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. 3, from 01/04/2015 to 31/09/2015
Place of review meeting:	Brussels
Date of review meeting:	29 January 2016
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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*

This is the fourth review of the project covering the 25-31 month period, assessing the project´s progress and the adherence to suggestions made at the previous review.

The majority of the project work in this period has been devoted to develop the clinical relevance of different models, and its user adaption and requirements. An important effort has been done with respect to clinical drivers and concepts have been clarified. A rather significant change of direction following the recommendations of review #3 has been undertaken by the consortium.

The work reported is of good quality and has overall stayed in line with what was suggested in previous review. The expected deliverables have been released on due date, and are well and clearly written, emphasizing the clinical needs that the CHIC project supports.

This interim review has been organized to assess the refocusing on clinical orientation. A clinical coordinator has been appointed and a new deliverable D2.5 has been issued with the purpose to provide the usability viewpoint of clinicians when using the system.

Detailed descriptions of scenarios and demonstrators illustrating the interactions of the clinician using the hypermodels for clinical decision support were shown. A dedicated framework (CRAF) featuring the clinician's working environment has been designed. The demonstration was effective and proved that the clinical dimension is well addressed. This gives confidence regarding the clinical relevance, usability and acceptability of the future system. The increased emphasis on satisfying the requirements of the clinicians in the fields was very visible and encouraging for the remaining work of the project.

The recommendations given at the last review have all been addressed by the project even where it resulted in significant changes in resource allocations, management structure or partner responsibilities. The responsiveness demonstrated by the project has been impressive. The project did decide to maintain four targeted types of cancer rather than three, as recommended, but gave very valid reasons for this.

.The review was well prepared, with a detailed accompanying documentation. All participants were very reactive on reviewers' comments and questions. Detailed responses to the recommendations made during the previous review have been provided by written form and commented during the review. Altogether, responses and actions launched are highly relevant and address well the recommendations.

Technical achievements have been completed as expected and delivered in conformance with the DoW during the period. The deliverables are of expected scientific quality and are accepted.

Progress with dissemination activities were presented as well as some of the preparative work for the final deliverables on exploitation (no deliverables scheduled at this time) and were well targeted.

An amendment to the DoW is under preparation and figures provided for resources reallocations are consistent with the work to be done until the end of the project and the remaining budget.

The management is very professional and effective. Partners are all committed. Internal communication and relationships inside the consortium are still very good.

The consortium delivered an additional deliverable D2.5 Clinical relevance of the CHIC project - describing the integrated workflows of the scenarios from a clinical perspective. This is an excellent deliverable demonstrating well the clinical relevance of the work done by far in the project. Additionally periodic interim progress report was produced. Integration of the components is in progress, this was well demonstrated during the review with the nephroblastoma demonstrator.

Resources consumption and costs reported are globally consistent with work performed and delivered results, and have been accordingly modified with necessary changes identified at the previous review.

To be mentioned is the appointment of the Assistant Clinical Coordinator and the Clinical Advisory Board.

In summary, the project has reviewed its workplan and governance structure in the directions necessary to implement the recommendations from the previous review and is on track with all this work. Significant increases in manpower allocations overall has been made and changes in resource allocations between partners. Also some minor changes to the timing of milestones and deliverables are being consolidated in a DoW amendment to be submitted in the next few weeks. Most of the recommendations from the previous review have been well and appropriately addressed by the consortium.

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.

The work and deliverables, as well as use of resources, of the period under review have been accepted.

Clinical relevance of the CHIC project has been adequately addressed in D2.5, which elaborates concisely and extensively in the description of the integrated workflows of the scenarios from a clinical perspective. Emphasis has been placed in understanding the integration of the functional architecture and the infrastructure in each clinical setting. Concepts have been clarified and new needs have been identified.

The quality of the work done during the period is good, the stated objectives have been achieved. The use of resources has been modified slightly on the cost categories and tasks of the partners. There is still high potential for impact on the cancer research and treatment practices.

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.

Clinically Relevant Application Framework (CRAF) tool to be developed in each clinical scenario. Future reviews should demonstrate the applicability of CRAF for the other types of cancer considered in the project, as well as the ability of the system to deal with incomplete sets of data. Special attention should be paid to relevant standards, model integration, conflict resolution in integration, and to integration of software components and tools.

The key tasks for the coming period are:

1) **integration** – finalise integration of models, hypermodels, tools and components into a usable, reliable, valid and useful clinical environment. The final CHIC environment needs to cover the other 3 cancer types as planned in DoW and possibly demonstrate the feasibility of the hypermodelling approach in general.
2) **evaluation** – collect feedback, as much as possible, from the clinicians and cancer researchers from the adaptability, usability and usefulness of the developed CHIC environment.
3) The **user-friendliness** of the developed CRAF platform can be further improved by considering the development of visual, workflow-based interfaces, guiding the user through the selection and execution of different alternative hypermodelling strategies and providing support during the interpretation of the prediction results e.g. comparative evaluation of alternative treatment strategies.
4) The further **development and refinement** of the hypermodelling strategies should also consider the development of hypermodelling best practices and guidelines for the clinicians.

5) The hypermodelling strategy should also develop dedicated strategies for **conflict resolution** in situations when models originating from different sources (e.g. bio-physical vs. data-driven) produce conflicting results and thus cannot be further integrated.

The time remaining is short, manpower allocations have been increased significantly; a first estimate is the "burn-rate", which will have to be 30% higher in the 3rd and 4th year than they were in year 2. This is challenging and will require a lot of monitoring and management.

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 apparently been attained, and a clear clarification of the asked for Clinical Relevance has been issued. The project has progressed well already in this direction as witnessed by the demonstration conducted at the review

The results are of expected scientific level and quality. There is fruitful interaction across workpackages and good integration across 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.

All the work packages are already active and have been advancing according to the roadmap described in DoW Annex 1. The relevant WP activities for this review are as follows:

WP1: Project Management. The project management is of good quality. Almost all project activities are progressing according to the plan and the engagement and the motivation of the research partners is high. The consortium also managed to attract two new members to CHIC External Advisory Board.
Periodic progress report delivered.
Clinical coordinator and clinical advisory board nominated. FORTH has taken a role as technical coordinator. Management has been working well. Several partners have adjusted their person month efforts to provide a realistic budget breakdown.

WP2: User Needs and Requirements. The focus during the reporting period was bases on thorough analysis of necessary requirements to achieve acceptance of the hypermodelling approach by clinicians and patients. The WP produced D2.5 devoted to the clinical relevance of the integrated hypermodelling workflows for the proposed clinical scenarios. This is an excellent report starting from an end-user narrative of the clinical application and going backwards to technical specifications. Work done was well demonstrated in the review with a focus on nephroblastoma patients. The demonstrator showed well the integration of models and their use in cancer treatment planning.

WP8: Model and Data Repositories. The work package advanced well performing the development of web services for model/tool and in silico trial repositories, together with the development of more functionalities for the web services for the clinical data repository. Deliverable D8.3 “Implementation of the interfaces of the CHIC repositories” has been

delivered. It describes the interfaces to four resources: the hypermodel repository, the clinical data repository, the metadata repository and the insilico trial repository.

WP12: Dissemination and Exploitation. The work package reported on a very broad range of different dissemination activities. The visibility of the project is well maintained both in the scientific and public space. Newsletters were edited and 134 dissemination events during the first 30 project months. Interfacing with other projects is active.
Exploitation activities have been started: information collected from partners, CHIC exploitable outputs have been identified; 23 altogether. For each output TRL levels are defined and information collected to understand sustainability.
Three potential exploitation paths have been identified for CHIC platform: as a clinical decision support system, generic research exploitation and educational exploitation. Exploitation will be further discussed in the consortium with the Innovation radar questionnaire.
The most important task of the work package for the remaining period of the project will be the development and implementation of realistic exploitation strategies for the project outputs.

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).

No specific milestone was scheduled for the period under review. The two deliverables submitted are of good quality, substantial and informative. Both are accepted.

STATUS OF DELIVERABLES			
No.	**Title**	**Status** *(Approved/Rejected)*	**Remarks**
3rd Project interim report	3rd Project interim report	A	Good report
D2.5	**Clinical relevance of the CHIC project**	**A**	Provides the viewpoint of the clinician in using the hypermodels for clinical decision support in order to guarantee the clinical relevance, usability and acceptability of the CHIC outputs. The approach starts from the scenarios previously established for the hypermodels of the 3 main cancer types (nephroblastoma, glioblastoma and non-small cel lung) and the additional prostate cancer. The interactions between the clinician and the system are mediated by a dedicated end-user front-end, CRAF (Clinically Relevant Application Framework) that triggers all the necessary functionalities of the CHIC platform. For each scenario, the clinically meaningfull steps and interactions of the clinician using the hypermodel are described in details,

			distinguishing between steps that take place outside and inside the CHIC platform. Finally, several possible demonstrators are described for each type of cancer, and the timeline for the availability of their components is provided. The methodology used is very adequate. The presentation is sound and convincing.
D8.3	**Implementation of the interfaces of the CHIC repositories**	**A**	This deliverable describes the interfaces to the CHIC repositories (clinical data; models/tools; in-silico trial; semantic metadata) in terms of web services and their interactions. The presentation relies on the service oriented paradigm adopted for the CHIC architecture. Access to the repositories and exchange of data between applications are achieved through a web interface consisting of (5) http methods using the REST (representational state transfer) principle. The data model of the first 3 repositories are provided and commented. The API's of all services associated are carefully described with their definition, parameters and detailed examples. The semantic metadata repository uses the RICORDO software suite to represent semantic annotations as RDF triples. This approach provides full access to the RICORDO API's for the management of knowledge, including knowledge driven querying facilities and ontology management. The document provides a clear specification of the functionality associated with the system repositories and how they can be invoked from external applications or services. It is a comprehensive piece of work that provides a sound basis for further steps of the project.

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.

After the refocusing of the project, objectives are still highly relevant but achieving them will require a lot of coordination over the last 15 months of the project. Furthermore, the feasibility of achieving all of the project objectives will depend on the development of realistic integration strategies guaranteeing the composition of robust, accurate and reproducible hypermodel environment

The scientific approach and methodology are relevant as demonstrated by the quality of the deliverables and by presentations and demonstrations given at the review meeting.

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.

Figures as provided are consistent with the work to be done until the end of the project and the remaining budget.

Relative to Personnel costs, still the project seems to under spend on the manpower budget - although not all numbers were in yet. A challenge remains underway, with the Project needing to increase use of resources by 30% for the last two project years.

b. Deviations

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

A revised budget including reallocation of resources will be provided in the amendment to the DoW under preparation.

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[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 project management is very professional. Managerial and technical leadership are effective. The deliverables are of expected quality and substantial. They reflect an effective organisation of the work and a suitable coordination between all involved parties.

The management has been very busy with implementing the reorientation of the project. This work has been done very well and successfully..

The recommendations made at the previous review were explicitly summarised and all implemented - even where it implied substantial changes.

b. Collaboration and communication

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

Coordination between the participants is good, with high evidence of collaboration and communication between participants.

A lot of cooperative spirit has been shown, and a will and talent to collaborate to implement change.

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.

No sign of underperformance or loss of interest is observed. All partners have attended the review and were very reactive on experts' questions. The review was well prepared. Presentations and demonstration were effective

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)?

The expected scientific impact of the project is still high, and should ever be improved with the focus on clinical orientation. The hypermodeling approach and tools show decisive progress and with many potential applications beyond the healthcare domain.

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.

Results from evaluation workshops and consultations of the clinicians should be carefully collected and used to guide the ongoing work and results.

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.

Discussion on the sustainability and maintenance issues of the CHIC project via the proposed Study Trial and Research Centre (STaRC) have been started, project outcomes identified and their sustainability are under analysis. Innovation radar questionnaire will be filled by the consortium.

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 intense and has raised interest in the specialised community targeted.

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 and are now playing an important driving role for the integration work aligned with the recommendations from the last review.

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 consortium is well linked and networked with other EU projects and initiatives in the VPH-domain. The project utilises also well earlier work and builds connections to research community. Interaction with the standardisation bodies is not evident.

6. OTHER ISSUES

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

None

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SIGNED:

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