The ACGT Exploitation Plan Update 3 (2009)

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ABSTRACT: This document is the second update of the ACGT Initial Exploitation plan. Published annually for each of the 2nd and subsequent years of the project, updates present the results of the work performed to date, issues encountered, any modifications to the original exploitation plan created as well as list of immediate tasks for the year to come.

In the present version of the exploitation plan we focus on the options that any ACGT-like infrastructure has in connection with exploitation. Specifically we consider ACGT as either an infrastructure, an integrated environment of CT-related services and resources and finally a research project. Each of these viewpoints implies different issues and challenges and consequently different exploitation priorities. In this document we take each viewpoint in turn and discuss the concomitant implications.

Finally, in this plan update we report on the progress with respect to the previous plan objectives, reassesses the risk factors and where appropriate presents corrective steps planned for year 4 (2009)

KEYWORD LIST: exploitation plan, update of plan, report on activities, exploitation materials, exploitation options

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Contents

1 Scope of the Exploitation Plan Update

1.1 Exploitation Plan Overview

ACGT aims to provide open source tools, resources and infrastructure that in principle target all major stakeholders with an interest in clinical trials and research in a post genomic environment. The project covers a very wide scope of activities and needs, often contradicting (e.g. the need for easy access to clinical data and the requirement for protection of personal information), and attempts to address these with technological solutions that in some cases are based on shifting or incomplete standards and immature underlying IT platforms.

Effort so far has focused on providing the proof of the original concept of the project, namely to support clinical trial research in multi-centric, multi-platform, international environments. This has been achieved to a significant degree at the time of writing of this report. However, by necessity, the solutions provided are technically complex at all the levels of the ACGT architecture, including the data repository, security and end-user services levels to name but a few.

This complexity implies a steep learning curve as well as a significant commitment of time from any third party who would be interested to use and benefit from ACGT results. A consequence of this is that these third parties are seeking assurances for the continued existence and support of the ACGT infrastructure after the official end of this project before they commit any personal resources on learning and using ACGT outcomes. This challenge has been identified since the previous version of the plan but although progress has been made in certain aspects, the main question of who actually undertakes to support post project-end still remains unanswered.

Integration with legacy systems and resources, together with end users' requirement to support 'simple' activities (like data exchange between some of these existing systems) pose additional challenges to the consortium which often finds itself in the position of providing a sledgehammer to crack the proverbial nut.

On top of these technical challenges, the landscape is not very clear either, on both the legal and ethical levels which ACGT attempts to address. One of the conclusions from the legal experts group of the consortium (see Deliverables D10.x) is that on many of the core issues, there is significant fragmentation at the European level which of course presently makes it quite difficult to deploy an international multi-centric infrastructure that meets all national requirements.

These challenges have become increasingly clear as the consortium has begun shifting its focus from establishing the technical feasibility of the original concept and design to deploying the resources, tools and services in end user environments. It is precisely these challenges that the present third version of the exploitation plan aims to address. It does so by organizing the exploitation opportunities and challenges according to three distinct viewpoints of ACGT. These are the following:

1. ACGT as an infrastructure
2. ACGT as an integrated environment of resources, tools and services for end users
3. ACGT as a research project

Each of these viewpoints poses slightly different requirements from an exploitation point of view. For example stressing the infrastructure nature of the project implies that additional effort should be spent in providing the underlying IT-expert-oriented tools that will facilitate the creation of resources and services for end users. On the other hand stressing the services nature of ACGT implies that effort should be spent on creating a consistent and complete set of end-user oriented services that support present end users tasks in actual environments (e.g. hospitals) and add significant and well understood value.

To date progress has been made on all of these fronts. However the results are not complete with respect to any of the above mentioned viewpoints (with the exception of the 'research project' viewpoint which of course poses fewer demands on the exploitability of the end result) and as a consequence a major goal of this version of the plan is to discuss the implications relating to each viewpoint and provide support for the decisions made and the exploitation-related work selected for the final period of the project.

1.2 Purpose of the Document

The purpose of this document is to provide an update on the exploitation plan focusing on exploitation options available to the consortium, achievements to date, issues identified and specific exploitation activities taken. It aims to justify the actions that the consortium has decided to take during the final period of the project providing a consistent organizational framework for these actions as well as a basis for predicting expected results.

As was the case with the two previous versions of this document, it serves management board members by providing a tool to help manage the work during the final period of the project.

Finally an important goal is to capture and make available to other interested parties (be they other research consortia, policy makers or other stakeholders) the experiences gained by the consortium in connection with infrastructure based projects in the area of clinical trials support but also more generally, life science related IT systems.

1.3 Who is this document for?

The primary target audience of this document is the Project Management Board (PMB) and partners who are responsible for exploiting the results of their work. Chapter 4 has been written specifically with parties external to ACGT in mind. It targets policy makers, researchers as well as IT managers who are active in the area of MIS and the support of multi-data, multi-centric IT systems that are deployed in a clinical or more generally health related environment.

1.4 Structure of the Document

This document is arranged in 4 main chapters, as follows:

Chapter 2 discusses the main activities carried out in accordance with the second version of exploitation plan, results to date and any issues that have arisen.

Chapter 3 explores exploitation options that have been identified and considered by the consortium in connection with each of three different viewpoints of the nature of the project, namely

- ACGT as an IT infrastructure
- ACGT as a set of resources and services for researchers and clinicians, and
- ACGT as a research project in the field of post-genomic clinical trials support

Chapter 4 discusses issues identified and presents an update on the risk factors identified in the previous versions of the Exploitation Plan, specifically whether they have materialised or not and if so what corrective action is proposed.

Chapter 5 focuses on specific partners (primarily the SMEs in the consortium that are driven by commercial objectives) and reports on their achievements and activities in exploiting their work in the project.

Finally, chapter 6 presents the plan proposed for the period 2009-2010 taking into account findings and the work carried out in the third year of the project.

The Appendices provide additional information and details on a number of issues discussed in the main part of the document.

1.5 Document Versions and Update Procedure

This document is the second annual update to the original exploitation plan published in March 2007 (deliverable D16.1). It presents the exploitation work package results as they stand at the time of publishing and discusses changes that are considered necessary in response to results and findings that transpired during the reporting period.

All communications regarding the current version or future amendments should be sent directly to Andreas Persidis, Biovista at andreasp@biovista.com and copied to acgt-wp16@inria.fr .

2 Update on Work to Date

The main objectives of the exploitation task for the third year of the project were the following:

1. to ensure the consolidation of the minimum set of demonstrable resources and infrastructure that will act as reference points in any discussion with third parties
2. to liaise with other work-packages (namely WP15 and WP14) in order to ensure the coordinated creation of exploitation related materials that can be used as exploitation opportunities arise
3. to pursue exploitation opportunities in a controlled fashion by carefully managing third party expectations and at the same time maintaining interest in project developments.

In addition to the above and as the consortium has made initial contacts and inroads, it is becoming increasingly clear that a number of 'soft factors' (such as sustainability of the resources and the infrastructure) play an equally important role in the further use of project outcomes and have therefore been attracting the increasing attention of the PMB.

With the above in mind, the achievements during the reporting period are as follows:

1. **European Breast Cancer Conference-06 (Berlin 14/4/08):** ACGT hosted a workshop addressed at EBCC attendees. Approximately 80 delegates attended the various sessions with circa 50 of them providing their contact details and subsequently receiving the ACGT Newsletter. One observation was that while the medical/biology oriented presentations maintained audience interest, the technical/IT oriented ones did not fair so well, reflecting more the synthesis of the audience than the quality/content of the technical presentations themselves. Future efforts will need to match more closely the message with the expected audience.

2. **ACGT – EORTC:** The contract with EORTC is now signed. The main points of the collaboration are as follows:
    - A review of the security infrastructure of ACGT by EORTC staff with a view to provide appropriate comments from an experienced group of end users (included in deliverable 13.2)
    - Provision of CRF from EORTC with the aim of improving the ACGT Master Ontology
    - Provision of data from a recently closed EORTC trial which has extensive clinical, imaging and biological data.
    - Provision of access to the protocol and CRF of the MINDACT trial so as to see the degree to which ACGT infrastructure meets the needs of this trial.

3. **Identification of recipient of ACGT news**: During the reporting period effort has been spent in identifying additional researchers and other individuals who may have an interest in ACGT related developments and resources on offer. In addition to the personal contacts identified in the previous period two new contact lists have been generated, one with individuals active in child nephroblastoma and one with those active in breast cancer. The lists comprising over 50 and over 240 contacts respectively will be used as recipients of the ACGT Newsletter and other noteworthy ACGT news. Those who react more favourably will be contacted with further uptake of ACGT outcomes in mind.

4. **NeoBIG**: NeoBIG is a multi-organizational, multi-national effort in which pharmaceutical companies have a major stake. NeoBIG aims to organize and set up next generation clinical trials in the area of breast cancer R&D. Partner Jules Bordet arranged a meeting with the NeoBIG consortium to explore the potential for ACGT to be the platform of choice that will support NeoBIG in its future work. Due to the confidential nature of this work, involved partners (FORTH, Custodix, Biovista, Lausanne, Saarland, Phillips, FHG) were requested to sign a CDA. Following the first meeting, an internal ACGT meeting was held during the latest consortium meeting in Vienna (26-29/1/09). While in theory partners agreed that the ACGT platform is capable of providing the necessary solution, long term support and other requirements of NeoBIG mean that an unequivocal 'Yes' at this point in time is not possible. ACGT members have decided to explore this internally and deliver an official position in due time. NeoBIG is considered a major opportunity for the long term support of the ACGT infrastructure and considerable effort will be invested in the final period of the project to explore it.

5. **Generation of Additional Training Materials**: Tools that address non expert users must be accompanied by training materials and so effort was spent in order to generate these materials (user manuals, tutorials etc) for the publicly available tools. These materials refer to the ACGT OV and have been made available to the training work package (WP14) that is integrating them in the ACGT portal

6. **The STaRC Initiative**: STaRC is an initiative originally conceived by the University of Saarland (Prof. N. Graf) based on the experience of ACGT and some of the challenges that have been identified by the consortium so far. These challenges refer to the deployment and uptake of ACGT services and infrastructure by third party stakeholders, in particular hospitals and clinicians involved in Clinical Trials. STaRC is intended to be a '**S**tudy, **T**rial **a**nd **R**esearch **C**entre' that will exploit clinically relevant aspects of ACGT. The main tasks of STARC will be:
    - Simplification of the clinical trial process
    - Patient empowerment
    - Combining clinical and molecular biological and genomic data in single patients leading to personalized medicine
    - Facilitating translational research
    - Continually improving curricula of medical schools and medical education

   Appendix 2 presents in more detail the STaRC initiative.

7. **ACGT Competition**: The ACGT competition is still being pursued by the PMB as it is believed to help with the uptake of project results. The ACGT Competition is scheduled for the end of 2009 – beginning of 2010. Initial versions of supporting materials (competition announcement etc), have been prepared. Remaining issues will be dealt in year 2009.

8. **Usage scenario**: University of Saarland and Biovista collaborated in a usage scenario that represents actual current research carried out by Saarland. The research aims to characterise nephroblastoma antigens and the literature mining services were used to support and accelerate this task. As soon as the research is completed, a case study report will be prepared to record the experience and be used as 'exploitation material'.

9. **Thalassaemia International Foundation (TIF):** TIF is an international foundation that supports research, awareness and educational activities related to beta-thalassaemia. TIF is interested in deploying a patient record system at 4-8

collaborating hospitals in Cyprus (to start with) and later on in other countries with which it has ties. The management of patient records is along the lines envisaged by ACGT. Following a host of earlier communications, a meeting was set up in Nicosia (25-26/9/08). The presentation generated keen interest – in a recent communication TIF have said that they want to move ahead but are short on funds and are currently looking at national and other funding options. We expect to have a clear position in Q3-Q4 of 2009.

10. **Capture the experience from creating the reference implementation**: Deliverable D9.3 has begun to address this objective. However due to its complexity the task has been extended into the final period of the project. The envisaged document is now planned for publication in Q1 2010.

11. **Center for Data Protection**: the CDP is now fully operational and is providing services not only to ACGT but also other 3rd parties. It has recently provided its support to the iLINK proposal being submitted by a subgroup of the ACTG consortium to the April '09 EC call (see also Appendix 4).

12. **Follow on proposals and projects**: ACGT has already resulted in a number of follow on proposals and projects that have been submitted and are running by sub-groups of the present consortium. In particular
    - a STREP (CancerCanum) was submitted in the previous ICT call is coordinated by FORTH and includes NTUA-ICCS and Uni. Saarland.
    - A new proposal from FORTH, Saarland, NTUA and CviT and Queen's College – London in the action line "international collaborations in VPH".
    - The Coordination and Support project Eurocancercomms has already received funding from the "Science in Society" programme. One of the main objectives of Eurocancercomms is to establish an integrated model for a Europe-wide comprehensive cancer information and policy exchange portal. This exchange portal will be hosted by eCancer[1]. eCancer, Philips and FORTH are partners in both iLink and Eurocancercomms. ACGT participants include IEO (Coordinator), FORTH, SIVECO and Philips.

In summary, during 2008 progress has been made in connection with the use (actual and potential) of ACGT results by interested third parties and the generation of materials that can be used in support of the longer term exploitation actions taken.

From a technical point of view many issues have been resolved. However the complexity of ACGT, the problem it addresses and the outcomes it produces means that a significant amount of additional supporting materials need to be created so as to facilitate the deployment and usage of project outcomes by third parties.

The exact nature of these materials depends on the intended audience and usage. The next chapter discusses the options we have explored for ACGT and the implications of each, in terms of the necessary exploitation-related work that they entail.

3 Partner-Specific Exploitation

ACGT is of course a very complex and large undertaking and our main concern is tis exploitation as a whole. However, the consortium comprises a number of partners each of which could and does exploit their work in a multitude of ways that can compliment the efforts taken at the consortium level.

With this in mind, we report in this section on specific exploitation activities and results by individual partners. We have selected those results that although primarily benefiting the partner himself, impact ACGT by providing case studies of ACGT compliant resources and services in actual use.

3.1 NTUA-ICCS

NTUA-ICCS has been developing the Oncosimulator technology which has exploitation potential as discussed below:

- Simulation code: Novel algorithms for the cytokinetic and mitotic potential initialization of an imageable real tumour.
- Simulation code: The entire simulation modules addressing the cases of nephroblastoma and breast cancer response to chemotherapeutic treatment.
- Clinical methodologies: the protocols for the clinical validation of the Oncosimulator for the cases of nephroblastoma and breast cancer chemotherapy treatment.
- Software: the technological modules' software and their integration software. This includes standard and virtual visualization of the tumour, image processing of the tumour and the RecipeeSheet facilitating parametric exploration and adaptation of the code.

Following completion of the clinical adaptation, optimization and validation procedure, the above parts of the Oncosimulator will constitute exploitable knowledge or products applying to the basic science and the clinical sectors which NTUA intends to pursue.

3.2 Biovista

The literature mining services that are being made available through the ACGT infrastructure are driving Biovista's work in the area of adverse event prediction and drug repositioning. This technology uses published literature and related resources (e.g. the GO ontology) to make predictions of adverse events, identify biomarkers and reposition drugs with high accuracy, low cost and without the need for a large number of costly experiments. To date Biovista has used this technology to offer services to commercial clients and academic initiatives. The latest successful use of this, is the CTSA Pharmaceutical Assets Portal (http://www.ctsapharmaportal.org/) whose purpose is *"…to forge relationships with the pharmaceutical/biotech industry with the intent to facilitate the transfer of the investigational drugs and biologics for academic research."*

Biovista has also been using this technology to develop its own IP portfolio of repositioned drugs having submitted 5 patent applications in the period from September – December 2008. Some of these predictions have already shown statistical significance in animal model experiments and as a consequence the company is expecting to generate significant commercial interest in the near future.

3.3 FORTH

FORTH has been the main developer of the Workflow Editor and Enactment Environment (WEEE). FORTH being an academic institute focuses its exploitation on the use of its tools in further R&D projects. The following is a list of actions to date:

An initial exploitation of WEEE has been developed in the context of "Genotype-To-Phenotype Databases: A Holistic Solution (GEN2PHEN)" project. One of the GEN2PHEN project's objectives is the delivery of a Grid infrastructure (based on existing standard technology, systems, tools and services) to enable efficient integration and sharing of data and analytical tools, high-performing G2P explorations enabling respective studies querying operations.

FORTH in collaboration with EBI developed a case study scenario (called GG2P) that enables the discovery of genotype to phenotype associations and predictive models, and supports Genotypic to Phenotypic association studies. The methodology in the context of the GG2P scenario has been implemented with the aid of Web Services, Scientific Workflows and operated in a grid environment. For the realization of the GG2P scenario parts of the ACGT Grid infrastructure such as the Data Management System, the service repository and the WEEE were used. The scenario was demonstrated during the 3rd General Assembly Meeting (GAM3) & 5th Steering Committee Meeting (SCM5) of Gen2Phen project 18-20 February, 2009 at Leicester, UK. The consortium of GEN2PHEN has shown significant interest for the usage of WEEE.

Additionally, exploitation and further development of the WEEE has been added in a number of EU project proposals in which FORTH is involved.

4 Exploitation Options for ACGT

ACGT is a complex and multifaceted project that presents a number of exploitation opportunities, each of these addressing a different group of stakeholders. Moreover, the requirements of each imply a different focus in terms of plans and goals, strategic actions taken and supporting materials generated.

With substantial resources and time it is possible to pursue all these options simultaneously. In the context of ACGT however with its limited resources and time, this is not an option. It has therefore become essential to recognise these alternatives and organise them in such a way that the PMB can plan its exploitation work for the final period of the project in a coordinated and manageable manner.

We recognise three distinct viewpoints of ACGT.

a. ACGT as an infrastructure

b. ACGT as an integrated environment of resources, tools and services for end users

c. ACGT as a research project

In the sections that follow we explore each of these in terms of their implications for the exploitation of project outcomes.

4.1 ACGT as an infrastructure

ACGT is in large part an IT infrastructure project. It aims to create an integrated environment for the running of services and the exchange of data and other resources based on a layer sitting, architecturally, on top of grid technologies.

Like any similar undertaking, its success would be measured on the basis of the use of this infrastructure by third parties. This use is in turn increased, the easier it is for these parties to use the infrastructure and the greater the benefit they derive from such use. Clearly, each specific success criterion poses different requirements to the infrastructure developers. In the following table we have therefore listed the main ones we consider are pertinent to ACGT. For each criterion we have also identified the corresponding requirements. These then act as a guide for work that would need to be undertaken and supporting actions and resources created during the remainder of the project. Table 4.1 below lists these criteria:

Criterion	Metric	Implication for ACGT
Ease of development for the infrastructure	1. Underlying technologies used 2. Supporting documentation	I1: Ensure availability of documentation. The ACGT competition will act as a focal point for collecting, organizing and presenting this.
Number of end user	The more the better	I2: Resources already

resources		committed. The ACGT competition is expected to generate more.
Number of tools/resources that support the development of compliant services	The more the better	I3: Need to organise and present what exists in a more accessible manner. WP14 will be assuming a more active role in this.
Expected longevity of the infrastructure	1. Assurances for financial support of infrastructure 2. Credibility of assurors 3. Track record	I4: Visible and official partner commitments where possible
Compliance of infrastructure with existing standards		I5: Document and present visibly in web, portal and other access points.
Infrastructure robustness	High score in robustness tests	I6: Test extensively and document problems and fixes where appropriate.
Number of existing users	Either a large number of users or a smaller number of high profile ones.	I7: The ACGT competition aims to address the first metric. The EORTC, NeoBIG and indeed University of Saarland are considered high profile end users.
Performance	Speed of applications	I8: It is early days and actually getting jobs done in the first place is more important than the speed at which they run.
Availability of system	1. Low downtime	I9: Monitoring system already in place. Possibly make this more prominent and open for public access.
Supporting tools (e.g. usage and uptime monitoring, etc)	Number, findability and ease of use of these tools	I10: Document them extensively, make them easily searchable (via the Portal)

Table 4.1: Exploitation criteria for the ACGT infrastructure

4.2 ACGT as an integrated environment of resources, tools and services for end users

In addition to an infrastructure, ACGT aims to offer non-IT expert end users (namely clinicians, bio-researchers and patients) a set of services that support current tasks and processes that are employed in their working environments (such as the design and management of a clinical trial). This set of users is not interested or indeed able to use the tools and resources aimed at the IT systems expert in their organization; on the other hand

they are looking for s/w tools and resources that support them in carrying out well understood, daily tasks.

From an exploitation potential point of view the criteria and metrics of success focus on the services and resources themselves. Table 4.2 list the main ones and once again the implications for ACGT in terms of necessary exploitation-related work.

Criterion	Metric	Implication for ACGT
Nature of resources	• Resources must address a variety of actual, valuable tasks	I1: The consortium has selected 'usage scenarios' with the involvement of the end users. Need to use these with 'live data' and document as case studies.
Number of resources	• The more the better	I12: Most probably we need to create more resources. The ACGT competition aims to address this.
Supporting materials	• Documentation • On-line tutorials	I13: Create more supporting materials. (see WP14)
Integration with legacy systems	• Integration should be transparent to end user	I14: No attempt to address this so far. Need to be aware of what is needed to achieve this integration. Probably need to create relevant documentation.
Integration with other ACGT services and resources	• Number of other ACGT resources with which each service can be combined to support more complex workflows	I15: Basic integration achieved for the selected use-case scenarios. Need additional tests between all available resources and services
Quality	• As measured by accepted metrics (application specific)	I16: Define metrics, create and organize tests as applicable, conduct tests and report findings
Performance	• Application specific metrics. • Possibly availability of comparative information	I17: Define metrics, create and organize tests as applicable, conduct tests and report findings
Track record	• History of use	I18: Create a log of use and provide some basic access to it
Real and perceived utility	• The resource is seen to offer true value to its end users	I19: Requires actual use by end users, creation of relevant evaluation questionnaires and analysis of results
Local support requirements	• Ideally these should be minimal	I20: Documentation of what is needed and list of

		solutions offered
Long term professional support	• Assurances of technical support by trusted assuror	I21: Visible and official partner commitments where possible

Table 4.2: Exploitation criteria for the ACGT resources

4.3 ACGT as a research project

ACGT is of course an EU co-funded project and as such can also be exploited in the context of the broader EU research community. Typically this type of exploitation focuses on the following possibilities:

1. **Interactions with other EU or other national projects**: here the objective is to explore complementarities and where appropriate cross-pollinate with results from the other projects. ACGT is already in contact with projects such as caBIG, EGEE and others. This activity is planned to continue until the end of the project.

2. **Follow-on projects**: Various follow-on proposals are currently being put together by subgroups of the ACGT consortium.

3. **Dissemination activities**: WP15 has been pursuing this possibilities and the relevant deliverables report on progress to date. Partners are also publishing papers in peer reviewed journals as well as making presentations at a variety of fora. This activity will continue until the end of the project and beyond.

5 Issues Involved and Risk Factor Assessment

5.1 Issues

An ongoing activity of the exploitation work package is to monitor the progress of work within the consortium as well as developments in the target industry and application area with a view to their contribution to the exploitation of project results. In this section we discuss previously identified as well as new issues that affect project exploitation and present adjustments to the plan itself

Update on previously identified issues

1. **Not enough infrastructure and services in place**: this concern from the previous version of the plan has been partly addressed, especially in the infrastructure side of the equation. It is presently felt that the lower level tools and resources that are required to support end-user oriented resources and services are now in place and operate reasonably well. The concern now is more on the 'completeness' and consistency of the available set of end user services so as to support existing workflows and tasks in end user partner environments (like Jules Bordet, University Hospital Saarland and others). Considerable effort has been spent in the past year to define scenaria that represent actual tasks and workflows and make sense to end users (doctors, researchers, etc.). It is now felt that the goal has been achieved with respect to IT specialists in these end-user environments who should be able to install and operate an ACGT environment. On the other hand the non-IT end user services are more fragmented and hence at the present point in time support only simple operations. The consortium is aware of this and as partners are gaining confidence in the underlying infrastructure more effort will be spent in the latter services. The ACGT competition is an additional measure that we hope will generate even more end-user applications.

2. **Technical issues**: While many of the lower level integration problems have been addressed it is accepted by the consortium that developing ACGT compliant applications is not an easy task. The experience of the development of the reference implementation has been documented but there is still a need for the preparation of additional materials that will make the entire experience for third parties smoother and more straightforward. It is felt that we will not be able to prepare all of these in the time remaining. As a consequence of this the ACGT Ready certification initiative has been dropped in favour of the ACGT Competition. (see more below)

3. **Competing efforts**: ACGT has been pursuing links with CaBIG and EGEE. To date these are still rather loose and limited to the presence of members from each consortium to events organised by the others and a general exchange of ideas and updates. WHAT ARE THE LESSONS we've learnt so far from these interactions?

4. **Critical Mass**: A concern from the previous reporting period was that "*ACGT [does not] represent enough critical mass in terms of both contributors to and users of the infrastructure and resources of the ACGT environment to help 'prime the pump'*". This is still true and as decided in v2 of the plan, the consortium has attempted to recruit third parties (both users and contributors) on a case by case basis. EORTC And the BIG initiatives are examples of actions taken to date. We will be able to report on our progress on these fronts at the end of the project.

5. **Anti spam laws**: while the Newsletter has continued to be produced on a regular basis the hoped for impact has not materialised. We believe that one factor that is certainly not contributing is the conservative approach taken with respect to our email campaign. We have adopted an opt-in policy rather than the more commonly accepted opt-out policy. While this is safer from an anti-spam perspective, it is much less efficient. As a consequence, circulation figures are rather low, as reported in the corresponding dissemination deliverable (D15.3). Compounding this is the rather small number of first level contacts of consortium members that have been the first recipients of the Newsletters (less than 1000). With the above in mind the PMB is strongly considering changing its policy from opt-out to opt-in. Given that at this point in time ACGT has more results that it can talk about and that a track record of previous issues has been established, it is felt that this is still not a bad point in time to make this policy change and hope to see results before the end of the project.

6. **Will we be around 'tomorrow'?**: This refers to a concern by potentially interested third parties whether the consortium and the ACGT infrastructure will be active after the end of the project. To date there is no firm commitment by any partner to maintain their part of the infrastructure. On the other hand we are pursuing the option of follow-on projects and proposals are being considered.

New Issues

7. **Legal Considerations**: At European level there is still great heterogeneity in the area of security and data protection regulations in medical networks. This makes European cooperation in the E-health area difficult, especially if genetic personal data shall be exchanged. Therefore ACGT developed a network that is compliant with the relevant European legislation. Part of the network is the newly created Center for Data Protection (CDP) that serves as a legal entity responsible for compliance with data protection regulations and serving as a legal entity to conclude the necessary contracts with. CDP offers its services to other European projects as well and will help to exploit the legal results of ACGT. In our view, this framework represents a good practice model with a great deal of exploitation potential not just for ACGT but rather for any other project related to the health care sector.

8. **Intellectual property**: ACGT has been analyzing the situation. As foreseen, IP-issues tend to be a hindering factor in data exchange: On the one hand participating clinicians have serious reservations against sharing (raw) patient data as their possession is an important (and not always legally protected) factor in scientific competition. On the other hand patients' (sometimes economic) interests in the outcome of the research are not always sufficiently covered by trial setups and results' exploitation. ACGT has been developing an analysis of the situation bringing decision makers into the position to allow patients and clinicians proper participation in the exploitation process. The outcome of our research can serve as a basis for

European project managers in the E-health area to identify intellectual property issues in an early stage of the project's lifecycle. Advice in this area is an (also commercially) exploitable result of ACGT.

5.2 Risk Factor Assessment

As stated in earlier versions of this document, by risk factors we understand events, developments or actual exploitation materials that can lead to a "below expectations" adoption of ACGT offerings and work. These risk factors represent technological, human, commercial and working environment parameters and are presented in Table 5.1. This table is reproduced from D16.2 with the last column ("Update") discussing each factor in view of the experiences of the third year of the project.

	Risk Factor	Check Point	Corrective Measure	Update
1	Preparation of exploitation materials falls behind schedule	Middle of year 2 and on a continuous basis thereafter	• Tight management schedule and reallocation of resources if and where appropriate	Production of these materials, namely the accompanying documents is less than what is ideally desired. This has become quite clear in the case of materials needed to support the ACGT Ready certification initiative which as mentioned elsewhere has now been abandoned.
2	Early prototypes fail to raise interest	At time of first deployment of prototypes – end of year 2	• Actions to elicit feedback for assessment of reasons for failure	The large scale prototype planed for May 2008 was created and demonstrated at Review 2. The consortium is now concentrating on stability issues. At the same time these prototypes have been put in the hands of end users and at the consortium meeting in Vienna (January 2009) tutorial sessions were run for their benefit. This and similar actions are considered necessary to help end users get started on the 'ACGT learning curve'.
3	Use Case studies not convincing	At time of first deployment of prototypes – mid to end of year 2	• Rationalization of case studies to ensure they represent clear, present and	We are constantly discussing and redesigning the usage scenarios and adding new ones. The consortium is

			important needs of ACGT's targeted end user communities • Involvement of further end user groups	also examining the requirements of the BIG initiative with the aim of providing a solution to a present issue they are addressing.
4	Final offerings fail to meet expectations	Years 3 and 4 of the project	• Report listing reasons of failure, lessons learned and recommendations for other groups	Not Applicable at this point in time.
5	Failure to identify and 'enlist' the most active PAGs	Year 3	• Assessment of reasons and new plan based on findings, to be implemented in year 4	The consortium has decided not to pursue this target group.
6	Legal/ethical impediments to widespread use	Year 3 once use of tools go beyond prototype demonstration phase	• Realignment of objectives and/or content of demonstrators • List of recommendations for s/w and other resource developers • Recommendations/requests to groups dealing with legal/ethical issues	Not Applicable at this point in time but see also relevant section below.
7	Personal agendas reduce adoption	End of year 3 and year 4	• Actions to assess reasons of failure • Realignment of demonstrators • List of recommendations for s/w and other resource developers	Not Applicable at this point in time.
8	Competing initiatives achieve critical mass or backing by important stakeholder groups overshadowing ACGT	Start of Year 3, once ACGT has obtained initial momentum and initial conclusions can be drawn. On a continuous basis	• Actions to assess reasons of failure • Intensification of effort to establish alliances and recruit early adopters. • Repeat of the ACGT Competition initiative	We have established links with other initiatives in the space (EGEE and caBIG) and a basic exchange of information provides the PMB with reasonable reassurances that ACGT is still competitive.

		thereafter.	in Year 4. • As a final measure towards Q2 of year 4, intensification of effort to align ACGT with those initiatives ("If you can't beat them, join them" tactics)	
9	Awareness efforts lag	End of year 2 and on a continuous basis thereafter	• Identification of new target groups to contact • Follow up actions with initial contacts • Assessment and corrective actions by the PMB	By now ACGT consortium members have published and presented at a reasonable number of events. However even though visits are increasing, there is some concern about general visibility as this is captured by the traffic of the ACGT web site. The consortium has considered adding entries to Wikipedia which help increase overall visibility and awareness.
10	Technological developments in the area of Grid services render ACGT options obsolete	Year 2 and on a continuous basis thereafter	• Recommendations for adoption of alternative technological base	There is already talk (e.g in the recent calls for EC proposals) of 'cloud computing' as the next thing to follow the 'grid'. It is still early days and at this point 'cloud computing' might only confuse potential end users. In the end of the day the PMB believes that the winners will be those who offer useful services in a transparent and well integrated manner.
11	Failure to convince 3rd parties s/w providers to contribute to ACGT	End of Year 3 and beyond	• Assessment of reasons and recommendations for corrective measures • Search and selection of additional 3rd parties whose priorities align with ACGT	We are still lacking sufficient materials and critical mass that would convince 3rd parties to develop ACGT compliant resources and services. The PMB is hoping that the competition will address this to a certain extent.
12	Working environment and administrative complications	Year 2 at time of deployment of first prototypes in	• Assessment of reasons, recommendations for corrective measures	The PMB is still not able to assess this at this point in time. We consider the BIG opportunity discussed at

	hinder adoption	ACGT user partner working environments and on a continuous basis thereafter	and where appropriate relevant guidelines • Possible changes to case studies and/or prototypes	the Vienna CM in January 2009 as an important challenge in this respect. A task force has been set up to work on it and we will report in the net version of this plan.
13	Legal and ethical considerations provide larger than expected restrictions	Year 2 at time of deployment of first prototypes in ACGT user partner working environments and on a continuous basis thereafter	• Report on exact nature and reason of difficulties. • Recommendations for action. • Reports to appropriate legal/ethical committees	Significant output is being generated by the consortium. It is felt that at this point in time, it is not possible to deploy a European wide solution easily. However the consortium has been acquiring experience in how to navigate these waters and we report in the deliverables of WP!0 as well as in the relevant section below.

Table 5.1: Exploitation Plan Risk factors - update

In summary at the end of the third year of the project, we are still faced with the issues identified in the previous version of this plan. The PMB's present decision and course of action is to focus on a narrower set of objectives (still pretty challenging) in order to demonstrate the fundamental utility or not of the infrastructure and services developed. It is felt that the present version of this plan reflects this decision and shows how to achieve the present goals.

6 Exploitation Plan for 2009 - 2010

The results to date and issues encountered during the third year of the project have necessitated and adjustment to the second version of exploitation plan as described in deliverable D16.2.

In this section we discuss the changes decided by the PMB as well as the actions selected from the analysis of the exploitation options discussed in chapter 4.

1. **Push for additional higher level services**: This is still a goal for the final period of the project. The consortium will continue to work on usage scenarios that are compelling for the end user. At the same time scenarios that illustrate the usage of the lower level resources of the infrastructure will continue to be pursued so as to encourage third parties to develop ACGT compliant resources. This is also necessary as background work that will support the ACGT competition (see below)

2. **ACGT Competition and ACGT Ready Initiatives**: The PMB has decided to drop the ACGT Ready initiative mainly due to the large set of documentation required to make this possible during the term of the project. On the other had the ACGT Competition is still considered viable and the necessary work will begin in Q2-Q3 of 2009. Given the 6 month extension to the project, the competition itself is now expected to take place early in 2010.

3. **Capture the experience from creating the reference implementation**: As a first step to creating the necessary documentation that will be required by third parties (both s/w contributors and end users) it has been decided to capture the experience for the creation of the reference implementation. This document will aim to present the technical problems encountered and the solutions adopted, highlight potential pitfalls, list all the underlying tools that need to be in place before ACGT compatible services can be made to work and in general help third parties with the installation and deployment of their own services. This is an arduous task involving the close collaboration of technical experts in more than one partner organizations. This effort is planned for the first half of 2008 and will result in a technical deliverable that will be publicly available.

4. **The ACGT Video**: Following the consortium meeting in Irakleio (Sept 08) the PMB confirmed its intention to develop the ACGT video. An experienced partner (CAID www.caid.gr) has been identified and a number of bilateral meetings already held with the goal of defining the scope, target audience and other relevant parameters of the video (see also Appendix A). The production cost (estimated at roughly 30-40K Euros) will be secured from the reallocation of funds from existing partners. The PMB will also decide whether to produce a single video (aimed at the general public) or two videos, with the second aimed at clinicians.

Additional tasks

We list below specific tasks that correspond to each of the items in column 3 of Tables 4.1 and 4.2 of Chapter 4.

- **I1:** Review and where necessary prepare additional documentation relating tot the infrastructure and architecture so as to support s/w developers.
- **I3:** Review, organize and present tools that support the development of ACGT compliant services. Collaborate with WP14.
- **I4**: Explore the possibility to obtain official partner commitments to support their part of the ACGT infrastructure.
- **I5**: Document and present visibly in the web, portal and other access points the relevant standards with which each system module complies.
- **I6:** Test extensively and document robustness related problems and fixes where appropriate.
- **I7:** Organise the ACGT competition – create a competition category that focuses on supporting tools for s/w developers. Continue pursuing the EORTC, NeoBIG and University of Saarland end-user case studies.
- **I8:** If possible gather service performance related data and present them in easily digestible format.
- **I9:** Make the existing services monitoring system more prominent and open for public access.
- **I10**: Implement a “service search” module and integrate it with the Portal.
- **I11:** Aim to run the ‘usage scenarios’ with ‘live data’ and document experience as case studies.
- **I12**: Create a category in the ACGT competition for end user applications.
- **I13:** Create more supporting materials for the end user applications (coordinate effort with WP14)
- **I14**: IF possible attempt to integrate with a legacy system in one end-user environment. Document the experience.
- **I16 –I17**: Define metrics, create and organize tests as applicable, conduct tests and report findings. Collaborate closely with WP13.
- **I18:** Create a log of use and provide some basic access to it
- **I19:** In collaboration with WP13 create relevant evaluation questionnaires, analyse results and present in format for end user consumption.

- **I20:** High level documentation to support local installations.

- **I21**: Where possible, obtain collect and present in appropriate format official partner commitments to technical support of services they are offering.

The tasks discussed above will be pursued during the final period of the project.

7 APPENDICES

Appendix 1: The ACGT Video

The ACGT video is considered as an important instrument for promoting the entire work of ACGT and attracting in the future additional interest in the general space of clinic-genomic trials and supporting technologies. To date a number of meetings have been held at the PMB level as well as between the exploitation work package and the third party (CAID www.caid.gr) that has been selected to undertake its production.

The objective of the meetings so far has been educational for both parties: CAID experts have been introduced to the scope and goals of ACGT, while ACGT members have been 'educated' on some basic parameters, capabilities and limitations of story-telling and video production.

The table below lists some of the main issues that are pertinent to our case and our current initial choices:

ISSUE	**INITIAL DECISION**
Goal of the video	To create broad awareness of ACGT work, drive enquiries from potential interested parties and generate support for continuing the work
Scope of content	Present challenges with clinical trials and bio-research and the possible role of IT in achieving better patient care
Target audience	General public, clinicians and bio-researchers
Main message	Clinical trials contribute significantly to better therapies but there are challenges to solve. IT infrastructure and systems are making significant advances and support post-genomic CTs. Optional: There are still legal and ethical complications at the EU level.
Materials to use	Interviews with ACGT participants including: M. Tsiknakis, N. Graf, C. Desmedt, N. Forgo, S. Rueping and others. Possibly free materials (computer animations) on the diseases or IT infrastructure
Visually appealing materials	Obtima, Oncosimulator, Workflow editor
Duration	20-30 minutes
Dissemination channel	European TV channels and the EC
Language / Subtitles	English / German and French
Shot on location?	Yes, as the budget allows
Use of animations and other 'enhancing' materials	Budget allowing
Is the video is person, task centric or technology centric?	Task and technology
Use a professional science narrator/presenter?	Being considered. Will depend on cost.

The Video Storyline

The storyline describes the content and flow of the 'story' being told by the video. It has to be engaging, flow naturally and be complete in terms of the message to the audience.

To begin with, we aim to produce a video to inform the general public but also to introduce clinicians to some of the possibilities that the ACGT infrastructure has to offer.

The following list shows the main elements of the video 'story'

- Possibly start with a patient story
- Scenes from the hospitals / bio-research labs / IT labs?
- Patients appear in video? Do they tell their story?
- Some complex diseases can benefit from technologies and resources that are geographically scattered – if only we had integration now…
- Examples of data and resources… maybe some biology here that is also quite visual? Visits to 1-2 labs
- The problem of data access/integration
- Privacy issues
- The ACGT s/w tools to address all this
- The closing concept? What message do we leave the viewer with?

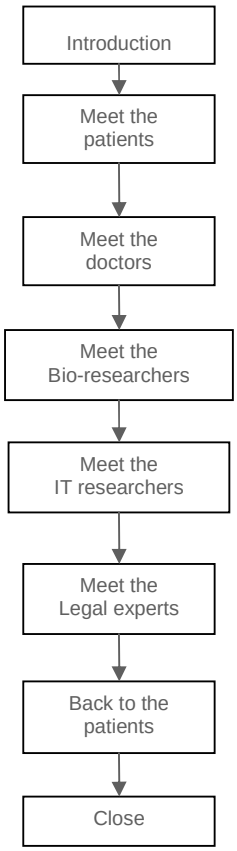
The following list shows the main introductory messages and the sequence of presentations:

- Drug development has given us many success stories and advances recently but if you think about it Drug Development is about managing the unknown
- Our knowledge of biology, disease mechanisms and drug action is incomplete and patchy. At the same time many diseases, as indeed the human body are highly complex. We often think we have it right only to be proven wrong when the drugs are given to the public
- In the age of "big data science" pharmas, doctors and bio-researchers are turning to IT for support
- This is the 'story' of an EU project that aims to provide such support using advanced grid, modeling, simulation, data exchange and other technologies
- Interviews with various stakeholders with opportunity to present issues and needs from their own perspective
    - Meet the patients (this is contingent on a number of factors)
    - Meet the doctors
    - Meet the bio-researchers
    - Meet the IT experts
    - Meet the legal/bioethics experts

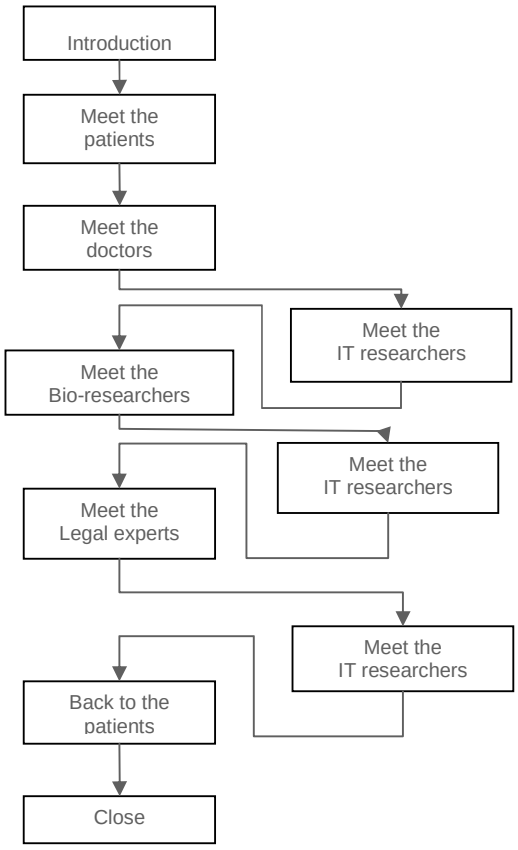
The following concluding message is foreseen:

- Back to the overall picture
- Our ability to heal is increasing
- IT technologies are leveraging existing knowledge to accelerate our learning and drug discovery process
- We are living in the 'Big data science' era and this needs sophisticated IT tools access, integrate and analyze this for better use
- We also need to harmonize standards procedures etc at the EU level to allow all this to happen
- Closing remark: Patient X has good reason to feel hopeful …

There are also options on the sequence of presentations and below we recognize at least 2 that will be considered: the linear and the interlaced sequences:



Linear sequence



Interlaced sequence

In the 'interlaced' sequence the relevant IT systems, services and interviews follow the presentation of each end-user presentation (doctors, bio-researchers, legal experts) linking directly the various challenges with their IT solution.

Appendix 2: The STARC initiative

STaRC is an initiative originally conceived by the University of Saarland (Prof. N. Graf) based on the experience of ACGT and some of the challenges that have been identified by the consortium so far, in connection with the deployment and uptake of ACGT services and infrastructure by third party stakeholders, in particular hospitals and clinicians involved in Clinical Trials.

Background and Experience to date

Despite recent advances clinical care of patients still faces a number of non-medical challenges that hinder the more rapid deployment and use of supporting systems that could eventually lead to better health care. The following is a list of some of the more important ones:

On the physician side:

- There is a time lack for physicians being kept informed about all the new developments in medicine, even in their specialized field. Every week hundreds of new papers are published. To find the most relevant, to read them all and to judge them as important for the own work is impossible.

- Today teamwork is of utmost importance. No physician is able to treat a patient with cancer by his own. He always has to communicate and work together with other specialists in medicine. As a result a lot of so called Cancer Comprehensive Centres are established to facilitate the interdisciplinary work. But up to now no IT infrastructure is supporting this by storing all relevant data in a database, so that every treating physician will have immediate access to the history, diagnosis, treatment and other relevant data of patients in an anonymous and secure way.

- Physicians do not get feedback of how efficient they are working. They do not have any statistics regarding the survival of their patients compared to the survival of all patients with that kind of cancer. There is no benchmarking telling them they are doing good or bad.

- Physicians do not know about the possibilities of modern IT technologies that could help them to support them in daily care of patients, or in developing new clinical trials. The lack of this knowledge leads to a lack of requests and requirements to IT people for the creation of new and user friendly tools in this respect.

- Physicians do not (want to) enter patients in clinical trials because they are not well informed about the meaning and impact of clinical trials (fear of experiments with their patients, simply not used to enrol patients in clinical trials, etc.)

- In most curricula of Medical Schools Clinical trials are missing, so that students will not learn about the benefits of clinical trials

On the patient side:

- Only a minority of patients are enrolled in prospective clinical trials. The reason for this is manifold:
- As explained in deliverable 2.4 Chapter 2, the conduct of investigator initiated trials in Europe is characterized by redundant paperwork, liability tangles and unending bureaucracy.
- There is no financial and/or administrative support to cover the overhead of clinical trials
- The burden of European regulations contrasts the available resources to increase the number of new clinical trials
- Infrastructures in hospitals or outpatient facilities are lacking (no data manager, etc.)
- Patients do not want to enter a clinical trial, are not informed at all about clinical trials or in the best case are simply not well informed about the meaning and impact of clinical trials (fear of taking part in an experiment, etc.)
- Today patients do use the internet to get information about their disease. There is no way how a patient can trust such information. Often information is contradictory and alienates patients. Even if patients do find relevant information, they may not understand the medical language used in these information. More patients are asking for second opinions regarding their disease. This is time consuming for physicians, expensive for the health care system and often unsatisfying for patients. They often get different and contradictory answers resulting in the question: “And what should I do now?”
- There exists no database for clinical trials with an easy way of access for physicians or patients in Europe. This is unacceptable for two reasons:
    - A physician is not able to find the best trial that fits the need for his patient
    - A trial chairman might build a new trial that is still running by another physician

Some of these challenges are addressed by ACGT. ACGT provides a platform by offering an IT-infrastructure that facilitates the creation and running of Clinical Trials. Beyond that the seamless integration of heterogeneous data from molecular biology, imaging and clinics is given making it possible to run queries across different trials. ACGT is in line with the legal and ethical regulations and provides tools – like ObTiMA –helping end-users in conducting clinical and clinico-genomic trials. As a result many requests are coming from scientific and clinical societies or research groups to use ACGT for running clinical trials. There are always two major concerns about ACGT: maintenance and sustainability

No clinician or end-user will work with real data in an infrastructure that does not guarantee the maintenance of data. On the other hand, without the use of real data the ACGT infrastructure can not be validated in a clinical setting. Therefore the following clinical scenarios, trials and registries are more or less piloting the usability of ACGT for clinico-genomic trials.

It is also obvious that maintenance and sustainability always need a staff of people dealing with the needs of users in ACGT. ACGT can not run by itself. Access to ACGT has to be monitored, a submission system for the Ontology is only part of the task to keep the Master Ontology updated on a regular basis, new tools are required for analyzing data by increasing the number of clinico-genomic trials and because of progress in science, etc.. None of these processes runs automatically. If there is no support in this regard, ACGT can not be sustained. Self standing tools and software need glue to build an IT infrastructure that is usable in the future. Such a structure may also provide a basis for all kinds of information regarding clinico-genomic trials throughout Europe. At the moment such a kind of comprehensive information is lacking. For example there is no access to the EudraCT database available to the public, meaning that a clinician can get no info what clinical trials are open for entering his patients. Asking for such information from EMEA, the following answer is provided by email:

> Access to the EudraCT database is unfortunately not available to the public. I would therefore recommend you contact an EU Member State Competent Authority for guidance on this issue.
> For contact details for all EU Member State Competent Authorities (Human & Vet), please see the link below:
> http://www.hma.eu
>
> For clinical trial information in European countries, outside of the EU, please contact each country respectively. A list of all European countries, that are not in the EU, is available on the following link: http://www.europa.eu/abc/european_countries/index_en.htm
> (Please see sections "Candidate countries" and "Other European countries")
>
> Should you have any further questions or queries, please feel free to contact me.
> Kind Regards,

The creation of a Study, Trial and Research Centres in Europe can exploit clinical relevant aspects of ACGT. The name of such a 'Study, Trial and Research Centre' can be STaRC.

Figure A2-1: Logo of STaRC

The main tasks of STARC are:

1. Simplification of the clinical trial process
2. Patient empowerment
3. Combining clinical and molecular biological and genomic data in single patients leading to personalized medicine
4. Facilitating translational research
5. Continually improving curricula of medical schools and medical education

Figure A2-2 gives all tasks of STARC.

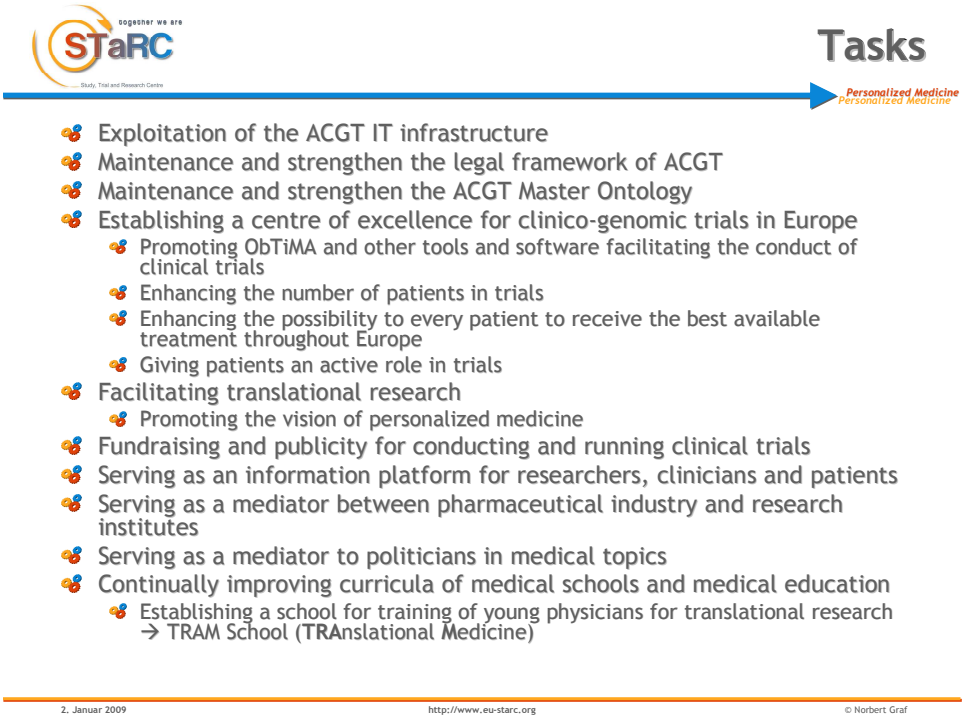


Figure A2-2: All tasks of STaRC

The structure envisaged for STaRC is that of a CRO (Contract Research Organization) (figure 3) that can easily work together with other Organizations, Registries and external Centres. STaRC is more than a Comprehensive Cancer Centre (CCC), because of the following reasons:

1. it will deal with patients having cancer and all other kind of diseases
2. it is also a research organization fostering translational research
3. it has educational and teaching aspects

4. it links patient care with research and teaching
5. it has an IT infrastructure
6. it has a structure to provide help for patients throughout centres and countries within Europe
7. it provides a security framework for patients
8. it empowers patients
9. other organizations and pharmaceutical companies can cooperate

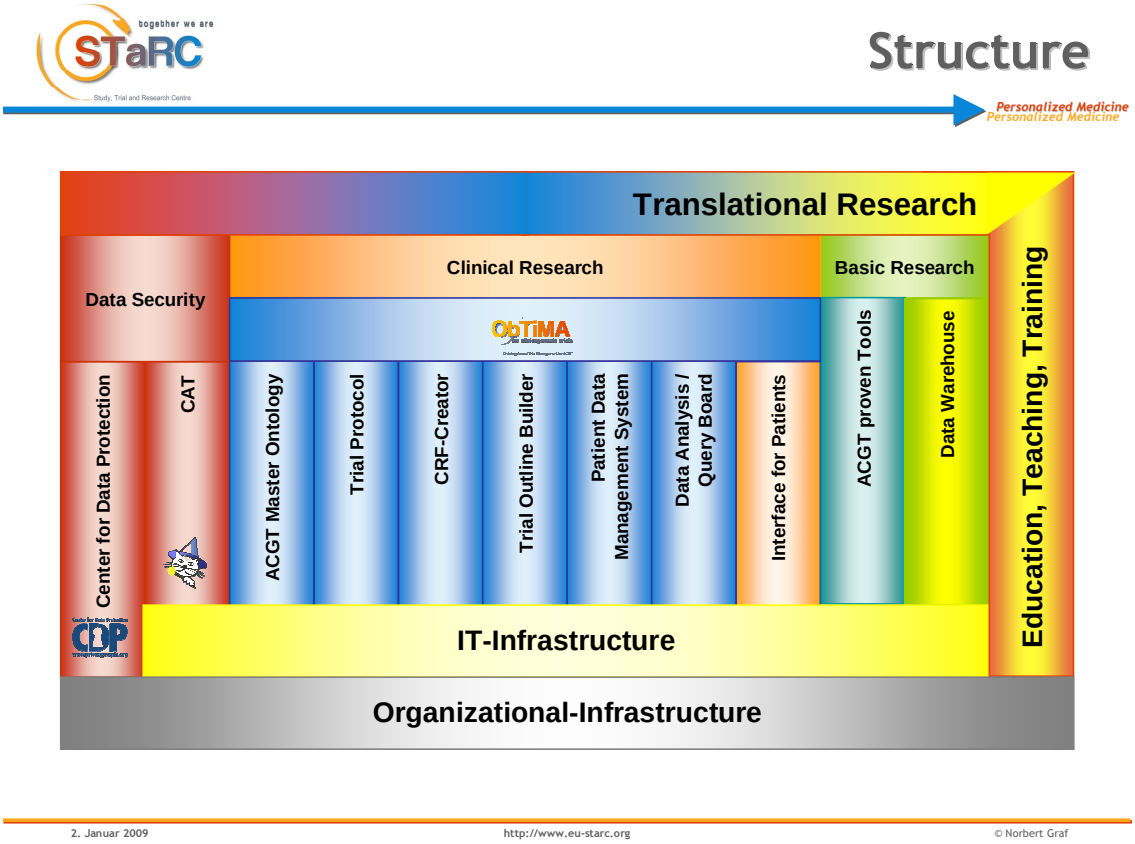


Figure A2-3: Structure of STaRC.

One of the most important software tools for running clinical trials is ObTiMA (Ontology based Trial Management Application). ObTiMA is an open source software developed within ACGT by different partners based on the idea of Norbert Graf:

- Fraunhofer, IBMT in St. Ingbert
- Foundation for Research and Technology Hellas (FORTH), Institute of Computer Science, Vassilika Vouton P.O Box 1385, GR-71110 Heraklion, Crete, Greece
- Meme Media Laboratory, Hokkaido University N-13, W-8 Sapporo, 060-8628 Japan

This software will be used in STaRC to run clinical trials. A proposal for the organizational infrastructure is given in figure A2-4.

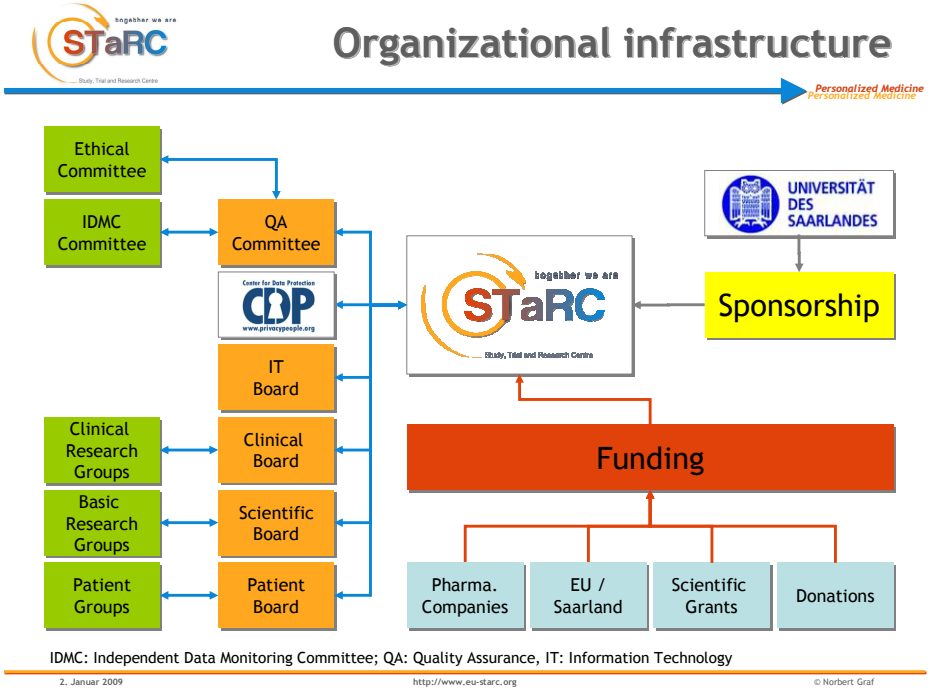


Figure A2-4: A proposal of the organizational infrastructure of STaRC

This proposal is under discussion to find the best infrastructure for starting STaRC. There is a great chance to develop STaRC in a way that it will get a Centre for running clinical Trials within Europe. The University of the Saarland, Custodix, the 'Center for Data Protection' and the Meme Media Institute at the University of Hokkaido, Japan are agreeing to build STaRC in the Saarland area. A close connection to the University of the Saarland is attempted by the Medical Faculty.

Partners that have expressed interest to be involved in STaRC are:

- University of the Saarland (Medical Faculty (Dep. Paediatric Oncology), IFOMIS, Fraunhofer (IBMT))
- Biovista, Athens, Greece
- Custodix, Brussels, Belgium
- FORTH, Heraklion, Greece
- University of Hokkaido, Japan, UoH
- STaRC will be leaded by the Dep. of Paediatric Oncology and Haematology.

In STaRC three main topics are identified for exploitation of ACGT results. These topics are

- Service
- Research and Development (R&D)
- Education, Teaching

The proposed involvement of the different partners to the 3 topics is given in Table A2-1.

Service	Research & Development	Education, Teaching
UdS	UdS	UdS
Custodix	IFOMIS	
(IFOMIS)	Fraunhofer	
	FORTH	
	UoH	
	Custodix	
	Biovista	

Table A2-1: Participation of the different partners in the 3 identified topics.

Appendix 3: Study of nephroblastoma antigens using literature mining services

In this usage scenario, partner University of Saarland used the literature mining services to assist the research and discovery process related to the study of nephroblastoma antigens. The following is a brief account of the work performed:

After the nephroblastoma antigens were identified in the first pool of sera, blood from 16 patients was analysed and a set of 16 antigens with a frequency between 6,25% and 62.5% positive clones were detected and reported in January 2009.

The literature mining services were used to identify specific literature as well as undiscovered relations out of literature concerning cell pathways, genomics and diseases related to the antigens. The performance of the search was done for each antigen in relation to the different classes offered (e.g. Genes, Pathway, Diseases, etc), the relation between the antigens and the relation between antigens and diseases and anatomical structures and tissues.

Over- and under expressed genes, already published in context of Nephroblastoma were analysed. The main benefit obtained was the possibility to discover literature references for antigens related to topic and terms that are often used in literature in the context of Nephroblastoma (e.g. Wilms tumour, WT 1, WT 2, Kidney, etc…). During the work with the literature mining services, it became clear that not all of the Antigens are published already. Nevertheless the possibility to add new items to the database and search literature giving these items a class was very user-friendly. One problem is the different typing and nomenclature in literature. The rapid change in nomenclature and individual typing is not a real problem but it takes time testing if items can only be found using different spellings.

In the next step two novel analysis tools Genetrail (http://genetrail.bioinf.uni-sb.de/) and Webgestalt (http://bioinfo.vanderbilt.edu/webgestalt/) were used to further characterize the antigens and to find significant statistical entries in established biomolecular databases (e.g. KEGG-Pathways, Transpath-Pathways, Transfac, DIP, HPRD, INTACT, etc.). The results of these data searches will be included in the literature search as well, once they are interpreted.

During the usage scenario, the literature mining service was used for daily work under special circumstances as well as to discover its potential in identifying relevant literature in rare oncological diseases. Literature in the context of medical procedures and therapy for rare diseases could be reviewed in a very efficient way and the tool was found to help in daily medical work.

One important lesson learned was that in leading edge research, the ability to deal with new ‘entities’ such as new genes etc. is an important requirement for semantic-based systems. The Master Ontology submission system, the Ontology Viewer and all tools that use such entities must therefore be able to deal with new entities in a seamless, consistent and user-friendly way.

Appendix 4: CDP letter of support to iLINK proposal

3/27/2009

To whom it may concern

Letter of intent

Dear Madam, dear Sir,

herby I may certify that the Center for Data Protection – a nonprofit organization under Belgian law committed to data protection and data security – is willing and able to serve as a data controller and/or legal entity for contracts to be concluded on data protection and data security within the iLink consortium. We strongly support the consortium and the project's goals.

Prof. Dr. Nikolaus Forgó

Appendix 5: Person-Month Allocation for Year 4

During period 3 most partners did not use their planned resources for exploitation. Once again most effort is spent on resolving technological issues. For the final period of the project the total allocated PM effort is 34.7 PMs as shown in the Table below:

PARTNER	PMs
ERCIM	1
FORTH	3
INRIA	0
UvA	0
PHILIPS	0.5
UB	2
SIB	1
LUNDU	0
UMA	0
UPM	0
FHG	3
BIOVISTA	9
UOC	0
UHANN	1
PSNC	2
CUSTODIX	2
HEALTHGRID	3
ICCS	1.2
USAAR	2
SIVECO	2
FUNDP	0
UH	1
UOXF	0.5
UHOK	0
IEO	0.5
TOTAL	**34.7**

Appendix 6: Partner Contact Persons for Exploitation Issues

ORGANIZATION	#	NAME SURNAME	POSITION	EMAIL	TEL
ERCIM	1	**Remi Ronchaud**	Project Manager	remi.ronchaud@ercim.org	+33 4 92 38 50 12
FORTH	2	**Manolis Tsiknakis**	Principal Investigator and Leader	tsiknaki@ics.forth.gr	+30 2810 391690
FORTH	2	Angelina Kouroubali	Affiliated Research Scientist	kouroub@ics.forth.gr	+30 2810 391680
PHILIPS	5	**Erwin Bonsma**	Senior scientist	erwin.bonsma@philips.com	+31 40 27 42675
PHILIPS	5	Anca Bucur	Senior scientist	anca.bucur@philips.com	+31 40 27 44609
Jules Bordet Institute	6	**Christine Desmedt**		christine.desmedt@bordet.be	+32 2 541 31 07
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