EUROPEAN COMMISSION
Information Society and Media Directorate-General

ICT addressing Societal Challenges
ICT for Health

Brussels, 09 MARS 2009
DG INFSO-H1/ RB/egc D (2009) 110087

Mr Remi Ronchaud (ACGT)
ERCIM
Route des Lucioles, 2004
F-06902 SOPHIA ANTIPOLIS
FRANCE

REGISTERED MAIL

Subject: Contract No. IST-2004-026996 Project ACGT
Outcome of the fifth Review held in Brussels on 10th December 2008

Dear Mr Ronchaud,

I refer to the fifth review of ACGT project which was held in Brussels on 10th December 2008. The review report, giving in full the findings of the review session, is enclosed. In their report, the reviewers' overall assessment for ACGT is a good to excellent project and the reviewers confirm all the submitted and reviewed Deliverables are approved, except:

- D15.5 "Revised Dissemination Plan"

and they recommend that the project can continue without modifications.

The Commission is in agreement with the review report and requests the consortium to address all its comments and recommendations. The Commission also requests the consortium to submit revised version of the rejected Deliverable by 27 March, 2008.

In view of the above, the Commission considers that the consortium is performing well and that the project can continue accordingly.

Please acknowledge receipt of this letter and inform your partners of its content.

Yours sincerely,

Ragnar Bergstöm
Project Officer

Enclosure: Review report

c.c.: *Mrs Tuula Hyorinen, Mr Gérard Comyn*

Commission européenne, B-1049 Bruxelles / Europese Commissie, B-1049 Brussel - Belgium. Telephone: (32-2) 299 11 11.
Office: BU31 6/46. Telephone: direct line (32-2) 2956415. Fax: (32-2) 2960181.

E-mail: ragnar.BERGSTROM@ec.europa.eu

Consensus

Project Review Report (FP6) for NoE / IP

Project no	IST-2004-026996
Project acronym	ACGT
Title	Advancing Clinico-Genomic Trials on Cancer: Open Grid Services for Improving Medical Knowledge Discovery
Instrument type	Integrated Project
Thematic Priority	Information Society Technologies – ICT for Health
Start date of project	1 February 2006
Duration of project	48 months
Total Budget	16,747,206€
EC contribution	11,887,000€
Date of review	10 December 2008
Place of review	Brussels, Belgium
Period covered by review	from 1 February 2008 to 31 October 2008
Coordinator name	Remi Ronchaud
Coordinator organisation	GEIE ERCIM
Name(s) of reviewer(s)	Elena Tsiporkova - Olle Björk – David Ingram
Name of rapporteur	David Ingram

1. EXECUTIVE SUMMARY

With a short description on what the project is about. Includes key results and overall comments on the project's technical progress, management, and exploitation and whether it should: proceed as is, or proceed with some modifications, or whether remedial action is needed.

The ACGT project aims to deliver the cancer research community an integrated Clinico-Genomic ICT environment, through an integrated workplan. The environment is being validated with three ongoing clinical trials on cancer. Progress is demonstrated at each review through a series of key exemplar applications that are progressively integrating an innovative approach, deploying a new high level master ontology focused on clinical trials.

This is the fifth review of the program and progress has been demonstrated at each review. The end result of the project will facilitate connection and integration of different clinical research projects. It is a base for a pan-European project or even local or hospital based clinical research. In the past reviews it was discussed that it is important to test the ACGT in realistic clinical environments. It was also discussed that a wider dissemination of the project is necessary to receive information and evaluation from potential end users.

The momentum of the project remains good and a good communication environment has been sustained through the consortium, with deliverables delivered mainly on time. In this review period, a range of new clinical test scenarios has been explored and detailed discussions started with relevant partner organisations that might become involved in the wider evaluation (eg EORTC) and use and dissemination (eg BIG and SIOP) of the infrastructure. As reported before, maintaining the Obtima trial builder as a main driver of clinical research community engagement is necessary if the complexity of the tasks is to be kept under good control with implementable solutions that work in real life. Progress in implementation of the Obtima administrative functions was demonstrated but the development of the Hokaido graphical interface for mapping phasing and progress of clinical interventions is not yet showing substantive progress.

The documentation of the Master Ontology (Del. 7.5) has been improved, as recommended in the previous review. The structure, completeness and scalability will require ongoing evaluation as the full range of functions supported by the ontology are implemented and tested. The extension of the ontology to new cancer domains will certainly be facilitated by introducing modularity, i.e. splitting the Master Ontology in a set of smaller ontologies, which are relatively easy to maintain and validate. There was some indication that clinical investigators are finding the ontology difficult to work with and thought is being given to a user interface that invokes sections of the ontology, but accessed and controlled through more clinically understandable terms and categories of information. This new approach needs to be handled with care as it may also affect consistent query generation, as well. A comparative evaluation of the ontological foundations of ACGT and CaBIG is a high priority for completion within this project.

The project remains at a crucial stage, consolidating progress, looking inwards, and building sustainable partnership, looking outwards. For the remainder of the project, we recommend restricting new activity, focusing on completing existing workplan functionality to a level that can reasonably be disseminated, in modular fashion, to new collaborating centres. We also recommend focusing on a small and synergistic set of external partnerships. The leadership and motivation of the consortium continues to be outstanding. A 6-month extension of the project is highly desirable. We strongly support this and understand it can be achieved within the existing resource framework.

2. ORGANISATION AND LOGISTICS

Comments on the review meeting: Were timing and schedule adequate? Were copies of the slides distributed in advance? Were demonstrations performed well?
Comments on the reports and deliverables received: timely reception, completeness, had the reviewers enough time to study the documentation?
Comments on the partners present at the meeting: were all there? (See list of participants, list of reports and deliverables & agenda (appended to this report)).

Comments:

All aspects of the review meeting were excellently managed. The demonstrations had clearly been a huge team effort and we congratulate the team on these efforts.

Documentation was delivered rather late, considering the amount of material required to be assimilated by the reviewers. In general there is still a tendency to repeat too much of the material. A number of detailed recommendations were made at the meeting, as discussed throughout this report.

The plans for an advisory board for the ACGT should, in time, also include representation from key partner organisations such as EORTC, BIG and SIOP.

The consortium, as always, presented professionally and the dialogue with reviewers worked well. The relevant partners were represented at the meeting.

3. OVERALL OBJECTIVES OF THE PROJECT

Have the main objectives for the period been achieved?

Yes ☒ No ☐ Partially ☐

Comments:

The end point is well understood and steps are being taken to focus on engagement with the wider community of cancer clinical trials. There remains a significant gap between the perspectives of users in real clinical trials environments and the more technical preoccupations of the project.

Are the project's objectives (a) still relevant and (b) still achievable within the time and resources available to the project?

(a) Yes ☒ No ☐ Partially ☐

(b) Yes ☐ No ☐ Partially ☒

Comments:

The relevance is indisputable but usability remains an issue. In narrowing the scope of future technical innovations, clinical trials and organisational partnerships, it is hoped that the remaining considerable challenge of optimising the master ontology, trial builder and security management can be met, within the context of an external critical review by new partner organisations and detailed evaluation by end users based on practical usage.

The full development, dissemination and exploitation of the ACGT infrastructure is clearly a 5-10y endeavour and will require a detailed business and scientific strategy – embracing formal organisational partnerships, commercial activity and participation in open scientific communications. It remains important to make sure that goals are realistically prioritised so that the really important practical outcomes that are looked to from this project are not compromised by spending too much resource on goals that will take longer to achieve. The project needs to leave a solid platform for what comes next and capturing fully the knowledge gained within the consortium is essential for this.

Do you recommend changes in the objectives of the project in order to keep up with current state-of-the-art?

Yes ☐ No ☒ Partially ☐

Comments:

See above comments

4. PROJECT WORKPLAN AND RESOURCES

A. WORKPLAN

Has the project as a whole been making satisfactory progress, notably in relation to the Description of Work (Annex I to the contract)?

Yes ☒ No ☐ Partially ☐

Comments:

As discussed above, there is progress on all fronts, but with considerable technical, clinical research and organisational challenges still to be faced. Progress with the Master Ontology, Obtima and data security/confidentiality remains the main technical challenge. Securing relevant interest and participation remains the principal clinical research challenge. The oncosimulator and its related visualisation services are finding an increasing international framework of collaborative research for their future development.

Is the work planned in each work package (WPs) on schedule for the reporting period?

Yes ☒ No ☐ Partially ☐

Comments:

Some minor delays were noted; these were not considered significant to the generally timely advance of the work plan.

Have planned milestones and deliverables been achieved for the reporting period?

Yes ☒ No ☐ Partially ☐

Comments:

See above

Future workplan: Is the work-plan coherent and are the timing of milestones and future activities of the project still valid?

Yes ☒ No ☐ Partially ☐

Comments:

See comments from previous reviews; continues to plan

B. RESOURCES AND EXPENDITURES

Have resources been deployed as foreseen in Annex I, overall and for each participant (**see Table 3 - Budget vs. Actual Costs and Table 4 - Person-months Status Table from the Periodic Management Report**)?

Yes ☐ No ☐ Partially ☐

Comments:

Not applicable

Have expenditures been demonstrated as being economic and necessary for the work performed (Are expenditures consistent with the work achieved? Are the major cost items appropriate?)

Yes ☐ No ☐ Partially ☐

Comments:

Not applicable

5. WORKPLAN OF NoEs and IPs

A. WORK CARRIED OUT IN THE PREVIOUS REPORTING PERIOD

Has the overall *Implementation Plan* (IPs) or *Joint Programme of Activity* (NoEs) been adhered to as described in the *Description of Work (Annex I of contract)*?

Yes ☒ No ☐ Uncertain ☐

Comments:

See above

For NoEs: Is there evidence of real integration and restructuring of activities between partners (to be evaluated against Indicators of Integration, e.g. exchanges of personnel, shared infrastructures, joint research and training activities, changes of research orientation of individual partners to better integrate into the NoE, etc).

Yes ☐ No ☐ Partially ☐ Not applicable ☒

Comments:

B. WORK PLANNED FOR THE NEXT 18-MONTH PERIOD

Is the proposed update to the *Implementation Plan* (IPs) or *Joint Programme of Activity* (NoEs) for the next 18-month period satisfactory

a. from scientific/technical point of view

Yes ☒ No ☐ Uncertain ☐

Comments:

See previous comments. A detailed comparative evaluation of the ACGT and CaBIG project methodologies and implementations is highly desirable within the next project period.

b. from management point of view including use of resources

Yes ☒ No ☐ Uncertain ☐

Comments:

The project requires extension, which can, we understand, be achieved within currently allocated resources. The balance of future funding to the different activities should be reviewed in the light of the focus and prioritisation suggested in this review.

c. concerning non-scientific activities (dissemination, science-society issues, further integration etc)

Yes ☒ No ☐ Uncertain ☐

Comments:

There were good examples given of the project being presented at international meetings and in discussions with clinical trials organisations. The roles foreseen for the advisory board have been slow to develop. These should be easier to develop now that the project has a credible end-to-end demonstration and is showing evidence of engagement in alliances with other groups involved in cancer clinical trials and cancer research infrastructure. The modular structure adopted for services that might be fulfilled making use of the ACGT infrastructure will be important in maximising options for dissemination, through scalable and cost-effective partnerships.

6. CONSORTIUM PARTNERSHIP

Is there evidence of meaningful cooperation and integration between all the partners?

Yes ☒ No ☐ Partially ☐

Comments:

Again, this is a very commendable feature of the consortium, its partners, leadership and culture.

Have the partners contributed as planned to the project and tasks assigned to them?

Yes ☒ No ☐ Partially ☐

Comments:

Do you identify any conflicts or evidence of underperforming partners, lack of commitment or change of interest of any partners?

Yes ☐ No ☒ Partially ☐

Comments:

Do you recommend changes in partnership?

Yes ☐ No ☒

Comments:

The formal alliances with EORTC, BIG and SIOP are welcomed.

7. MANAGEMENT

Has the technical management performed as required (efficient, effective accomplishment of planned technical management tasks)?

Yes ☒ No ☐ Partially ☐

Comments:

The project exhibits strong and effective leadership.

Has the administrative and financial management performed as required (efficient, effective accomplishment of planned tasks, including proper handling of the consortium agreement, intellectual property rights, technical collective responsibility, sub-contracting, competitive calls)?

Yes ☒ No ☐ Partially ☐

Comments:

These aspects are also excellently managed, as evidenced, still, by an almost complete absence of problems in this area.

Has (electronic) information and communication networks been established as required to support interactive working between the teams involved?

Yes ☒ No ☐ Partially ☐

Comments:

The website, published material and BSCW server all seem to be good and working well.

Is the consortium interacting in a satisfactory manner with other related 5th and 6th Framework projects or other R&D programmes addressing aspects of ERA, e.g., EUREKA, eTPs, etc)?

Yes ☒ No ☐ Partially ☐

Comments:

Communication, meetings and new project proposals with other international consortia in this field.

8. USE AND DISSEMINATION OF KNOWLEDGE

Does the project have significant exploitation potential?

Yes ☒ No ☐ Partially ☐

Comments:

As fully discussed in previous reviews.

Is the Plan for the Use and Dissemination of Knowledge [please refer to the Guidance notes on Project Reporting in FP6 (Appendix 1) (see http://www.cordis.lu/fp6/find-doc.htm#reporting)] developing in a satisfactory manner?

Yes ☐ No ☐ Partially ☒

Comments:

See previous comments concerning slower than hoped for progress with advisory/governance structure for moving ACGT into a practical clinical trials phase of use. That said, the scope of the project is extremely ambitious and it is important to communicate about discrete, clear and demonstrable modules of the ACGT infrastructure that can bring specific added value to the wider research community.

Have the contractors disseminated project results and information as foreseen by the contract and the plan for dissemination and use of knowledge (publications, conferences…)?

Yes ☒ No ☐ Partially ☐

Comments:

See previous comments

Where relevant, are potential users and other stakeholders in the research being suitably involved in the project?

Yes ☒ No ☐ Partially ☐

Comments:

Wider engagement with potential end users and relevant research organisations is essential, as being pursued by the Consortium.

9. OTHER ISSUES

Can you identify any policy-related regulatory issues emanating from the project at this stage?

Yes ☒ No ☐ Partially ☐

Comments:

This matter was addressed in detail in previous review comments and the situation remains as set out there. The continued and practical progress of the project is heartening.

Has promotion of gender equality been successful?

Yes ☒ No ☐ Partially ☐

Comments:

See previous review comments

Have the science and society issues related to the topics of the Integrated Project been adequately handled?

Yes ☒ No ☐ Partially ☐

Comments:

Has the training programme being adhered to as described in the contract?

Yes ☐ No ☐ Partially ☒

Comments:

Some delay in this aspect, as discussed above.

Is the project fulfilling its contractual commitments, if any, concerning ethics and safety?

Yes ☒ No ☐ Partially ☐

Comments:

See previous comments.

10. OVERALL ASSESSMENT

☐ Unsatisfactory project (The project has failed to achieve critical objectives and/or is not at all on schedule)

☐ Acceptable project (The project has achieved most of its objectives and technical goals for the period with relatively minor deviations)

☒ Good to excellent project (The project has fully achieved its objectives and technical goals for the period and has even exceeded expectations)

Recommendations

☒ the project should continued without modifications

☐ the project should continue with the following modifications (technical or administrative):

The project should focus on testing and evaluation with real clinical data.

☐ the project should be terminated (list main reasons):

Are there other issues you wish bring to the attention of the Consortium and/or the Project Officer?

Yes ☐ No ☒

Comments:

11. VISIBILITY ACTIONS

Please flag characteristics of the project which may be of interest to the Commission's services and visibility actions:

☐ high visibility/media attractive project

☒ project with an impact on EU policies

☒ project with a major role for women

☐ project with a significant impact on health, safety, environment

☒ project with ethical issues associated

☒ substantial breakthrough character

☐ significant impact on employment

☐ significant participation from outside EU

☐ involvement of the top researchers in the field

☐ involvement of the top economic actors in the field

Comments:

Name(s) and signature(s) of the reviewer(s):

Olle Björk

David Ingram

Elena Tsiporkova

Date:

12. 3 APPENDICES

Appendix 1
Status and approval of project reports and deliverables

Deliv. number	Title	Status (submitted/ delayed)	Accepted/ Rejected/To be modified	Comments	Deadline for (re) submissions
D1.1.4	Six Monthly Progress Report (month 25 to 30)	submitted	accepted	Contains quite some typos, there is a considerable overlap and repetition between the different WPs achievements (e.g. WP2 & WP7 and WP15 & WP16).	
D2.4 (due month 30)	Report on additional user-driven scenarios in post-genomic clinical trails on cancer	submitted (30/11/08)	accepted	Exhaustive, clear and well motivated.	
D4.4 (due month 33)	Gridge-GridR integration	submitted (28/11/08)	accepted	No information concerning testing, evaluation and performance has been provided.	
D5.5 (due month 32)	Initial high-level model definition of an ACGT-specific Clinico-Genomic EHR	submitted (28/11/08)	accepted	Rather abstract and synthetic exposition. It is not clear how the proposed model of the Genomic EHR will be integrated with the rest of the ACGT framework.	
D7.5 (due month 32)	Demonstration of final mediation access tools and services	submitted (14/11/08)	accepted	The mapping process and the query building remain extremely complex for a user who is not acquainted with the principles of semantic mediation. Adequate training materials on the structure of the ontology and on the functionalities of the mapping and query tools are needed in order to make it possible for clinicians to perform meaningful data queries. Pages 19-20 contain a couple of sentences, which are probably user's feedback on the mapping tool. However these are not supplied with any explanation and seem out of context.	

D7.6 (due month 38)	**Prototype of the Ontology Submission subsystem**	submitted (18/11/08)	accepted	The prototype definition is well thought and sound. However it will not be trivial in practice to mobilise all the different users (contributors, ontology experts, domain experts) in order to guarantee consistent evolution and maintenance of the master ontology.	
D7.7 (due month 38)	**Design principles of the ACGT Master Ontology: Examples and Discussion**	submitted (December 2008)	accepted	The document is written in a quite philosophical and abstract style. The usage of a specific jargon does not make it really accessible for non-experts in ontology engineering. The **242** different relations used at present in the master ontology is quite alarming. One should carefully revise these and try to reduce their number by defining higher level relations, which could replace several of the existing relations.	
D8.3	**Report on the refinement and optimisation of the algorithms and codes, and the initial clinical validation and adaptation of the "Oncosimulator"**	submitted (15/09/08)	accepted	Major effort has been put into detailed sensitivity analysis of the model parameterisation. There is as yet rather little experimental evidence justifying how well the model mirrors and supports practical clinical management of cancer treatments. This should now become the main focus of work, so that appropriateness and utility of the model can be explored and improved.	
D9.4 (due month 30)	**Semantic Integration in ACGT**	**Delayed**			
D11.4	**Requirements and guidelines for developing secured ACGT services**	**delayed** (draft available)			

D12.6 (due month 30)	**Review and extension of the ACGT clinical studies**	submitted (28/11/08)	accepted	One needs to consider several alternative and statistically sound validation scenarios in the multi-centre and multi-platform study. Expression data for 75 patients might be not sufficient to perform robust supervised training and validation.	
D13.2	**Intermediate evaluation report** (*Overview of second integrated demonstrator of the ACGT platform*)	**delayed** (submitted partially December 2008)			
D14.3 (rejected previously)	**Demonstration and Report of training modules**	**delayed**			
D14.4	**Training workshop for end-users on ACGT Technologies & methodologies**	**delayed**			
D14.5	**Methodology for ACGT service integration in the ACGT portal on the Business Process Layer**	submitted (28/11/08)	accepted	Very exhaustive and well written document.	
D14.6	**First report on ACGT Portal usage, online training modules development and evaluation**	submitted (30/11/08)	accepted	One needs to devote more time on designing adequate usability questionnaires. The proposed version assumes that each clinician understands terminology as 'GUI', 'widgets', 'interface', etc.	
D15.4	**Organisation and report of a project Conference**	**delayed**			
D15.5 (rejected previously)	**Revised Dissemination Plan**	re-submitted (06/11/08)	**rejected**	The document is not of a vey high quality and appears more as a draft (see for example the bottom of page 21) than as a final version. The proposed dissemination plan remains vague and general.	

Appendix 2

List of participants

Name	Organisation
Anca Bucur	PHILIPS – Electronics Nederland B.V.
Remi Ronchaud	GEIE ERCIM
Manolis Tsiknakis	FORTH
Stelios Sfakianakis	FORTH
Radu Gramatovici	SIVECO ROMANIA
Brecht Claerhout	CUSTODIX
Luis Martin	Universidad Politecnica de Madrid
Andreas Persidis	BIOVISTA – A. PERSIDIS & SIA O.E.
Nobert Graf	USAAR – Universitaet des Saarland
Christine Desmedt (Monday & Tuesday only)	Institut Jules Bordet
Thierry Sengstag	SIB – Institut Suisse de Bioinformatique
Juliusz Pukacki	PSNC – Instytut Chemii Biooganicznej pan w Poznaniu
Stefan Rüping	Fraunhofer IAIS
Mathias Brochhausen	USAAR – Universitaet des Saarland
Nikolaus Forgo	UH – University Hamburg
Georgios Stamatakos	ICCS (NTVA) – Institute of Communications and Computer Systems
Lefteris Koumakis	FORTH
Alberto Anguita	UPM

Reviewers	
Ragnar Bergström	European Commission
David Ingram	Private Expert
Elena Tsiporkova	Private Expert
Olle Björk	Private Expert

Appendix 3
ACGT review meeting

European Commission, Avenue de Beaulieu 31, 1160 Brussels
Metro Beaulieu

AGENDA	
	SESSION I – Management Presentation of Project Progress
9:00 – 9:10	Opening of review meeting [Ragnar Bergström]
9:10 – 9:15	Introduction of project participants [Remi Ronchaud]
9:15 – 9:40	Project Contractual and Financial overview – [Remi Ronchaud] ➲ 15" presentation ➲ 10" discussion
9:40 – 10:05	Project Scientific and Technological Progress [Manolis Tsiknakis] ➲ 15" presentation ➲ 10" discussion
10:05 – 10:30	New Trials and Scenarios [Norbert Graf] ➲ 15" presentation ➲ 10" discussion
	SESSION II – Project Demonstrator
	The project will present progress towards its scientific and technological objectives by focusing on an integrated demonstrator supported by the ACGT platform. The demonstrator this time relates to important bioinformatics tasks. The demonstrator will be accompanied with focused presentations in an attempt to *reveal the technical and scientific issues addressed* and to discuss project progress beyond what has been shown in the Annual Review in May 2008. The demonstrator, together with discussions, is scheduled to take 1 hour and 30 minutes (i.e. 10:45 – 12:15)
10:30 – 10:45	***Short Break***
10:45 -11:00	Introduction of the MCMP Scenario [Thierry Sengstang] ➲ 10" presentation (Scientific background, what's new, etc) ➲ 5" discussion
Part A	Data mining of public data (independent bioinformatician) ➲ Creation of GridR-based service by Jane Doe o Download and use public data (upload in DMS) o Publication of newly created service in ACGT o GridR (interactive access through portal)
PART B	Mining of real data (bioinformatician attached to a clinical trial) ➲ Data integration and VOs o Real data are used

	○ Describe user creation and rights assignments ○ Data preparation steps (including legal aspects) ○ Anonymization process extended ○ Data access (BASE), extension to Illumina data : slides describing principles ○ Semantic integration : Ontology tool (Luis) ○ Mapping and query building tools ➲ Build-up of scenario ○ Service discovery ○ Construction of bioinformatics workflow ○ Presentation of workflow editor (new functionalities, easy!) ○ Demonstration of execution monitoring
12:15 – 13:15	***Lunch***
13:15 – 13:40	Status of the effort for incremental development and evaluation of the Master Ontology [Matthias Brochhausen] ➲ 15" presentation ➲ 10" discussion
13:40 – 14:00	Methodology for Third Party Service Integration [Stelios Sfakianakis] ➲ 10" presentation ➲ 10" discussion
14:00 – 14:25	Status of ObTiMA development [Norbert Graf] ➲ 15" presentation ➲ 10" discussion
14:25 – 14:50	Progress in the development of the Oncosimulator [George Stamatakos] ➲ 15" presentation ➲ 10" discussion
14:50 – 15:10	Main technical challenges addressed [Stefan Rueping] ➲ 10" presentation ➲ 10" discussion
	Session IV – Planning of activities for the next period
15:10 – 15:30	Short overview of the ACGT planning for the next reporting period [Manolis Tsiknakis] ➲ 10" presentation ➲ 10" discussion
15:30– 16:00	Reviewers' discussion (Reviewers and Commission only)
16 :00 – 16:15	Feedback and recommendations
16:15	Conclusion of the meeting ➲ Planning for the 3rd Annual Review