 - 9 November 2007	Martín L, Bonsma E, Anguita A, Vrijnsen J, García-Remesal M, Crespo J, Tsiknakis M, Maojo V. "Data Access and Management in ACGT: Tools to solve syntactic and semantic heterogeneities between clinical and image databases".
Proceedings of the American Medical Informatics Association (AMIA - Annual Symposium) 2007. 11-14 Nov 2007, Chicago, IL (USA)	Martín L, Anguita A, de la Calle G, García-Remesal M, Crespo J, Tsiknakis M, Maojo V. "Semantic Data Integration in the European ACGT project".
Proceedings of the American Medical Informatics Association (AMIA – Annual Symposium) 2007. 11-14 Nov 2007, Chicago, IL (USA) [In Press]	Pérez-Rey D, Anguita A, Crespo J, Maojo V. "An Ontology-based and Distributed KDD Model for Biomedical Sources".
Conference - pending approval	Dennis Wegener, Thierry Sengstag, Stelios Sfakianakis, Stefan Rüping, Anthony Assi "GridR: An R-based grid-enabled tool for data analysis in ACGT clinico genomics trials", submitted to 3 rd IEEE International Conference on e-Science and Grid Computing

Lecture Notes in Computer Science 4561, pp.569-575, 2007.	D.D.Dionysiou, G.S.Stamatakos, K.Marias "Simulating cancer radiotherapy on a multi-level basis: biology, oncology and image processing",
Lecture Notes in Computer Science 4561, pp.703-709, 2007.	K.Marias, D.Dionysiou, G.S. Stamatakos, F.Zacharopoulou, E.Georgiadi, T.G.Maris, I.Tollis "Multi-level analysis and information extraction considerations for validating 4D models of human function",
Press on Physical Review E.	A. d'Onofrio "Rapidly acting anti-tumoral anti-angiogenic therapies" in press on Physical Review E.
Journal publication; accepted for future publication	Tsiknakis M., Brochhausen M., Nabrzyski J., Pucacki J., Sfakianakis S. ; 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": Accepted for future publication in <i>IEEE Transactions on Information Technology in Biomedicine</i> , Digital Object Identifier 10.1109/TITB.2007.903519
June 2007 - Clin Cancer Res. 2007	<u>Desmedt C, Piette F, Loi S, Wang Y, Lallemand F, Haibe-Kains B, Viale G, Delorenzi M, Zhang Y, d'Assignies MS, Bergh J, Lidereau R, Ellis P, Harris AL, Klijn JG, Foekens JA, Cardoso F, Piccart MJ, Buyse M, Sotiriou C; TRANSBIG Consortium.</u>
Article turned in for publication / foreseen for next year	J. Herveg, "Panorama des responsabilités liées aux services et aux produits de la santé en ligne en droit européen", in <i>Revista de Direito Medico e da Saude and Editions hospitalières</i> .
Article turned in for publication / foreseen for next year	J. Herveg, "Autonomie et Droit au respect de la vie privée", in <i>Revista de Direito Medico e da Saude and Editions hospitalières</i> .
Cancer Informatics, submitted 2007	Graf N, Hoppe A, Sofra N, Stamatakos G: Clinical requirements regarding <i>In Silico Oncology</i> .
ERCIM News 69, Special Issue: The Digital Patient. pp. 22-23, April 2007.	R.G. Belleman, M. Scarpa and B. Stolk. <i>Interactive Simulation and Visualization for Cancer Treatment Planning with Grid-Based Technology</i> .
finalized manuscript, to be submitted	A. d'Onofrio (corr. author), A. Gandolfi and A. Rocca. <i>The dynamics of tumour-vasculature interaction suggests low-dose, time-dense antiangiogenic schedulings</i> .
Dossier médical et données médicales de santé, Bordeaux, Ed. Hospitalières, 2007, pp. 183-19	J. Herveg, "La protection des données médicales en droit européen", 6.
Dossier médical et données médicales de santé, Bordeaux, Ed. Hospitalières, 2007, pp. 243-258.	J.-M. Van Gysegheem, "L'information génétiques et le traitement des données à caractère personnel",
Press in the book "Aspects of Nonlinear Modelling" Birkhauser Publishing (E. Venturino and R. Hodskings eds.)	A. d'Onofrio " 'Noisy Oncology': some Caveats in using Gaussian Noise in Mathematical Models of Chemotherapy.
in From Genes to Personalized HealthCare : Grid Solutions for the Life Sciences, IOS Press, 2007, vol. 126, pp. 219-228.	J. Herveg, "Does Healthgrid Present Specifics Risks with Regard to Data Protection ?",
on press on Physical Review E	A. d'Onofrio. <i>Rapidly acting anti-angiogenic antitumor therapies</i> .
manuscript in preparation	A. d'Onofrio

Research article	<i>“Strong time dependence of the 76-gene prognostic signature for node-negative breast cancer patients in the TRANSBIG multicenter independent validation series.”</i>
submitted	P.Cerai and A. d’Onofrio (corr. auth). <i>A bi-parametric general model for the tumor angiogenesis and anti-angiogenesis therapy.</i>
submitted	A. d’Onofrio (corr. auth.) and A. Gandolfi. <i>A family of models of angiogenesis and antiangiogenesis anticancer therapy.</i>
submitted to Cancer Informatics.	N.Graf, A. Hoppe, D.Dionysiou, G. Stamatakos <i>“Clinical requirements regarding In Silico Oncology”</i> ,
submitted to Mathematical Biosciences.	D.D.Dionysiou and G.S.Stamatakos <i>“Introducing operator notation to in silico oncology: the paradigm of imageable glioblastoma treated with radiotherapy. Clinical validation based on RTOG study 82-02”</i> ,
submitted to the Journal of Theoretical Biology.	G.S.Stamatakos and D.D.Dionysiou <i>Introduction of Hypermatrix and Operator Notation into a Discrete Mathematics Simulation Model of Malignant Tumour Response to Therapeutic Schemes In Vivo. Some Operator Properties,</i>
Internal report. UvA, May 2007.	Z.R. Rahhal. <i>Interactive Distributed Computing Middleware.</i>
Internal report. UvA, June 2007.	T. de Kler. <i>Integration of the ARToolKitPlus optical tracker into the Personal Space Station.</i>
Internal report. UvA, June 2007.	P.M. Geldof. <i>Generic Computing on a Graphics Processing Unit.</i>
Internal UVA Report, June 2007	T. de Kler. <i>Integration of the ARToolKitPlus optical tracker into the Personal Space Station.</i> Internal report. UvA, June 2007.
Internal UVA Report, June 2007	P.M. Geldof. <i>Generic Computing on a Graphics Processing Unit.</i> Internal report. UvA, June 2007
Internal UVA Report, May 2007	Z.R. Rahhal. <i>Interactive Distributed Computing Middleware.</i> Internal report. UvA, May 2007.
Bio-Med-Grid Workshop Proceedings, To appear in special issue of CMST (Computational Methods for Science and Technology) in January 2008.	BIO-MED-GRID Workshop Proceedings are under preparation and will appear in January 2008. ACGT contributed papers include: Manolis Tsiknakis (FORTH, Heraklion, Greece): <i>Advancing Clinico-Genomic Trials on Cancer with the ACGT Infrastructure</i> Desmedt Christine (Institute of J. Bordet, Brussels, Belgium): <i>New Insights Into Breast Cancer Biology and Subtyping</i> Mathias Brochhausen (IFOMIS, Saarland, Germany): <i>ACGT Cancer Ontology</i> Andreas Persidis (Biovista, Athens, Greece): <i>Browse-directed search: a new way to mine the scientific literature.</i> Georgios Stamatakos (NTUA, Athens, Greece): <i>Oncosimulator</i> Francesca Buffa (University of Oxford, UK): <i>A hypoxia metagene in head and neck cancer and its relation to prognosis of multiple cancers</i> Nikolaus Forgo (University of Hannover, Germany): <i>A legal data-protection framework for transnational research in genetics and cancer: the ACGT-approach.</i> Jarek Nabrzyski (PSNC): <i>Grids for Life Sciences</i>

6 Disseminated Project Results

Description	Details
Patents, Software prototype...	.
Literature Mining prototypes	<p>Biovista has been demonstrated the grid-enabled versions of its literature mining s/f to various existing and potential customers including organizations such as: BiogenIdec, Novartis, Pfizer, Eli Lilly, Qiagen, Millpore, University of Virginia and others. These early prototypes are intended to generate initial interest by the target groups.</p>
	<p>Gridge software (www.gridge.org) was extended with new features needed by the ACGT project, namely: multiple credential support, implementation of new security policy for ACGT inside GAS, new GUI client for GAS, deployment of portal client for GAS, deployment of improved Globus authorization layer, implementation and deployment of new authorization plug-in for SW-GRAM, work on implementation of JSDL support for GRMS, work on parametric jobs support for GRMS, support for Fraunhofer Institute IAIS in development of client for GRMS.</p> <p>The Gridge toolkit is freely available for anyone who wants to build their own Grid infrastructures. The website reaches around 50.000 hits each week.</p>

7 Person Month Status Report

1 February - 31 July 2007

CONTRACT N°: 026996		AC Partners - Own Staff																									
ACRONYM: ACGT																											
PERIOD: 01/02/2007 31/07/2007																											
TOTALS		1-ERCIM	2-FORTH	3-INRIA	4-UVA	5-PHILLIPS	6-JUB	7-SIB	8-LUNDU	9-UMA	10-LUPM	11-FHG	12-BIOVISTA	13-UJC	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	
WP1 - Consortium Management act.	Act. WP total: 1,00																										
Project Management	Plan. P total: 1,00																										
WP2 - RTD/Innovation activities	Act. WP total: 5,30				0,50		0,50							0,50						1,38				0,09		1,33	
User Needs Analysis and Specificati	Plan. P total: 1,50				0,50																						
WP3 - RTD/Innovation activities	Act. WP total: 3,00																										
Architecture and Standards	Plan. P total: 2,00																										
WP4 - Demonstration activities	Act. WP total: 3,00															3,00											
Biomedical GRID technology Layer	Plan. P total: 3,00															3,00											
WP4 -RTD/Innovation activities	Act. WP total: 3,00																										
Biomedical GRID technology Layer	Plan. P total: 3,00																										
WP5 - Demonstration activities	Act. WP total: 4,31															2,00				0,22				0,09	2,00		
Distributed Data Access, Tools and /	Plan. P total: 3,00															2,00									1,00		
WP5 - RTD/Innovation activities	Act. WP total: 4,31																										
Distributed Data Access, Tools and /	Plan. P total: 3,00																										
WP6 - Demonstration activities	Act. WP total: 1,84				0,50																				0,67	0,67	
Knowledge Management and Discov	Plan. P total: 1,17				0,50																				0,67		
WP6 - RTD/Innovation activities	Act. WP total: 1,84																										
Knowledge Management and Discov	Plan. P total: 1,17																										
WP7 - Demonstration activities	Act. WP total: 1,82						0,33													1,40				0,09			
Ontologies and Semantic Mediation	Plan. P total: 1,82																										
WP7 - RTD/Innovation activities	Act. WP total: 1,82																										
Ontologies and Semantic Mediation	Plan. P total: 1,82																										
WP8 - Demonstration activities	Act. WP total: 5,56				2,00														2,25	0,31					0,67	0,33	
Technologies and Tools for in-silico	Plan. P total: 2,33				2,00																				0,33	0,33	
WP8 - RTD/Innovation activities	Act. WP total: 5,56																										
Technologies and Tools for in-silico	Plan. P total: 2,33																										
WP9 - Demonstration activities	Act. WP total: 1,43														1,00					0,10					0,33		
The integrated ACGT Environment	Plan. P total: 2,33														1,00										1,33		
WP9 - RTD/Innovation activities	Act. WP total: 1,43																										
The integrated ACGT Environment	Plan. P total: 2,33																										
WP10 - RTD/Innovation activities	Act. WP total: 1,54																			0,25		0,20	1,00	0,09			
Ethical, Legal and QA Issues	Plan. P total: 1,54																										
WP11 - Demonstration activities	Act. WP total: 2,00															2,00											
Trust and Security	Plan. P total: 2,00															2,00											
WP11- RTD/Innovation activities	Act. WP total: 2,00																										
Trust and Security	Plan. P total: 2,00																										
WP12 - Demonstration activities	Act. WP total: 4,10						0,50							1,00						0,60						2,00	
Clinical Trials	Plan. P total: 4,10																										
WP12 - RTD/Innovation activities	Act. WP total: 4,10																										
Clinical Trials	Plan. P total: 4,10																										
WP13 - RTD/Innovation activities	Act. WP total: 1,33															1,00										0,33	
Evaluation and Validation	Plan. P total: 1,00															1,00											
WP14 - Training Activities	Act. WP total: 2,33																	0,25					0,33				
Training	Plan. P total: 1,33																										
WP14 - RTD/Innovation activities	Act. WP total: 2,33																										
Training	Plan. P total: 1,33																										
WP15 - RTD/Innovation activities	Act. WP total: 2,33						0,25							0,50		1,00		0,25							0,33		
Dissemination	Plan. P total: 1,33															1,00											
WP16 - RTD/Innovation activities	Act. WP total: 2,33																								0,33		
Market Investigation and Exploitation	Plan. P total: 2,33																										
Actual total	38,55				3,00		1,58						2,00		15,00		0,25	2,25	4,26		0,20	1,33	0,35	3,67	4,66		
Planned total	20,66				3,00										14,00										3,66		
Total PM																											
Actual total	298,95	5,10	24,65	6,00	15,00	18,20	6,48	6,03	14,00	12,00	26,00	19,00	15,80	7,99	7,16	29,83	11,75	8,59	9,57	17,90	8,00	6,90	8,32	6,35	3,67	4,66	
Planned total	300,67	7,66	24,00	6,00	10,33	18,33	8,65	7,00	11,33	13,50	23,66	25,14	18,66	5,99	8,00	30,32	10,33	15,00	7,32	13,50	7,66	5,99	5,99	7,99	3,66	4,66	