TECHNICAL REVIEW REPORT

Information and Communication Technologies
ICT

Project acronym:	CHIC
Project title:	Computational Horizons in Cancer:Developing Meta- and Hyper-Multiscale Models and Repositories for In Silico Oncology
Grant agreement number:	600841
Funding scheme:	Collaborative project
Project starting date:	01/04/2013
Project duration:	48 months
Coordinator:	Institute of Communication and Computer Systems National University of Athens (Greece)
Project web site:	http://www.chic-vph.eu

Period covered by the report:	Period No. 1, from 01/10/2013 to 31/03/2014
Place of review meeting:	Brussels
Date of review meeting:	03/09/2014
Experts:	*Tor BLOCH* *Henry KANOUI* *Jorge MARTINEZ de HURTADO* *Pirkko NYKÄNEN* *Elena TSIPORKOVA*
Project officer:	Dr Jaakko AARNIO

Individual report	☐
Consolidated report	☒

SEVENTH FRAMEWORK PROGRAMME

European Commission
Information Society and Media

1. OVERALL ASSESSMENT

a. Executive summary

Please give your overall assessment of the project, commenting on the following:

- *main scientific/technological achievements of the project*
- *quality of the results*
- *attainment of the objectives and milestones for the period*
- *adherence to the workplan, any deviations (whether justified) and remedies (whether acceptable)*
- *take-up of the recommendations from the previous review (if applicable)*
- *contribution to the state of the art*
- *use of resources*
- *impact*

CHIC proposes the development of a suite of tools, services and secure infrastructure that will support accessibility and reusability of VPH mathematical and computational hypermodels. The CHIC tools, services, infrastructure and repositories will provide a collaborative interface for exchanging knowledge and sharing work in an effective and standardized way. Clinical adaptation and partial clinical validation of hypermodels and hypermodel oncosimulators will be undertaken. CHIC will test and validate the overall architecture defined in the VPHOP project.

This is the SECOND review of the project covering the first 12 month period, furthermore assessing the corrective measures suggested at the previous interim review.

The majority of the project work in this period has been devoted to establish the basis, (from the technical, clinical, user requirements, legal and dissemination perspectives), setting up the system architecture and correct user interfaces, together with all the legal and clinical implications.

The work reported is of good quality and has overall improved from the interim review. Nearly all deliverables have been released on due date, with the few delays not compromising final results. They are very well written and homogeneous, despite the number of different contributors.

Dissemination issues have been very well addressed, with participation in many events (workshops, conferences, etc.), and publication of scientific papers. Activity on exploitation still remains at an early stage.

Resources consumption and costs reported are globally consistent with work performed and delivered results. However, high difficulties in recruiting senior researchers forced partner FORTH to hire junior staff. No information was provided on the impact on the expected level of skills and experience. This matter should be urgently clarified.

There is good cooperation between partners, especially between clinicians and IT specialists; all seem committed and actively participated in the review meeting. Project management looks effective.

The presentations made at the review were an indispensable contribution to fully understand the real contents of some deliverables. The demonstrations of the platforms were basic and mostly illustrative of the technical advances of the project. The key for the project to reach its goals is to have convincing demonstrators, showing clear clinical relevance, as early as possible. At this stage the project is progressing over a broad front; it might be worth considering concentrating on a few "use cases", so as to produce tangible results to be shown.

The biggest worry at this stage is the lack of clarity of the goals connected with the (partial) GCP validation.

A clear and explicit Gantt chart documenting which services are available to the clinicians, when and from where, should have been presented, as was suggested in previous review.

b. Recommendations concerning the period under review

Please give your recommendations on the acceptance or rejection of resources, work done and required corrective actions – e.g., resubmission of reports or deliverables, further justifications, etc.

Data protection and IPR issues have been adequately and extensively addressed (D4.2 and 4.3.1). However a note is made relative to the internal IPR in the consortium. It was recommended during the previous review that an IPR agreement be signed between all partners. An initial format has been provided (Annexed to 4.3.1), but no information has been given as to its effective acceptance and signature. If it has been signed by any partners, a hard copy should be provided. If it has not, it is strongly recommended to do it as soon as possible (do not wait until M42).

c. Recommendations concerning future work

Please give your recommendations – e.g., overall modifications, corrective actions at WP level, re-tuning of the objectives to optimise the impact or to keep up with the state of the art, better use of resources, re-focusing, etc. Where appropriate, indicate the timescale for implementation.

- Internal IPR agreement to be signed. This has extensively been considered in D4.3.1, specifically in chapters 5.2.2.3 (p40), 5.6.1.2 (p54), and 6 (p66). All annexes should be signed by now.
- Special attention should be paid to relevant standards, model integration, conflict resolution in integration, and to integration of software components and tools.
- Usability of the developed tools in clinical practise should be improved.
- The hypermodelling strategy should also develop dedicated tactics for conflict resolution in situations where models, originating from different sources (e.g. bio-physical vs. data-driven), produce conflicting results, and thus cannot be further integrated.
- A Randomised Clinical Trial should be designed for each type of cancer, once the respective hypermodel is in place. As such, it is the only scientific manner in which it can be proven to be of any utility and future sustainability. Of course this would also require an Ethical Committee approval.
- Clarify recruitment issues at FORTH and provide an accurate list of involved staff.
- A contingency plan should be devised in case a clinical significant disruptive development occurs during hypermodelling of each cancer scenario.

d. Assessment

☐ Excellent progress (the project has fully achieved its objectives and technical goals for the period and has even exceeded expectations).

☒ Good progress (the project has achieved most of its objectives and technical goals for the period with relatively minor deviations).

☐ Acceptable progress (the project has achieved some of its objectives; however, corrective action will be required).

☐ Unsatisfactory progress (the project has failed to achieve key objectives and/or is not at all on schedule).

2. OBJECTIVES and WORKPLAN

a. Progress towards project objectives

Assess to what extent the objectives of the project for the period have been achieved. In particular, please indicate if the project as a whole has been making satisfactory progress in relation to the Description of Work (Annex I to the grant agreement) and comment on the interaction between the work packages and the level of integration demonstrated.

The project has progressed in conformance with the DoW, the objectives set for the reported period have been attained. The contractual deliverables are of high quality and were overall issued on schedule. There is apparently great cooperation between work packages as well as among individual participants.

b. Progress in individual work packages

For each work package (WP), assess the progress in relation to the Description of Work (Annex I of the grant agreement). Please also report and comment on any delays, reasons for them and any remedial action taken. Specify the work packages concerned.

WP1 – Project management

Work and activities performed along the first 12 months of the project are comprehensively described in the 2nd interim report. The project management is of good quality and effective. All the work packages have been started and the engagement and the motivation of the research partners is high.

Progress accomplished in each work packages and individual tasks (with details on the work achieved by each contributing partner), issues raised (if any) and their resolution, as well as project management meetings, events and dissemination activities (conferences and paper submission or publication in scientific journals), have been documented.

Recruitment issues with FORTH, should be solved with the Commission and Project Management.

The presentation at review showed that the project has progressed as expected; the objectives set for the reported period have been fulfilled. The milestones have been attained; the contractual deliverables are of good quality and were issued on schedule or with agreed delay.

WP2 – User needs and requirements

Progressing according to the schedule. D2.2 of comprehensive and high quality. The focus was on initialising the collection of state of the art knowledge about building hypermodels,

working on the development of realistic use case and scenarios, and the collection of data from different cancer domains.
During the period, the state of the art for building hypermodels study was conducted and the scenarios underpinning the user needs and requirements were finalized. The corresponding deliverables D2.1 and D2.2 were produced, which completed tasks 2.1 and 2.2. Other tasks started as scheduled or slightly in advance.
The focus was on the extraction of user needs and requirements from defined use case scenarios. The collection of multiscale data for the purpose of several hypermodelling scenarios has been also performed. The project has established a systematic interaction with the p-medicine project.

WP3 - Clinical and Translational science scenarios
Started and progressing according to the schedule. No deliverable due for the period. The work package concentrated on exploration and collection of data for the three different cancer types considered by the project. Close cooperation with WP2 have produced D2.2
Data specifications have been developed and retrospective data collection ongoing in the specified cancer cases.
The main activities consisted in the definition and collection of multiscale data sets of the 3 different cancer types for the validation of the CHIC environment. The work is progressing according to the schedule.
Detailed specifications of the data collected for the three different cancer types considered by the project have been developed. Ethical approval has been granted for the clinical scenarios.

WP4 - Legal and ethical framework
A great effort has been made as shown both in D4.2 and D4.3.1, with extensive research on Data Protection and IPR issues. A comprehensive and detailed analysis of the issues related to *the* ethical and the legal requirements for sharing data is presented. External issues have been approached. Internal IPR analysis has produced a preliminary IPR agreement to be signed by all partners. .
Task 4.2 has been completed; task 4.3 has been started and is progressing according to the schedule. The corresponding deliverables D4.2 and D4.3.1 have been released on due time. It is worth to notice that a position paper drafted on the basis of the first results obtained has been circulated among the VPH community to get feedback from the research community.
An initial data protection and data security framework for the project has been developed and data protection contracts for data providers, end users, and the trusted service provider have been drafted and circulated to the partners.

WP5 - IT architecture
Tasks progressing according to schedule. D5.1.1 delivered on time and of great quality. An evaluation of existing architectures and private cloud technologies, and selection to be used by the consortium, has been presented.
Architecture views- functional, information, deployment, security- have been presented. An information model, e.g. in the form of an entity-relationship model, has not yet been presented. Interplay between the technical architecture and the clinical model is not yet made explicit. The resource allocation for architecture seems low (90 mm's), might need modification.
A dedicated architecture board has been set up to lead the design of the system architecture and the evaluation and selection of appropriate technological solutions. The first results are reported in D5.1.1 that was submitted with a slight delay. All 3 tasks of WP5 are active and progressing in conformance with the schedule.
The work package developed an initial CHIC IT architecture and an initial data protection (security) framework within the CHIC environment. An initial deployment of the CHIC private cloud infrastructure has been performed.

WP6 Cancer Models and Hypermodel Design
A first review of existing models already available or under refinement or development from consortium partners was provided (task 6.1). The hypermodelling "strategy" strategy has been provided in D6.2 and D7.1. The work package carried out an extensive work regarding cancer hypomodelling and hypermodelling strategies.

Many models at various levels of granularity have been documented. A classification scheme of 13 perspectives has been proposed and adopted for the models.
Strategies for hypomodelling and hypermodelling have been refined and the conceptual platform for design and development has been presented.
The first results (as reported in D7.1) look promising at this stage.
As requested, a glossary has been produced and features a very useful contribution. Work is progressing satisfactorily, but FORTH has still problems in staff recruitment. Although the impact at the moment is again qualified as "minimal", the issue should be immediately resolved.
An initial generic conceptual platform to serve as a standardized framework for the design and the development of multiscale hypermodels has been developed. A formal description of any cancer model based on 13 perspectives has been proposed and adopted by the consortium. The initial process of integration of biomechanics modelling into discrete-entity discrete-event multiscale cancer modelling has also been designed.

WP7 – Hypermodelling infrastructure
Started and progressing according to the schedule. The focus was on the definition of the component models of the ICT hypermodelling infrastructure. Work has only just started on how to link the existing and future components (hypomodels). For this Json (Java Script Object Notation) was mentioned as a favoured candidate.
An infrastructure to execute the models has been proposed and HOT maps for knowledge management for literature mining, semantic annotations, mappings to ontologies has been installed. Demonstrations were shown on breast cancer and lung cancer.
An initial hypermodelling platform has been installed on the basis of VPH-HF, existing software from project partners. Progresses regarding model annotation and tagging have been also achieved using software components and ontologies available from previous work. All these components are being analyzed for the specific needs of the project and will be updated and enhanced accordingly. First results on model executions have been released in deliverable D7.1.
The focus was on the definition of the component models of the ICT hypermodelling infrastructure.The set of 13 perspectives, proposed by WP6, from which each model should be viewed and a corresponding (semantic) metamodel should be created has been adopted by WP7. The VPH-HF, being the core technology for the CHIC hypermodelling IT architecture, has been successfully installed.

WP8 – Models and data repositories
Started and progressing according to the schedule. No deliverable due for the period. The work package focused on the analysis of models/tools and clinical data specifications, collection of knowledge representation requirements for multiscale cancer biology and initiated the design of a semantic interoperability framework
A data upload tool was demonstrated to show data upload from various clinical sources with varying data formats. apiNATOMY tool will be used to manage visual ontologies and semantic metadata.
Work achieved to date mainly regards the definition and analysis of data, as well as the requirements and specification of the models and data repositories and study of candidate technologies for implementation. A first level of integration and a first version of related services have been completed. Preliminary work regarding semantic management issues (knowledge representation, ontologies and semantic interoperability) has also been conducted. Work has progressed as expected.

WP9 – Image processing and visualization.
This work package focused on the analysis of the user requirements, at this stage the modellers' in particular, for the visualization toolkit and image analysis toolkits. Task 9.1 has progressed as expected and issued Deliverable 9.1 on time, with inputs from T6.1. The work produced is of good quality and is considered as a solid basis for the specification work. Significant preparatory work for task 9.8 (starting month 8) could also be achieved. Input to WP2 necessary to produce D2.2.
On the basis of the user requirement the work consisted mainly in the identification and evaluation of various image processing tools in view of defining the approach of

visualization and developing the visualization module. Preliminary software implementation and test were also achieved. Work is progressing well, although FORTH could not recruit senior researchers as needed by the complexity of the tasks.
User requirements for multimodal brain tumour segmentation have been finalized. The major components of the image registration tool have been identified and initial trials on clinical images have been conducted.

WP10 - Integrated platform
An evaluation of portal frameworks and technologies was conducted and a development installation of a portal to be used for CHIC was set up. D10.1 presented the choices selected for the portal.
The architecture for the platform has been planned and the end user portal has been set up. A generic stub specification that allows hypermodels and dataflows integration has been presented.
This WP has progressed according to the schedule and installed the project portal integrating tools from other WP's together with a set of technical guidelines to support further software development activities in task 10.1. Some basic features of the cloud based platform were demonstrated during the review. All other tasks of the WP have been launched and are progressing according to the schedule. Here again, FORTH reports difficulties in recruiting experienced staff.

WP11 - Clinical adaptation and validation
Progressing according to schedule. D11.1 produced on time and of high quality. The aggregate results of the surveys presented as annexes should have been made available for analysis of clinicians needs and requirements.
Criteria for model adaptation validation have been presented and the questionnaires outlined. Each workpackage is to follow the validation plan. Still missing the detailed methodology for each criteria validation.
The definition of basic policies for the evaluation and validation of hypermodels has been initiated and published in D11.1. Tasks 11.1 and 11.2 have been started (slightly in advance on the schedule) and are progressing normally.

WP12 - Dissemination plan
The dissemination issue receives a great attention and it is clear that it is considered as a key aspect of the project success. A full dissemination strategy is presented in D12.1. and a concise kit has been presented in D12.2
Newsletters published, some delays with the printed newsletters. Overall, high activity in dissemination: 70 events during the 1st project year. Special attention needed for dissemination to clinical professionals.
The project partners have been extremely active in participating to conferences and workshops and publishing scientific contributions. The web presence has been enhanced and a dissemination kit has been created. However, the release of D12.6 (issue 1 of the project newsletter) has been delayed due to unforeseen workload at the partner in charge
The work package produced elaborated dissemination plan covering different activities and potential stakeholders of the project results

c. Milestones and deliverables

Indicate whether the planned milestones and deliverables have been achieved for the reporting period (please give more detailed comments first and then fill in the summary table below).

Milestones 3 and 8 have been attained. Milestone MS27 has been achieved as scheduled. Milestone M15 was reached on mid-June only since the delivery of D5.1.1 and D7.1 was postponed by 2-3 months after the outcomes of the 6 months review. The other contractual deliverables have been issued on time. All deliverables are of overall good quality, substantial and informative. All are accepted.

STATUS OF DELIVERABLES			
No.	**Title**	**Status** *(Approved/Rejected)*	**Remarks**
D2.1	State of the art knowledge for building hypermodels	Approved	Good report, well presented state of the art. Model integration is not fully discussed.
D2.2	Scenario-based user needs and requirements	Approved	Scenarios well presented.
D4.1	Initial analysis of the ethical and legal requirements	Approved	Good, comprehensive report.
D4.2	Initial analysis of the copyright-related legal requirements for the sharing of data	Approved	Good report, complete analysis.
D5.1.1	The CHIC technical architecture- initial version	Approved	A preliminary plan for the architecture. Missing details on information view.
D6.1	Cancer hypermodelling	Approved	Adequate report
D7.1	Hypermodelling specifications	Approved	Model integration requires more elaboration and risk analysis and mitigation strategy for potential conflicts in integration.
D7.10	Hypermodelling definitions-v4	Approved	Presenting definitions for models.
D10.1	The CHIC portal	Approved	Basic structure and outlook, could be more informative and better in usability.
D11.1	Evaluation and validation criteria for clinical adaptation	Approved	Criteria for validation of model adaptation presented. Missing details on evaluation methodology for each criteria.
D12.1	Dissemination plan	Approved	Adequate report.
D12.2	Dissemination kit	Approved	Good, improves sharing of information and results.
D12.6	Periodic newsletters	Approved	
	CHIC Project Periodic Report	Approved	Good report.
	First Interim report	Approved	Good report.

d. Relevance of objectives

Indicate whether the objectives for the coming periods are (i) still relevant and (ii) still achievable within the time and resources available to the project. Assess also whether the approach and methodology continue to be relevant.

The project objectives are still highly relevant and achievable within the remaining time and resources. The relevance of the scientific approach and methodology were assessed by the quality of the deliverables and explanations given during the review meeting.

However, the feasibility of achieving all of the project objectives will depend on the development of realistic integration strategies, which will warrant the composition of robust, accurate and reproducible hypermodels.

e. For Networks of Excellence (NoEs) only

Assess how the Joint Programme of Activities has been realised for the period and whether all the planned activities have been satisfactorily completed.
NA

3. RESOURCES

a. Assessment of the use of resources

Comment on the use of resources, i.e. personnel resources and other major cost items. In particular, indicate whether the resources have been utilised (i) to achieve the progress and (ii) in a manner consistent with the principle of economy, efficiency and effectiveness[1]*. Note that both aspects (i) and (ii) have to be covered in your answer. The assessment should cover the deployment of resources overall and by each participant. Are the resources used appropriate and necessary for the work performed and commensurate with the results achieved? Are the major cost items appropriate? In your assessment, consider the person months, equipment, subcontracting, consumables and travel.*

Personnel costs

Reported personnel expenditures are globally consistent with the amount of work performed to achieve the project objectives. The principles of economy, efficiency and effectiveness have been respected. In general, partners have committed skilled staff in time and volume according to the workplan.

However partner FORTH still reports high difficulties in recruiting senior researchers and was forced to hire junior staff instead. For this reason FORTH consumed 45 junior pm instead of the scheduled 12 senior pm in WP's 6, 9 and 10. Even if this has no impact on the budget, it is questionable whether 4 juniors can provide the same skills as 1 senior researcher. This matter should be urgently clarified.

Other expenditures

No specific comment. Look adequate and quite reasonable.

b. Deviations

If applicable, please comment on major deviations with respect to the planned resources.

No significant deviations reported

[1] "The principle of economy, efficiency and effectiveness refers to the standard of "good housekeeping" in spending public money effectively. Economy can be understood as minimising the costs of resources used for an activity (input), having regard to the appropriate quality and can be linked to efficiency, which is the relationship between the outputs and the resources used to produce them. Effectiveness is concerned with measuring the extent to which the objectives have been achieved and the relationship between the intended impact and the actual impact of an activity. Cost effectiveness means the relationship between project costs and outcomes, expressed as costs per unit of outcome achieved." Guide to Financial Issues, Version 02/04/2009, p.33.

4. MANAGEMENT, COLLABORATION AND BENEFICIARIES' ROLES

a. Technical, administrative and financial management of the project

Assess the quality and effectiveness of the project management, including the management of individual work packages, the handling of any problems and the implementation of previous review recommendations. Comment also on the quality and completeness of information and documentation.

The management has been adequate. The role of the participants and their mutual relationships are clearly stated, with provision for quality assurance, quality criteria and risk analysis. There is a contingency plan in place.

The structure and contents of deliverables reflects an effective organisation of the work and a suitable coordination between all involved parties. All project documents (deliverables, periodic report, etc.) were delivered on time and were very informative.

A Consortium Agreement relative to IPR issues should have been signed by now, so that IPR usage between partners be clarified.

The recommendations made at the previous review were well considered and satisfactorily answered. However, a clear documentation of services addressing clinicians is still lacking.

b. Collaboration and communication

Comment on the quality and effectiveness of the collaboration and communication between the beneficiaries.

There is good coordination between partners. The consortium works with efficiency. Evidence of collaboration and knowledge transfer among partners is exemplified by the work done in the first deliverables which gathers expertise and contribution from many different participants.

c. Beneficiaries' roles

Give an assessment of the role and contribution of each individual beneficiary and indicate if there is any evidence of underperformance, lack of commitment or change of interest.

All partners seem fully committed. All have attended the review and were very reactive to experts' questions.

5. USE AND DISSEMINATION OF FOREGROUND

a. Impact

Is there evidence that the project has so far had, and is it likely to have, significant scientific, technical, commercial, social or environmental impact (where applicable)?

If successfully completed, the project should have a high impact in scientific and clinical terms. Large scale hypermodeling is a real challenge and the demonstration of a feasible approach would be a decisive progress. Clinical and social consequences should also be important in optimizing the diagnostic, assessment of evolution and treatment of cancer diseases helping thus to improve the patient's quality of life.

b. Use of results

Comment on whether the plan for the use of foreground, including any updates, is still appropriate. Comment also on the plan for the exploitation and use of foreground for the consortium as a whole, or for individual beneficiaries or groups of beneficiaries, and its progress to date.

IPR agreements are in progress, but not yet finalised.

Exploitation activities are still at a preliminary stage. It is expected that deliverable D12.3, to be released at month 24, will include a first market study including the positioning of CHIC potential results in the current offer, and preliminary partners' individual exploitation plans.

c. Dissemination

Assess whether the dissemination of project results and information (via the project website, publications, conferences, etc.) has been adequate and appropriate.

Scientific dissemination has been relatively intense. 10 presentations at international conferences and participations in 4 workshops have taken place. 7 scientific peer-reviewed papers have been published or accepted, and 3 submitted.

Communication to a larger public has also been considered through the project web site, and 2 online or newspaper articles. Unfortunately, the first release of the project newsletter (D12.6) had to be postponed due to a work overload in the partner in charge.

d. Involvement of potential users and stakeholders

Indicate whether potential users and other stakeholders (outside the consortium) are suitably involved (if applicable).

User organisations are involved as consortium members. Although some contacts with other potential customers have taken place in the frame of the dissemination above, more efforts should be made to develop such actions in the future.

e. Links with other projects and programmes

Comment on the consortium's interaction with other related Framework Programme projects and other national/international R&D programmes and standardisation bodies (if relevant).

The project has already very close interactions with p-medicine and VPH-Share thanks to CHIC partners participating in those projects. The project also intends to re-use some

of the results of other projects (some already finished) e.g. VPHOP, TUMOR, ContraCancrum, RICORDO and ACGT.

6. OTHER ISSUES

If applicable, comment on whether other relevant issues (e.g. ethical issues, policy/regulatory issues, safety issues) have been handled appropriately.

The ethical and legal situation regarding the sharing of data electronically within Europe and beyond have been particularly well analyzed (cf. comments on Deliverable D4.1).

Name(s) of expert(s):
Tor BLOCH *Henry KANOUI* *Jorge MARTINEZ de HURTADO* *Pirkko NYKÄNEN* *Elena TSIPORKOVA*
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