

Six Monthly Progress Report

February 2009 to July 2009 (Month 37 to 42)

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ABSTRACT:

This deliverable presents the full range of activities during the period February 2009 to July 2009 (Month 37 to 42), including management, dissemination technical and scientific activities in accordance with the Description of Work.

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Executive Summary

ACGT Objectives

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

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

In addition the project is developing

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

Finally, the project has also focused with more emphasis on its dissemination activities, is engaging in a closer dialog with several of the relevant end-user communities, and is formulating a range of concrete exploitation plans.

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Project objectives and major achievements over the reporting period

The current reporting period was a period of intense technical, integration and evaluation activities of the project, which we will briefly describe below.

The ultimate objective of the ACGT project is the development of a secure semantic grid services infrastructure which:

- will facilitate the seamless and secure access to heterogeneous, distributed multilevel databases;
- will provide a range of semantically rich re-usable, open tools for the analysis of such integrated, multilevel clinico-genomic data;
- in the context of discovery-driven (eScience) workflows and dynamic VOs;
- in compliance with existing ethical and legal regulations.

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

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

In specifying this architectural blueprint of the ACGT technological platform, corresponding specifications of other relevant projects have been thoroughly studied. Of particular relevance are the Cancer Biomedical Informatics Grid (caBIG) in the US and the CancerGrid project in the UK. The infrastructure being developed uses a common set of services and service registrations for the entire clinical trial on cancer community.

During the reporting period we have been focusing on delivering final implementations of the core components and their integration up to a stage where they can effectively support in-silico investigation. Mature service implementations have been used in providing integrated demonstration of the capabilities, characteristics and constraints of the architectural framework defined, and have been used for supporting the evaluation, training and dissemination activities of the project. Technical integration issues, that have arisen, have been addressed and most have been successfully resolved.

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

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

- a) One of our key scientific challenges is related to "achieving semantic integration of heterogeneous, distributed and multi-level clinical and genomic data". Theoretically, semantically consistent data integration may be achieved through different approaches:
 - Everyone adopts a single, core model.
 - Everyone has its own model but follows interchange standards (communication, messaging) between the models.

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- Everyone agrees on common data elements (CDEs) with systematic unambiguous formats e.g. data descriptions (data types, terminologies, coding), meta data and information models.
- Everyone uses a predefined knowledge representation framework (classes, attributes, definitions, identification principles) and inference mechanisms (inclusions, exceptions, constraints, reasoning etc).

In responding to this challenge the project is pursuing – among the various alternatives – the use on a global schema. As a result our "semantic integration approach" requires the definition and seamless integration of three main components, comprising the core of the Semantic Mediation layer. These components are:

- > The ACGT Master Ontology on Cancer
- The mappings between ontology elements and data access services schemas.
- ➤ The **Semantic Mediator**, a software controlling the translation of queries and integration of results.
- Additional components that are used for overcoming several issues in the data integration process are the Mapping Tool, the Data Cleaning module—for retrieved instances—, and the Query Preprocessing Module—for literal homogenization in queries.

During the reporting period our work related to this "challenge" consisted of:

Activities aiming at finalizing the implementation of our Master Ontology on Cancer and its validation wrt to its completeness and adequacy. In specific we have

Tested of ObTiMA's CRF creator thus checking coverage of the ACGT MO

February to March 2009 IFOMIS spent creating Case Report Forms (CRFs) using ObTiMA's CRF creator. IFOMIS was given that task in order to check whether the coverage of the ACGT MO was sufficient to create CRFs for two of the clinical studies at hand, namely SIOP and the Rhabdoid Study.

2. Reviewed and optimized of the ACGT MO

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

The consistency is constantly checked while working with the owl-File, using the Pellet reasoner.

3. Validation of conceptual design by means of terminology techniques (Ongoing)

In order to validate our conceptual design we decided to collaborate with terminology experts outside ACGT to get an impression on the completeness of our representation.

The 200 abstracts we worked on in the first round proofed to be too small a basis for successfully providing terminological comparison. Therefore, IFOMIS hired a student assistant to create three corpora of up to 1500 abstracts, one for each disease (nephroblastoma, mamma carcinoma, rhabdoid tumour). This task is now fulfilled and the corpora were delivered to IAI for analysis. For rhabdoid tumour only around 500 abstract have been found. Results will be delivered end of August 2009.

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4. Networking with the OBO Foundry

Communication with the OBO Foundry is maintained in our efforts to make the ACGT MO part of the Foundry. Most of the criteria of the OBO Foundry have already be fulfilled (s. last 6 monthly report), but at the moment getting the MO accepted hinges on providing textual definitions for the classes. A student assistant has started to work on this task - under supervision of Dr Mathias Brochhausen-, but the definitions are not yet included in the owl file. However, it needs to be understood that this is obstacle that can and will be overcome in the near future.

- Activities related to the remaining components of the mediation process. Namely:
 - 1. Integration of the Query Tool in the ACGT Portal
 - 2. Implementation of a security layer for accessing the Semantic Mediator
 - 3. Final implementations of the remaining components of the mediation process (Mapping Tool, the Data Cleaning module, and the Query Preprocessing Module).
 - 4. Design and implementation of a wrapper for an ArrayExpress for the multi-level data integration experiment.
- b) Our second main objective and challenge relates to the "provision of a range of semantically rich re-usable, open tools for the analysis of such integrated, multilevel clinico-genomic data". Towards this direction, the main activities during the reporting period relate to:
 - Finalized development and integration of generic web-service for command-line applications with ACGT security services (GAS), data storage (DMS) and job submission and control (GRMS).
 - Extension of the modular programmatic framework (mAPI) to provide support for secure metadata repository. This enhancement increases interoperability between ACGT secure services and external Web-services in a protected way.
 - Development work on combinatorial literature search and client additions.
 - Rewrote the bibliography search, and proper error handling was implemented.
 - GridR testing and debugging
 - Support for mediator queries over Command-line services.
 - Work on the final ACGT meta-data specifications continued. Development of the metadata repository as a secure web-service (supporting credential access) was completed.
- c) Our third main objective and related challenges are linked to the need for supporting "discovery-driven (eScience) workflows and dynamic VOs". In responding to this challenge the project has been developing services for virtual organisation set-up and management and a technical framework supporting the definition and seamless execution of the grid of scientific workflows. To this end during the reporting period the project has:
 - Development on the version v2.0 of the ACGT Workflow Editor was completed, including the incorporation of the Biomoby data type ontology matching in the workflow editor
 - Implementation of generic proxy services for the integration of external bioinformatic services (Biomoby services) was completed.
 - Improve the performance of the credential delegation process by employing a main memory based repository for the proxy credentials.
 - Development on the Proxy Services framework for making possible the secure, authenticated, and authorized invocation of Grid ACGT Services from within BPEL Workflow Enactors.
 - Integration of the Semantic Mediator and the Dynamic Data Access Services (DAS) in the workflow environment by implementing the corresponding proxy services.
 - Investigations of state of the art in machine learning techniques for recommender engine, in particular community-based approaches and similarity-based approaches

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- Implementation of the "Query as Service" concept in the workflow Editor so that semantic queries of the Mediator can be shared among users and workflows.
- Embedding intelligence into the ACGT Workflow and service environment by developing of Magallanes, a Service to be used as automatic / intelligent workflow composition tool that can be used from the workflow editor.
- Development of jORCA, a standalone client, for executing command line services in the ACGT environment.
- Development of a bioinformatics data standardization formatter aimed to facilitate data standardization by using configurable XPath rules and regular expressions enabling the automatic identification of data types and performing the appropriated transformations.
- d) Our final challenge and hence an additional dimension of activities during the reporting period - relates to the need for supporting all the previous mentioned functionalities in a way that is in full agreement with the existing legal and regulatory framework in the European Union. Towards this challenge – during the reporting period – the main activities of the project have been:
 - Has developed a new version of Grid Authorisation Service (GAS) and deployed in the ACGT infrastructure. This new version adds advanced functionality such as wildcards for resources.
 - Requirements and guidelines for developing secured ACGT services have been adapted to take into account the comments from the internal review.
 - Development and release of new registration and delegation applets with enhanced functionality. It is now possible to select an identity out of a list, store credentials on portable devices and log in automatically at successful delegation.
 - Further specification and completion of the implementation of the role based secure access control (RBAC) to ObTiMA and user roles and rights management, as well as implementation of secure Data Access Services (compliant to OGSA DAI) for ObTiMA
 - Definition of the requirements for the integration of the Anonymization Tool (CAT) with ObTIMA.
 - CAT has been evaluated further by actively using the tool in de-identification of ACGT patient data.
 - Finally our work on D11.6: ACGT guide with administrative documentation of ACGT security and VO management has started.
 - Continuous support has been given to partners for further integration of new services in ACGT and troubleshooting bugs.

In parallel to these technical activities several other critical tasks were performed. Namely:

- Analysis of legal requirements concerning data, genetic material and scientific outcome and their implications has been completed.
- Analysis of licenses used/to be used in ACGT and their legal requirements and implications has been completed.
- Analysis of the GRID-infrastructure and its legal implications has been completed.
- Risk analysis concerning the data security and data protection framework has begun and is progressing very nicely.
- The negotiation of contracts between partners and ACGT is in progress.
- An in depth analysis on the current legal situation to know if the data protection framework drawn in the D10.2 is reached, has started.
- e) At the same time two other areas of important work in the project have significantly moved forward. These relate to the implementation of ObTiMA, an open source Ontology based Trial Management System, and the implementation and validation of a computational framework for modeling in-silico tumor growth and response to therapy. With respect to ObTiMA, during the reporting period, the following have been performed:
 - Importing of the clinical trial for Nephroblastoma cancer (SIOP) in ObTiMA
 - Integration of OGSA DAI services for accessing the ObTiMA database
 - Final implementation of an Advanced Ontology viewer

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- Final implementation of a CRF creator
- Implementation of v1.0 of a Web Service for the integration of the Trial Outline Builder with ObTiMA
- Implementation of v1.0 of a Web Service for communication with the ACGT submission system for maintenance of the ACGT Master Ontology.
- Implementation for Audit trial functionality
- Implementation of the functionality for CRF validation
- Reviewing and updating of the Obtima database scheme

With respect to the Oncosimulator, during the reporting period, the following have been performed:

- Completion of the numerical study wrt the behaviour of the simulation models, through a study of the convergence of the algorithms and codes concerning both Wilms tumour and breast cancer, and a comprehensive study of the stability/sensitivity of the algorithms and codes concerning both Wilms tumour and breast cancer with respect to several critical parameters.
- Provision of an advanced integrated version of the simulation and the technological modules constituting the Oncosimulator including, a) Optimization of the simulation codes and their execution. Consideration of normal tissue treatment complication limits, b) Internal parallelization of the simulation code in order to considerably lower the execution time needed, c) Interactive visualization of the tumour before, during and after the application of a therapeutic scheme/schedule [both real and simulated] and adaptation of visualization techniques to the actual data and the improved versions of the simulation module have been achieved, and d) An advanced version of the OncoRecipeSheet module has been produced and tested for numerous combinations of model parameter values. Further optimization work is in progress.

Finally, the project has devoted significant effort in establishing its evaluation and validation framework and initiating the process for continuous, user-driven, evaluation. To this respect new user evaluation sessions has been organized during the reporting period. Non-ACGT members were assessing the usability of the ACGT data-mining platform. Also, the legal and security framework of the ACGT environment were externally evaluated and were found globally in-line with current state-of-the-art practices in clinical data management by EORTC. Minor improvements to related deliverables were suggested. The difficulty to deal with the antinomy between availability of genomic data for research and the need to ensure patient privacy was recognized, as well as the importance to provide proper training to end users of such a complex environment. Yet the global strategic choices made in the project sound appropriate. The results from the evaluation sessions were used to improve the usability of the security services (e.g. an evaluation of the registration and login mechanism has been performed). This included the evaluation and comparison with solutions adopted in other similar EU projects.

We should also report that, there were deviations from the project work programme concerning the training workshops. The delay registered in previous reporting periods since these activities had to wait for the core ACGT services to reach a certain state of development, in which they are ready to be exposed and demonstrated to the ACGT users. Also, further delays resulted from the fact that there is a gap between the actual state of the ACGT services and the technical documentation available from other Work Packages due to continuous improvement of the services.

This gap will be covered in the next 6 months by focusing on filling the ACGT Handbook (already created and maintained). The wiki content provides up-to-date, community reviewed content, for the training related activities. Several methods of producing training materials (online tutorial content and offline handouts) from the content in the ACGT Handbook are scheduled in the following 6 months, to support the training sessions.

In addition to these RTD activities the project has also focused with more emphasis on its dissemination activities, and is gradually engaging in dialog with several of the relevant end-user communities and is gradually formulating a more concrete exploitation plan.

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Workpackage progress report over the period

Workpackage 1 - Project Management

• Partner Responsible : ERCIM

• Contributing partner(s): ERCIM, FORTH

Reporting Period: 01/02/2009 – 31/07/2009

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

-The Workpackage has the following major objectives:

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

- Objectives during reporting period

The main objectives for the period were:

- The preparation of the third annual report (reporting period 01/02/08-31/01/09)
- The annual review held on 23-24 April 2009
- The preparation of the next implementation plan Month 36 54

- Progress towards objectives

Significant efforts were devoted to the administrative tasks, due to the fact that the project was preparing the third Periodic Management Report and the annual review. The scientific management activities, since a range of activities are progressing was much more demanding, requiring continuous monitoring and full functioning of the Technical Management Committee that has been previously established.

- Main Activities & Tasks worked on

- Participation in all PMB meetings during the period
- Planning and participation in the conference calls
- Definition of the Agenda and issues to be discussed
- Close monitoring and follow up of deliverables and technical developments
- Identification of implementation bottlenecks and actions for their prompt resolution
- Coordination of efforts for the production of the DoW for the final implementation period.
- Coordination of the preparation of the project Review (April 2009)
- Coordination, collection of partners' contributions and submission of the third periodic Management report
- Answer the clarifications required by the European Commission after the analysis of the PMR

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Major Achievements towards planned objectives, identify main partners Involved

- The management has devoted significant efforts in making sure that this ambitious project will meet its annual objetctives and address the recommendations of the intermediate review held in December 2008.
- Deviations from the project work programme, and corrective actions taken/suggested
- List of deliverables, including due date and actual/foreseen submission date

Periodic Management Report (PMR) submitted on 15 April 2009 Third Periodic Activity Report (PAR) submitted on 10 April 2009

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

N/A

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Workpackage 2 – User Needs Analysis & Specifications

- Partner Responsible : USAAR
- <u>Contributing partner(s):</u> Forth, UvA, Philips, IJB, SIB, LundU, UMA, UPM, FHG, Biovista, UOC, PSNC, Custodix, ICCS, USAAR, SIVECO, UOXF.BP, UHoK, IEO
- Reporting Period: 01/02/2009 31/07/2009
- Workpackage objectives and starting point of work at beginning of reporting period

-The Workpackage has the following major objectives:

- This WP will continue to elaborate on the various requirements from a clinical point of view that are necessary for the proposed ACGT platform.
- To update guidelines for clinical trials (e.g. ICH and GCP), tools and software for the management of clinical studies and needs for clinico-genomic integration (including technological, legal issues, ethics, security, quality control, etc.).
- To refine requirements and assessment of the relevance (from the point of view of the clinical research) of the architectures and applications that are developed.
- To ensure the feasibility of implementing and to increase the number of clinical studies for cancer into ACGT based on specific clinicogenomic scenarios
- To define and implement usability criteria as part of the quality process for the evaluation of developed tools and software driven by clinicians and other endusers.
- To define criteria for a submission system for tools, software and data from an enduser perspective
- To define criteria for the selection of tools, software and data from a clinical perspective.
- To elaborate maintenance criteria for ACGT (together with WP16)

- Objectives during reporting period

Again the main focus was laid on clinical aspects of the project as done in the last periods. The implementation of the Rhabdoid Tumour Registry in ObTiMA was a major workload. In this respect the work was concentrated on the following major areas during the fourth period of ACGT:

Continuation of work regarding user requirements and functionality of the Ontology based clinical data management system (ObTiMA)

User needs for clinicians and basic researchers for ObTiMA including the user friendly integration of the Master Ontology, Roles and rights Management, Pseudonymization

Those specific clinico-genomic scenarios that were implemented in the clinical studies as defined in WP12 are further developed. Work was done in integrating them into the trial builder

- Progress towards objectives

Further progress was done in developing requirements and functionality of ObTiMA to get a tool for clinicians that will help to increase the number of clinical trials in ACGT.

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- Tasks worked on and achievement made with reference to planned objectives, identify contractors involved.

The main tasks carried out by USAAR:

The main focus was laid on the user requirements and the functionality of ObTiMA and the search for new trials and scenarios for ACGT. This task is leaded by USAAR (Norbert Graf). Deliverable D2.5 was finished and submitted. Over the entire period IFOMIS stayed in contact with Saarland University Hospital and FHG [IMBT] in order to discuss ontology related questions regarding the development of the Trial Builder. Major progress is done regarding the Clinical view and the maintenance of the Master Ontology. Multiple meetings and discussions about technical issues with project partners (FHG [IBMT], Hokkaido University, Custodix, IFOMIS, FORTH) took place to enhance feedback between developers of ObTiMA and the users. Since July 2009 one additional person (Holger Stenzhorn) is coordinating the work on ObTiMA.

This WP continued to elaborate on the various requirements from a clinical point of view that are necessary for the proposed ACGT platform. ACGT and ObTiMA were presented at several international Meetings by USAAR:

- 1. 1st International Rhabdoid Tumour meeting, Boston USA, 9th to 11th of March 2009
- 2. 2nd Edition of the ERCIM-ETSI Infinity Initiative, Meeting of the NoE VPH: Session 4: Why standardisation is absolutely necessary? Session Chair and Speaker: Norbert Graf (USAAR) The need for standardization from a clinical perspective. Sophia Antipolis, France, 2nd -3rd of April 2009:

 $\underline{\text{http://www.etsi.org/WebSite/NewsandEvents/Past_Events/2009_BIOICT_INFINITYINITIATIVE.asp} \underline{x}$

http://portal.etsi.org/docbox/Workshop/2009/200904 BIOICT/Standardization Infinity 2009 GRAF .pdf

- 3. SIOP-Europe Meeting Brussels regarding Clinical Trials in Paediatric Oncology, 29th of April, 2009
- 4. Rhabdoidtumor Meeting in Münster, Germany, 7th of May 2009, Norbert Graf gave a talk regarding ObTiMA for the Rhabdoid Tumour Registry
- 5. I-BFM Meeting in Bergamo, 8^{th} 10^{th} of May 2009, Norbert Graf presented ACGT and ObTiMA
- 6. Joint Meeting of ACGT and ContraCancrum in Heraklion, Crete, 6th of July 2009

Review Meeting

The periodic review was organized by USAAR and held in Homburg from 23rd to 24th of April 2009.

Main Focus

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

ACGT and ObTiMA were presented to different clinical groups in different workshops and meetings (list of meetings and dissemination activities are reported in the dedicated tables on part 5 and 6 of the report).

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Special focus was given to EORTC, SIOP, I-BFM and GPOH. These groups all are interested and are willing to use the ACGT infrastructure, if a guarantee is given that ACGT and ObTiMA will be maintained.

To increase the number of clinical trials for cancer into ACGT a lot of effort was done in organizing local meetings and attending other meetings The European Rhabdoid tumour Registry will use the TrialBuilder as soon as there is a functioning prototype. The same will be done with the next SIOP nephroblastoma trial.

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

Together with WP16 the elaboration of criteria for maintenance of ACGT has been continued. During this period the state of the art review was updated on a regular basis, regarding current guidelines for clinical trials, the assessment of tools and software for the management of clinico-genomic studies and trials. The user needs for clinico-genomic integration (including technological, legal issues, ethics, security, quality control, etc.) was consolidated within the corresponding WPs.

The main tasks carried out by IFOMIS: Review/Extension of ACGT MO

- Testing of ObTiMA's CRF creator/ Checking coverage of the ACGT MO
- Review and optimization of the ACGT MO
- Validation of conceptual design by means of terminology techniques (Ongoing)
- Networking with the OBO Foundry/ Working on textual definitions for the MO
- Networking with Theseus Medico
- Preparation of publications

Testing of ObTiMA's CRF creator / Checking coverage of the ACGT MO

February to March 2009 IFOMIS spent creating Case Report Forms (CRFs) using ObTiMA's CRF creator. IFOMIS was given that task in order to check whether the coverage of the ACGT MO was sufficient to create CRFs for two of the clinical studies at hand, namely SIOP and the Rhabdoid Study. Integrating the classes for the Rhabdoid Study took place in January 2009 and progressed slightly into February. The result with respect to domain coverage was that the reality representation of the ACGT MO fitted the two studies, yet some constraints were missing, which were needed to get the full view of the ontology in ObTiMA's ontology viewer. The missing constraints were added to the ontology and the CRFs completed.

Review and optimization of the ACGT MO

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

After creating the CRFs the MO was thoroughly revised and some issues with defined classes had to be resolved. In the future, IFOMIS will aim at minimizing the object properties in the owl file to a number smaller than 60. This, of course, needs to be coordinated with all users within the ACGT system (Mediator, ObTiMA).

Of course, the consistency is constantly checked while working with the owl-File, using the Pellet reasoner.

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Validation of conceptual design by means of terminology techniques (Ongoing)

A critical aspect for the success of the ACGT MO is whether we manage to provide a correct and complete representation of the given domain. In order to validate our conceptual design we decided to collaborate with terminology experts outside ACGT to get an impression on the completeness of our representation.

In this task we co-operated with the Institut für Angewandte Informationsforschung (IAI, Institute for Applied Information Science) located at Saarland University. We were in contact with the director of the institute, Prof. J. Haller, and a PhD student (G. Grigonyte).

The 200 abstracts we worked on in the first round proofed to be too small a basis for successfully providing terminological comparison. Therefore, IFOMIS hired a student assistant to create three corpora of up to 1500 abstracts, one for each disease (nephroblastoma, mamma carcinoma, rhabdoid tumour). This task is now fulfilled and the corpora were delivered to IAI for analysis. For rhabdoid tumour only around 500 abstract have been found.

Results will be delivered end of August 2009.

IFOMIS is working on a publication on these efforts together with IAI:

Networking with the OBO Foundry

IFOMIS is keeping contact with the OBO Foundry to make the ACGT MO part of the Foundry. Most of the criteria of the OBO Foundry have already be fulfilled (s. last 6 monthly report), but at the moment getting the MO accepted hinges on providing textual definitions for the classes. A student assistant has started to work on these under supervision of Mathias Brochhausen, but the definitions are not yet included in the owl file. However, it needs to be understood that this is obstacle that can and will be overcome in the near future.

Networking with Theseus Medico

As already declared in the last report the ACGT MO has been adopted by researchers outside ACGT, namely by the German Theseus Medico project. Our contact there is Pinar Wennnerberg (Siemens, Germany) who is collaborating with the DFKI (German Research Center for Artificial Intelligence) on semantic issues related to Theseus Medico. IFOMIS has kept in touch with Mrs Wennerberg to learn the needs of that project and to provide help with their using the ACGT MO.

Preparation of publications

IFOMIS took charge in providing a software demonstrator of ObTiMA for the International Conference on Biomedical Ontologies in Buffalo, USA. The demonstrator raised a lot of interest among the participants, interestingly enough mostly from bioinformaticians with no connection to the clinical sphere.

The main tasks carried out by Philips:

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

The main tasks carried out by UPM:

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

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The main tasks carried out by UMA:

UPM group has developed a requirement gathering process involving the mapping tool and query tool user interfaces. It has been a main goal to make these interfaces user-friendly. The requirements were gathered from different points of view, with the aim of generating personalized interface for different profiles. UPM has worked closely with end-users as well in defining use-case scenarios for demonstration purposes

The main tasks carried out by UvA:

Continuous work in designing and visualization of the OncoSimulator experiments

The main tasks carried out by IEO:

In the framework of WP2, IEO mainly developed theoretical research activities, by continuing focusing on antiangiogenic therapy.

Theoretical modelling of combined chemo- and antiangio-therapy, with particular focus on the investigation of the causes of sudden reactivation of the disease during the therapy.

Theoretical Investigations on the laws of growth of a tumour and of chemotherapy, with the extension of the classical Gompertz model.

Theoretical investigation on delivering of chemotherapy combined with antiangiogenic therapy

Theoretical and epistemic investigations on Phase 0 clinical trials

The main tasks carried out by ICCS:

ICCS continued to contribute to the definition of the Oncosimulator particular module specifications and their interdependencies from both the end user (clinician, basic researcher, general public) point of view - in tight collaboration with the clinical partners (USAAR, IJB) - and from the technical point of view in tight collaboration with the technical partners (UvA, INRIA, FORTH, FHG, PSNC, UHok et al.)

The main tasks carried out by UoC:

UoC, in close collaboration with FORTH, has continued working in the scenario that is based on the Prognochip clinico-genomic study and aiming at extending pathological characterization of samples, completing clinical information about the patients and capturing the requirements for deployment of the ACGT infrastructure.

The main tasks carried out by Biovista:

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

The main tasks carried out by SIB:

SIB continued analysis of bioinformaticians/data miners' requirements in the context of the scenarios adopted for demonstration and testing:

- TOP/PseudoTOP: Data mining on breast cancer data (in-depth analysis of data collected at a single site)
- MCMP multi-centric multi-platform scenario (integration of datasets collected at two different sites and using different microarray platforms in clinical research)
- SIOP (integration of ObTiMA with the ACGT data mining environment)

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The user requirements for the TOP/PseudoTOP and MCMP have lead to scenarios that have been shown in the reviews and will be demonstrated at the Japan Meeting in September 2009.

The user requirements for the SIOP clinical trial (Wilms tumor) have started to be analyzed at the very end of the period. This process is currently ongoing.

The main tasks carried out by Custodix:

A short review of user requirements regarding VO and resource management was performed. The different use case scenarios are evaluated and possible needs are discussed with end-users continuously. Further user needs analysis through the results of the evaluation sessions in Vienna and Oxford was done.

The main tasks carried out by UOXF:

In the framework of WP2, UOXF continued to develop research activities in the context of the MCMP scenario described in WP12 and more generally methods for the development and validation of prognostic/predictive signatures, and meta-analysis of publicly available datasets. Furthermore, they have been assessing feasibility and usability of the ACGT platform in the context of genomic clinical studies and trials carried out at OXF.

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

There are no deviations according to the plan

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

D2.5: Report on requirements for an ontology submission system and for the selection of tools, software and data within ACGT submitted in April 2009.

<u>List of milestones, including due date and actual/foreseen achievement date</u>
 Milestone 2.1 was achieved at month 6.
 No further milestones foreseen for this reporting period

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Workpackage 3 – Architecture and Standards

- Partner Responsible : PSNC
- <u>Contributing partner(s)</u>: FORTH, Philips, LundU, UMA, UPM, FHG, BIOVISTA, Custodix, LUH, USAAR
- Reporting Period: 01/02/2009 31/07/2009
- Workpackage objectives and starting point of work at beginning of reporting period

-The Workpackage has the following major objectives:

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

- Objectives during reporting period

- evaluation and validation of the ACGT environment architecture including taking care of the consistency of the architecture and providing guidelines for the services developers: we need to take care of the new services and scenarios that are developed in ACGT, and provide the guidelines for them to be compliant with the overall ACGT system.
- monitoring of standards development: it is ongoing work focused on the new achievements in the standard development, and trying to adopt the some work in that area for the ACGT infrastructure
- research on interoperability issues in a context of ACGT architecture design: we need to answer the question how flexible is the proposed architecture in the context of replacing particular components of whole layers; that is very important issue in the context of transferring the ACGT technologies (bio-medical oriented) to the other grid environment, or just using external resources for the ACGT users.

- Progress towards objectives

The first part of deliverable describing final architecture was prepared and submitted to BSCW server

- Main Activities & Tasks worked on

The main activity of the reporting period was concentrated on describing final ACGT architecture.

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

- Major Achievements towards planned objectives, identify main partners Involved
 All technical WPs were conducting their development according to architecture proposed
- <u>Deviations from the project work programme, and corrective actions taken/suggested</u>
 There were no serious deviations from the work programme.

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

There were no deliverables expected for the reporting period.

• <u>List of milestones, including due date and actual/foreseen achievement date</u> All planed milestones were accomplished.

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Workpackage 4 – Biomedical Grid Technology Layer

- Partner Responsible : PSNC
- Contributing partner(s): FORTH, UMA, FHG, BIOVISTA, Custodix, ICSS, SIVECO
- Reporting Period: 01/02/2009 31/07/2009

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

-The Workpackage has the following major objectives:

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

- Objectives during reporting period

- grid infrastructure maintenance: we need to take care of the grid services deployed in the ACGT environment; we will manage all required updates and try to add new machines to the testbed
- New test cases for grid/services monitoring portal: there are new services and scenarios developed in ACGT, so it will be necessary to provide testing procedure for it, and incorporate it to the existing testing framework of ACGT.
- Support in installation and configuration of Grid services: we will help to use existing grid infrastructure for the new services developed within ACGT; we will also be able to support developers who are creating new services compliant with the ACGT infrastructure
- Support in accessing grid services from different clients Recipe sheet and visualization services integration: there are new scenarios exploiting grid infrastructure; we will be able to support coding of client part of the tools communicating with the grid.
- Support and implementation of VO management portlets: the portlet is required for the administrators of resources to be able to design security policy for their resources. The work will be done with cooperation with WP10, WP14 and will be part of the ACGT security infrastructure.
- Logging service deployment of distributed logging service for ACGT infrastructure: the distributed logging service is required to debug workflows that are run in ACGT environment.

- Progress towards objectives

There was significant progress in all planned areas, especially in development and deployment of global logging system

- Main Activities & Tasks worked on

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The main activity of WP4 was focused on development and deployment of logging service for the ACGT environment. The distributed logging service called Toth was successfully deployed in the ACGT testbed.

The other important activities of reporting period:

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

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

- Tuning and improvements of Grid Services

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

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

There were some significant improvements in GRMS to support Oncosimulator scenarios (WP8).

- Major Achievements towards planned objectives, identify main partners Involved
 All partners taking part in WP4 were involved in maintaining grid infrastructure on their resources
- <u>Deviations from the project work programme, and corrective actions taken/suggested</u>
 There were no serious deviations from the work programme
- <u>List of deliverables, including due date and actual/foreseen submission date</u>

There were no deliverables expected for the reporting period.

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

All planed milestones were accomplished.

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Workpackage 5 – Distributed Data Access and Applications

- Partner Responsible : PHILIPS
- Contributing partner(s): Philips, FHG-IBMT, UPM, LundU, USAAR, Uhok
- Reporting Period: 01/02/2009 31/07/2009

• Workpackage objectives and starting point of work at beginning of reporting period

-The Workpackage has the following major objectives:

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

- Objectives during reporting period

Implementation of the data access services (including literature sources and public databases)

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

Definition and evaluation of the neoBIG scenario

Guidelines and recommendations for database management systems to be integrated with the ACGT infrastructure

- Progress towards objectives

Extended the capabilities of the Data Access Services such that it can be specified when transferring results to the DMS, that already existing files should be overwritten.

Provided support with DAS and contributed to the integration work for the demonstration in Japan.

Requirements collection and analysis for the neoBIG data sharing scenario.

Started investigation into other technologies and tools related to the ACGT technologies and tools. Initiated the selection and evaluation of the caBIG tools relevant for the neoBIG scenario: caGRID, caIntegrator, caCORE, caTISSUE, caARRAY, Rembrandt project.

Elaborated guidelines and recommendations for integrating clinical data sources into the ACGT platform. We consider two aspects. First review available Open Source database solutions for storing the different types of clinical trial data after anonymisation. Next describe how this data can be made accessible inside the ACGT platform by way of the data access services. Detailed instructions are provided for each data access service. We also discuss our experiences so far, illustrate what is possible but also describe the open issues.

Further development of Obtima:

- Importing of the clinical trial for Nephroblastoma cancer (SIOP) in Obtima
- Integration of OGSA DAI services for accessing the Obtima database

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- Advanced Ontology viewer
- Advanced CRF creator
- Initial Web Service for the integration of the Trial Outline Builder (developed by

U. Hokkaido) with Obtima

- Web Service for communication with ACGT submission system for maintenance of the ACGT Master Ontology (developed by FORTH)
- Initial implementation for Audit trial functionality
- Initial implementation for validation of CRFs
- Reviewing and updating of the Obtima database scheme
- Assigning of CRF categories to CRFs

Development of specifications and User documentation:

- Contribution to the development of the specification for demonstration of Obtima on the Review (April 22- 24th 2009, Homburg)
- Contribution to the specification of scenarios for the first integrated demonstrator of the ACGT platform
- Development of initial specification for usability test
- Development of the initial User manual documentation
- Further specification of Web Service for the integration of the Trial Outline Builder with Obtima
- Contribution to the further specification of the role based secure access for Obtima resources (CRF categorisation, Informed consent)

Demonstration of ObTiMA:

- April 22nd-24th 2009 Review (Homburg)
- June 25th-26th 2009 Demonstration of ObTiMA on the consortium meeting in Oxford by executing of usability tests (evaluation session)
- July 24th 2009, Buffalo NY, USA demonstration of Obtima on the International conference on Biomedical Ontologies (by M. Brochhausen)

- Main Activities & Tasks worked on

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

Definition and evaluation of the neoBIG scenario

Guidelines and recommendations for database management systems to be integrated with the ACGT infrastructure

- Major Achievements towards planned objectives, identify main partners Involved Further development of Obtima (FHG)

Requirements collection and analysis for the neoBIG scenario (Philips, IJB)

Elaboration of guidelines and recommendations for database management systems to be integrated with the ACGT infrastructure (Philips)

Contribution to the demonstrators for the annual review (all)

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

No deviation to report for the reporting period

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- List of deliverables, including due date and actual/foreseen submission date
 - D5.6 Requirements analysis and consolidation of the neoBIG scenario (month 42 / month 46)
 - D5.7 Guidelines and recommendations for open source database management systems to be used with the ACGT integration platform (month 44/ month 44)
- List of milestones, including due date and actual/foreseen achievement date

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Workpackage 6 – Data Mining and Knowledge Discovery Tools

- Partner Responsible : FHG
- Contributing partner(s): UMA, SIB, INRIA, UOXF, EIO, UvA
- Reporting Period: 01/02/2009 31/07/2009

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

-The Workpackage has the following major objectives:

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

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

- Objectives during reporting period

- Implementation if integrated demonstrators in collaboration with WPs 4,5,7 & 9
- Progress towards implementation of intelligent support for knowledge discovery using rich meta data

- Progress towards objectives

- Implementation of end-to-end demonstrator
- Definition of metadata scenarios and necessary metadata elements

- Main Activities & Tasks worked on

- Scenario definition for metadata usage
- Implementation, refinement, and testing of knowledge discovery services,
- Development of increasingly complex scenarios to demonstrate the usability of end-to-end knowledge discovery in ACGT
- Optimization of the visualization capabilities and user interfaces of the ACGT platform

- Major Achievements towards planned objectives, identify main partners Involved

METADATA

- UMA: Development metadata repository as secure web-services (supports credential
 access). This activity is also reported in WP11, but the changes involved an almost complete
 re-write of the code due to web service architecture requirements and therefore consumed
 significant development effort. The metadata repository is mainly used in WP6 and therefore
 we report this task also there.
- FORTH: Participation on the discussions about the file related metadata and the different approaches for supporting them.
- FHG: discussion about file-related metadata and provenance information.
- FHG: Requirements analysis for recommender engine for workflows, services, and data, based on machine learning approaches.

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• FHG: Investigations of state of the art in machine learning techniques for recommender engine, in particular community-based approaches and similarity-based approaches

IMPLEMENTATION AND TESTING OF SERVICES

- UMA: Extension of the modular programmatic framework (mAPI) to provide support for secure metadata repository. This enhancement increases interoperability between ACGT secure services and external Web-services in protected way.
- UMA: Finalized development and integration of generic web-service for command-line applications with ACGT security (GAS), data storage (DMS) and job submission and control (GRMS). This web-service will be used to provide functionality from UMA applications (Engene and Prep).
- BIOVISTA: development work on combinatorial literature search and client additions
- BIOVISTA: rewrote the bibliography search
- BIOVISTA: proper error handling was implemented
- SIB: GridR testing (in the context of global testing)
- FHG: GridR testing and debugging
- UMA: Support for mediator queries over Command-line services (UMA).

SCENARIOS AND DEMONSTRATION

- UMA: Initial development of workflow scenario for two-color gene-expression data (based on a mini-scenario developed by SIB and UMA). This includes using pre-processing and normalization tools from Engene and Prep+07 as web-services.
- FHG: Demonstrator setup and testing
- FORTH: Implementation of various services for the realization of the Pathway scenario, demonstrated in the project review at Homburg.

VISUALISATION AND USER INTERFACES

- UvA: expanded the availability of the visualization services for use by several partners within the scope of the OncoRecipesheet Interface.
- UvA: created two software packages for the interactive visualization of large graphs/networks for an in-house developed direct-touch interactive graphics device, the UvA Multi-Touch Table.
- UHOK: collaboration with UvA on the design and control of visualisation services, in connection to the OncoSimulator.
- FHG: Optimization of the GridR user interface following feedback from end-user validation and usability testing.
- Deviations from the project work programme, and corrective actions taken/suggested

None

- List of deliverables, including due date and actual/foreseen submission date
 - D6.6 Interoperability of ACGT knowledge discovery services with existing bioinformatics tools (T0+48)
 - D6.7 Prototype and report of the final the ACGT analysis environment (To+50)
- <u>List of milestones, including due date and actual/foreseen achievement date</u>

 The integrated ACGT analysis environment (month 50), part of major project milestone M12

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Workpackage 7 – Ontologies and Semantic Mediation Tools

- Partner Responsible: UPM
- <u>Contributing partner(s):</u> FORTH, FHG, PHILIPS, OXFORD, BIOVISTA, USAAR, IFOMIS, UPM
- Reporting Period: 01/02/2009 31/07/2009
- Workpackage objectives and starting point of work at beginning of reporting period

-The Workpackage has the following major objectives:

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

To develop a semantic mediation layer that integrates distributed and heterogeneous biomedical databases. This mediator is supported by the ACGT Master Ontology, which provides the necessary semantic background by modelling the domain.

To fully exploit powerful languages, such as OWL, in order to provide mediation services across a wide range of information sources, resulting in the implementation of the ACGT semantic mediation tools and services.

The core of the ACGT platform is formed by the semantic mediation layer. This is composed of several mediation services, and supported by the ACGT Master Ontology. The services will be provided to a number of tools developed inside the ACGT project, as well as endusers, who will get access to a query system that integrates a great number of biomedical sources concerning clinical trials on cancer

To, ultimately, develop the mediation technologies required for achieving a vertical integration among many different levels of granularity (molecular, cellular, tissue, organ, individual and population)

- Objectives during reporting period:

To provide friendly access to the mediation service to both end users and client layers within the ACGT platform

To document describing the main methods, techniques and procedures for the semantic integration of clinic-genomic data developed during the complete project.

- Progress towards objectives

- Main Activities & Tasks worked on:

Maintenance and extension of the ACGT Master Ontology (MO)

Development of the following tools and systems:

- Ontology submission system
- Query tool interface
- Mediator features

Major Achievements towards planned objectives, identify main partners Involved

Review of the ontology, both in terms of entries and in terms of constructions, and making of suggestions for its real use in clinical trial units in the UK. (OXFORD)

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Integration of ObTiMA into ACGT environment using the ACGT Mediator Query Tool via OGSA DAI services (FhG-IBMT)

Developing tools to automatically create ontology mapping files during setting up a trial for the mediator (FhG-IBMT)

Automatically uploading of the ontology mapping files to the ACGT Mediator (FhG-IBMT)

Testing of ObTiMA's CRF creator/ checking coverage of the ACGT MO (IFOMIS)

Review and optimization of the ACGT MO (IFOMIS)

Validation of conceptual design by means of terminology techniques (IFOMIS)

Networking with the OBO Foundry/ Working on textual definitions for the MO (IFOMIS)

Networking with Theseus Medico (IFOMIS)

The 'show pub trends viewer' for a selected node (BIOVISTA)

Advanced search i.e. the ability to search nodes not only in their title but also include other properties of the nodes (BIOVISTA)

Work on Submission Tool (FORTH):

- Add new Master Ontology Version functionality
- View changes between two MO versions
- View Class/Relation History
- New submission web service through Obtima
- Manual/Help Functionality

Work on the Semantic Mediation tools (UPM):

- Integration of the Query Tool in the ACGT Portal
- Implementation of a security layer for accessing the Semantic Mediator
- Design and development of an ArrayExpress wrapper for the multi-level data integration experiment.
- Deviations from the project work programme, and corrective actions taken/suggested

No deviation to be reported

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

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Workpackage 8 – Technologies and Tools for In Silico Oncology

- Partner Responsible : ICCS
- <u>Contributing partner(s)</u>: FORTH, INRIA, UvA, IJB, FHG, ICCS, UdS, UHok, IEO, UOXF (informal contributor)
- Reporting Period: 01/02/2009 31/07/2009
- Workpackage objectives and starting point of work at beginning of reporting period

-The Workpackage has the following major objectives:

The objective of this WP is to develop the "Oncosimulator", a technologically advanced and user friendly system able to spatiotemporally simulate within well defined reliability limits tumour growth and tumour and normal tissue response to chemotherapy for the cases of breast cancer and nephroblastoma in the patient's individualized context.

- Objectives during reporting period:

- i) Numerical study of the simulation models' behaviour.
- ii) Provision of an advanced integrated version of the simulation and the technological modules constituting the Oncosimulator.
- iii) Use of further real inhomogeneous medical data in order to adapt, optimize and validate the Oncosimulator (simulation and technological modules).
- iv) Integration of the "Oncosimulator" service into the entire ACGT platform.

- Progress towards objectives:

- i) A rather thorough numerical analysis of the parametric subspaces corresponding to the tumour types and chemotherapy schedules considered has been performed.
- ii) An advanced version of the simulation and technological module(s) has been produced and demonstrated during the annual April 2009 review in Homburg, Germany.
- iii) Refined analysis and utilization of 8 sets of multiscale data concerning nephroblastoma and 27 sets of breast cancer multiscale data.
- iv) An exploratory discussion of the overall ACGT platform level integration issue took place at the University of Oxford during the June ACGT plenary meeting.

- Main Activities & Tasks worked on

T8.1 Completion of the numerical study of the simulation models behaviour

i. A thorough study of the convergence of the algorithms and codes concerning both Wilms tumour and breast cancer.

The study has been successfully completed.

ii. A comprehensive study of the stability/sensitivity of the algorithms and codes concerning both Wilms tumour and breast cancer with respect to several critical parameters.

An extensive stability and sensitivity study has been implemented.

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- T8.2 Provision of an advanced integrated version of the simulation and the technological modules constituting the Oncosimulator
- i. Optimization of the simulation codes and their execution. Consideration of normal tissue treatment complication limits
- ii. Several optimization aspects have been dealt with.
- iii. Internal parallelization of the simulation code in order to considerably lower the execution time needed.

A parallelization version has been produced for the nephroblastoma code.

iv. Automation of the execution of different instances of the simulation code on a cluster via a portal

Improvements on an earlier version of the submission code have been implemented.

v. Automation of the execution of different instances of the code on grid architectures via a portal

Improvements on an earlier version of the submission code have been implemented.

vi. Interactive visualization of the tumour before, during and after the application of a therapeutic scheme/schedule [both real and simulated]

Adaptation of visualization techniques to the actual data and the improved versions of the simulation module have been achieved.

vii. Execution and parametric exploration of the simulation code through the development of subjunctive interfaces

An advanced version of the OncoRecipeSheet module has been produced and tested for numerous combinations of model parameter values. Further optimization work is in progress.

UHok in tight collaboration with ICCS coordinated cross-site integration and testing of OncoSimulator processing and interface components, including preparation for demonstration at annual review. OncoRecipeSheet interface distribution, bug fixes and enhancements have been performed.

T8.3 Use of further real inhomogeneous medical data in order to adapt, optimize and validate the Oncosimulator (simulation and technological modules)

This task is being implemented in tight collaboration with WP12. (Pseudo)Anonymized real medical data [clinical, imaging, histopathological, molecular and actual treatment data] are being collected and used in order to adapt, optimize and validate the Oncosimulator.

T8.4 Integration of the "Oncosimulator" service into the entire ACGT platform

The process of the Oncosimulator's integration into the overall ACGT platform is in progress. It is envisioned that by the end of ACGT's lifetime the Oncosimulator will be accessible and through and run on the overall ACGT infrastructure.

- Major Achievements towards planned objectives, identify main partners involved

The major achievements towards planned objectives include the following (partners involved are given in parentheses):

- Achievement of an advanced integration level of the various simulation and technological modules of the Oncosimulator (ICCS, UHok, UdS, UvA, IJB, INRIA, FHG, FORTH, IEO).
- Exploitation of sets of real multiscale medical data for the adaptation and optimization of the Oncosimulator. Initial predictive trends have been identified (ICCS, UdS, IJB, UvA, FHG).
- <u>Deviations from the project work programme, and corrective actions taken/suggested</u>
 No major deviations have been identified.
- <u>List of deliverables, including due date and actual/foreseen submission date</u> None in the reporting period

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

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Workpackage 9 – The Integrated ACGT Environment

- Partner Responsible : FORTH
- <u>Contributing partner(s)</u>: UvA, Philips, IJB, SIB, LundU, UMA, UPM, FHG, BIOVISTA, UoC, PSNC, Custodix, ICCS, UHok
- Reporting Period: 01/02/2009 31/07/2009
- Workpackage objectives and starting point of work at beginning of reporting period

-The Workpackage has the following major objectives:

- To demonstrate large scale system integration within the ACGT environment
- To implement the workflow layer for achieving composability of applications and services
- To investigate the evolution of the ACGT integrated platform proposing enhancements to all levels with respect to functionality and performance

- Objectives during reporting period

During this reporting period the objectives included the prototyping of the infrastructure with the non-ACGT ("third-party") tools and services and the provision of more intelligent user guidance in the workflow environment

- Progress towards objectives

The work has been progressed according to the objectives. The generic framework defined in the workflow environment for supporting the Grid security was used for the integration with the Biomoby third party service registries. Additionally we have worked for the better integration and stability of the environment and the better exploitation of the service related metadata in the workflow composition process.

Main Activities & Tasks worked on

- Initiate the work on third party service integration in order to extend the coverage of the bioinformatics tools available in the ACGT platform
- Design and experiment on possible ways to provide a more "intelligent" workflow environment
- Improve the stability and performance of the ACGT Workflow Environment
- Resolve technical integration issues
- Prepare and submit the Deliverable 9.4 "Semantic Integration in ACGT"
- Major Achievements towards planned objectives, identify main partners Involved

Main tasks carried out by FORTH:

- Development on the ACGT Workflow Editor
- Implementation of generic proxy services for Biomoby services
- Incorporation of the Biomoby data type ontology matching in the workflow editor
- Organize the discussions about the "semantic interoperability of services" in ACGT and the work with respect to the metadata descriptions.

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- Improve the performance of the credential delegation process by employing a main memory based repository for the proxy credentials.
- Development on the Proxy Services framework for making possible the secure, authenticated, and authorized invocation of Grid ACGT Services from within BPEL Workflow Enactors.
- Integration of the Semantic Mediator and the Dynamic Data Access Services (DAS) in the workflow environment by implementing the corresponding proxy services.
- Implementation of the "Query as Service" concept in the workflow Editor so that semantic queries of the Mediator can be shared among users and workflows.
- Preparation of Deliverable 9.4
- Perform the usual responsibilities implied by the leading of a WP such as the preparation of the necessary paper work.

Main tasks carried out by SIB:

Workflow environment testing

Main tasks carried out by UMA

- Support in repository for specification of mime types for tool (services/workflow) parameters.
 A mime type specifies the format of the input/output.
- Embedding intelligence into the ACGT WF and service environment by developing of Magallanes, a Web-Service interface to be used as automatic / intelligent workflow composition tool that can be used from the workflow editor. This software is also provided as desktop and web clients with the following features:
- DataType, Tool and Functional Category Search for service and datatype discovering in a google-like style.
- Automatic workflow composition and basic visualization and by-hand pruning tool.
- Use of feedback for statistics purposes.
- Development of worker for jORCA, standalone client, to execute command line services in ACGT environment.
- Development of a bioinformatics data standardization formatter aimed to facilitate data standardization by using configurable XPath rules and regular expressions enabling the automatic identification of data types and performing the appropriated transformations. As a plug-ins based system, it can be used to develop specialized clients and friendly data editors, covering an important aspect of service interoperability; with direct application to service integration.

Main tasks carried out by UPM

Work on resolving issues to integrate the mediator and the query tool in the ACGT platform

Main tasks carried out by BIOVISTA:

- Work on further integration with the workflow manager
- Update content in the ACGT wiki
- Work on the integration with ACGT monitoring service
- Deviations from the project work programme, and corrective actions taken/suggested

None in the reporting period

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

Deliverable 9.4 was prepared and made available for submission to the EC on April 2008

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

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Workpackage 10 - Ethics, Legal and QA issues

- Partner Responsible: LUH
- Contributing partner(s): LUH, Custodix, UH, USAAR, IJB, UOXF, FUNDP
- Reporting Period: 01/02/2009 31/07/2009
- Workpackage objectives and starting point of work at beginning of reporting period
 - -The Workpackage has the following major objectives:

- Objectives during reporting period

- 1. Analysis of intellectual property rights concerning the data, the genetic material and the scientific outcome
- 2. Analysis of the intellectual property issues concerning computer software and licensing
- 3. Analysis of the GRID infrastructure and its legal implications, especially concerning intellectual property rights
- 4. Risk analysis regarding the data security
- 5. Risk analysis regarding data protection
- Negotiation of contracts between partners exchanging data via the ACGT network and the consortium.
- 7. Survey on patients' perspectives and needs regarding informed consent and data protection

- Progress towards objectives

- 1. The analysis of legal requirements concerning data, genetic material and scientific outcome and their implications has been completed.
- 2. The analysis of licenses used/to be used in ACGT and their legal requirements and implications has been completed.
- 3. The analysis of the GRID-infrastructure and its legal implications has been completed.
- 4. Risk analysis concerning the data security and data protection framework is in progress.
- 5. The negotiation of contracts between partners and ACGT is in progress.
- 6. The survey on patients' perspectives and needs regarding informed consent and data protection is in progress.
- 7. Writing on the consent in matter of research;
- 8. In depth analysis on the current legal situation to know if the data protection framework drawn in the D10.2 is reached?

- Main Activities & Tasks worked on

- In depth analysis of the intellectual property issues in ACGT (LUH)
- In depth analysis of legal risks regarding the data security and data protection framework is in progress (Custodix and LUH)

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- Meetings with ACGT-partners (especially with WP11) took place/are planned for the analysis of risks regarding the data security and data protection framework is in progress (Custodix, FUNDP, LUH)
- Discussions on the contracts to be signed by participants exchanging data via the ACGT network (FUNDP, Custodix, LUH, IJB, UOXF)
- WP10/11 meeting took place.
- Meeting of the non profit organization CDP took place.
- The survey on breast cancer patients was accepted by the local ethics committee of Hamburg on 15 May 2009 (UH)
- The survey on patients affected by breast cancer was submitted to the institutional review board of Oxford University Hospital (UH).
- The data collection in collaboration with the German Cancer Registry ended in July successfully with a return rate of about 50% (UH).
- During the reporting period input was given regarding quality assurance and actual international guidelines. USAAR participated in the Satellite WP 10 meeting during the Consortium meeting in Oxford. The Deliverables during the reporting period were reviewed internally (USAAR).
- IJB carried out the translation of the patient questionnaire in French and Dutch. IJB further had many internal meetings to review the questionnaires, to identify the patients we would submit the questionnaire to and to talk with them. By the end of July, IJB had the filled questionnaires for 42 patients and IJB continues the work to hopefully reach the 100 filled questionnaires by the beginning of October.
- Patient questionnaire study: plan and application to ethical committee, we are answering their points and re-applying (UOXF)
- Contracts: evaluated and provided comments and corrections needed for Oxford signature, this is under review by legal department (UOXF)
- MCMP dataset preparation for sharing: anonymisation, provided consent Forms (UOXF)
- FUND Crid organized a European Summer University from 06th to 8th of July 2009 in Namur with an attendance of about 90 persons)
- Major Achievements towards planned objectives, identify main partners Involved
- Presentation of ACGT during several meetings with experts in the field and professional exchange (Tilburg, Berlin,) (LUH).
- Analysis of legislation and literature regarding the analysis of the intellectual property issues in ACGT (LUH).
- Analysis of legislation and literature regarding the analysis of legal risks regarding the data security and data protection framework is in progress (LUH).
- Cooperation with WP11 regarding the analysis concerning the data security and data protection framework (LUH, CUSTODIX).
- Deviations from the project work programme, and corrective actions taken/suggested
 - None
- List of deliverables, including due date and actual/foreseen submission date
 - D10.6.2 Results of the international and national empirical survey on patients' and parents of minor patients' perspectives and needs T0+51 (UH) is in progress
 - D10.7 Analysis of the most important Intellectual Property issues resulting from the chosen ACGT architecture (submitted as foreseen in month 40)

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- D10.8 Risk analysis concerning the data security and data protection framework (due/foreseen month 49) is in progress
- List of milestones, including due date and actual/foreseen achievement date
 - MWP10.3 Analysis of the most important Intellectual Property issues (achieved as foreseen in month 40)
 - MWP10.4 Risk analysis concerning the data security and data protection framework (due/foreseen month 49)

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Workpackage 11 – Trust and Security

- Partner Responsible : CUSTODIX
- Contributing partner(s): IJB, UMA, UPM, Fraunhofer, LUH, PSNC, Custodix, FUNDP, UH
- Reporting Period: 01/02/2009 31/07/2009
- Workpackage objectives and starting point of work at beginning of reporting period

-The Workpackage has the following major objectives:

The main objective of WP11 is to create a working environment in which sensitive patient data processing for research is compliant with the relevant regulations "by default". Using provided documentation and guidelines the developers can create services that will live up to the data protection expectations. Additionally the task of monitoring ACGT security and privacy requirements remains important and are revisited and evolved based on feedback acquired during the project.

- Objectives during reporting period

In this final stage of the project evaluation and monitoring of services has come more to the foreground. Improved usability of the (security) tools and management of security will enable end users and administrators to use the ACGT infrastructure safely and effectively.

- Progress towards objectives

- => A new version (1.17) of GAS has been developed and deployed in the ACGT infrastructure. This new version adds advanced functionality such as wildcards for resources.
- => D11.5: Requirements and guidelines for developing secured ACGT services has been adapted to take into account the comments from the internal review.
- => A draft for D11.4: Finalized ACGT security architecture (Merged with D3.3: The ACGT technical architecture: Final Specifications) has been shared with WP3 for initial consolidation.
- => Work on D11.6: ACGT guide with administrative documentation of ACGT security and VO management has been started.
- => CAT has been evaluated further by actively using the tool in de-identification of ACGT patient data.
- => Continuous support has been given to partners for further integration of new services in ACGT and troubleshooting bugs.
- => In cooperation with WP5 support is provided for dynamic data access services integrated in the security framework.
- => A 2nd evaluation session of the ACGT infrastructure, including the registration process and login has been performed during the consortium meeting in Oxford. The findings of the evaluation session have been used to improve the usability of the registration process and login process.
- => First steps towards centralised logging have been taken and discussed during the Technical Management Committee meetings.
- => During the HealthGrid conference ACGT has been represented in an expert panel for the RADICAL project.
- => Continuous integration sessions through Skype provide a constant source for feedback and allow quick action when problems are encountered.

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- => Development and release of new registration and delegation applets with added functionality. It is now possible to select an identity out of a list, store credentials on portable devices and log in automatically at successful delegation.
- => Further specification and development the role based secure access to ObTiMA and user roles and rights management (together with FORTH): CRF categorisation, Informed consent
- => Supporting of secure OGSA DAI services for ObTiMA
- => Discussions about the specification of integrating CAT with Obtima in the Technical Parallel Session of the Consortium Meeting (Oxford, June 2009)
- Main Activities & Tasks worked on
- Major Achievements towards planned objectives, identify main partners
 Involved
- Deviations from the project work programme, and corrective actions taken/suggested

No deviations from the work programme for this reporting period and no corrective actions required

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

No deliverables are foreseen for this reporting period.

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

M9: The final ACGT architecture (M36)

M12: Integrated demonstration of the ACGT architecture and technologies. (M38)

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Workpackage 12 - Clinical Trials

- Partner Responsible : IJB FORTH IMBB
- <u>Contributing partner(s)</u>: UHANN, UH, USAAR, Biovista, EIO, UOXF, UoC, SIB, Custodix, FUNDP.
- Reporting Period: 01/02/2009 31/07/2009
- Workpackage objectives and starting point of work at beginning of reporting period

-The Workpackage has the following major objectives:

- Implement the ACGT post-genomic clinical trials collecting multilevel clinical information for the validation of the ACGT infrastructure.
- Identify and address the various harmonization issues related to cross-platform and multicentric post-genomic data collection.
- Implement various advanced post-genomic analyses including expression profiling, genotyping, proteome and metabolome profiling methodologies.
- Promote post-genomic medicine according to the ethical, regulatory and technical requirements.
 - Objectives during reporting period

- Progress towards objectives

- (a) Two clinical trials were previously selected as the ACGT clinical trials:
- 1. The TOP trial: This multi-centric trial, which is coordinated by IJB, investigates preoperative chemotherapy treatment and responses in order to identify indicative
 individualized patients' profiles. The accrual of this trial has been closed in August 2008.
 Gene expression analyses have been carried out on the 121 with available gene
 expression profiles which led to the identification of a gene expression signature which
 was associated with response to epirubicin. This signature was also validated in two
 independent datasets. These results were presented at large international conferences
 (cfr WP15). The re-consent procedure is still ongoing and 45 patients have reconsented up to now. This trial is also contributing data for the oncosimulator on an
 ongoing basis.
- 2. The SIOP trial: The Nephroblastoma study and trial protocol 2001 started accrual in June 2001 and is coordinated by USAAR. In 2006 the first patient did enter the ACGT Nephroblastoma trial after approval of an amendment of the SIOP 2001/GPOH trial by the ethical committee (Landesärztekammer des Saarlandes). During the reporting period, the enrolment of patients into the SIOP nephroblastoma trial and the antigen scenario trial was ongoing. 13 antigens are characterised and the results from laboratory findings undergo statistical analysis at the moment. Lot of work was spent for the contribution of clinical and imaging data from this SIOP trial for the oncosimulator (for more details see WP 8).

Additionally, IEO carried out the clinical part (and the preliminary electronic duties) of the Trenett study, and started collecting and pre-validating the data.

The clinical partners are also continuously interacting with the other WPs to answer all the questions they may have regarding these trials.

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- (b) The Multi-centric multi-platform scenario: Clinical partners in ACGT own a unique data set of gene expression, namely RNA extracts from biopsies of 73 patients have been hybridized each on two different microarray platforms (Illumina and Affymetrix). This data set is called Multi-Centric Multi-Platform (MCMP). A signal scaling method developed in the context of this project (quantile-scaling) showed that signal from different technological platforms can be combined when a suitable signal preprocessing step is applied. A classical cross-validation procedure showed that biologically consistent gene-expression signatures can be derived from the mixture of raw signal issued from different platform without requiring complex meta-analytical approaches. This work was conducted jointly by SIB, UOXF and IJB.
- (c) <u>Identification of scenarios for testing</u>: In order to validate the ACGT data-mining environment, simple yet clinically realistic scenarios have to be identified for as actual implementation. Taking into account the IT development requirements (most importantly that anonymization cannot be formally guaranteed while the infrastructure is in development), a previously published dataset from the Transbig clinical trial has been recast into an "ACGT clinical trial". The scenario is adapted to the current stage of development of the platform (namely requiring only simple (simulated) CRFs, a subset of the MO, and the use of the core data-mining tools). Preliminary work on the actual ACGT trial SIOP has also been conducted, but has been suspended at the end of the reporting period. ACGT-based data-mining on this trial will be resumed once the security of the ACGT data-mining environment will have been thoroughly tested. This activity was conducted jointly between SIB, IJB and USaar.
- (d) Different initiatives have been taken to <u>promote post-genomic studies conducted in the context</u> <u>of ACGT</u> as well as to get feed-back from the clinical community:
- 1/ ACGT pursued the collaboration with the Breast International Group (BIG) to investigate whether ACGT could help with data-sharing issues linked with their new research program (collaboration with WP5).
- 2/ During the Consortium meeting in Oxford the first usability sessions for the creation of post-genomic clinical trials using the ObTiMA system developed in ACGT were performed and use scenarios were produced. The system and the creation of the trials was tested by trial creators from the team of Marian Taylor/ University hospital of Oxford. A second meeting for the set up of post genomic clinical trials involving all three groups of end-users will take place during the next period.
- 3/ The collaboration with the European Organization for Research and Treatment of Cancer (EORTC) is ongoing through a subcontract with IJB.
 - Main Activities & Tasks worked on (see above)
 - Major Achievements towards planned objectives, identify main partners Involved
- Deviations from the project work programme, and corrective actions taken/suggested
 None
- List of deliverables, including due date and actual/foreseen submission date
 No deliverable was planned during this period.
- <u>List of milestones, including due date and actual/foreseen achievement date</u>
 No milestones were foreseen during the reporting period

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Workpackage 13 – Evaluation & Validation

- Partner Responsible : SIB
- <u>Contributing partner(s)</u>: SIB, FhG, FORTH, Philips, Siveco, UPM, UMA, LundU, UvA, INRIA, IJB, Biovista, PSNC, Custodix, ICCS, UHok, USaar, UOXF
- Reporting Period: 01/02/2009 31/07/2009
- Workpackage objectives and starting point of work at beginning of reporting period

-The Workpackage has the following major objectives:

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

- Formulate evaluation criteria, verification procedures and feedback report guidelines
- Coordinate local validation activities and feedback reports
- Coordinate formal usability evaluation of the ACGT platform

- Objectives during reporting period

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

- Definition of a consistent set of scenarios for the review, illustrating the progress of the development of the ACGT environment
- Conduct regular testing of the platform on the basis of the scenarios designed for earlier reviews.
- Conduct first evaluation activities: specially regarding the Master Ontology, the legal and security framework (EORTC), and the data-mining environment.

- Progress towards objectives

The ACGT Master Ontology is constantly reviewed with respect to usability (by the ACGT services, e.g. the mediator and ObTiMA) and completeness. The clinical partners are constantly asked to hand in reviews on the coherence and correctness of the representation of clinical reality. In addition an assessment of the adequacy of the Master Ontology to the OBO-foundry acceptation rules has been conducted. This activity is coordinated by USaar.

USaar is conducting a continuous internal review, evaluation and validation of ObTiMA (and other tools and software), working extensively with WP13 usability engineer.

Clinical and technical partners of the project took an active part in the Oxford evaluation session coordinated by SIB and FhG, 25th -26th of June 2009. Evaluators external to the ACGT project (biostatisticians at UOXF) were involved in the session. The recordings of Oxford evaluation sessions are under evaluation by the usability engineer and the global outcome of the sessions will be documented in the next period (Deliverables D13.2b). The most important findings of the sessions have been conveyed internally to the development teams.

A scenario based on previously used data sets has been defined for the ACGT workshop in Japan. The implementation of the scenario will be the guiding thread towards a fully integrated demonstrator involving ObTiMA and the data mining tools.

As reported in the previous period, Skype-based debugging sessions regrouping developers of the platform across Europe took place on a regular basis, enabling a coordinated effort to solve technical issues. This continuous integrated-testing effort will be reconducted in the next periods.

The University of Amsterdam has gathered performance data from the use of their visualization services by the OncoRecipesheet, developed in WP8. Based on this data,

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several criteria have been updated to increase the quality, performance and availability of the visualization services.

FORTH has installed and maintains the Request Tracker, a tool to ensure the proper followup of development issues.

Discussions took place during the Oxford meeting to consider strategies for the final integration of the ACGT tools, including in particular the OncoSimulator (all Technical partners).

- Main Activities & Tasks worked on

See above

- Major Achievements towards planned objectives, identify main partners Involved

A new user evaluation session has been organized during the reporting period. The session took place as a parallel session of the consortium meeting in Oxford, in June 2009. Non-ACGT members of the Oxford clinical community were assessing the usability of the ACGT datamining platform. FhG and SIB were coordinating the evaluation session, while the ACGT TMC members were providing in-room or remote support.

The legal and security framework of the ACGT environment was found globally in-line with current state-of-the-art practices in clinical data management by EORTC. Minor improvements to related deliverables were suggested. The difficulty to deal with the antinomy between availability of genomic data for research and the need to ensure patient privacy was recognized, as well as the importance to provide proper training to end users of such a complex environment. Yet the global strategic choices made in the project sound appropriate. The results from the evaluation session in Vienna were used to improve the usability of the security services (e.g. an evaluation of the registration and login mechanism has been performed). This included the evaluation and comparison with solutions adopted in other similar EU projects. (Custodix)

The usability of ACGT tools by end-users was assessed continuously, by technical partners and bioinformaticians for the data-mining environment (SIB, FhG, UOxf, FORTH, UMA, UPM, Philips, and Siveco) and by clinicians for ObTiMA (USaar).

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

The actions occurring in WP13 depend largely on the developments that take place in other WPs (notably technical WPs). Progress is in-line with the rest of the project.

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

D13.2 First evaluation report - Due: Month 30, July 2008

This deliverable was pending due to the lack of a full user-grade demonstration infrastructure. The deliverable has now been split in two parts D13.2a and D13.2b which will be delivered separately: The first part addresses the evaluation of the master ontology and of the legal and security framework of ACGT, while the context scenarios collected by FhG through user interviews form the bulk of this deliverable. These scenarios define the framework of enduser evaluation which result will be reported in Deliverable D13.2b. Delivery dates: D13.2a September 2009, D13.2b Spring 2010.

D13.4 Specifications of the April 2009 demonstrator

This deliverable was introduced to describe the various components of the April 2009 review demonstrator. It was submitted in April 2009. Main contributors were: SIB, FhG, FORTH, Philips, Siveco, UPM, UMA, IJB, Biovista, PSNC, Custodix, USaar, UOXF, ICCS, UHok.

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

An evaluation session using the fully integrated ACGT environment and based on the context scenarios collected earlier will take place during the next reporting period.

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Workpackage 14 – Training and Portal

- Partner Responsible: SIVECO
- Contributing partner(s): FORTH, SIB, UMA, FHG, BioVista, Custodix, HealthGrid,
- Reporting Period: 01/02/2009– 31/07/2009
- Workpackage objectives and starting point of work at beginning of reporting period

-The Workpackage has the following major objectives:

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

- Objectives during reporting period

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

- Progress towards objectives

- All the services that became available during the reporting period were integrated at the interface level (through portlets) into the ACGT Portal
- -Several training materials and Contextual help for all the existing portlets has been added in the ACGT Portal
- The ACGT Handbook has been started (as a Wiki site) to provide consortium and usercommunity reviewed content. The content will be used for other online and offline training materials supporting training sessions.

- Main Activities & Tasks worked on

T14.2 Final implementation of the ACGT Portal

This task continued the development of the ACGT Portal:

- Redesign of the front-end and the back-end from the needs for "evaluation and validation" point of view (SIVECO, SIB) in the ACGT Portal
- The registration process was simplified (Custodix, SIB, SIVECO)
- Improvement of the User Interface in both the public and private areas of the Portal (SIB, HealthGrid)
- Integration of Magallanes and Victoria search engine in Metadata Portlets (UMA)
- Development of the DMS Portlet (SIVECO) added direct download feature and integration with Metadata Portlets for searching services compatible with a given file

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- Development of the Data Access Portlet, a portlet that allows users to: create dynamic data sources to be used by the ACGT services and query the existing data sources using SPARQL(Phillips)
- Added contextual help to Metadata, DMS and Data Access portlets in order to facilitate their usage(SIVECO, UMA, SiB)
- Updating of the Metadata Registration Portlet (SIVECO)
- Development of the VO Management Portlet (PSNC, Custodix)
- Presentation of Literature Mining Services in the ACGT Portal (BioVista)

T14.3 Training modules for Clinical and Biological investigators and students

- Data Mining Tutorial for the demonstration in April 2009 (SIVECO)
- User training material for the ACGT Workflow Environment (FORTH), pending full videos next reporting period
- Setting up of WIKI for WP14 partners to prepare the Training Handbook; Maintenance of the ACGT Handbook http://handbook.eu-acqt.org/ (HealthGrid)
- Training of partners on the use of the WIKI
- Writing and coordination of the first iteration of the ACGT Handbook (SIB, FHG, Forth, SIVECO)
- Video training materials (Creating an Aminoacid Sequence object, Launching services, Launching GRID services with authentication) (UMA, SIVECO)
- Tutorial for Magallanes search and use; documentation material for the jORCA application (UMA)
- Initial user documentation User manual and Obtima Tutorial under internal review will be updated in the ACGT Handbook during the next reporting period (FHG)
- Final production (SIVECO) of deliverable D14.3 for resubmission.
- Research and review of training environment tools (SIVECO, HealthGrid)

T14.4 Organisation of Summer School and Scientific Workshops

Various formal training sessions, in conjunction with other "clinical" oriented events and conferences for end-users, and informal training sessions for ACGT members on security services.

- User guidance and training (Evaluation sessions in Oxford) (SIB, Custodix)
- Training to ACGT members on security services in ACGT (Custodix).
- Regular teleconferences with WP15 leader and other stakeholders
- Participation at workshop in the HealthGrid conference to define action plan for training WP (HealthGrid)
- Definition of training protocols until the end of the project including target groups and dates for training (HealthGrid)

T14.5 Production of an ACGT Educational Video

Representatives from CAID, the Centre of Applied Industrial Design - a non-profit organisation whose mission is training in on /offline multimedia research with the goal of promoting cultural and science communication - attended the ACGT meeting in Oxford, UK. The CAID representatives began an initial assessment of the communication needs of the project with the goal of developing a storyline for the education of citizens and clinicians and the need for and aspects of clinical trials. Their role in the meetings was one of consultancy, explaining the diverse factors to consider in the production of video to be used for training purposes.

Having understood some of the technical specificities of video production, as well as the interest in producing such educational material, the consortium has agreed that the activity of

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video production should be subcontracted to independent experts. FORTH, responsible for the subcontracting activity, must launch a call for tender in compliance with Greek national legislation. The specifications of the call have been detailed and the call will be launched in early November with an expected two-month delay before video production will be undertaken.

- Major Achievements towards planned objectives, identify main partners Involved The main achievement of this reporting period was the increased collaboration with other WPs and partners (SIB, HealthGrid, FORTH, UMA, FHG) for the user manuals, contextual help included in the ACGT portlets and the creation of the ACGT Handbook.

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

There were several deviations from the project work programme concerning the training workshops. The delay registered in previous reporting periods with these activities was determined by the need to wait for the ACGT services to reach a certain state of development, in which they are ready to be exposed and demonstrated to the ACGT users. Also, further delays come from the fact that there is a gap between the actual state of the ACGT services and the technical documentation available from other Work Packages due to continuous improvement of the services.

This gap will be covered in the next 6 months by focusing on filling the ACGT Handbook (created and maintained by HealthGrid, joint editorial effort SIVECO) The wiki content provides up-to-date, community reviewed content, for the training related activities. Several methods of producing training materials (online tutorial content and offline handouts) from the content in the ACGT Handbook are scheduled in the following 6 months, to support the training sessions.

The training materials will be more focused on the user needs revealed by the demonstration activities - such as detailed user-oriented tutorials for the Registration and Login processes.

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

D14.3 Demonstration and Report of training modules, due and submitted on Month 21, was initially rejected. Resubmitted March 2009 and accepted.

D14.4, D14.5, D14.7 – First and second Training workshop for end-users on ACGT Technologies & methodologies and for service providers on ACGT, due in Month 30, 36 and 42, marked as delayed in previous reporting period, foreseen submission date T0+48 D14.8 - The final ACGT portal, and online training modules development and evaluation report, delayed to T0+50

D14.9 – The ACGT Educational Video will be scheduled for delivery in T0+50.

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

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Workpackage 15 - Dissemination

Partner Responsible : HEALTHGRID

• Contributing partner(s): All partners

Reporting Period: 01/02/2009 – 31/07/2009

• Workpackage objectives and starting point of work at beginning of reporting period

-The Workpackage has the following major objectives:

- Objectives during reporting period

Produce quarterly Newsletters

Global maintenance of the website

Support to the project with production of dissemination material: Posters, Leaflets

Preparation of presentations in the HealthGrid conference in Berlin

Mainstreaming activities with WP16 exploitation

Preparation for the project review

Start planning for the ACGT conference

- Progress towards objectives

2 ACGT newsletters produced

Workshop held in Oxford during consortium meeting with WP16 on mainstreaming activities with WP15 partners

Preparation of the Japan's workshop

Preparation of the presentation at HealthGrid conference

Production of dissemination material for the partners going to attend conferences (leaflets)

Leaflet preparation for ACGT workshop in Japan in September

- Main Activities & Tasks worked on

Production and writing of the ACGT Newsletter Spring edition

Theme was on the ACGT production environment. The newsletter was sent to ACGT mailing lists. Partners used the newsletter to progress discussing with other organizations. The newsletter aim to reach communities proves a success

Production and writing of the ACGT Newsletter Summer edition

Newsletter sent to mailing list, additional persons and organizations were added (150 new)

Poster design and production:

<u>ACGT poster for the IMPAKT conference on Breast cancer:</u> 3 posters were created and presented at the IMPAKT conference

ACGT poster for Annual meeting of the American Society of Clinical Ontology (ASCO):

Participation to Vienna consortium meeting:

Presentation made on activities

Discussions about future events

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Discussions about the Japan workshop with Hokkaido

Participation to Oxford consortium meeting:

Presentation of the latest developments in dissemination

Workshop on organizing the event in Japan for mid September

Preparation of the legal and ethical article for the summer newsletter with WP leader

Edition of the ACGT website

Insertion of news, events, publications on website Insertion of new contents for the communities

Maintenance of the ACGT website

Update on major security updates

Tests for configuration and updates on website

Design on parts of website

Rationalisation of web pages after releases from web tools

Publications in scientific journals, specialized papers and press releases

Accepted: 14 in journals

Submitted (waiting for reply): 7 in journals

Publication in conferences: conference papers and proceedings

Presented: 12
Waiting for reply: 1

Presentations in conferences and workshops

13 presentations in conference and workshops, including not yet delivered speeches

Invitations from conferences are ongoing and papers/presentations will be presented in the next reporting period

Organization of the ACGT sponsoring for the HealthGrid conference in Berlin (29th June to 1st of July 2009) including dissemination material (poster)

Presentation of ACGT with the EU-AsiaGrid project during the APAN (Asian Pacific Advance Network 28th edition conference on healthgrids conference in Kuala Lumpur, 22nd July 2009: Distribution of 150 leaflets to the conference

Demonstrations at conferences and events

5 demonstrations made during the reporting period

Events and relevant articles/publications inserted on the website

All interesting events and articles have been inserted on the website, after approval from editorial board

Project review meeting in Germany

Presentation of all activities made during the reporting period

Discussions with reviewers on how best to address dissemination in the future

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- Major Achievements towards planned objectives, identify main partners Involved

Dissemination during workshops

Design of posters for the Impakt conference

Strong presence at HealthGrid conference with demonstrations and ACGT represented as a sponsor

Publication of 2 newsletters showing the progresses of work and impact from ACGT Publication of newsletter on e-health newsletter

<u>Deviations from the project work programme, and corrective actions taken/suggested</u>

No deviations from the work programme

submission for the review

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

D15-5 (revised dissemination report): re-submission for the review in Homburg D15-4 (Report on organisation of scientific events and participation in conferences):

All deliverables were presented to the reviewers and accepted

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

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Workpackage 16 – Market Investigation & Exploitation

- Partner Responsible : BIOVISTA
- Contributing partner(s): IJB, USAAR, CUSTODIX, FHG, FORTH
- Reporting Period: 01/02/2009 31/07/2009

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

-The Workpackage has the following major objectives:

For the remainder of the project WP16 aims to:

- 1. Pursue new specific collaborations with end user groups as an ongoing task
- 2. Prepare and organise the ACGT Competition

- Objectives during reporting period

During the reporting period the objective was to

- 1. Consolidate the EORTC and BIG collaborations, consider ACGT continuation
- 2. Begin work on the ACGT competition

- Progress towards objectives

- OBJ1: this is an ongoing activity. EORTC is now a fully integrated partner. ACGT has contributed to BIG 'user need analysis' for a new BIG research project
- OBJ2: in progress. Competition scheduled for early Q2 2010.

- Main Activities & Tasks worked on

Task 16.5 ACGT Collaborations

Task 16.6 The ACGT Competition

Major Achievements towards planned objectives, identify main partners Involved

- 1. ACGT pursued the collaboration with the Breast International Group (BIG) by contributing the user's need and requirements analysis for the development of the data-sharing platform that will be used for their new research program.
- 2. Regarding the sub-contract that was done with the EORTC, they delivered to ACGT a detailed analysis of the security architecture and made some important recommendations.
- 3. Draft versions of a number of introductory documents required for the competition have been prepared.
- 4. We have been contemplating the continuation of ACGT in order to address a major end user concern about its sustainability. STaRC (Study, Trial and Research Centre) is a proposal that was developed mainly by USAAR with an intention to exploit ACGT results. The structure of **STaRC** today is a CRO (Contract Research Organization) that can easily work together with other Organizations, Registries and external Centres. The STaRC initiative has already secured funding by the local government of the Saarland and the University of Saarland for 2 years. During that period a business plan will be put together to ensure the sustainability of STaRC.
- Deviations from the project work programme, and corrective actions taken/suggested

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No deviation from the planned activities has occurred with the exception of the preparation of the ACGT competition. The consortium is aware of the intended deadline and target period of the competition (early Q2 2010) and feels confident that the deadlines will be met. A major concern is the stability of the platform and the underlying technologies so as to enable third parties to easily take part in the competition. This has been one of the main objectives for the entire group of technology providing partners during the reporting period. The main effort on the preparation is planned for the fall of 2009 in time for a late 2009 - early 2010 public announcement of the competition

<u>List of deliverables, including due date and actual/foreseen submission date</u>

No deliverables were foreseen for the reporting period

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

No milestones foreseen for the reporting period

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Consortium Management

Project Meetings (including WP technical meetings)

Title	Place and Date	Main conclusions
TMC integration meeting	St. Augustin (Germany) 02- 03 April 2009	Preparation and final integration for demonstrators for ACGT review.
WP8: OncoSimulator integration workshop	UvA (Amsterdam), 15 – 21 April 2009	Focussed efforts achieved integration of the simulator, Grid services, visualisation services and front-end interface to support the subsequent review demonstration.
WP8 Technical Meeting	Amsterdam, 15-16. April 2009	Preparation of Oncosimulator demo for review
WP5: ObTiMA/TOB integration workshop	FhG IBMT (Sankt Ingbert), 15 –22 April 2009	Focussed efforts achieved integration of ObTiMA front-end and TOB facilities to support the subsequent review demonstration.
Oncosimulator integration meeting	Amsterdam, The Netherlands, 15-16 April 2009	Provision of an advanced integrated version of the Oncosimulator (simulation + technological modules).
Pre-review Meeting	Homburg, Germany, 20 – 22 April 2009	
WP8 annual April 2009 review preparatory meeting	Homburg, Germany, 21- 22 April 2009	Initial predictive trends of the Oncosimulator were identified based on real sets of multiscale medical data.
Review meeting	Homburg (Germany), 23- 24/04/2009	ACGT review
ACGT Tech. meeting	Oxford, 25-26 May 2009	ACGT video shootings on location, plan for competition and video production
WP8: OncoRecipeSheet hands-on session	Oxford, 24 June 2009	Some intended users of the OncoRecipeSheet installed the system on their PCs and made a guided exploration of its interface. This provided valuable feedback on aspects requiring stabilisation and/or enhancement.
WP8 meeting focused on the RecipeSheets	Oxford, UK, 24 June 2009	Addressing of several points related primarily to the RecipeSheets efficiency, including the parameter value combinations for which creation of a tumour is impossible. A number of possible extension scenarios of the Oncosimulator concerning the immune system response and anti-angiogenetic treatment have been proposed.
Consortium Meeting	Oxford, 25 – 26 June 2009	State of project, definition of future steps, parallel evaluation session by external health scientists
Plenary ACGT meeting with extensive WP8 conribution	Oxford, 25-26 June 2009	A discussion on the envisaged integration of the Oncosimulator into the overall ACGT architecture platform has taken place.
Joint Meeting of ACGT and ContraCancrum	Heraklion, Crete, 6 July 2009	

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Local meetings:

Title	Place and Date	Main conclusions
Local ObTiMA Meeting	Homburg, 6 March 2009	Development of CRF for Rhabdoid tumour
Int. Rhabdoidtumour Meeting	Boston USA, 9-11 March 2009	
GPOH Meeting	Hannover, Germany, 19-20 March	Presentation of ObTiMA to trial chairman of Paediatric Oncology
Meeting of the SIOP Nephroblastoma biology group	London, 28 April 2009	Demonstration of ACGT and ObTiMA
SIOP-Europe Meeting	Brussels, 29 April 2009	How to continue with Clinical Trials in Paediatric Oncology in Europe
Benelux Venture Forum - presentation	Ghent, 27-29 May 2009	Results immature for a VC investment in a Newco
Rhabdoidtumor Meeting in Münster, Germany,	Münster, 7 May 2009	Norbert Graf gave a talk regarding ObTiMA for the Rhabdoid Tumour Registry
I-BFM Meeting in Bergam	Bergamo, 8-10 May 2009	Norbert Graf gave a talk regarding ACGT and ObTiMA
ACGT-MerckSerono meeting	Lille, 27 May 2009	Discussion with AstraZeneca ACGT and possible continuation of work with an IMI project. More discussions scheduled before the next IMI call.
Benelux Venture Forum - presentation	Ghent, 27-29 May 2009	Results immature for a VC investment in a Newco
National meeting of the RIRAAF network (Research network on adverse reaction to allergens and medical drugs)	Madrid, Spain, June 2009	Presentation of the design and first prototype of a database to contain clinical and molecular data on allergic response to allergens and medical drugs.
National meeting of OLEAGEN project (Generation of genomic tools in olive and application to the analysis of fruit and oil quality and agronomical traits)	Baeza, Spain, June 2009	Report on the genomics projects management tools and sequencing data, assembly and gene expression datamining tools
DynaNets	Amsterdam, 3-4 June 2009	Kick-off meeting, project's interest on interactive graph visualization
CrossOver	Reading, 7-8 July 2009	Collaboration on interactive visualization in virtual reality environments
Local Meeting on Ontology Development and Maintenance	Saarbrücken, 25-26 June 2009	
ACGT and ObTiMA for Cardiology	Homburg, 28 July 2009	Meeting between the Competence Centre for Paediatric Cardiology, Berlin and ACGT people of UdS. The IT-Infrastructure and ObTiMA was presented by Norbert Graf. The Competence Centre for Paediatric Cardiology has great interest to use this infrastructure for their clinical research. They do not want to build an IT Infrastructure by their own, if an existing one fulfils all their requirements.
Local ObTiMA Meeting	St. Ingbert, IBMT, 31 July 2009	Further development of ObTiMA
TMC skype conference	Merelbeke (Belgium)	Review of Vienna Evaluation session of 26-29/01/2009 and updates of improvements
TMC skype conference	Merelbeke (Belgium)	Preparation of the September Japan demonstration

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Use and Dissemination

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

Dates	Name	Participant profiles	Туре	Nb Part.	ACGT Partner responsible /involved
2-6 March 2009	OGF25 Conference, Grid technologies in e-Health session	Session organizer and speaker	Conference	whole conference: 200 Session: 30	Juliusz Pukacki (WP3, WP4) - session organizer and speaker Giorgos Zacharioudakis (WP9) - speaker.
5 March 2008	Session "Grid technologies in e-Health" in the context of EGEE User Forum/OGF25 International Event, Catania, Italy, March 2-6, 2009	Software developers, Grid specialists	European Level	around 40	J. Pukacki (PSNC), G. Zacharioudakis (FORTH)
07-11 March 2009	Rhabdoid Tumour Meeting, Boston, USA,				USAAR
15-21 March 2009	BioHackathon 2009, Database Center for Life Sciences; The University of Tokio, Japan	Software developers (bioinformatics)	Discussions and collaborative software development	66	UMA (participation only) Presentation of web-service discovery, integration and automatic workflow composition tools (jORCA, Magallanes, etc.)
2-3 April 2009	2 nd Edition of the ERCIM-ETSI Infinity Initiative, Meeting of the Not PVH: SESSION 4: WHY STANDARDISATION IS ABSOLUTELY NECESSARY? Session Chair and Speaker: Norbert Graf (USAAR) - The need for standardization from a clinical perspective. Sophia Antipolis, France http://www.etsi.org/WebSite/NewsandEvents/Past_Events/2009_BIOICT_INFINITYINITIATIVE.aspx http://portal.etsi.org/docbox/Workshop/2009/200904_BIOICT/Standardization_Infinity_2009_GRAF.pdf				USAAR
28 April 2009	Wilms Tumour Biology Group Meeting of SIOP-RTSG in London				USAAR
27 May 2009	Hearing of the Committee for Education, Research and Technology Assessment of the German Parliament on "Individualized Medicine"	Scientists Politicians, Journalists	Parlamentary Hearing, National	250	UH
27-28 May 2009	SBS Annual Meeting, Lille	Researchers from academia and industry	Conference	120 – at the presentation, 2000	Biovista
10 June 2009	"Biological Databases and how to protect them from a sui generis right perspective – ACGT Project" at University of Tilburg	Academics	Lecture	20	LUH
19 June 2009	Networks for eScience	Research, commercial	Workshop	50	UVA
24 June 2009	"Retrieval von Teilnehmern an Interventionsstudien auf der Grundlage molekularer Eigenschaften (INTER-	Scientists	Workshop	30	UH
26 – 26 June 2009	"Genetisches Wissen" (Genetic Knowledge)	Scholars, the public	Conference	50	UH
29 June - 01 July 2009	Healthgrid 2009 Conference	HG2009 representing ACGT in the RADICAL workshop expert panel Participant and demo support	Conference	150	Custodix Juliusz Pukacki (WP3, WP4)
29 June 2009	Live demo and presentation at the Healthgrid 2009 Conference in Berlin	Software developers, Grid specialists	European Level	Around 100	M. Tsiknakis (FORTH), T. Sengstag (SIB), L. Koumakis (FORTH)
6-8 July 2009	Technology and Health: Law and Ethics	Lawyers, researchers, physician, computer scientist	European Summer School	90	FUNDP - Crid
July 2009	International Summer School in IT Law at LUH	Academics	Lecture	20	LUH
July 2009	"Einatmen. Ausatmen. Zur Herstellung von Intimität im elektrischen Zeitalter" at International Summer School oft he University of Vienna at Strobl/Austria	Academics	Lecture	30	LUH

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> Scientific publications

Material	Title	Authors	Journal/Conf/Proceedi ngs	Date
Publication	In silico' oncology for clinical decision making in the context of nephroblastoma	Graf N, Hoppe A, Georgiadi E, Belleman R, Desmedt C, Dionysiou D, Erdt M, Jacques J, Kolokotroni E, Lunzer A, Tsiknakis M, Stamatakos G	Klin Padiatr	2009 May-June
Publication	Genomic Grade Index Is Associated With Response to Chemotherapy in Patients With Breast Cancer	Liedtke C, Hatzis C, Symmans WF, Desmedt C, Haibe-Kains B, Valero V, Kuerer H, Hortobagyi GN, Piccart-Gebhart M, Sotiriou C, Pusztai L.	J Clin Oncol	2009 Apr 13
Publication	HER-2 as a target for breast cancer therapy	Ignatiadis M, Desmedt C, Sotiriou C, de Azambuja E, Piccart M.	Clin Cancer Res	2009 Mar 15
Publication	Quantitation of HER2 expression or HER2:HER2 dimers and differential survival in a cohort of metastatic breast cancer patients carefully selected for trastuzumab treatment primarily by FISH.	Desmedt C, Sperinde J, Piette F, Huang W, Jin X, Tan Y, Durbecq V, Larsimont D, Giuliani R, Chappey C, Buyse M, Winslow J, Piccart M, Sotiriou C, Petropoulos C, Bates M.	Diagn Mol Pathol.	2009 Mar
Publication	Development and validation of gene expression profile signatures in early-stage breast cancer	Desmedt C, Sotiriou C, Piccart-Gebhart MJ	Cancer Invest	2009 Jan
Publication	Phosphorylated ERalpha, HIF-1alpha, and MAPK signaling as predictors of primary endocrine treatment response and resistance in patients with breast cancer.	Generali D, Buffa FM (joint first), Berruti A, Brizzi MP, Campo L, Bonardi S, Bersiga A, Allevi G, Milani M, Aguggini S, Papotti M, Dogliotti L, Bottini A, Harris AL, Fox SB	J Clin Oncol	2009 Jan
Publication	Surgical Aspects in the treatment of patients with unilateral Wilms'tumor - a report by the SIOP 93-01/ German Society of Pediatric Oncology and Hematology	Fuchs J, Kienecker K, Furtwängler R, Bürger D, Thüroff JW, Hager J, Graf N	Ann Surg	2009
Publication	Value and difficulties of a common European strategy for recurrent Wilms tumour	Spreafico Filippo, Pritchard Jones Kathy, Bergeron Cristophe, de Kraker Jan, Dallorso Sandro, Graf N for the International Society of Pediatric Oncology Renal Tumor Study Group (SIOP-RTSG)	Expert Reviews Anticancer Therapy	2009
Publication	On Optimal Delivery of Combination Therapy for Tumors	A. d'Onofrio, U. Ledzewicz, H. Maurer and H. Schaettler	Mathematical Biosciences	August 2009
Publication	The cooperative and nonlinear dynamics of tumor-vasculature interaction suggests low-dose, time-dense antiangiogenic schedulings	A d'Onofrio, A. Gandolfi and A. Rocca	Cell Proliferation	2009
Publication	On the interaction between the Immune System and an exponentially replicating Pathogen	A d'Onofrio	Mathematical Biosciences and Engineering	2009
Publication	Delay-induced Oscillatory dynamics of Tumor-Immune System Interaction	A. d'Onofrio, F. Gatti, P. Cerrai and L. Freschi	Mathematical and Computer modelling	Submitted in 2009
Publication	Phase 0 microdose trials and the role of computational sciences in translational research	S. Camporesi and A. d'Onofrio	British Journal of Cancer)	Submitted in 2009
Publication	Chemotherapy in vascularized tumours: effects of pruning and of multistability	A. d'Onofrio and A. Gandolfi	Journal of Theoretical Biology	Submitted in 2009
Publication	A generalization of Gompertz law compatible with the Gillenberg- Webb model for tumour growth	A. d'Onofrio. A. Fasano and B. Monechi	Bulletin of mathematical biology	Submitted in 2009
Publication	Role of motility and chemotaxis in the pathogenesis of Dickeya dadantii 3937 (ex Erwinia chrysanthemi 3937)	María Antúnez-Lamas, Ezequiel Cabrera Ordóñez, Emilia López-Solanilla, Oswaldo Trelles, Andrés Rodríguez and Pablo Rodríguez- Palenzuela	Applied of Environmental Microbiology	2009
Publication	Prep+07: improvements of a user friendly tool to preprocess and analyse microarray data	Victoria Martín-Requena; Antonio Muñóz-Merida; M.Gonzalo Claros and Oswaldo Trelles	BMC-Bioinformatics	2009
Publication	jORCA: Easily integrating bioinformatics web services	Victoria Martín-Requena, Javier Ríos, Maximiliano García, Sergio Ramírez and Oswaldo Trelles	Oxford Journal Bioinfomatics	Submitted August 2009
Publication	mAPI: A modular framework for the integrated use of distributed resources	Sergio Ramirez; J. Rios; M. Garcia; J. Karlsson and Oswaldo Trelles	Engineering and	Submitted May 2009
Publication	BioHackathon 2008: standardization and interoperability for bioinformatics web services and workflows	UMA	The Oxford Database Journal	Submitted June 2009
Publication	Magallanes: a web services discovery and automatic workflow composition tool	Javier Rios, Johan Karlsson and Oswaldo Trelles	BMC Bioinformatics	July 2009
Publication	Center for Data Protection (CDP)	Nikolaus Forgo	ACGT Newsletter Edition 4, Spring 2009	2009 Mar
Publication	ACGT Newsletter Spring and Summer 2009	All Partners	ACGT Newsletter Spring and Summer 2009	2009

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Material	Title	Authors	Journal/Conf/Proceedings	Date	Venue
Conference Paper	Homogenising access to heterogeneous biomedical data sources	Erwin Bonsma and Jeroen Vrijnsen	Proc. of the BMIINT AIAI 2009 Workshop	April 2009	Thessaloniki
Conference Paper	In silico oncology: a top-down multiscale simulator of cancer dynamics. Studying the effect of symmetric stem cell division on the cellular constitution of a tumour	G.S.Stamatakos, E.Kolokotroni, D.Dionysiou, E.Georgiadi, S.Giatili	Medical Physics and Biomedical Engineering World Congress 2009	2009 September	Munich
Conference Paper	Building a System for Advancing Clinico-Genomic Trials on Cancer	Stelios Sfakianakis, Norbert Graf, Alexander Hoppe, Stefan Ruping, Dennis Wegener, Lefteris Koumakis, and George Zacharioudakis	Proc. of the BMIINT AIAI 2009 Workshop	April 2009	Thessaloniki
Conference Paper	Discovery of Genotype-to-Phenotype Associations: A Grid- enabled Scientific Workflow Setting	Lefteris Koumakis, Stelios Sfakianakis, Vassilis Moustakis, and George Potamias	Proc. of the BMIINT AIAI 2009 Workshop	April 2009	Thessaloniki
Conference Paper	Cross-platform Integration of Transcriptomics Data	Georgia Tsiliki, Marina Ioannou, and Dimitris Kafetzopoulos	Proc. of the BMIINT AIAI 2009 Workshop	April 2009	Thessaloniki
Conference Paper	Web-based Authoring and Secure Enactment of Bioinformatics Workflows	S. Sfakianakis, L. Koumakis, G. Zacharioudakis, M. Tsiknakis	4th International Workshop on Workflow Management (ICWM 2009)	4-8 May 2009	Geneva
Conference Paper	Workflows for Intelligent Monitoring Using Proxy Services	Stefan Rüping, Dennis Wegener, Stelios Sfakianakis, Thierry Sengstag	Proceedings of HealthGrid 2009	June 2009	Berlin
Conference Paper	A Semantic Infrastructure for the Integration of Bioinformatics Services	Giorgos Zacharioudakis, Lefteris Koumakis, Stelios Sfakianakis and Manolis Tsiknakis	International Conference on Intelligent Systems Design and Applications (ISDA 09), Special Session on Intelligent Systems Design and Applications in the Health Domain	30 Nov - 2 Dec 2009	Pisa
Conference Paper	Towards closing the gap between user data and standardized input	Alfredo Martínez, Paul Gordon, Christoph W. Sensen and Oswaldo Trelles	Workshop NETTAB 2009 Mathematics and Computer Science Department	10-13 June 2009	Catania
Conference Paper	jORCA: Making the use of bioinformatics web services easier	Victoria Martin-Requena, Javier Rios, Maximiliano García, Sergio Ramirez and Oswaldo Trelles	ISMB ECCB 2009	27 June - 2 July 2009	Stockholm
Conference Paper	Qnorm: A library of parallel methods for gene-expression Q- normalization	José Manuel Mateos-Duran; Pjotr Prins; Andrés Rodríguez & Oswaldo Trelles	The Bioinformatics Open Source Conference (BOSC)	27 June - 2 July 2009	Stockholm
Conference Paper	Victoria: navigating to a new style of searching for web-services and workflows	Johan Karlsson, Javier Ríos Oswaldo Trelles	The Bioinformatics Open Source Conference (BOSC)	27 June - 2 July 2009	Stockholm
Conference Paper	Web Services across an European Biomedical GRID Infrastructure	Maximiliano García, Johan Karlsson, Sergio Ramirez and Oswaldo Trelles	Bioinformatic Journeys-Lisboa	Submitted August 2009	Lisbon

Material	Title	Authors	Journal/Conf/Proceedings	Date	Venue
Poster Presentation	Predicting the efficacy of anthracyclines in breast cancer (BC) patients: Results of the neoadjuvant TOP trial	C. Desmedt, E. Azambuja, D. Larsimont, G. Rouas, A. Di Leo, S. Delaloge, C. Duhem, V. D'Hondt, M. Piccart, C. Sotirioun behalf of the investigators of the TOP trial	Annual meeting of the American Society of Clinical Oncology (ASCO)	May 2009	Orlando
Poster Presentation	ACGT: A platform to facilitate clinico-genomic research on breast cancer	Christine Desmedt, Norbert Graf, Nikolaus Forgo, Brecht Claerhout, Anca Bucur, Georgios Stamatakos, Juliusz Pukacki, Thierry Sengstag, Stefan Rüping, Manolis Tsiknakis on behalf of the ACGT consortium	IMPAKT Breast Cancer Conference	May 2009	Brussels
Poster Presentation	Infrared (IR) imaging: A new tool to refine breast cancer prognosis	A. Bénard, C. Desmedt, V. Durbecq, G. Rouas, D. Larsimont, C. Sotiriou, E. Goormaghtigh	IMPAKT Breast Cancer Conference	May 2009	Brussels
Poster Presentation	Integrating the molecular subtypes of breast cancer into a novel prognostic model	B. Haibe-Kains, C. Desmedt, F. Rothé, M. Piccart, G. Bontempi, C. Sotiriou	IMPAKT Breast Cancer Conference	May 2009	Brussels

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Material	Title	Speakers	Journal/Conf/Proceedings	Date	Venue
Presentation	Predicting the efficacy of anthracyclines in breast cancer (BC) patients: The results of the TOP trial and their validation in the BIG00-01 trial.	C. Desmedt, E. Azambuja, D. Larsimont, F. Lallemand, B. Haibe-Kains, J. Selleslags, S. Delaloge, C. Duhem, JP Kains, B. Carly, M. Maerevoet, A. Vindevoghel, F. Cardoso, G. Rouas, V. Durbecq, R. Salgado, JM Nogaret, I. Veys, JC Schobbens, D. Noterman, A. Di. Leo, V. D'Hondt, M. Piccart-Gebhart, C. Sotiriou	Annual meeting of the American Association for Cancer Research (AACR)	18-22 April 2009	Denver
Presentation	Gene expression signatures can predict the efficacy of anthracyclines in HER2-negative and HER2-positive breast cancer (BC) patients: The results of the TOP trial and their validation in the BIG1-00 trial.	C. Desmedt, B.Haibe-Kains, E. Azambuja, D. Larsimont, S. Delaloge, C. Duhem, A. Di Leo, V. D'Hondt, M. Piccart-Gebhart, C. Sotiriou on behalf of the investigators of the TOP trial	IMPAKT Breast Cancer Conference	May 2009	Brussels
Presentation	tion Homogenising access to heterogeneous biomedical data sources Erwin Bonsma		BMIINT workshop	24 April 2009	Thessaloniki
Presentation	The need for standardization from a clinical perspective	Norbert Graf	Meeting of the Network of Excellence "Virtual Physiological Human" during ERCIM-ETSI Infinity Initiative	2-3 April 2009	Sophia Antipolis
Presentation		Alberto d'Onofrio	Mathematical and Computational Approaches in Biology and Medicine Scientific workshop	15-16 June 2009	University of Warsaw Poland
Presentation	Interactive Visual Exploration	Robert Belleman	IPA workshop	38458	Helvoirt, Netherlands
Presentation	Service-oriented interactive visualization in the ACGT project	Paul Melis	IPA workshop	38458	Helvoirt, Netherlands
Presentation	Graph exploration on a multitouch table	Laurence Muller	IPA workshop	38458	Helvoirt, Netherlands
Presentation	Interactive Visual Exploration of Graphs and Networks	Robert Belleman	Networked Visualization for e-Science	19 june 2009	Amsterdam
Presentation	The ACGT Workflow Editing & Enactment Environment	J. Pukacki G. Zacharioudakis	EGEE User Forum/OGF25 Session" Grid technologies in e-Health"	5 March 2009	Catania Italy
Presentation	Biovista: literature mining platform and its various applications	Andreas Persidis	Annual SBS conference	26-30 April 2009	Lille, France
Presentation	Healthgrids	Yannick Legré	Asia-Pacific Advanced Network APAN 28th meeting	22 July 2009	Kuala-Lumpur
Presentation	The ACGT WorkflGrid Technologies for Cancer Research in the ACGT Project ow Editing & Enactment Environment	Giorgos Zacharioudakis	EGEE User Forum/OGF25 Session" Grid technologies in e-Health"	5 March 2009	Catania Italy
Presentation	Biological Databases and how to protect them from a sui generis right perspective – ACGT Project	Marcelo Corrales	Lecture at university of Tilburg	10/06/2009	Tilburg
Presentation	ACGT	Nikolaus Forgo	Lecture at International Summer School in IT Law	July 2009	Hannover
Presentation	Einatmen. Ausatmen. Zur Herstellung von Intimität im elektrischen Zeitalter	Nikolaus Forgo	Lecture at International Summer School of he University of Vienna	July 2009	Strobl

Material	Title	Authors	Event	Date	Venue
Demonstration	Ontology-based Clinical Trial Management System (ObTiMA) Software	Brochhausen M., Weiler G., Schera F., Rauch J., Graf N., Kiefer S.	International Conference on Biomedical Ontologies	24 July 2009	Buffalo NY USA
Demonstration	Visualization software developed for ACGT	Robert Bellman & UVA	Bachelor's science day (60 participants)	7 March 2009	Amsterdam
Demonstration	Demonstration of visualization software developed for ACGT	Robert Bellman & UVA	Human-Computer Interaction symposium (25 participants)	20 March 2009	Amsterdam
Demonstration	The Cave Automated Virtual Environment	Robert Bellman & UVA	SARA Computing and Networking Services (15 masters's students)	26 June 2009	Amsterdam
Demonstration	A semantic grid services platform in support of efficient knowlegde discovery from multilevel biomedical data	M. Tsiknakis, T. Sengstag, L. Koumakis	HealthGrid conference	29 June 2009	Berlin

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Disseminated Project Results

Description	Details
Software prototype	Implementation of the first release of ObTiMA (Ontology based Trial Management System for ACGT)
Software prototype	Data access service for the BASE database
Software prototype	Generic OGSA-DAI activity that delivers query results to the Gridge Data Management System
Software prototype	Contribution to the integrated demonstrator
CAT	Custodix Anonymization Tool

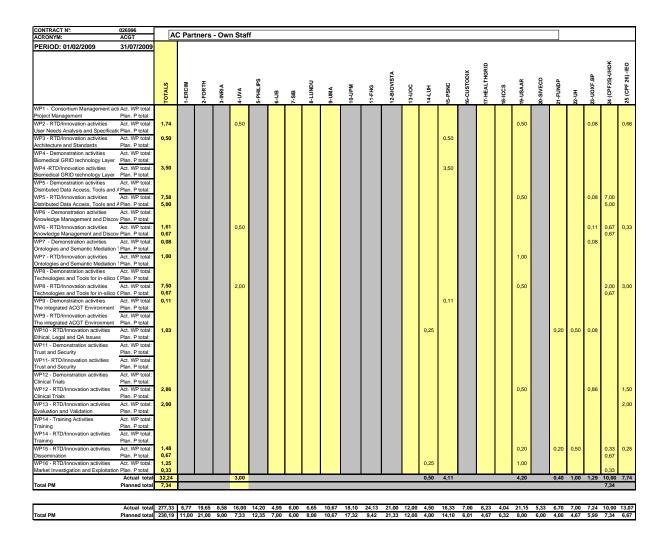
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Person Month Status Report

1 February - 31 July 2009

ACGT Person-Month	Status Tab	le																									
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PERIOD: 01/02/2009	31/07/2009	OTALS	1-ERCIM	2-ғоктн	3-INRIA	4-UVA	5-PHILIPS	6-1JB	7-SIB	8-LUNDU	9-ОМА	10-UPM	11-FHG	2-BIOVISTA	13-UOC	4-LUH	15-PSNC	CUSTODIX	HEALTHGRII	18-ICCS	9-USAAR	-SIVECO	FUNDP	동	23-UOXF.BP	24 (CPF25)-UHOK	(CPF 26) -IEO
		ı			균	4		ū	7	₽	<u> </u>	_	7	12	13	4	5	-91	17.	6	6	Ŕ	Ŕ	Ŕ	ន់	24	25
WP1 - Consortium Management a Project Management WP2 - RTD/Innovation activities User Needs Analysis and Specificit WP3 - RTD/Innovation activities Architecture and Standards WP4 - Demonstration activities Biomedical GRID technology Laye WP4 - RTD/Innovation activities Biomedical GRID technology Laye WP5 - Demonstration activities	Plan. P total: Act. WP total: titic Plan. P total: Act. WP total: Plan. P total: Plan. P total: Act. WP total: Act. WP total: Act. WP total: Act. WP total:	8,61 9,31 7,84 4,27 5,48 5,64 1,10 1,12 11,68 11,76	6,51 7,33	0,66 0,67 0,33 0,33 1,00 1,00	1,50 0,67	0,50 0,33 0,50 0,33	0,20 2,00 0,67 1,00 0,67	0,33	0,33 0,22		1,00 1,00	0,30 0,33 1,00 0,33 0,33	0,44 0,42 0,33 0,33	0,33	1,00 0,33		0,50 0,56 2,61 3,11 0,10 0,12 8,16 8,89	0,25		0,04 0,07 0,12 0,20	1,98 0,67	1,00			0,33 0,33		0,33 0,33
Distributed Data Access. Tools and																											
WP5 - RTD/Innovation activities Distributed Data Access, Tools and WP6 - Demonstration activities Knowledge Management and Disc	Act. WP total: d A Plan. P total: Act. WP total:	23,70 19,91		2,00 2,00	1,00		8,00 7,33	1,00 0,67		1,33 1,34		2,00 2,00	3,64 1,67	0,33	1,00 0,67					0,13 0,23	3,93 2,00				0,67 0,67		
WP6 - RTD/Innovation activities	Act. WP total:	29.95		2,00	3,00	0,75			0,33	3,33	4,33		7,21	7,00											1,67		0,33
WF9 - RTD/IIII/Ovalidit activities Knowledge Management and Disc WP7 - Demonstration activities Ontologies and Semantic Mediatio WP7 - RTD/Innovation activities Ontologies and Semantic Mediatio WP8 - Demonstration activities	Act. WP total: Plan. P total: Plan. P total: Act. WP total:	23,34 0,33 0,33 27,04 21,12 0.85		2,00 2,00 2,00 2,00	1,33	0,75	1,00 1,67		0,33	1,00 2,00	4,33 4,33 0,33 0,67	1,33 11,00 8,00	0,67 0,67	4,00 3,33	0,67					0.10	7,04 2,00				1,67 1,67 0,33 0,33		0,67
Technologies and Tools for in-silice WP8 - RTD/Innovation activities Technologies and Tools for in-silice WP9 - Demonstration activities The integrated ACGT Environment WP9 - RTD/Innovation activities	Act. WP total: O (Plan. P total: O (Plan. P total: Act. WP total:	1,00 14,53 15,34 2,03 2,96 24,74		1,00 1,33 6.00	4,08 3,66	0,67 6,00 3,00 0,50 0,33 2,00	1.00	0,33 0,67	0.84	0.33	3.00	2.00	0,34 1,67	0,33	1,00		0,53 0,97	2.00		0,33 2,58 3,67	1,20 0,67						2,00
The integrated ACGT Environment WP10 - RTD/Innovation activities Ethical, Legal and QA Issues WP11 - Demonstration activities Trust and Security WP11- RTD/Innovation activities	Plan. P total: Act. WP total: Plan. P total: Act. WP total: Plan. P total: Plan. P total: Act. WP total:	17,27 21,07 14,51 0,75 0,67 4,57		6,00		1,00	0,67	0,33 0,67 0,67	0,67	0,33	2,00	1,00	1,33	2,67	5,00 2,00	3,67 3,67	0,32	1,33 0,50 0,50 0,75 0,67 1,75		0,60	0,10 0,33		5,30 3,34	5,50 3,67	0,33 0,33		
Trust and Security WP12 - Demonstration activities Clinical Trials WP12 - RTD/Innovation activities Clinical Trials WP13 - RTD/Innovation activities	Plan. P total: Act. WP total: Plan. P total: Act. WP total: Plan. P total: Act. WP total:	4,78 0,80 1,33 11,67 15,90 17,54		1,00 1,00 1,00		1,00	1,00	0,33 2,00 2,00 0,33	0,67 1,33 2,33		0,67	0,33	6,33	0,33	3,00 6,00		0,45	1,67		0,18 0,23 0,08	0,80 0,67 0,80 0,67 0,50				1,35 1,33 1,00		2,67 2,67 2,00
Evaluation and Validation WP14 - Training Activities Training WP14 - RTD/Innovation activities Training WP15 - RTD/Innovation activities	Plan. P total: Act. WP total: Plan. P total: Act. WP total: Plan. P total: Act. WP total:	11,81 4,35 8,50 5,31 9,19 12,97	0,03 0,67 0,20	1,00 0,50 1,00	1,67	1,00	0,67	0,67 0,33 0,33	1,67 1,00 1,00 0,25	0,33 0,33 0,33 0,33	0,67 0,34 1,00 0,33	1,00 1,67	0,33 0,57 0,33	1,00 1,67 1,00 1,00 2,00	0,50			0,67 0,25 0,17 0,25 0,17 0,25	0,50 0,67 1,33 5,16	0,13 0,20 0,33 0,03 0,03 0,05	0,33	2,33 2,33 1,33 1,33	0,33	0,50	0,27		1,00
Dissemination WP16 - RTD/Innovation activities Market Investigation and Exploitation	Plan. P total: Act. WP total: on Plan. P total: Actual total	12,74 8,18 10,05 245,09	1,67 0,03 1,33 6,77	0,67 1,00 1,33 19,65	0,67 8,58	0,33	0,67 14,20	0,34 0,33 0,33 4,99	0,34 0,25 0,33 6,00	0,33 6,65	0,33	1,33	24,13	1,00 4,00 3,00 21,00	0,67 0,50 0,33 12,00	0,33 0,33 4,00	12,22	0,33 0,33 7,00	2,00 0,57 0,67 6,23	0,07 0,20 0,40 4,04	0,33 0,30 0,33 16,95	0,67 0,67 0,67 5,33	0,33 6,30	1,00 6,00	0,33 5,95		5,33
Total PM	Planned total	222,85	11,00	21,00	9,00	7,33	12,35	7,00	6,00	8,00	10,67	17,32	9,42	21,33	12,00	4,00	14,10	6,01	4,67	6,32	8,00	6,00	4,00	4,67	5,99		6,67

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