Appendix I

Brief description of the work performed

For the period 1st February 2006 to 31st January 2007

ACGT Contract n°026996

PARTNER 01 – ERCIM

WP1 : Project Management

The objective of this Workpackage is to ensure a strong and coherent administrative and financial management of the Network. This activity can be subdivided in two main parts: (i) Administrative and Financial Coordination; (ii) Scientific Coordination. This activity is lead by ERCIM, represented by Rémi Ronchaud, with the support of the ERCIM Office team.

The administrative coordination was concerned first and foremost with the implementation of the project's management architecture, including decision-making processes, and the establishment of efficient communication mechanisms for knowledge and information exchange (e.g., BSCW shared workspace, mailing lists, on-line reporting tools).

During this first year of activity, the main activities and achievements of the Managements have been focusing on:

- Implementation of the project's general organization and of the management architecture;
- Assistance and support to Scientific Management;
- Preparation of the internal working documents (templates);
- Definition of procedures and guidelines (reimbursement, costs claims, votes and communication protocol);
- Validation of partners financial figures and coordinates;
- Reception and transfer to all partners of the advance payment;
- Validation and monitoring of partners efforts and contributions to the project
- Implementation of the ACGT partner database;
- Preparation of the six monthly activity Report. Regular efforts were devoted to the collection of every partner's contribution to the periodic report (work description and effort figures in person-months).
- Definition of the dissemination strategy
- Preparation of dissemination material: ACGT poster, leaflet and give away material
- Supervision of the information flow within the project and support of collaborative tool (BSCW)
- Interaction with related initiatives to lay a grounds for cooperation

The Management has also been preparing and organising the plenary project meetings during the reporting period. Additional Management board and technical meetings have also been organised to support the scientific coordination effort across disseminated teams and workpackages.

The two ACGT Plenary meetings are detailed hereafter:

- ACGT Kick off Meeting in Juan les Pins, France, 27-28 February and 1rst of March 2006
- ACGT Plenary and Technical Meeting in Malaga, Spain, 23 to 26 January 2007

In addition, a periodic audio conferencing services has been implemented to support monthly exchanges among ACGT Participants. Audio conferences are jointly chaired by the Project coordinator and the Technical Director. If necessary to address a particular issue, additional audio conferences can be organised. Specific agenda and actions are defined for every audio conference, hence avoiding other costly and time consuming meetings.

WP15 : Dissemination

ERCIM has been contributing to the dissemination activity in several ways:

- Preparation of the first ACGT flyer
- Participation to the design and implementation of the ACGT web site
- Implementation of internal dissemination support tools (BSCW, audio conferencing services)
- Preparation of several press articles distributed in newspapers, Cordis News, electronic news boards and ERCIM News Magazine, distributed over 10 00 copies worldwide.
- Participation to the conception and design of the ACGT poster
- Presentation of the ACGT project during the EuroBio 2006 in Paris, France.
- Representation of the ACGT project during the IST 2006 Conference in Helsinki
- Contribution to the preparation of the Initial Dissemination Plan (D15.2)

WP16 : Market Investigation and Exploitation

- Our participation in WP16 has been limited to the reviewing of D16.1, Initial Exploitation plan. ERCIM has also been identifying potential commercial pharmaceutical companies to ensure the dissemination of the future project results in cooperation with WP15, but with a view towards supporting the technology uptake by relevant industrial stakeholders in the field.

PARTNER 02 – FORTH

FORTH is participating in ACGT through a number of its Institutes and Research Groups. Specifically, the Institute of Computer Science-ICS (Biomedical Informatics Laboratory and Information Systems Laboratory), the Institute of Molecular Biology and Biotechnology-IMBB (Laboratory for Post-Genomic Technologies) and the Institute of Chemical Engineering and High Temperature Processes-ICE-HT (Metabolic Engineering and Systems Biology Laboratory) are participating in ACGT.

WP1: Project Management

FORTH is responsible for the scientific-technical management of the project. The technical coordinator, Manolis Tsiknakis, is heading the Management Board and the External Advisory Committee. His role is also to ensure that the ACGT efforts are coordinated and in-line with the timing and expectations. As such, he is directing the scientific work of the project; supervising the creation of the DoW for the upcoming period, monitoring the time schedule and the timing of the related activities, recommending appropriate actions to rectify delays, creating and maintaining the conditions necessary for successful and effective collaboration and acting as the scientific representative of the network.

The person responsible has devoted substantial efforts for:

- The preparation of project presentation material.
- The organisation of a several technical meetings, either at the project level or at a WP level and formulating the agenda's for project technical meetings.
- The initiation of a number of discussions on technical as well as strategic issues.
- The continuous monitoring of the technical project activities.
- being in frequent communication with members of the External Advisory Board requesting their views on critical (scientific and/or strategic issues)
- Participating in all of the project meetings, conference calls and/or SKYPE meetings.

He initiated the formation of the Technical Management Committee (to assist him in the management of the complex and multidisciplinary technical challenges of the project) and by making sure that technical issues are appropriately identified, raised, discussed and decided upon.
He is also collaborating regularly with the administrative coordinator and is supervising the WP Leaders.

WP2: User Needs Analysis and Specifications

FORTH undertook the responsibility for the production of the Deliverable D2.1. FORTH's staff has made significant contributions for the deliverable by contributing to the work leading to the production of the deliverable, as well as towards preparing several contributions in the Deliverable.

In addition FORTH participated in several meetings and actively contributed to the discussions and the user needs elicitation process.

Our work focused on:

- Work focused on the preparation of a state-of-the-art document, entitled «*Integrated "-omic" studies for disease-specific diagnosis, early diagnosis, prognosis and therapy design: current status, directions and challenges*». The report presents the contribution of all current "-omic" technologies in clinical research of complex diseases and emphasizes the need for the technical and scientific integration of all "-omic" platforms for attaining the long-term objective of personalized medicine. In addition, the development of novel computer-based data storage, data visualization and educated integration tools that can effectively capture and integrate

genomic, transcriptomic, proteomic, metabolomic and clinical data towards the process of bringing systems biology information to clinical practice, is high-lighted.

- The preparation of the sections of the Deliverable 2.1 related to state of the art wrt Workflow Management and Enactment Systems and technological Standards as well as Metadata Standards and a review of metadata related work in the domain of bio-informatics.
- Holding regular meetings with the clinical users at the University of Crete, for eliciting user needs and requirements. In the context of this work a multi strategy knowledge discovery scenario for the discovery of evidential and strong relations/correlations between patients' genomic (i.e., gene-expression) profiles with respective clinico-histopathology profiles was defined and elaborated. The scenario is based on the smooth integration of three data-mining operations: clustering (of genes), association rules mining – ARM (between clinical features and indicative gene-clusters- the metagene features), and feature-selection (for the selection of most discriminant genes). Appropriate contributions were prepared with respect to this scenario for D2.1, and other Deliverables.

WP3: Architecture and Standards

FORTH made significant contributions to the work of this WP. It studied the architectural approaches of other projects and initiatives and provided contributions to the technical discussions related to the functional ACGT architecture.
It actively participated in the following technical seminars /workshops (WP3 "Architecture and Standards")

- "Entering into Grid" seminar from University of Crete, 16-17 March 2006, Heraklion-Greece, four participants from ICS-FORTH. Emphasis was given to the presentation and hands-on tutorial of the architecture, technologies, and standards of the EGEE Grid.
- "gLite seminar" from EGEE – EMBRACE, 9-13 October 2006, Clermont-Ferrand-France, one participant from ICS-FORTH

WP4: Biomedical GRID technology Layer

One of the more technical achievements was the setup of a Grid test bed (in collaboration with WP4) and the deployment of initial services at the sites of different partners. In the context of these activities, FORTH actively participated in the technical seminars/workshops "GT4 – Gridge tutorial" held in Poznan-Poland, on the 4-5th December 2006.

Subsequently, FORTH purchased the technology required for the development of the ACGT Grid node in its premises. The infrastructure today includes:

- a four Linux workstations (dual processor) cluster in FORTH as the local ACGT Grid node
- Globus toolkit and various grid components
- OGSA-DAI toolkit.

On the basis of this infrastructure, and in collaboration with WP5, WP6 and WP9 activities, FORTH is proceeding with the implementation of a proof-of-concept demonstrator of the "Complex query Scenario".

WP5: Distributed Data Access, Tools and Applications

Participation in various discussions related to accessing distributed data access and the different models to implement it. Preparation of a survey of relevant work with references to the major approaches (Global-As-View, Local-As-View). An evaluation of the corresponding advantages and disadvantages of each approach was performed.

Using the local Grid technology layer developed (see WP4) FORTH set up an "experimental infrastructure" consisting of clinical databases (Top CT data base), and a BASE compliant microarray database. We evaluated OGSA-DAI and OGSA-WebDB and provided technical arguments for their utilization in the ACGT architectural framework as the technologies to be used in ACGT for the implementation of the data access services. FORTH was also an active participant of the "OGSA-DAI technical workshop" that took place on the 23rd of January 2007 at Malaga-Spain.

In addition we have begun implementation of the OGSA-DAI based data access services to the Clinical and Genomic Databases of our experimental test-bed,

WP6: Knowledge Management and Discovery Tools

FORTH's involvement in WP6 is mainly to address and provide solutions for the data-mining and knowledge-discovery issues related to ACGT. In this context FORTH were actively involved into the following R&D activities:

- Elaboration of the requirements stemming out from the "*multi strategy knowledge discovery scenario"* and made concrete contributions to the WP6.1 deliverable.
- A prototypical implementation of the technologies and tools required by the scenario was initiated and preliminary results have been assessed. A full GRID-enabled and workflow-based operationalisation of this scenario is in progress – to be demonstrated during the first ACGT official review on a real-world clinico-genomic case study.

Moreover, FORTH customised in the context of the ACGT-Cretan infrastructure a *mediator* for integrated access to patients' gene-expression (from a BASE server) and respective clinical and histopathology data (from respective clinical information systems). The mediator and respective operations are appropriately linked with respective data-mining operations (as the ones mentioned above).

FORTH's researchers and staff involved in WP6 activities participated in all ACGT related meetings.

WP7: Ontologies and Semantic Mediation Tools

Our work focused on the study of the cases of heterogeneity in mapping medical and genomic information systems to a core ontology. In the context of this we undertook the task of

- Mapping of the BASE to a core Ontology (CIDOC)
- Mapping of a Clinical database schema (CIS) to a core Ontology (CIDOC)

Through our findings we made contributions to the relevant ACGT deliverables and also the following technical report was produced "Haridimos Kondylakis, Martin Doerr, Dimitris Plexousakis, Mapping Language for Information Integration, 2006, Technical Report 385, ICS-FORTH, December 2006"

We have also collaborated closely with IFOMIS on introducing a generic model of scientific observation into the ACGT Master Ontology. FORTH researchers (Dr Martin Doerr) participated in a dedicated meeting that took place at IFOMIS in Dec. 2006, and contributed to the formulation of the ACGT strategy with respect to Ontology development and maintenance. We are also focusing on evaluating automated ways of building and extending ontologies.

We have made significant contributions to the production of D2.1 and also to Deliverable 7.1-Consolidated Requirements on ontological approaches for integration of multi-level biomedical information.

FORTH has also initiated the organization of a scientific workshop, jointly with IFOMIS, on "Ontologies and Information Systems for the Semantic Web", to take place during the 26th International Conferences on Conceptual Modelling (ER 2007), November 5-9, 2007, New Zealand"

WP8: Technologies and Tools for in-silico Oncology

FORTH's involvement on WP8 is mainly to address and provide solutions for the image analysis requirements but also assist in the refinement and validation of in silico models.

FORTH has worked on setting the proper environment for the local data storing and handling. Also, image analysis scenarios have been developed for the validation and the visualization of the 'oncosimulator' predictions. It has been concluded that the segmentation of regions of interest (e.g. delineation of nephroblastoma before and after therapy), is a crucial step for initializing and validating the in silico models. FORTH has proposed a number of algorithms; however, 'ground truth' segmentations from the clinicians will be required to validate the automatic ROI extraction algorithms.

Additionally, an image analysis scenario for geometrical normalization and quantification of temporal imaging data has been designed. This will be beneficial for better assessing temporal changes after treatment and comparing them to the simulation predictions. The tools are currently been optimised for the nephroblastoma SIOP 2001/GPOH and breast cancer TOP data of WP8.

FORTH was also a co-organizer of a scientific dissemination event, the Second International Advanced Research Workshop on *In Silico* Oncology (**http://www.ics.forth.gr/bmi/2nd-iarwiso/**) that took place at Kolymbari, Crete, Greece on September 25 and 26, 2006.

WP9: The integrated ACGT Environment

FORTH coordinates the Workpackage, and performed a number of responsibilities implied by the leadership of a WP such as the preparation of the necessary paper work.

We undertook the planning for the kick-off meeting of the WP, which was organized, prepared and held on the 29th of September 2006 in Crete, Greece.

Subsequently we

- Performed an analysis of the integration requirements of ACGT and study of the state of the art approaches in other projects (e.g. caBIG) and in relevance with the current technological standards.
- Investigated the interoperability problems introduced by specific technological approaches (e.g. WSRF Grid Services) and raise these issues for discussion in the technical meetings of ACGT.
- Performed a survey of the open source workflow tools with roots in the business process management field and the respective industry standards such BPEL 2.0
- Set up "trial experiments" with the objective of evaluating open source workflow platforms (e.g. Taverna Workbech workflow editor and enactor and the accompanied tools and technologies and the TRIANA workflow editor and enactor) and investigated their applicability to the ACGT environment

We were also heavily involved in the initial preparation and production of the Deliverable 9.1 - "Integration Guidelines" and the elicitation of the integration needs of other work packages.

We have led the discussions with EGEE with respect to exploring the functionality offered by EGGE and its evaluation with respect to the ACGT requirements. In the context of this work we represented and presented the ACGT project in the EGEE 06 Conference on the 25th of September 2006 at Geneva, Switzerland.

Finally we have prepared and submitted the paper: "Extending Workflow Management for Knowledge Discovery in Clinico-Genomic Data" by Stefan Rüping, Stelios Sfakianakis, Manolis Tsiknakis, in the Healthgrid 2007 conference that will take place in Geneva at 24-27 of April 2007.

WP10: Ethical, Legal and QA issues

Our work in this WP was only minor (as foreseen). We have contributed material to the legal and ethical experts regarding the national regulatory framework and provided "models" for the patient consent forms to be studied and taken into consideration for the design of the ACGT consent form.

WP12: Clinical Trials

FORTH has the joint leadership of the WP. Dimitris Kafetzopoulos is in constant collaboration with the co-leader Christine Desmedt (IJB) and have devoted significant efforts towards the coordination of the activities of the WP.

Specifically, FORTH's work focused on:

- Detailed specification of the ACGT TOP trial, in terms of its objectives and design.
- The preparation for the implementation of the trial.
- Discussion of the study protocol with the local clinical researchers at the UoC
- Localisation of the study protocol and the consent form
- Preparation of its laboratory facilities for the post-genomic analysis required
-

In addition FORTH's researchers (specifically M. Klapa) are working actively in defining additional trials and studies to be supported by the ACGT infrastructure. Specifically, the activities related to the:

- Production of a technical document describing the contribution and influence of metabolic profiling and especially GC/MS metabolomics in clinical cancer research with emphasis in samples of affected individuals' biofluids (i.e. blood, urine). Specific emphasis was given at the central human fluidic reservoir, blood, and its products (plasma and lymphocytes) in all stages of clinical practice and research of these patients.
- Experimental design document for the application of GC/MS metabolomics in blood and urine samples of healthy and breast cancer individuals according to the clinical trial SOP that had been proposed. A thorough experimental protocol, based on the groups previous experience with human samples and other systems and literature, was described within this experimental design context.
- We have already initiated research to optimize the above-mentioned protocol for GC-MS metabolomics of (lymphocytes and plasma) from healthy individuals. The significance and novelty of this work is two-fold: (a) regarding the technology development level, it will provide valuable experience and information towards establishing and standardizing the experimental metabolomics protocol for plasma and lymphocytes research towards its application in breast cancer affected individuals, while (b) concerning the scientific level, it will provide high-throughput metabolic data, not to-date available, leading to at least some initial clues regarding the metabolomic profile of healthy individuals. The latter will help the discussion regarding the compounds, which are determinable in biofluids and could play a role as potential biomarkers for the early, accurate diagnosis, and monitoring of patients' response to the specific chemotherapy regimens described at the paragraphs 5, 6, 7 of the ACGT TOP trial.

Finally, Dr kafetzopoulos travelled extensively for meetings with other ACGT clinical partners in making sure that end users, clinicians and biomedical researchers are taken on-board the project. These activities have been successful and WP12 is now moving forward without any foreseen difficulties.

WP13: Evaluation and Validation

FORTH contributed to the initial activities lead by SIB aiming at the formulation of a rigorous evaluation framework. We have assisted in the final production of evaluation form to be employed during the implementation phase for monitoring and reporting the “production process”” of ACGT tools and services.

WP14: Training

No training activities have been undertaken during the first reporting period. Nevertheless, we foresee that the planned effort will be allocated to training activities during the next 6 months of project implementation.

WP15: Dissemination

FORTH has contributed significantly for the production of the final D15.2 deliverable, and has continuously provided with material the Web development team.

In addition it played a vital role in the scientific dissemination of the project, the organisation of a number of scientific workshops and the wider promotion of the project. Specifically:

- Scientific Workshop, May 30th 2006, Budapest, Hungary Theme: Advancing Clinico Genomics: Information Integration and Knowledge Discovery Issues, Co-organised with the ERCIM BMI WG (http://www.ics.forth.gr/bmi/ercim/events.html)

- 2nd International Advanced Research Workshop on In Silico Oncology: Advances and Challenges, 25-26 September 2006, Kolymbari - Crete, Greece, Co-organised with the ERCIM BMI WG

- Preconference workshop, IEEE Information Technology and Applications in Biomedicine Conference (ITAB 2006), Nov. 2006, Co-organised by ACGT in collaboration with the the “SmartHEALTH” Integrated Project – (Full Title: Smart Integrated Biodiagnostic Healthcare), the “LOCCANDIA” Targeted Research Project - (Full Title: Lab – On – Chip profiling for CANcer DIAgnosis), and the “MATCH” Specific Targeted Project - (Full Title: Automated Diagnosis System for the Treatment Cancer by discovering mutations on tumor suppressor genes.)

FORTH’s staff has produced several scientific publications, both journal articles and conference papers, presenting the vision and architectural approaches of the project. It also participated in a number of concertation activities of the project, such as caBIG, EGEE, etc.

PARTNER 03 – INRIA

WP2: User Needs Analysis & Specifications

The contributions to this work-package are analyses and specifications needed for the studies in package 6, 7 and 8. More precisely:

- We have produced a report on visualization interfaces (see the part about WP 7).
- We achieved a specification of the classification needs on clinical data. Particularly, we looked into the choice of an integration of our developments in the R framework.
- We made an analysis of the sequential version source code of the onco-simulator in order to specify parallelizable parts.

WP6: Knowledge Management and Discovery Tools

We are contributing to the development and implementation of a data analysis tool for clustering objects (i.e. individuals or variables). This tool called **chavl** is based on very original probabilistic similarity measures between objects to be clustered that take in to account the nature of the descriptive variables. In the ACGT environment, this tool may be useful for investigating the connexion between the genomic data and the clinical data in two steps: 1) perform clustering on the patients based on genomic data and 2) study the association between the clusters of patients and clinical attributes with the help of the discrimination coefficients described in the following article.

Israël-César Lerman ; "Coefficient numérique général de discrimination de classes d'objets par des variables de types quelconques. Application à des données génotypiques", Revue de Statistique Appliquée, 2006, LIV (2), pp. 33-63.

At this stage, chavl program is available in FORTRAN 77 and is being tested on genomic and clinical data. It has also been sent to some ACGT partners for testing and we are in contact with IJB in order to obtain the real data for the patients from TOP trial for testing. The negotiations on the “Terms of Use” with IJB are in progress. Other partner institutes are also contacted for obtaining the real data.

Implementation of chavl in R environment is being studied: specification and feasibility analysis have been worked out.

WP7: Ontologies and Semantic Mediation Tools

As part of the preparation of the DoW document, INRIA Rennes has produced a document for WP7 about the current state of the art on "Visual interfaces to query data model and data". The document has been written taking into account the point of view of the end users of the ACGT platform, which are supposed not being specialized in database technologies. The document describes some of the well-known tools available today, giving some hints of what could be implemented for the ACGT platform.

WP8: Technologies and Tools for in-silico Oncology

In this work package, the IRISA-INRIA bioinformatics team is involved in the optimization of the onco-simulator code. More specifically, larger data set and better model definitions increase the volume of computations. To keep a reasonable computation time, a parallel execution of the onco-simulator is envisioned. Today, a sequential version running on the Window operating system exists and is the base for further developments either on cluster or grid. The two alternatives have to be considered.

We have modified the existing code to make it running onto the Linux system. A direct compiling of the code showed diverging results between executions on Windows or on Linux. A deep analysis has revealed that floating point behaviour was the cause of the problem. Actually, small bugs have been detected and corrected in the original code, providing similar results whatever the operating systems.

In addition, profiling of the code has been done to localise the potential parallelism. Even if the code we have studied won't be the final code, we have got expertise on the structure of the onco-simulator, and should help to parallelize the next version.

WP14: Training

No activity

WP15: Dissemination

As far as we concerned, the dissemination took place during several events, which are:

- Our participation to ACGT meetings in Chania (Crete), Madrid (Spain), Athens (Greece) and Malaga (Spain).
- Our participation to conferences such as:
  - Conference EGC (knowledge extraction and management) in Namur (Belgium).
  - Conference JOBIM (French conference in Bioinformatics) in Bordeaux (France).
- We also visited Potsdam University (Germany) in order to study the representation of genomic knowledge in the framework of ASP (Answer Set Programming).

PARTNER 04 – UvA

WP2: User Needs Analysis and Specifications

- Conducted analysis of interactive 3D visualization needs in WP6 and WP8
- Evaluated state-of-the-art in interactive 3D visualization in context of WP6 and WP8
- Evaluated interactive workflow environments from context of visualization
- Summarized user needs analysis and evaluation of state-of-the-art
- Contributed input for Deliverable 2.1

WP3: Architecture and Standards

- Installed and tested initial version of ACGT Grid software on internal systems
- Performed experiments with initial version of ACGT Grid software for interactive 3D visualization
- Performed experiment with Grid software from other projects
- Contributed feedback on initial version of ACGT Grid software
- Start of design of a scenario for in-silico simulation and interactive 3D visualization

WP6: Knowledge Management and Discovery Tools

- Evaluated existing visualization tools
- Summarized and classified existing visualization tools into ACGT categories
- Design completed of interactive distributed visualization framework
- Work started on prototype of interactive distributed visualization framework
- Contributed input for Deliverable 6.1

WP8: Technologies and Tools for in-silico Oncology

- Contributed visualization ideas to WP8
- Initial experiments performed on visualization of in-silico simulation data
- Specification of interactive graphics devices and software framework started
- Work on visualization hardware prototype started
- Work on prototype interactive visualization framework started
- Performed comparison of NTUA simulation model with other cellular automata
- Development on Cellular Automata Modelling Environment and Library (CAMEL)
- Contributed input for Deliverable 8.1

WP9: The integrated ACGT Environment

- Evaluation of existing workflow environments
- Interface design for interactive visualization with web services started
- Design of a bridge mediator between interactive visualization and grid resources
- Prototype built of an interactive visualization scenario using grid resources

WP13: Evaluation and Validation

No activity (workpackage not yet started).

WP15: Dissemination

- Demonstrations given of prototypes of ACGT interactive 3D visualization environment
- Produced stills, photographs and videos of prototypes of ACGT interactive 3D visualization environment and hardware prototype
- Selection of methods created to generate publication quality visualizations from ACGT data
- Contributed visualizations and animations of ACGT data for ACGT website, poster, presentations
- ACGT work presented in lectures “Scientific Visualization and Virtual Reality” at University of Amsterdam
- Participated in ACGT meetings:
    - March 2006: Project kick-off meeting, Nice
    - September 2006: Plenary meeting, Crete
    - January 2007, Plenary meeting and OGSA-DAI workshop, Malaga

PARTNER 05 – Philips

WP1: Project Management

- Took part in ACGT MB meetings
- Provided presentations on progress and future research directions for WP5
- Contributed to the ACGT informal review – presentation for WP5
- Contributed to the risk management document for WP5

WP2: User Needs Analysis and Specifications

- Supported clinical users in expressing the technical requirements in the clinical scenarios.
- Learning into genomics and clinical trials.
- Carried out experiments with tools used in the clinical trials.
- Detailed review of D2.1, and review from architectural perspective with respect to the ACGT platform.

WP3: Architecture and Standards

- Investigated relevant standards to which our solution for distributed data access should be compliant (HL7, DICOM, IHE).
- Investigated interaction of the data access services and applications with the Grid access services, and how our services will fit in the general ACGT architecture.
- Took part in WP3 workshops (Grid technology) and meetings.

WP5: Distributed Data Access, Tools and Applications

- Carried out preparatory work for Task 5.1 and Task 5.5:
    - Workshop at IJB to collect relevant requirements with respect to data access for the TOP trial.
    - Workshop at UdS to collect relevant requirements with respect to data access for the SIOP trial, and with respect to the tools for creation, management and monitoring of clinical trials.
- Subsequently followed up with discussions to gather detailed information with respect to database schema and common queries for SIOP CRF database, and database views for TOP CRF database (Oracle Clinical). Also installed BASE (provided by Lund University) to obtain schema of this database. The resulting information has been documented in Deliverable 5.1.
- Close cooperation with UdS to work out Antigen scenario by an iterative process.
- Initiated the use of wiki for collaboration within ACGT project, which involved setting up a trial wiki and presenting its capabilities. We have ensured that a suitable wiki was set up, and created the initial content.
- Subsequently continued to contribute content, such as the biomedical and technical glossaries at wiki.
- Together with UdS (Norbert Graf), prepared and organised a Requirements Engineering workshop during the consortium meeting in Crete. The workshop revolved around three topics that we had identified, where inter-workpackage discussions were needed. The topics were: querying, data access and data collection.
- Specified and analysed the user requirements with respect to data access using a scenario-based architectural approach, CAFCR.
- Developed a system architecture and selected relevant technologies for implementing a solution.

- Explored relevant technologies, such as OGSA-DAI, DICOM, web services.
- Investigated web services technology using scenario SC2 from D2.1 as a case study. More specifically, we carried out Step 1 of the scenario solely by using existing web services. For this, web service clients were used that were provided by the web service provider (EBI).
- Subsequently we worked on building a web service client using a different web service toolkit. This led to the identification of significant incompatibility issues, which triggered further investigation of the current level of web service interoperability. Results are reported in Deliverable 5.1.
- Evaluated OGSA-DAI and decided on using it within ACGT as the interface for the data access services. Identified what functionality it does not (yet) support, where we therefore need to carry out further work.
- Also started using OGSA-DAI to build data access services for image data servers, using DICOM. For this, we have been looking into the DICOM protocol. This was also reported on in Deliverable 5.1. DICOM also provides a useful example how limitations of underlying data sources affect the wrappers for these services.
- Held a technical session in Malaga to discuss technical issues around developing an OGSA-DAI web service to access DICOM data.
- Worked on the development of prototypes of OGSA-DAI-based heterogeneous data access services.
- Wrote document 5.1. Consolidation of user requirements with respect to distributed data access and applications.

WP7: Ontologies and Semantic Mediation Tools

- Worked on the definition of the main interactions between WP5 and WP7:
  - Interface between the mediator and the data services
  - Queries to be supported by the data access services, semantics, syntax
  - Query language and data model to be exposed by the data access services to the mediator.
- Took part in WP7 meetings and workshops.

WP9: The integrated ACGT Environment

- Started investigation on how to integrate the data access services and applications with other architectural components of the ACGT platform.

WP15: Dissemination

- ACGT and WP5 presentations within Philips Research, e.g. the biomolecular research department.
- Presentations of ACGT work and vision to our customers from Philips Medical Systems
- Dissemination of the ACGT work in other external collaborations, e.g. to our partners from the Virtual Laboratory for eScience project.
- Took part in the Corporate Research Exhibition 2006 event, in May 2006. ACGT was disseminated in our presentations and at our stand.

WP16: Market Investigation and Exploitation

- Contributed to the Technical Report for ACGT exploitation
- Started investigation on the potential business relevance of ACGT for Philips

PARTNER 06 – IJB

WP2: User Needs Analysis and Specifications

WP2 and WP12 are the two clinical WP's of the project. Since IJB is co-leader of WP12, it interacted on a regular and continuous basis with this WP. For example IJB participated to the WP2 meeting in April 2006 and participates in the clinical/researchers' user needs discussions.

WP5: Distributed Data Access, Tools and Applications

IJB provided details regarding the different data requirements and specification for the breast cancer TOP ACGT clinical trial. This was done through e-mail contacts and three meetings at IJB with WP5 representatives and members from IJB.
A first set of anonymized data is being prepared to be sent to Philips. Preparations for the regular transfer of anonymized data were done together with WP10 and WP11.

Deliverable D5.1 "Consolidated requirements and specifications for data access" was reviewed.

WP7: Ontologies and Semantic Mediation Tools

IJB has contributed to the ongoing discussions in this WP regarding:

- The ontology: several members of IJB reviewed the Master Ontology with respect to its clinical accuracy and utility. IJB also provided critical information to IFOMIS regarding breast cancer to be incorporated in the ontology.
- The CRF creator: IJB provided the CRF from the TOP trial to FHG and IFOMIS so that they could test the ontology-driven clinical trial builder.

WP8: Technologies and Tools for in-silico Oncology

Together with the Institute of Communication and Computer Systems (ICCS) (WP8) a trial for the clinical validation of the In Silico Oncology simulation model for breast cancer was developed, discussed and finalized. The aim is to predict the response to epirubicin preoperative chemotherapy in breast cancer. IJB provided data specifications for the in-silico modelling of breast cancer cases in the context of the TOP trial though a meeting between WP8 and IJB in Brussels in June 2006 and through regular e-mail exchanges.
A first set of anonymized data is being prepared to be sent to ICCS. Preparations for the regular transfer of anonymized data were done together with WP10 and WP11.

Deliverable D8.1 "Consolidated requirements (including information flows) of the in silico simulation models" was reviewed.

WP9: The integrated ACGT Environment

Preparation of a set of data to be used for demonstration purposes. Otherwise, relatively minor participation in discussions and issues through email exchanges.

WP10: Ethical, Legal and QA Issues

IJB participated in the elaboration of the patient information sheet and informed consent. IJB also contributed to the ongoing discussions of this WP through regular e-mail exchanges and initiated contact with the ethical & legal WP of the European Network of Excellence TRANSBIG in order to have a joint meeting between these two groups.

Deliverable D10.1 “Production of informed-consent form in compliance with the clinical trials, post-genomic research and genetic data handling requirements” and D10.2 “The ACGT ethical and legal requirements” were reviewed.

WP12: Clinical Trials

IJB is leader of this WP together with FORTH; therefore the majority of IJB’s contribution to ACGT regards this WP.
Specifically, additionally to the contribution already described in the other WP’s, IJB’s work involved:

- continuous specification of user needs and requirements to the different WP’s, also through regular discussion with other clinical partners
- coordination of the ACGT breast cancer TOP study
- elaboration of a document specifying the different clinical and technical specification of the TOP trial
- the process to provide access to data from the TOP trial collected before the initiation of ACGT (this was done in collaboration with WP10 and WP11 to ensure that all legal, ethical and requirements were met).
- Together with FORTH, coordination of the different WP’s deliverables (cfr report of WP12).

WP13: Evaluation and Validation

The following deliverables were reviewed by members of IJB:

- D1.4 Risk analysis of ACGT
- D5.1 Consolidated requirements and specifications for data access
- D8.1 Consolidated requirements (including information flows) of the in silico simulation models
- D10.1 Production of informed-consent form in compliance with the clinical trials, post-genomic research and genetic data handling requirements
- D10.2 The ACGT ethical and legal requirements
- D15.2 Initial Dissemination Plan

In this review process, we focused on the clinical point of view.

WP14: Training

We focused in providing a clinical and research oriented point of view on the general organization of the ACGT training platform. This was done during the different ACGT meetings. We also had several internal discussions at IJB about the necessities of such a training platform to be efficient for the end-users.

WP15: Dissemination

- IJB is involved in the editorial board and the work involved significant contributions to the various dissemination materials and the ACGT Web site (IJB also participated to the WP15 meeting in November 2006).
- IJB started a dissemination programme on ACGT via internal and external presentations (for example at the EORTC Annual Meeting, St Gallen Breast Cancer Symposium) and with representatives from the Breast International Group (www.breastinternationalgroup.org).

PARTNER 07 – SIB

WP2: User Needs Analysis and Specifications

Two scenarios based on published data sets were proposed and the corresponding data made available.

WP6: Knowledge Management and Discovery Tools

SIB contributed to writing D6.1. Identified scenarios suitable for initial WP6 development, based on the tools and data types used. One of the published-data based scenarios was made completely explicit (i.e. data processing steps and expected results are available), thus usable for demonstration purpose in WP6. The corresponding data were made available to the consortium through a ACGT-specific database (BASE at LundU).

WP7: Ontologies and Semantic Mediation Tools

No activity

WP9: The integrated ACGT Environment

Familiarization with web services technology, viewed as essential to develop relevant evaluation and validation scenarios in the context of WP13, was conducted.

WP12: Clinical Trials

Review and familiarization with the ACGT clinical trials was conducted. A scenario based on the TOP trial -TOP light- was proposed that can be used in the context of a demonstrator using ACGT clinical data. The nature of the dataset suitable for that purpose was discussed with IJB which led to a selection of a subset of 10 patients for testing.

WP13: Evaluation and Validation

A preliminary survey of Evaluation and Validation procedures was conducted among ACGT partners. WP13 kick-off meeting took place during the MB meeting in Chania (Crete). A review of quality control procedures specially focused on standards available from ISO and IEEE was conducted. Relevant concepts were identified which resulted in a template document for Evaluation and Validation procedures submitted for evaluation in technical work packages. A scenario-based evaluation of the whole infrastructure by end-user was proposed, and the collection of scenarios to be used for actual validation was initiated. A template for validation form to be used by end-users was prepared.

WP15: Dissemination

Provided graphical material related to high-level genomics data analysis.

PARTNER 08 – LundU

WP2: User Needs Analysis and Specifications

- Meeting preparations
- Defining BASE user needs and specifications
- Reviewing D2.1.

WP3: Architecture and Standards

- Follow up on the documents produced in WP3 and anlysing their impact on BASE.

WP5: Distributed Data Access, Tools and Applications

- Adding Affymetrix support to BASE (needed for microarray data storage in the ACGT project) and performing ACGT needed modifications of BASE (such as adding web services).
- Work on D5.1.

WP6: Knowledge Management and Discovery Tools

- Adding R/BASE accessibility through web services: Planning of the web service functionality in BASE, review of Java-to-R and Perl-to-R software for the connection between R and BASE, development of a Perl module that connects to BASE using web services, and development of R-to-Perl software that can indirectly connect to BASE.
- Making BASE2 compatible with BASE1 analysis plug-ins: Creating a module for BASE to enable the system to execute already made analysis tools for old versions of BASE. This module includes a simplified way of installing the tool, exporting data in a BASEfile format (anticipated to be useful in future ACGT grid environment).
- Work on scenarios.
- Microarray encodings, meeting preparations and attendance
- Affymetrix algorithms support in BASE.

WP7: Ontologies and Semantic Mediation Tools

- Understanding of ontologies in ACGT context and meeting preparations and attendance.
- Research/knowledge mining of existing ontologies such as ontologies in connection with cancer.
- Drafting of how BASE will use and support ACGT ontology: Investigating how to implement the ability to use ontologies into BASE. This has included the understanding of existing microarray ontologies (MGED ontology, MO) and on drafting how BASE will use an ontology database (e.g. ACGT master ontology).

WP9: The integrated ACGT Environment

- Setting up and maintaining ACGT BASE server (currently used for testing purposes).

WP12: Clinical Trials

- Work on D12.3

WP15: Dissemination

Marketing ACGT at MGED9 and to NuGO (another EU funded project, http://www.nugo.org).
MGED is the Microarray Gene Expression Data Society, an international organisation of biologists, computer scientists, and data analysts that aims to facilitate the sharing of microarray data generated by functional genomics and proteomics experiments.

The current focus is on establishing standards for microarray data annotation and exchange, facilitating the creation of microarray databases and related software implementing these standards, and promoting the sharing of high quality, well annotated data within the life sciences community. A long-term goal for the future is to extend the mission to other functional genomics and proteomics high throughput technologies.

So MGED9 was the annual meeting of the society in Seattle, WA, USA, on September 7-10 2006.

We had a poster presentation and the audience was researchers and computer scientist. During the session we discussed BASE and ACGT with approximately 10-20 people, main focus was of course BASE but we also emphasis ACGT.

PARTNER 09 – UMA

WP2: User Needs Analysis and Specifications

- WP2 Action: inquiry of available tools. In this task we have prepared the inquiry including the initial set of tools and databases, distributed and collected it, and summarized the results.
- D2.1 contribution: bioinformatics methods and tools state of art. We have analyzed the data collected in the inquiry of available tools and presented the results and conclusions.

WP3: Architecture and Standards

- We have made a review of Data grids technology which is accessible at the BSCW/Wiki repository
- We have attended a technology specific workshop in Malaga for implementing data access modules using OGSA-DAI standard.

WP4: Biomedical GRID technology Layer

- We have attended a technology specific workshop in Poznan for implementing grid nodes using Globus Toolkit 4 and Gridge.
- We have implemented a grid node for the ACGT testbed.
- We have developed a prototype of service registry which integrates tools running as Globus jobs (available at http://mango.ac.uma.es/ACGT)

WP5: Distributed Data Access, Tools and Applications

- We have participated in the collection of requirements, at the Jules Bordet Hospital, for accessing clinical data.
- As part of the task T5.2 we have started data access layer specification, design and implementation.

WP6: Knowledge Management and Discovery Tools

- We have made a review of methods for visualization & interactivity in KDD which is part of D6.1.
- As part of the deliverable D6.1 we have defined requirements for KDD tools including pre-processing, normalization, clustering and association rules discovery of microarray data.
- We have proposed initial requirements of KDD tools metadata which have been included in the deliverable D6.1.
- We have worked on a proposal of a microarray data model as part of the task of specifying the methods for exchanging data between the KDD tools.
- We have developed an initial prototype of an interactive tool for the visualization of hierarchical clustering.
- Design and specifications of a Association Rules Discovering algorithm over gene-expression data. A first prototype demonstrating the main functionality is currently under development.

WP9: The integrated ACGT Environment

- Developed a prototype for the demonstration of service registry functionality. This prototype is accessible at http://mango.ac.uma.es/ACGT

- Development and implementation of several workflows (available at http://mango.ac.uma.es/ACGT; in the tab “Workflows”):

- Homology_search_and_Phylogenetic_study (Performs a homology and phylogenetic study)
- Structure_Information (Get all entries from different structure databases given a PDB ID)
- Basic_structure_study (Mutation and structure study from a PDB ID)
- gi_to_agi (Takes a given NCBI_gi and retrieves the AGI codes for it)
- DNA_Clustalw_Phylip (Runs clustalw and phylip services on DNA sequences)

- Participated in technical discussions addressing issues at various levels: service interoperability, workflow editors and enactors, services & workflows required metadata.

WP11: Trust and Security

No Activity

WP13: Evaluation and Validation

No activity

WP15: Dissemination

Papers: 11 papers published in international peer-review journals. Content:

- (2) Technology for data, services and CPU- power integration
- (9) Software and data analysis in biomedical domain

Congress: 12 communications to peer-review international workshops

- (8) Technology for data, services and CPU- power integration
- (2) Software and data analysis in biomedical domain
- (2) Communications on the on-going tasks in ACGT project

Other activities: Attendee and active participation in 6 technical meeting related to the tasks in which the UMA group is involved:

Dissemination courses: Attendee and/or active participation in training technical meetings:

- PSNC GT4 and Gridge Workshop- Poznan 4-5 Dec. 2006; PSNC.
- OGSA-DAI workshop June 23, 2007; Malaga
- Swiss Institute for Bioiformatics: BioMOBY.
- EMBRACE course: Web Services. Feb. 2007, Madrid, Spain
- Workflows over Grid-based Web services: General framework and a practical case in structural biology: Workflows in Bioinformatics; (Feb. 2007, Madrid, Spain)
- II Iberoamerican Bioinformatics workshop: Distributed execution of workflows at the INB (Dec. 2006; Bs. As. Argentina).
- Brainstorming about the myExperiment (myGrid) project: http://www.mygrid.org.uk/wiki/Portal (Sep. 2006)

PARTNER 10 – UPM

WP1: Project Management

UPM participated in periodic audio conferences, MB meetings (in Budapest, Crete, Athens, Crete and Malaga), in the analysis of shared documents, and contributed with general strategy suggestions. UPM analyzed the consortium agreement, and participated in the internal revision of deliverable D8.1. At an internal level, UPM prepared 6-month PAR and the annual PMR documents, and also coordinated WP7 regarding managerial issues.

WP2: User Needs Analysis and Specifications

UPM participated in documents analysis, and contributed with feedback about requirements, and in the discussions regarding scenarios. UPM also contributed to D2.1, and coordinated the contribution of other partners to this deliverable.

WP3: Architecture and Standards

UPM staff assisted to a Grid course held in Poznan (PSNC) on Dec 4-5, 2006. UPM also contributed to D3.1 with a description of the Semantic Mediator. An analysis on the state of the art regarding Grid architectures has been done. Finally, work regarding relation between WP3 and WP7 (situation of the Mediator in the ACGT platform) was carried out, with also a study of migration issues in Ontofusion from web services to grid services, including estimation of needed resources for his task.

WP5: Distributed Data Access, Tools and Applications

UPM attended WP5 meeting in Eindhoven, and a WP5 session in Crete. UPM has performed an analysis of database wrappers within the context of the Ontofusion tool, a study of the viability of web services for distributed heterogeneous data access and a study of the state of the art on ontologies. UPM has studied the coordination between WP7 and task 5.2 and the interfaces needed between WP5 and WP7 through the translation of real SIOP SQL queries into RDQL

WP6: Knowledge Management and Discovery Tools

UPM organized the WP6 and WP7 meetings joint meetings, held in Madrid in June 2006. The UPM has studied the interface between WP7 and WP6. UPM contributed to D6.1, providing a description of the mediator and a study of the state of the art on ontology-based KDD tools. Regarding the OntoDataClean tool for instance level pre-processing, several updates and improvements to the system were done, as well as the inclusion of algorithms which allow the system to semi-automatically generate cleaning ontologies, based on statistical heuristics. Also the study of ontology-based database preprocessing, leading to the publication of “OntoDataClean: Ontology-based Integration and Pre-processing of Biomedical Data” in ISBMDA 2006.

WP7: Ontologies and Semantic Mediation Tools

UPM organized the WP7 Kick-off meeting in Madrid, and le WP7 session in Crete, as well as several presentations in other meetings, including the informal review of the project in Brussels. UPM studied the state of the art on database integration and on several issues regarding challenges in relation with ontologies and images, grid and data mining. UPM analyzed the semantic mediation requirements, and written a major part of the deliverable D7.1. UPM designed the first draft for the semantic mediation layer architecture, and studied the integration of the

Master Ontology in the ACGT architecture. UPM has been designing WP7 demonstrator, and began its implementation. UPM performed analysis in ontology query languages and mapping formats for database integration in ACGT.

WP9: The integrated ACGT Environment

UPM contributed to D9.1, with a study regarding interoperability definitions inside the ACGT project, and the role of the ACGT semantic mediator. Also, a deep analysis of workflow annotation formats for automatic choreography of tasks is being carried out.

WP11: Trust and Security

UPM carried out a study of security issues in the scenarios used in the ACGT requirements analysis, obtaining a list of actions to perform to guarantee privacy. All scenarios were studied, identifying the key security points, for D11.1, as well as the participation in several security discussions during meetings

WP14: Training

UPM attended the courses given by the ACGT consortium:

- GRID technologies course in Poznan (2 people)
- OGSA-DAI course in Málaga (2 people)

WP15: Dissemination

UPM group has published the following papers and communications in relation with ACGT:

- L. Martín, V. Maojo, M. Tsiknakis, A. Anguita, G. de la Calle. *ACGT: Una plataforma europea para la ayuda a la integración de datos genéticos y clínicos para la terapia y el tratamiento personalizado en cancer*. INFORSALUD 2007

- M. Tsiknakis, V. Maojo, G. Potamias, A. Analyti, M. Brochhausen, S. Rueping, L. Martin, D. Kafetzopoulos. S*emantic grid services enabling ontology based integration and analysis of multilevel biomedical data*. IEEE Trans on Nanobioscience – Special issue on GRID & Ontology Applications 2006 (Submitted)

- Maojo V, Garcia-Remesal M, Billhardt H, Alonso-Calvo R, Perez-Rey D, Martin-Sanchez F. "Designing new methodologies for integrating biomedical information in clinical trials." Methods Inf Med. 2006;45(2):180-5.

- R. Alonso-Calvo, V. Maojo, H. Billhardt, F. Martin-Sanchez, M. Garcia-Remesal, D. Perez-Rey. *An agent- and ontology-based system for integrating public gene, protein, and disease databases.* Journal of Biomedical Informatics 40 (2007) 17–29

UPM has also given a lecture about database integration in the ACGT framework in Ioannina (Greece), during ITAB 2006 conference.

WP16: Market Investigation and Exploitation

UPM studied exploitation activities in relation with semantic mediation and database integration. UPM contributed to deliverable D16.1 with the results of this study.

PARTNER 11 – FHG

WP1: Project Management

- Participation in Management Board Meetings (Budapest, May 2006 and Athens, July 2006) and Management Board phone conferences
- Participation in the informal review (Brussels, November 2006)
- Participation in the Technical Management Committee

WP2: User Needs Analysis and Specifications

- Evaluation and design of user requirements for Clinical Trials
- Investigation on the state of the art of Clinical Trial Management systems
- Contribution to Deliverable 2.1 “User requirements and specification of the ACGT internal clinical trials”
- Collaboration: Participation in WP2 kick-off meeting (Saarbrucken, April 2006) - Several local WP2 meetings in Saarland with USAAR and IFOMIS (project partner 19)

WP3: Architecture and Standards

- Contribution to Deliverable 3.1 “The ACGT Initial Architecture”
- Approach for the integration of knowledge discovery tools into the ACGT Grid environment
- Approach for the integration of the Clinical Trial Builder into the ACGT Grid Architecture
- Collaboration: participation in the WP3 kick-off meeting (Eindhoven, Mai 2006)

WP4: Biomedical GRID technology Layer

- Initial actions to provide a ACGT Grid nodes
- Participation in the GT4 and Gridge tutorial (Poznan, December 2006)
- Collaboration: participation in the WP4 kick-off meeting (Eindhoven, Mai 2006)

WP5: Distributed Data Access, Tools and Applications

- Concept development for the Clinical Trial Builder and Clinical Data Management System
- Contribution to Deliverable 5.1 “Consolidated requirements and specifications for data access”
- Collaboration: participation in the WP5 meetings (Eindhoven, Mai 2006; Saarland, September 2006)

WP6: Knowledge Management and Discovery Tools

- Coordination of the WP6 activities
- Contribution to and editing of Deliverable 6.1 “Consolidated Requirement Analysis for Data Mining, Analysis and the Visualization Environment“
- Requirement elicitation for the data mining components of the ACGT environment
- Design and implementation of an initial demonstrator for the ACGT knowledge discovery environment, in particular a gridified version of the R / Bioconductor environment.
- Collaboration:WP6 kick-off meeting (Madrid, Mai 2006) - preparation and participation

WP7: Ontologies and Semantic Mediation Tools

- Contribution to ACGT Master Ontology: Specification of requirements and review
- Contribution to Deliverable 7.1 “Consolidated Requirements on ontological approaches for integration of multi-level biomedical information”
- Collaboration: WP7 kick-off meeting (Madrid, Mai 2006) - preparation and participation - Several local WP7 meetings in Saarland with IFOMIS (project partner 19)

WP8: Technologies and Tools for in-silico Oncology

- Contribution to Deliverable D8.1
- Design of an imaging data handling repository and specification of the imaging tools used by the physician. Image contouring of MRI and PET modalities are going to the supported by image collaboration tool. Physicians would be able to annotate the medical images and communicate with other physicians over TCP/IP protocol.

WP9: The integrated ACGT Environment

- Investigation on the State of the art of integration requirements and guidelines
- Definition of the integration requirements and guidelines for the ACGT environment
- Preparation of a draft version of Deliverable 9.1 “Integration requirements and guidelines”
- Requirement elicitation and design study for the workflow editing and enacting components
- Collaboration: participation in the WP9 meeting (Crete, September 2006)

WP11: Trust and Security

No activity

WP14: Training

No activity

WP15: Dissemination

- Dissemination of the ACGT project at the ECML'06 - European Conference on Machine Learning (Berlin, October 2006)
- Dissemination of the ACGT project flyer on the MEDICA trade fair (Düsseldorf, November 2006)

WP16: Market Investigation and Exploitation

No activity

PARTNER 12 – BIOVISTA

WP2: User Needs Analysis and Specifications

Work focused on the preparation of 2 technical documents;

1. ACGT-TR-2.1-1-BVA-v1: this document reviews commercial visualization software
2. ACGT-TR-2.2-1-BVA-v1: this document is the «Quality Assurance Review Results for Deliverable D2.1».

In addition Biovista participated in the discussions and user needs elicitation process. Biovista also demonstrated its literature mining technology to one of the two main user partners with which we are in collaboration on an existing medical problem of interest to them.

WP3: Architecture and Standards

Relatively minor participation in all discussions and issues through email exchanges and the various technical meetings of the project.

WP4: Biomedical GRID technology Layer

While no person effort was foreseen in the original DoW work was necessary and involved the 'gridification' of some of Biovista's literature mining modules. Work involved mostly familiarization, design and deployment of Grid technologies and infrastructure on the server and development of WSDL 'wrappers' for the modules. Finally an API has been published.

WP5: Distributed Data Access, Tools and Applications

No activity other than following work and discussions of WP.

WP6: Knowledge Management and Discovery Tools

Work focused on the preparation of 2 technical documents as well as developing prototype implementations of our literature mining technology for the Grid. The reports are the following:

- Technical Report *BVA-ACGT-6-1v1* "Biovista Technology Introduction": the report presents an introduction to 2 of Biovista's technologies, the BEA literature mining system and JAnaemia, an expert system for medical record management focused on beta thalassaemia.
- Technical Report *ACGT-TR-6.1-2-BVA-v1* "Consolidation of Requirements Analysis: The Biovista BEA system". The report discusses how Biovista's literature mining tool, can be developed to meet the objectives of the knowledge discovery component of the ACGT toolkit. It concludes with a use case scenario based on discussions with the user partners. The proposed scenario involves the identification of biomarkers.

Specific work on the prototype implementation involved the following:

- Lease and deployment of BEA server dedicated to the project
- Installation of BEA on server
- Access and training to a select subset of partners.
- Active Collaboration with 1 user partner (Saarland) on a current problem of theirs
- Selection and definition of 2 basic BEA operations to make available through grid (demo available)
- Development and deployment of a simple I/F to demonstrate functionality of prototype modules

WP7: Ontologies and Semantic Mediation Tools

Work focused on the development of a module for managing, querying and visualizing ontologies. The module has been applied to the Gene Ontology (G.O.). Biovista has also contributed to the ongoing discussions in this WP.

WP9: The integrated ACGT Environment

Relatively minor participation in all discussions and issues through email exchanges and the various technical meetings of the project.

WP12: Clinical Trials

Work focused on the preparation of 2 technical documents as follows:

- Technical Report *ACGT-TR-12.1-1-BVA-v1* "Clinical Trials Scenaria: The Biovista Viewpoint": The report presents major parameters involved in CTs and stakeholders involved. It then selects stakeholder-issue combinations and discusses scenaria of how ACGT might support activities in those scenaria.
- Technical Report *ACGT-TR-12.1-2-BVA-v1* "Clinical Trials Scenaria: The Biovista Viewpoint 2". The report discusses the antigen characterization scenario co-developed between the University of Saarland and Biovista.

WP15: Dissemination

Work involved significant contributions to the following:

- Various dissemination materials – involvement in the preparation and editing of the ACGT leaflet.
- The ACGT Web site – Biovista suggested the organization of the site on the basis of identifiable stakeholder groups.
- The preparation of technical report "ACGT-TR-15.1-1-BVA-v1". The report entitled "ACGT Web Site FAQs: Issues and Content for use" discusses the organization of the Frequently Asked Questions section of the site and presents initial content with which to seed the section.

WP16: Market Investigation and Exploitation

Most work carried out for this WP involved the background research, preparation and writing of Deliverable D16.1 "The ACGT initial exploitation plan".
In preparation of D16.1 Technical Report *ACGT-TR-16.1-1-BVA-v1* "ACGT Exploitation: Issues and models" reviews issues and possible exploitation models for open source s/w and makes initial recommendations to the consortium for which options to adopt.

Further work following the publication of this report was included directly into D16.1 itself.

In addition Biovista attended the following conferences, trade fairs and individual presentations:

- April 3-5: AACR Annual meeting, Washington DC. Biovista attends this conference on a regular basis. Contacts and information collected were used as input to the forming of the exploitation strategy.
- June 9th Paris: presentation at INSERM at the group of cancer specialists of Dr.Chouab.
- October 25-26: EuroBio exhibition and Trade Fair in Paris together with ERCIM. ACGT was collocated at the INRIA booth and we presented our text mining tool (BEA) and its intended use and evolution within the ACGT framework.

PARTNER 13 – UOC

WP2: User Needs Analysis and Specifications

- Participation in the SoA review wrt post-genomic clinical trials with a focus to breast cancer
- Specification of the user requirements in the context of such CTs
- Contribution to relevant deliverable (D2.1)

WP5: Distributed Data Access and Applications

Collaboration with FORTH for the elaboration of requirements for the development of the clinical trial management application and the (histopathological) image management tool required for the execution of the ACGT-TOP-trial locally.

WP10: Ethics, Legal and QA issues

Our work in this WP focused in contributions in the discussions wrt patient consent forms and in localising the ACGT Patient Consent form for the TOP trial, in which we are participating.

WP12: Clinical Trials

Participation in a series of meetings with the WP leader with the objective of:

- Studying and elaboration of the ACGT-TOP trial protocol
- Analysing the data flow within the Breast Cancer ACGT-TOP-trial
- Adaptation of the protocol to local conditions
- Translation of the protocol into Greek and preparation of the required material for submission to the local ethical committee for approval
- Initial preparation of the logistics for the implementation of the ACGT-TOP-trial
- Finally, actions have been taken towards patient recruitment.

WP13: Evaluation & Validation

No activity during the reporting period

WP14: Training

No activity during the reporting period

WP15: Dissemination

The project was presented internally to other colleagues in several occasions and also a presentation was made to the Regional Medical Congress of Crete.

We have participated in the following Project meetings:

1. Participation in two Consortium Management Meetings PMB (the meeting in Kolymbari, Crete – Sept 2006 and the Malaga Meeting – Jan 2007)
2. Participation in a series of regular meetings held locally with Dr Kafetzopoulos (WP12 Coordinator) and Dr Tsiknakis, for planning and monitoring project evolution locally.

PARTNER 14 – LUH

WP2: User Needs Analysis and Specifications

- A workpackage meeting with WP 2, 10, 11, 12 was organized, prepared and held in the Institute for Legal Informatics of the University of Hannover on 3rd of May 2006. During this meeting especially the data flows within clinical trials were discussed. Furthermore the quality of the data used for the trials was discussed (personal/pseudonymized/anonymized data).
- Legal consulting of WP 2 about the implementation of available software. Therefore software licenses were examined and explained (e.g. SAAM II).

WP10: Ethical, Legal and QA Issues

- A kick-off meeting was organized, prepared and held in the Institute for Legal Informatics of the University of Hannover on 3rd of May 2006.
- Definitions of important legal terminology were developed and sent out.
- The data flows within the clinical studies and in ACGT were identified, especially within the Nephroblastoma study carried out by USAAR.
- The quality of the data within ACGT was analyzed. Especially it was examined whether personal data has to be processed within ACGT or whether pseudonymized or anonymized data can be used for ACGT.
- An ACGT Data Protection Framework was examined and developed. It was described in detail in Deliverable 10.2 (see below).
- The Legal Aspects of informed consents were examined and explained in Deliverable 10.1 ("Production of informed consents"). Therefore:
    - The requirements of an informed consent were examined and explained.
    - The scope of an informed consent was analyzed.
    - Special attention was paid to the questions, which has to consent to the data processing (only the patient or also his/her relatives?), how long a consent is valid and the right of withdrawal and erasure.
- The Legal Requirements of ACGT and solutions for data protection issues were examined and explained in Deliverable 10.2 ("The ACGT ethical and legal requirements"). Therefore:
    - An analysis whether pseudonymous data can be seen as anonymous data was carried out.
    - Definition for additional knowledge that is attributable to the data controller was examined and developed.
    - An analysis of the role of a trusted third party in the process of aliasing was carried out.
    - An analysis whether the local physician can act as a trusted third party was carried out.
    - The establishment of a Data Protection Board was examined.
    - A Data Protection Framework was created for ACGT.
- All duties of a WP-leader were performed. In particular
    - we organised and documented several WP-meetings (particularly in Chania and in Malaga)
    - we organised all the paper work within WP 10
    - we were contact point for different legal questions of all the other partners within their tasks
    - we did consulting on questions of IP for WP 16

WP11: Trust and Security

- A workpackage meeting with WP 2, 10, 11 and 12 was organized, prepared and held at the Institute for Legal Informatics in Hannover on 3rd May 2006. Regarding WP 11 especially technical measures and options of data security were discussed.
- The ACGT Data Protection Framework was created in collaboration with WP 11. Especially the role of a Trusted Third Party, the technical framework, the implementation of anonymizing tools, the implementation of a Data Protection Board were discussed for example during two joint WP meetings on 28th September 2006 and 24th January 2007. Special attention was also paid to the role of the ACGT Data Protection Board and the question, what contracts are needed within the ACGT Data Protection Framework.
- D11.1 was reviewed.

WP12: Clinical Trials

- A workpackage meeting with WP 2, 10, 11 and 12 was organized, prepared and held at the Institute for Legal Informatics in Hannover on 3rd May 2006. Regarding WP 12 especially the data flow within the Breast Cancer ACGT-TOP-trial was explained and discussed, as well as confidentiality and the impact of a GRID infrastructure for trials like ACGT.
- Legal consulting of WP12 regarding the exchange of (genetic) data sets within the TOP-trial.
- Extensive Feedback to D 12.1 was given

WP14: Training

- Participation in the GT4/GRIDGE training held from 4th-5th December in Poznan.
- Participation in the OGSA-DAI training held on 23rd January in Malaga.

WP15: Dissemination

- The following articles were published:
    - Arning, Marian/Forgó, Nikolaus/Krügel, Tina: Datenschutzrechtliche Aspekte bei der Forschung mit menschlichen Genen; in:Hochberger, Christian/Liskowsky, Rüdiger (Eds.):INFORMATIK 2006-Informatik für Menschen Vol. 1, Bonn 2006, pp. 702-708
    - Arning, Marian/Forgó, Nikolaus/Krügel, Tina: Datenschutzrechtliche Aspekte der Forschung mit genetischen Daten; in:DuD 2006, pp. 700-705
- The following presentations about ACGT were held:
    - Data protection regarding human genetic research; Dresden, 5th October 2006 at the 36th annual summit of the Gesellschaft für Informatik
    - Bio-ethical considerations: Addressing the complex legal, regulatory and ethical issues in the post genomic era; Ioannina, 25th October 2006 at the ITAP 2006 Pre-Conference Workshop
    - Requirements for european multicentre trials including genetic data of subjects; Berlin, 8th December at the workshop “Personal Data Issues in European/International Medical Research Projects” organized by the Telematikplattform für Medizinische Forschungsnetze e.V.
- Participation in the WP 15 meeting in Brussels on the 8th November 2006. Legal advice was given about setting up a website and providing content.
- The content for the legal section of the ACGT-website was created and added in the ACGT-Wiki.

PARTNER 15 – PSNC

WP1: Project Management

Jarek Nabrzyski and Juliusz Pukacki from PSNC are involved in managing two workpackages of the project. Jarek Nabrzyski is also a PSNC representative in the Project Management Board. We participate in all the PMB meetings as well as all the phone calls.

WP2: User Needs Analysis and Specifications

We reviewed the D2.1 deliverable and based on it provided plans and design of Gridge extensions. PSNC took all the requirements of the clinical trials and used these requirements for designing the initial architecture of the project. PSNC provided also feedback to the requirements document when it comes to the parts of the deliverable concerning Grid technologies.

WP3: Architecture and Standards

PSNC was a lead partner of this Workpackage. We were main contributors to the deliverable D3.1 (ACGT Architecture). We attended and co-organized a joint meeting of WP3 and WP4 in Eindhoven. As the result of work done within this WP we have proposed an initial ACGT architecture, which will be the basis for all the technical development in the project.The architecture follows the layered structure. PSNC participates also in the OGF (Open Grid Forum), especially in such groups as JSDL (Job Submision Description Language), GSA (Grid Scheduling Architecture), BES (Basic Execution Services).

WP4: Biomedical GRID technology Layer

PSNC is a lead partner of this workpackage. We have proposed, led and organized an initial ACGT Grid testbed, which is already operational. Bogdan Ludwiczak (bogdanl@man.poznan.pl) is a contact point for this activity. The testbed deployment includes now such services as: Globus (Globus WebService Container, MDS4 Index Service, WS-GRAM, RFT, GridFTP, Globus pre-ws gatekeepr), Gridge Toolkit. The actual contents of the testbed can be viewed at http://moss1.man.poznan.pl:8080/webmds/.
We have also installed, together with Custodix, the ACGT CA.
PSNC provided also and organized already 3 training sessions to ACGT consortium: one on GridSphere, one on Gridge, Globus and grids, and one on OGSA-DAI. The training was done within the scope of WP4.

WP9: The integrated ACGT Environment

PSNC is working with other institutions on the integration activities. So far, we participated in integration with Oncosimulator team, as well as we started to work with workflow and visualization groups. PSNC has also participated and gave tutorials on PSNC's GridSphere portal toolkit.

WP11: Trust and Security

PSNC worked together with Custodix on trust and security deliverable D11.1 and was one of the main contributors to this deliverable. We were responsible for Grid-related security issues.

WP15: Dissemination

PSNC participates in dissemination activities. We gave several talks on ACGT. Jarek Nabrzyski gave a talk at Cracow Grid Workshop in 2006 and also in Shanghai in 2006 at the Grids@Asia workshop.

PARTNER 16 – Custodix

WP2: User Need Analysis & Specs

- Custodix provided the security contribution to deliverable D2.1 (User Requirements and Specifications of the ACGT internal clinical trial). In this contribution several existing grid based security technologies have been examined and explained in the context of ACGT. The State of the Art in privacy protection technology has also been discussed in the contribution.
- Based on previous experience with clinical trials and security an initial requirements analysis was made and provided to WP2 (cf. T2.2).

WP3: Architecture & Standards

- Custodix was assigned the ACGT internal review of D3.1.
- Custodix has actively participated in several workshops and meetings on standards such as WS/WS-RF, OGSA-DAI, … ; including (but not limited to) the WP3 kick-off in Eindhoven on 16th of may 2006 and the OGSA-DAI workshop in Malaga.

WP4: Biomedical Grid Layer

- Custodix has actively participated in the Gridge tutorial workshop at PSNC in Poznan aimed at setting Globus based grid nodes.
- Custodix has setup several grid nodes as part of the initial ACGT grid infrastructure. Extra effort was put into making necessary conversions to enable the software to run on Sun Solaris systems.
- Custodix has reviewed D4.1 which was incorporated into D11.1
- Joined the kickoff meeting for WP4 in Eindhoven on 17th of may 2006

WP9: Integrated ACGT Environment

- Custodix has actively worked together with PSNC to integrate the Gridge Authorization Service with the Globus infrastructure set up for ACGT.

WP10: Ethics, Legal and QA issues

- Custodix has actively attended to several WP10 meetings discussing legal and ethical issues within ACGT. Custodix' contributions encompass the technical aspects for solving legal data protection issues.
  e.g.: the joint WP2/10/11/12 workshop held in Hannover to discuss data workflows, patient consent, genetic data and pseudonymization.
- Custodix has been a leading partner in designing the ACGT Data Protection Framework (joint WP10-WP11 work)

WP11: Trust & Security

- An initial PKI infrastructure has been setup for ACGT and using this PKI several certificates have been distributed for the initial ACGT testbed.

- Custodix has been responsible for the deliverable D11.1 (Consolidation of security requirements of ACGT and initial security architecture).

This included:
    - Custodix contribution on data protection (including organising a WP11 at Custodix regarding consent)
    - Editting of the document

- The Gridge Authorization Service has been adapted for Sun Solaris and installed on the Custodix Infrastructure.

- Several Privacy Enhancing Techniques (PETs) have been evaluated for the use within the ACGT pseudonymization tools

- Participated in Management Board meetings as WP leader
    - Kick-off Meeting, Juan-Les_Pins (27 februari to 1 march 2006)
    - Management Board meeting, Budapest (30-31 may 2006)
    - Technical Management board meeting, Athens (11-13 juli 2006)
    - Consortium Meeting, Kreta (27-28 sept 2006)
    - Consortium & Management Board meeting, Malaga (24-26 jan 2007)
    - Telephone conferences
- Partiticated in the preparation and actual informal review in Brussels (29-30 nov 2006)

WP14: Training

- No Activity

WP15: Dissemination

- At the WoHIT (World of Health IT) Conference in Geneve ACGT has been presented as part of the Custodix pavilion.
- Joined the WP15 meeting in Brussels on 8th of November 2006 concerning the status of the ACGT Website

PARTNER 17 – HEALTHGRID

WP14: Training

HealthGrid has mainly given feedback and performed some proof-reading on documents produced within the training work package. Changes within Siveco, who is the leader of theWP14 training work package have caused delays and have made it more difficult to delegate tasks and involve other partners.

WP15: Dissemination

There is a deviation in PMs allocated to the WP 15: Justification is given for the change in the Appendix IV in which a table containing previous PM allocation and the new ones is added.

HealthGrid is the work package leader of the dissemination activity. During this first year, HealthGrid has performed the following tasks:

- Official launch of the project;
- Design of the external website. This website has been designed to fulfil the expectations and requirements of the exploitation activity (WP16) since the beginning.
- A wide-range of publicity material has been created and is available on the BSCW server. These include business cards, bookmarks, flyers, stand up poster;
- The internal website (intranet) is up and running allowing each activity to post items on their own pages; It is sustained by a BSCW server, hosted and maintained by ERCIM for documents sharing
- Setup of a wiki server with private zones for the specific needs of the various working groups of the project and to make collaboration easier.
- The ACGT style has been finalised (by HealthGrid, FORTH & ERCIM) and a style guide will circulate shortly.
- Documents templates have been developed. All of them are downloadable from the BSCW server (https://bscw.ercim.org/);
- WP15 held face-to-face meeting in Brussels on November 8th, 2006. Another one is foreseen in May/June 2007;
- Dissemination targets have been defined;
- Presentation of the ACGT project and/or distribution of dissemination material at various international events: ISGC2006, HealthGrid 2006, ICT for Biomedicine, AMIA2006, IST2006, eHealth2006
- Realisation of the Dissemination Strategy Plan

PARTNER 18 – ICCS

WP2: User Needs Analysis and Specifications

ICCS in collaboration mainly with USAAR and IJB formulated the *in silico* oncology user needs and provided the specifications for the *in silico* clinical trial.

WP3: Architecture and Standards

ICCS contributed to the formulation of the architecture and standards of the entire ACGT platform especially through the description of the input-output and code execution needs of the "Oncosimulator".

WP4: Biomedical GRID technology Layer

Although no PMs had been formally allocated to this workpackage, ICCS provided the needs and specifications of that part of the GRID layer that will be used for the support and execution of the "Oncosimulator". Furthermore, ICCS provided a simulation code of glioblastoma response to radiotherapy in order to test the GRID infrastructure before the ACGT specific tumour types had been addressed.

WP5: Distributed Data Access, Tools and Applications

ICCS contributed to the formulation of the distributed data access systems and tools through the description and analysis of the needs of the in silico oncology application and especially of the "Oncosimulator".

WP8: Technologies and Tools for *in silico* oncology

As the WP8 (in silico oncology) leader, ICCS provided the ground work and coordination for the implementation of this workpackage. Of special note was the provision of glioblastoma tumour growth and response to radiotherapy simulation code that was used by several partners as a starting point for the development of various ACGT technical modules. In the following an action list is given where ICCS had a mostly predominant involvement:

- Construction of a detailed block diagram outline of the Oncosimulator including, among other features, the exact types of input data, the submodules of the main computational biology body of the system, the format of the output etc. Definition of information flow.
- Determination of the exact type of clinical, imaging, histopathologic and molecular data necessary for the in silico oncology trial.
- Decision on the basic components of the image processing and visualization modules of the Oncosimulator.
- Setting of the proper environment for the local imaging data storing and handling.

WP9: The integrated ACGT Environment

ICCS contributed to the integration plan of the ACGT environment by crystallizing the "Oncosimulator" integration into the broader ACGT environment.

WP12: Clinical Trials

Although no PMs had been formally allocated to this workpackage, ICCS substantially contributed to the detailed design of the *in silico* oncology trial based on the two other clinical trials (nephroblastoma SIOP 2001/GPOH, University of Saarland, and breast cancer TOP trial, Institute Jules Bordet).

WP13: Evaluation and Validation

ICCS contributed to WP13 by providing the context for the evaluation and validation of the "Oncosimulator" as a module of the entire ACGT platform.

WP14: Training

ICCS proposed and formulated various cases for which the "Oncosimulator" will be used as a training tool. These include i.a. training of medical doctors, researchers, interested patients, technology providers.

WP15: Dissemination

A number of publications within both the strict and the broader ACGT context have been produced by ICCS and collaborating institutions. An initial description of the "Oncosimulator" for the needs the ACGT website has been produced. Furthermore, ICCS in collaboration with FORTH organized the 2nd Advanced Research Workshop on *In Silico* Oncology, that took place in Kolympari, Chania, Greece, 25-26 September 2006. This workshop was co-sponsored by ACGT.

WP16: Market Investigation and Exploitation

Although no PMs had been formally allocated to this workpackage, ICCS extensively contributed to the formulation of the ACGT exploitation plan with special focus on financially supporting new research and education.

PARTNER 19 – USAAR

WP2: User Needs Analysis and Specifications

The main focus was laid on clinical aspects of the project. The state of the art review in clinical trials was a main objective providing an elaborate and thorough review on all aspects which are relevant to ACGT. Task leader for T2.1 was Manolis Tsiknakis. In preparing the deliverable the following partners made significant contributions:

1. SOA in clinical trials – USAAR – Norbert Graf
2. SOA in Grid technologies and middleware – PSNC – Jarek Nabrzyski
3. Data access services – Philips – Anca Bucur
4. Modelling of the future clinico-genomic Electronic Health Record - Philips – Anca Bucur
5. Tools for the creation and management of clinical trials – FhG/IBMT&FORTH – G Weiler/S Kiefer & M. Tsiknakis
6. Data mining and knowledge discovery (DM/KDD) - Grid enabled DM/KDD – FhG – Michael May
7. Bioinformatics methods and tools - Grid enabled DM/KDD – SIB & UMA & FORTH –Thierry Sengstag & O. Trelles & G. Potamias
8. Biomedical (Cancer) Ontologies – IFOMIS – Anand Kumar (done both for WP2 and WP7)
9. Semantic mediation – UPM - Victor Maojo
10. In silico modelling and Simulation – ICCS – G Stamatakos
11. Workflows Management and Enactment Systems – FORTH&FhG/IBMT – M. Tsiknakis & S. Sfakianakis & S. Kiefer
12. Visualisation techniques and standards – Biovista&FORTH – A. Persidis & I. Tollis
13. Legal and Ethical Guidelines – UHANN – N Forgo
14. Security related issues – Custodix – Brecht Claerhout
15. Evaluation Methodologies - SIB - Thierry Sengstag
16. Online training platforms and standards - Siveco – O. Zelch & L. Majorescu

Deliverable 2.1 was finished and reviewed during this period. The Milestone and the expected results were achieved in time.

Together with the University of Malaga (UMA) a questionnaire regarding task T2.2 was carried out, disseminated and analyzed and interpreted. The results can be found on the BSCW server (https://bscw.ercim.org/bscw/bscw.cgi/117400).

The development of two scenarios for the ACGT nephroblastoma trial was carried out:

- Nephroblastoma antigen scenario
- Scenario for SAEs und SUSARs in clinical trials

These scenarios can be found on the BSCW server (https://bscw.ercim.org/bscw/bscw.cgi/99048), as well as in the WIKI of the ACGT project (http://wiki.healthgrid.org/index.php/ACGT:Index).

For the Antigen scenario - hospitals taking part in the ACGT Nephroblastoma trial - were contacted and asked for serum of patients. Up to now (31st of January 2006) 30 sera were sent to the laboratory performing the analysis of antigens. Phase I of the antigen scenario is finished with the experiments in the laboratory. The characterization of the antigens has started.

A schema for the development of new scenarios was defined. It can be found on the WIKI (http://wiki.healthgrid.org/index.php/ACGT:Scenarios/Development)

USAAR hosted the kick-off meeting of this work package at IFOMIS in Saarbrücken on April 7th 2006.

IFOMIS collaborated with clinical partners in order to integrate user needs into the ontology. On the other hand basic aspects of ontological engineering have been disseminated among the partners defining user needs.

Deliverable D1.4 'Risk analysis of ACGT' was reviewed and input given.

Norbert Graf contributed to deliverable D1.2.

Norbert Graf did participate in the Management Board telephone conferences

WP3: Architecture and Standards

A lot of effort was spent to convince the IT people of the University Hospital to build a Grid node at the University Hospital. Because of security reasons mentioned by the local IT people of the Hospital this is still not the case.

WP5: Distributed Data Access, Tools and Applications

Together with the Fraunhofer-Gesellschaft (FhG-IBMT) an enquiry regarding data management software and systems for clinical trials was done and analysed.
International guidelines in clinical research, clinical trials and studies were performed.

An analysis of clinical requirements for the development of an ontology based CRF-generator was carried out and has been intensively discussed during several meetings with members of IFOMIS (M. Brochhausen, H. Stenzhorn, C. Cocos) and Fraunhofer-Gesellschaft (FhG-IBMT)

USAAR hosted a WP 5 meeting in Homburg on the 5th – 6th September 2006.

Deliverable D5.1 "Consolidated requirements and specifications for data access" was reviewed.

WP7: Ontologies and Semantic Mediation Tools

The Institute for Formal Ontology and Medical Information Science (IFOMIS) has been active in Tasks 7.1, 7.2 and 7.3. This work package is the core effort of IFOMIS in this project. The main objective was the creation of a Master ontology for clinical trials on cancer. Considerable progress has been made on this task and it is being pursued further. In this effort, IFOMIS is closely collaborating with the Paediatric Haematology and Ontology Unit of University of the Saarland and with the Fraunhofer Institute for Biomedical Technology (IBMT) in St. Ingbert, in order to match our efforts the user needs as closely as possible. The close collaboration made a number of joint working sessions and meetings in Homburg (University Hospital) as well as in Saarbrücken (IFOMIS) necessary.

Anand Kumar wrote a detailed state-of-the-art review on "Biomedical Ontologies, Terminologies and Databases relevant to Oncology" which has been uploaded onto the BSCW server.

Mathias Brochhausen from IFOMIS has collaborated with other partners on two papers (first author: Manolis Tsiknakis) on the ACGT technical environment.

IFOMIS has worked out an extensive state of the art review for Deliverable 7.1 and contributed further material and comments to that document.

IFOMIS has been present in quite a number of special meetings, like the Technical Management Board Meeting, Athens, July 11-13 and the ACGT Pre-Review, Brussels, November 29-30. These contributions were important to present the basic ideas and features of the ACGT Master Ontology. However, these meetings have been an extra effort to IFOMIS.

IFOMIS (M. Brochhausen, H. Stenzhorn, C. Cocos) has worked constantly on that deliverable (7.2) which is due in month 15 of the project. This work is ontological engineering of clinical trials and all other aspects relevant to ACGT. The Master Ontology will provide the basis of data integration in the project.

Together with FHG IFOMIS is pursuing the idea of an ontology-driven clinical trial builder. This work includes research on possibilities to integrate the virtues of information models into ontology. In this effort Martin Doerr from FORTH visited IFOMIS and had a one-day meeting on December 18th with all IFOMIS researchers in ACGT and on BFO[1] representative.

Deliverable "D7.1 Consolidated requirements on Ontological approaches for integration of multi-level biomedical information" was reviewed.

WP8: Technologies and Tools for In-Silico Oncology

Together with the Institute of Communication and Computer Systems (ICCS) (WP8) a trial for the clinical validation of the In Silico Oncology simulation model for nephroblastoma was developed, discussed and finalized. The aim is to predict the response to preoperative chemotherapy in nephroblastoma.
A first set of anonymized data were send to ICCS. Preparations for the regular transfer of anonymized data were done

Deliverable D8.1 "Consolidated requirements (including information flows) of the in silico simulation models" was reviewed.

Norbert Graf did actively participate on the 2nd IARWISO Meeting in Kolymbari, Chania, Crete on the 25th and 26th of September 2006.

WP10: Ethical, Legal and QA Issues

Norbert Graf participated on the Kick-Off meeting of WP 10 in Hannover (3rd of May 2006).

The data workflow of the Nephroblastoma trial was generated and the way how clinical trials are run were shown and continuously discussed. The main focus was laid on clinical aspects giving the viewpoint of clinicians.
Relevant information regarding pseudonymisation / anonymisation in clinical trials were provided and continuously discussed, especially if biomaterial is used.

Input was given to D10.2 regarding the clinical aspects.

Deliverable D10.1 "Production of informed-consent form in compliance with the clinical trials, post-genomic research and genetic data handling requirements" and D10.2 "The ACGT ethical and legal requirements" was reviewed.

WP12: Clinical Trials

The ACGT Nephroblastoma trial was written (Alexander Hoppe, Norbert Graf). It can be found on the BSCW Server (https://bscw.ercim.org/bscw/bscw.cgi/99096).

CRFs for the ACGT Nephroblastoma trial were written (Alexander Hoppe, Norbert Graf). It can be found on the BSCW Server (https://bscw.ercim.org/bscw/bscw.cgi/99096).

[1] Basic Formal Ontology. BFO was developed by Barry Smith and Pierre Grenon and is constantly improved by IFOMIS and SUNY. BFO is the top level ontology used by the ACGT Master Ontology.

The ACGT Nephroblastoma trial was send to the ethical committee. The trial did pass the ethical committee and other necessary regulations. The inclusion of patients is possible. Data of the trial will be made available for ACGT during the next period.

The deliverable D12.1 includes the ACGT Nephroblastoma trial. This deliverable was also reviewed.

WP13: Evaluation and Validation

The following deliverables were reviewed by members of UdS

- D1.2- Definition and Guidelines for the Quality Assurance Process
- D1.4 - Risk analysis of ACGT
- D5.1 - Consolidated requirements and specifications for data access
- D7.1 - Consolidated requirements on Ontological approaches for integration of multi-level biomedical information
- D8.1 - Consolidated requirements (including information flows) of the in silico simulation models
- D10.1 - Production of informed-consent form in compliance with the clinical trials, post-genomic research and genetic data handling requirements
- D10.2 - The ACGT ethical and legal requirements
- D15.2 - Initial Dissemination Plan

Input is given in respect to usability criteria. The evaluation process has to recognize that the end-users have to work with the ACGT platform. Clinical input in the evaluation and validation is therefore most important.

WP14: Training

No activity

WP15: Dissemination

Mathias Brochhausen represented IFOMIS at a pre-conference meeting to ITAB 2006 in Ioannina, Greece, October 25. The topic of the workshop was “ICT Technologies for Cancer Research and Management in the Post-Genomic Era: Status and Challenges”. On this occasion IFOMIS presented the ontology-based approach of ACGT.

Input was given to the structure and content of the Homepage.

Alexander Hoppe participated actively in the ENGAGE Conference in Jakarta, Indonesia from the 9th - 16th of September 2006.

Alexander Hoppe did take part at the WP15 meeting in Brussels, 8th of November 2006.

Norbert Graf presented ACGT at a conference of the project ELAN2LIFE in Homburg, 11th May 2006.

Norbert Graf presented ACGT at the ICT for Biomedical Sciences in Brussels, June 29th – 30th 2006.

Norbert Graf presented ACGT at a Lymphoma conference in WUHAN, China on the 21st of October 2006.

Deliverable D15.2 ‘Initial Dissemination Plan’ was reviewed.

PARTNER 20 – SIVECO

WP2: User Needs Analysis and Specifications

- We have produced a state-of-the-art analysis on Web Portals
- We have produced a state-of-the-art analysis on online training platforms
- We have provided the consolidation of user needs analysis by evaluating the specific ACGT portal user needs

WP4: Biomedical GRID technology Layer

- We have developed the Gridsphere portal prototype as an interface layer of the ACGT GRID.
- We have adapted/developed specific portlets for implementing the basic functions of the ACGT portal, including:
    - authentication services
    - data management services
    - job execution and monitoring services
- We have contributed to the guidelines regarding the integration of service interfaces in the ACGT Portal

WP14: Training

- We have realized the analysis of the ACGT portal development, including:
    - Application of requirements engineering methods at the ACGT Portal level
    - Specific ACGT Portal scenarios
    - Specific ACGT Portal roles
    - Specific ACGT Portal functionalities, including customization, security, training and collaboration functions
    - ACGT Portal technical specifications
- We have analysed a reduced set of functional features of the ACGT Portal to be implemented in the prototype
- We have developed a functional prototype of the ACGT Portal, using the Gridsphere portal framework
- We have written a report on the ACGT prototype

WP15: Dissemination

No activity

WP16: Market Investigation and Exploitation

No activity

PARTNER 21 – FUNDP

WP2: User Needs Analysis and Specifications

No activity
In accordance with ERCIM's Email dd. 04.10.2006 (see appendix IV), Crid didn't have anymore PM allocated to WP2 for this period.

WP3: Architecture and Standards

No activity
In accordance with ERCIM's Email dd. 04.10.2006 (see appendix IV), Crid didn't have anymore PM allocated to WP3 for this period.

WP10: Ethical, Legal and QA Issues

Crid has elaborated:

- a document giving Definitions of important legal terminology (with UHANN) and identified the data flows within the clinical studies and in ACGT, especially within the Nephroblastoma study carried out by USAAR (with Custodix, USAAR, UHANN and FORTH,)
- an ACGT Data Protection Framework which is described in detail in Deliverable 10.2 (with FUNDP, UH, Custodix, UHANN)

Crid has produced:

- Like editor, the Deliverable 10.1 titled "Production of informed consents" (with FUNDP, UH, Custodix, UHANN). Therefore:
  - The requirements of an informed consent as a way of legitimization of sensitive data processing was examined and explained.
  - The scope of an informed consent was analyzed.
  - Special attention was paid to the questions, who has to consent to the data processing (only the patient itself or also it's relatives?), how long a consent is valid and the right to withdraw and erasure.
- Like contributor, the Deliverable 10.2 titled "The ACGT ethical and legal requirements" (with FUNDP, UH, Custodix, UHANN). The Legal Requirements of ACGT and solutions for data protection issues were examined and explained in. Therefore:
  - An analysis whether pseudonymous data can be seen as anonymous data was carried out.
  - Definition for additional knowledge that is attributable to the data controller was examined and developed.
  - An analysis of the role of a trusted third party in the process of aliasing was carried out.
  - An analysis whether the local physician can act as a trusted third party was carried out
  - The establishment of a Data Protection Board was examined
  - A first analyze of the legal duties of ACGT creating an infrastructure.

Crid was involved, as speaker, in Conferences, lessons and in the writing of article (see above).

WP11: Trust and Security

Crid has participated, as contributor (with UH and UHANN) to the production of the Deliverable 11.1 by producing general terms document and consent forms which has been modified in the Deliverable 10.1.
In accordance with ERCIM's Email dd. 04.10.2006, Crid didn't have any more PM allocated to WP11 for this period.

WP12: Clinical Trials

In accordance with ERCIM's Email dd. 04.10.2006, Crid didn't have anymore PM allocated to WP12 for this period.

WP14: Training

No activity

WP15: Dissemination

03.08.2006-07.08.2008	**Lessons** Université européenne d'été - Droit de la santé et Ethique Biomédicale	Student / post-graduate	International	60	FUNDP – Crid Jean Herveg
07.08.2006 - 11.08.2006	**Conference** 16th World congress on Medical Law in Toulouse	Medical people (lawyers, doctors, etc…)	International	800	FUNDP – Crid Pr. Yves Poullet Jean Herveg Jean-Marc Van Gyseghem
20.09.2006	**Conference** TG6 Meeting at EGTD 2006	IT public	International	50	FUNDP – Crid Jean-Marc Van Gyseghem
20.09.2006 - 23.09.2006	**Conference** Congrès société européenne de Télémédecine in Salamanque	Professors – Lecturer – representatives of states - Judges	International	100	FUNDP – Crid Jean Herveg
01.12.2007	**Internal training day (FUNDP – Crid)**	Researchers – Professors – Lecturers	Belgium	40	FUNDP – Crid Jean-Marc Van Gyseghem
08.2006	**Publication** "L'espace européen de la santé en ligne: vers un marché des données médicales", Journal de médecine légale, droit médical, victimologie dommage corporel, abstracts of the 16th World Congress on Medical Law,	Medical people (lawyers, doctors, etc…)	International		FUNDP – Crid Jean Herveg

WP16: Market Investigation and Exploitation

No activity - In accordance with ERCIM's Email dd. 04.10.2006 (see appendix IV), Crid didn't have anymore PM allocated to WP16 for this period.

PARTNER 22 - UH

WP2: User Needs Analysis and Specifications

UH contributed to WP2 by preparing and delivering chapter 21 (Ethico-legal issues related to multicentric, post-genomic Clinical Trials) to D2.1 (User requirements and specification of the ACGT internal clinical trial). The chapter 21.1 covers issues regarding protections of patients and patient's rights, integrity of the person and self-determination, and informational self-determination. The review and extraction of several ethico-legal documents are included in chapter 21.2 (Review of current law, guidelines and documents) as well as a review of the relevant laws and regulations in the countries where the clinical pilots and research will be carried out (Belgium, Germany, Greece and the UK) in Chapter 21.2.3 (National Laws and Regulations). Proofreading of other parts of D2.1 was done. Deviant from the scheduled PM allocation, we finished our work for WP2 within 4 PM.

WP3: Architecture and Standards

No activity. Different from what was initially projected, no ethical framing for architecture and standards was developed by UH in WP3, since preliminary ethical requirements were developed in WP2, and consolidated ethical requirements in WP10. Hence, the 2PM allocated to WP3 were shifted to WP10.

WP10: Ethical, Legal and QA Issues

Within WP10, UH was involved in D10.1 (Production of inform-consent form in compliance with the clinical trials, post-genomic research and genetic data handling requirements) and D10.2 (The ACGT ethical and legal requirements).
The "Patient Information Sheet" as contribution of UH to D10.1 was developed, circularized and finalized. Furthermore, an ethico-historical introduction to informed consent was written for D10.1 in chapter 2.1 (Ethical Aspects). Proofreading of other parts of D10.1 was done.
Since the start of the project we continuously collected and analyzed literature relevant for the assessment of ethical and legal requirements for ACGT in order to prepare our contribution to D10.2. Especially, literature was analyzed with respect to the following ethical issues: scope of informed consent and data feedback to individual patients. In addition, other ethical issues which may be of potential importance for ACGT have been identified and examined (e.g. patients' perspective, research involving children, communication processes). The final version of chapter 2 (Ethical Requirements) including abstract and conclusions was brought to completion as contribution of UH to D10.2. Proofreading of other parts of D10.2 was done. Due to the complexity of issues in D10.2, we expanded our PM from 8 to 12 for WP10 for the fist period of 18 months.

Collaborations within WP10

- May 3, 2006: Regine Kollek participated in the WP10 meeting with WP2, WP11 and WP12 in Hanover.
- September 28, 2006: Regine Kollek participated in the WP10 and WP11 meeting which took place in the context of the 2nd Consortium Meeting in Crete from September 27 to September 29, 2006.
- January 24, 2007: Regine Kollek and Imme Petersen attended a spontaneously organized WP10 and WP11 assembly in the context of the 3d Consortium Meeting in Malaga from January 24 to January 26, 2007.

WP11: Trust and Security

UH cooperated with WP11 in the course of the development of D11.1 (Consolidation of security requirements of ACGT and initial security architecture), especially with respect to questions of patient

information, informed consent, withdrawal of consent, and patient feedback. Contributions of UH involved investigation for and provision of relevant documents (i.g. different informed consent forms) and publications from the field of ethics, which are important for securing compliance of ACGT security architecture with ethical requirements and European and national legislation.

Collaborations within WP11

- May 3, 2006: Regine Kollek met WP11 during the WP10 meeting in Hanover.
- September 28, 2006: Regine Kollek participated in the WP11 and WP10 meeting which took place in the context of the 2nd Consortium Meeting in Crete from September 27 to September 29, 2006.
- January 24, 2007: Regine Kollek and Imme Petersen attended a spontaneously organized WP11 and WP10 assembly in the context of the 3d Consortium Meeting in Malaga from January 24 to January 26, 2007.

WP12: Clinical Trials

UH collaborated with partners from WP12 in the course of developments of the patient information sheet, which involved several rounds of feedback and redrafting of the patient information. Furthermore, advice on different issues regarding the ethical and legal aspects of patient data sharing within ACGT was given after studying relevant ethical and legal documents.

Collaborations within WP12: May 3, 2006: Regine Kollek met WP 12 during the WP10 meeting in Hanover.

WP15: Dissemination

Presentations

- May 27, 2006: Regine Kollek presented her paper "*The Individual to be found in Translation? Paradoxes of "Personalised" Medicine"* at the 1st International Conference on Ethics and Politics in Heraklion (Greece) from 24 May to 26 May, 2006, www.philosophycrete.edu.gr/.
- October 5, 2006: Regine Kollek presented her paper *"Design of Individual Donor Feedback Processes in Biobank Research"* together with Norbert Luttenberger (Institute for Informatics, University of Kiel) in the Workshop on "Electronic Data Custodianship" at the 36th Annual Meeting of the German Society of Informatics, a non-profit organization to promote informatics with about 25.000 members coming from all areas of business and science in Dresden (Germany) from 2nd-6th of October 2006, www.informatik2006.de/.
- October 9, 2006: Regine Kollek presented her paper "*The individual value of genetic information. Ethical and social considerations in the evaluation of genetic testing technologies*" at the ESF-IfW Conference on "The Global Health Economy: New Technology and Medical Decision Making – Normative Models and Empirical Practice" in Salzau Castle (Germany), 4 - 9 October 2006.

Websites

- In the course of the redesign of the ACGT website UH contributed content to the link "ethical aspects".
- UH established a description of ACGT project with a link to the ACGT website on its institutional homepage, http://www.uni-hamburg.de/fachbereiche-einrichtungen/fg_ta_med/index.html.

PARTNER 23 – UOXF

WP2: User Needs Analysis and Specifications

We have reviewed the literature and we have contributed to the assessment of the needs for the analysis of genomic trials. We have suggested some available tools and existing standards for genomic data analysis, and also some areas where tools are lacking and which would benefit from further research work. We have developed and contributed some of the analysis workflows (e.g. Studying the prognostic value of specific pathways for different tumours, Comparing the performance of supervised data mining algorithms). As the person working for ACGT at Oxford started in November this work couldn't be contributed in time to be incorporated into WP2 deliverable. Thus, some this work was included into WP6 (Data discovery) deliverable (see specifically sections 4 and 5 of WP6 first deliverable for more details).

We are generating workflows for an inter-centres and inter-platform gene expression microarrays comparative study (see WP12 for more details). The aim of this study is to assess the variability in gene expression microarrays, and of the prognostic and predictive profiles obtained from this technology, performed at different clinical sites and using different array methodologies in human breast cancer samples. The workflows for this study are been implemented in R and will be contributed to WP2 and WP6 during the next months.

Furthermore, in collaboration with the Istituto Europeo di Oncologia (IEO), ACGT partner 26, we started planning some new inter-centre studies. In this initial planning phase, we identified a number of pathways critical to cancer progression and prognosis (e.g. angiogenesis), and relative drugs of interest. The studies will use a variety of available state-of-the-art genomic, proteomic and imaging technology. The workflows regarding these studies will be introduced in a revised version of WP2 deliverable.

WP5: Distributed Data Access, Tools and Applications

The activity was limited to reading the documentation produced and contributing to discussion.

WP7: Ontologies and Semantic Mediation Tools

We have reviewed the existing initiatives and standards for ontology, specifically in breast cancer. We have contributed to the discussion on ontology development and we have provided material for the development of the ontology (e.g. examples of clinical and R&D forms in use in the UK in relation to clinical trials, clinical reporting forms, material regarding other ontology initiatives and existing standards, published papers and guidelines).
We have reviewed the first draft of the Master ontology for cancer.

WP10: Ethical, Legal and QA Issues

We have provided input for the development of deliverables 10.1 and 10.2 in the form of information on current UK ethics regulations, clinical trials documentation (e.g. examples of consent forms and information sheets used for clinical trials in the UK), and publications. We have contributed to the writing of the patient information and consent form in deliverable D 10.1.
We have reviewed the deliverables 10.1 and 10.2 for the ACGT internal review.

WP12: Clinical Trials

We have contributed to the first year deliverables, reviewed the documentation and provided input to the discussion on future ACGT clinical studies and trials.

We have been generating gene expression microarrays for an inter-centres and inter-platform gene expression microarrays comparative study in breast cancer. This study includes samples from breast cancer patients who had adjuvant chemotherapy only, adjuvant hormone therapy only, both these therapies, or no adjuvant treatment. We are contributing breast cancer samples where both Affymetrix gene expression microarrays (performed previously by IJB) and Illumina gene expression microarrays (that is been performed by UOXF) will be available for comparison. This study is not a clinical trial per se, but it will provide crucial information that will help in the analysis and comparison of large multiple-centres clinico-genomic trials. This study is also particularly interesting as it is part of a larger breast cancer genomic study (involving an historical series of 200 patients) where results from a variety of state-of-the-art genomic techniques such as DNA methylation, CGH analysis, microRNA analysis and miRNA analysis will be assessed and compared. We have been developing in the context of WP2 and WP6 analyses workflow for this study based on existing standards for the normalisation and processing of the data from these arrays.

As far as the collaborative studies between IEO and UOXF, we are setting-up a series of small (around 30 patients) non-randomized studies (but by year 4 of ACGT it is envisaged that randomized designs will be implemented), initially in breast cancer. The “neo adjuvant” model protocol will be adopted (not dissimilar to the TOP trial), so that the experimental intervention (new targeted molecules) takes place after baseline imaging, and after genomic/proteomic parameters have been measured in tissue and other biological samples (e.g. plasma, serum). Shortly after exposure to the novel agent, the same measurements are repeated. As surgery will be scheduled at this point, access to second sampling of tissue should be guaranteed. This will allow treatment response data to be generated, and treatment effects to be quantified using genomic, proteomic and imaging technologies.

WP13: Evaluation and Validation

We have contributed to the discussion and we have given feedback on criteria for evaluation. We are implementing in R one of the workflows that we have contributed and that will be used for validation (i.e. Studying the prognostic value of specific pathways for different tumours).

WP15: Dissemination

We have given feedback and suggestion for the development of the ACGT website. We have been gathering and preparing material on breast cancer trials and molecular biology to be incorporated into the web site.

PARTNER 25 – Uhok

WP2: User Needs Analysis and Specifications

UhoK has been involved in the Deliverable D2.1 User Requirements and Specification of the ACGT internal clinical trials, and wrote the chapter 13 state-of-the-art survey – “Tools for the visual orchestration of services”.

WP3: Architecture and Standards

WP4: Biomedical GRID technology Layer

WP5: Distributed Data Access, Tools and Applications

For WP3, WP4 and WP5: Participation in cross-WP technical meetings and discussions (Eindhoven 2 pers.; Chania 3 pers.; Malaga 4 pers.)

WP9: The integrated ACGT Environment

Wrote and distributed discussion document relating to UHok’s ACGT contributions.

WP15: Dissemination

No activity

PARTNER 26 - IEO

WP2: User Needs Analysis and Specifications

In the framework of ACGT project we started a pharmacogenomic study, which would greatly benefit from the ACGT computational framework.
In particular, our project is aimed to define the pharmacogenetic profile of non-small cell lung cancer (NSCLC) and transitional cell carcinoma (TCC) of the bladder by directly studying microdissected tumor samples by quantitative RT-PCR (TaqMan).
Gemcitabine is a deoxycytidine analogue with action mechanism similar to AraC. Its cytotoxic activity depends on the inhibition of the enzyme ribonucleotide reductase (RR) and on drug incorporation into the DNA during the S phase. To become active, gemcitabine is thought be transported into the cells by the intracellular transporter hENT and phosphorylated by the enzyme deoxycytidine kinase (dCK). Indeed, these two steps are rate-limiting for gemcitabine activation. On the converse, deoxycytidine deaminase (CdA) and endo-5'-nucleotidase (5'-NT) are responsible for gemcitabine inactivation.
In the last year, our group measured the expression levels of all of these genes involved in gemcitabine activation. Our results confirm that this method is feasible and reproducible. Statistical analysis will be performed to correlate the pattern of gene expression (GE) with the clinical outcome of the patient and to find out the chemoresistance/chemosensitivity threshold of GE. We analyzed the computational needs of this research and we decided to integrate in it some research activities in bio-informatics, bio-statistics and also in bio-mathematical modelling.

Furthermore, in collaboration with the Weatherall Institute of Molecular Medicine of Oxford University (ACGT Partner 23), we started planning some new studies requiring intensive computational support, which optimally fit in the framework of ACGT project. Both teams consist of integrated clinical and basis science groups, who wish to expand and strengthen their commitment to bioinformatics through ACGT.

We shall establish joint hypothesis-driven translational science and clinical protocols, also focusing on imaging end points (see also WP12).

In this initial planning phase, we identified a number of state-of-the-art cellular targets, critical to cancer cell survival, in which both partners are interested: Numb and notch, Angiogenesis, HDAC, Growth factor recepetor pathways.
The drugs of interest that will be investigated will include: Bevacizumab, Erlotinib, Lapatinib, Sorafenib and Sunitinib
We will focus mainly on the following experimental and theoretical methods to be tested and validated: NMR Imaging (IMM + IEO resp), Ultrasound (IEO), CT/PET (IEO), Circulating Endothelial (IMM + IEO) and Tumour cells (by Veridex Cell Search system at IEO), scanning with anti-Tenascin (IEO), Genomics: Affymetrix (IEO) – Illumina (IMM).
Both bio-informatics and bio-mathematical investigations will be performed, with interplay between them and between IMM and IEO.

WP6: Knowledge Management and Discovery Tools

We started assessing the potential contribution of our institute in terms of human resource and of our biological and bio-informatics research experience. Thus we focussed on two main categories: Software testers for the SWs of WP6 (mainly bio-medical researchers with computational experience); Developers contributing to WP6 both by "GRID-izing" their own existing SWs and by developing new SWs.
Among the previously produced IEO SWs, we individualised some candidate tools: *GenePicker* (H. Mueller's workgroup); *Splicy* (F. Ciccarelli's workgroup); *GAAS* and *My West* (M. Alcalay's workgroup).

Among the “in progress” research work, the H. Mueller’s workgroup developed an algorithm for the identification of cancer signalling pathways, and it is high priority for implementation and integration in the framework of WP6.

WP7: Ontologies and Semantic Mediation Tools

No activity in the first 12 months.

WP10: Ethical, Legal and QA Issues

The IEO contains a register of all patients who have attended since its inception eleven years ago. At present almost 10,000 new patients are seen each year, and 4,000 go in to clinical trials. At present 17,000 are in trial follow-up. There are five collections of tumour samples, the largest is 3000 breast cancer samples, and these are about to be centralised. The legal and ethical issues relevant to WP10 have just been exhaustively examined in IEO, in order to clarify who might do experiments on those banked tumour samples, and which informed consent procedures were appropriate within EU and Italian legislation.
We have recently installed a central Hospital based Tumour Registry, linked to the tumour bank. The first quality assurance study has been completed on data regarding 5,000 patients seen at IEO in the second half of 2006, and the result is exceptionally good with over 90% accuracy in most categories. This experience and methodology will be imported in to WP 10.

WP12: Clinical Trials

As far as the clinical pharmacogenetic studies, the following clinical trials are ongoing at IEO:

Clinical trial in bladder cancer
The primary aim of the study is to identify the relationship between the GE levels of deoxycytidine kinase (dCK), deoxycytidine deaminase (CdA), endo-5'-nucleotidase (5’-NT) and ribonucleotide reductase (RR) in transitional bladder cancer tissue and pathological response to treatment with gemcitabine. Eligible patients undergo a trans urethral resection (TUR). All tumour lesions but one, which will be the “marker lesion”, are resected. Histology examination is performed. Specimens from each patient are processed in order to obtain biological samples that will be processed for GE of enzymes involved into the Gemcitabine activity and microarrays for genotype profiling. Patients receive one course of weekly intravesical gemcitabine for a period of 6 weeks follow ed by two weeks of rest. Tissue samples, if any, are collected again to repeat the analysis for GE of enzymes involved into the Gemcitabine activity and microarrays for genotype profiling. Up to date 41 patients have been included in the study. Of the 31 evaluable patients for efficacy 11 experienced a pathological complete remission of the ML. Of the 11 responder patients: 7 patients were with intermediate risk, 3 with high risk (one non definable). Of the 20 non responder patients: 9 patients were with intermediate risk, 10 patients with high risk (one non definible). The GE has been analyzed on total cellular RNA extracted from tumor cells.
22 patients are evaluable for pharmacogenetic determinants (4 with pathological remission and 18 with stable disease).
Patients who achieved a pathological complete response to intravesical gemcitabine showed higher expression levels of dCK (median value 1.026) and lower levels of RRM2 (median value 0.820).
The calculated dCKhENT/RR expression ratio is a potential pharmacogenetic determinant predictive of pathological response to intravesical gemcitabine (p=0.012).
Clinical trial in NSCLC:
A pharmacogenomic model will be also applied to NSCLC.

This research project is designed to assess the impact of specific gene profiles on efficacy of gemcitabine in previously untreated patients with non-small cell lung cancer (NSCLC).

Patients with locally advanced NSCLC (stage IIIA or IIIB) will undergo surgical biopsy of mediastinal lymph nodes. Mediastinoscopy will be elective for patients with evidence of right paratracheal (R2 and R4), subcarenal (7) and left paratracheal lymph nodes (L4), mediastinotomy will be elective procedure for aorto-pulmonary and paraortic (5 and 6) lymph node biopsy.
Patients with metastatic NSCLC (stage IV) will undergo tumor biopsy by bronchial endoscopy or, if evidence of biopticable metastatic lesion, by ultrasound or CT scan guided tumor biopsy.
All the biopsy samples will be rapidly frozen and OCT embedded in liquid nitrogen, and suitably stored in a super freezer at -140°C. In parallel, all the information dealing with the clinical history of the patients, from whom the samples are coming from, will be filed in a specific database in order to be able to correlate biological findings of the tumor with clinical outcome of the patients.
All patients will receive a combination of cisplatin at a dose of 80 mg per square meter of body-surface area on day 1 plus gemcitabine at a dose of 1250 mg/m^2 on days 1 and 8, according to standard protocols. The cycle will be repeated every 3 weeks.
All patients will undergo staging procedures at baseline (computed tomography and whole body fluorodeoxyglucose positron emission (PET)). Following four cycles of chemotherapy the response rate will be estimated according to the Response Evaluation Criteria in Solid tumors (RECIST).
The fresh tissue from each biopsy will be analyzed by quantitative real-time PCR in order to quantitatively evaluate the expression of genes related to gemcitabine metabolism (hENT, RR, dCK, CdA and 5'-NT).

As far as the collaborative studies between IEO and Oxford University, we will start now a series of non- randomized trials, but by year 4 of ACGT it is envisaged that randomized designs will be implemented. We will study small cohorts of around 30 patients, initially with breast or lung cancer, then bladder cancer. Those trial participants will be studied intensively through "neo adjuvant" model protocols (not dissimilar to the TOP trial), so that experimental interventions, such as new targeted molecules will be administered after baseline imaging, and after genomic/proteomic parameters have been measured in tissue and other biological samples (e.g. plasma, serum, urine, sputum, ductal lavage specimens etc.). After short exposure to the novel agent, the same measurements will be repeated. As surgery will be scheduled at this point, access to second sampling of tissues will be guaranteed. This will allow comparative data to be generated and various new platforms to be validated.

WP13: Evaluation and Validation

No activity has been contributed to the WP13 as yet, as we are still inventarising, formulating and prioritising institutional activities which will be most synergistic with the ACGT programme.

WP14: Training

The IEO activity in this WP was focused in providing a biological and medical oriented point of view on the general organization of ACGT training platform. This was mainly done during two meetings we attended in the period: a first meeting in Milan at Ieo with prof. Tsinakis and the general ACGT meeting in Malaga.

WP15: Dissemination

We are starting ACGT-related research collaborations with some institution and researchers with which IEO collaborates from many years: **World Health Organization – International Agency for Research on Cancer:** (Prof. Peter Boyle, general director of WHO IARC); **The National Research Council of Italy** (Prof. A. Bertuzzi and Prof. A. Gandolfi); **The University of Pisa** (Prof. F. Giannessi, and Prof. Danesi).
Finally, a vigorous dissemination programme on ACGT has been started.