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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:	Interim Period, from 01/04/2016 to 31/10/2016
Place of review meeting:	Remotely
Date of review meeting:	21st November 2016
Experts:	Tor BLOCH Henry KANOUI Jorge MARTINEZ de HURTADO Pirkko NYKANEN Elena TSIPORKOVA
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Individual report	☐
Consolidated report	☒

SEVENTH FRAMEWORK PROGRAMME

European Commission

Directorate-General Communications Networks, Content and Technology

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 hypo- and hyper-models. 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.

This was the sixth review of the project covering the first part of period 4 (months 37 to 42 included). The objective was to ensure that the project is on track for demonstrating significant results and presenting comprehensive exploitation plans at the final review, together with approval of the deliverables submitted, and to prepare for the final review in which a strong recommendation has already been made to include important demonstrations and discussions about the future exploitation of the significant amount of results obtained.

The reported work is of high scientific quality. All deliverables are accepted. The refocusing on clinical usage is confirmed and significant effort towards dissemination of the CHIC concept addressing clinicians and other main stakeholders is reported. The recommendations at the last (interim) review have been addressed well by the Consortium

The review went swiftly, presentations were of quality and participants were very responsive to questions. Recommendations made at the previous review were well addressed. The overall impression is very positive and we are confident that the project will be a success from the scientific perspective, bringing significant advances of the state of the art on both conceptual and practical terms.

Questions from reviewers were answered by the project members present but the discussion was less lively than normal – being it a fact inherent to the communication medium.

Excellent progress was demonstrated in further refinement and consolidation of the developed hypermodels, development of the data protection and copyright framework, and deployment models for the technical architecture.

One very valuable achievement for this period is the proposed multi-phase methodology for the validation of hypermodels, following the four phases in drug development. However, it should be also considered that hypermodels are very dynamic entities and will need to be open to faster evolving scientific knowledge.

The participants are ready for launching the exploitation of results in clinical practice, and many efforts have been reported in this direction. However, the clinical validation of the system is a

mandatory prerequisite for securing a successful exploitation, task which takes time, and such an effort is not in the scope of the project.

The seven deliverables for the period are all accepted (D2.4; D4.3.2; D5.1.2; D5.2.2; D6.3; D7.4; D8.4).

All milestones of the period have been achieved.

The **recommendation of having a two-day final review in Heraklion** was reiterated and the dates were provisionally fixed to be in the period the 22-24 May 2017. Preparation to the final review should be focused on finalisation of the platform and on demonstrating its clinical relevance and usability and on elaborating the exploitation of the results for the cancer communities.

On the other hand, a significant under spending of resources was observed, and projections suggest that part of the allocated budget will remain unspent at the end of the project. We therefore recommend a 3-6 months extension of the project in order to start the clinical validation process with the remaining budget. The duration of this extension, as well as the choice and role of the participants to be involved, is subject to an agreement between the commission and the consortium.

b. Recommendations concerning the period under review

The progress achieved during this period is considered excellent, all deliverables and work done are accepted. The comments and recommendations given in the June 2016 review were addressed in the deliverables and in the review.

The previous review had asked for a clarification of the Prostate Cancer commitments of the project and a satisfactory clarification was presented at this interim review with D6.3 and its presentation

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.

The current version of the CHIC platform offers a lot of options: tools, models, security solutions, and it is not clear yet how usable and clinically relevant these tools and services are for the clinician or the researcher.

It is recommended to pay attention to the integration of the possible options into a comprehensive platform that is both usable and useful for the end user, and that can be integrated with the health care IT environment, to some extent at least. These issues were raised in D2.4 and it was concluded that more work is needed on the clinical relevance aspect of hypermodels, user training on hypermodels, and their operative validation.

Both proof-of-concept and clinical relevance are important to be demonstrated with adequate number of users to validate the developed models and hypermodels. Therefore, it is recommended to allocate sufficient resources to WP11 Clinical adaptation and validation during the remaining project duration.

The project activities in the remaining period should be focused on guaranteeing sustainability of the project results beyond the project life time. It is important to consider how the developed rich set of hypermodels and acquired knowledge can be best transferred to the scientific and clinical communities for the purpose of further research and disease treatment. It is necessary to consider how to facilitate the decision making process of clinicians and researchers with respect to how to select the most suitable model for a given context, what is the type of data needed, how to interpret the modelling results, etc.

Further development and refinement of the hypermodelling strategies should also consider the development of hypermodelling best practices and guidelines for the clinicians.

The research and clinical validation of the developed hypermodelling repository would benefit from additional 6 months extension of the project. This will also result in better technology and knowledge transfer results towards the interested communities

As there is clear under spending of resources up to now, and as the exploitation potential is high, the consortium is recommended to ask for extension of the project duration with 3-6 months to have the results finalised and the exploitation plans elaborated.

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.

Progresses are as expected, in time and quality. The review presentations and the submitted deliverables demonstrate convincing progress for the reporting period. All of the objectives for the reporting period have been achieved.

The project has made excellent progress towards objectives. However, there is still work to be done, especially with the clinical relevance, with the usability and understandability of the models for the user, and with the integration of the CHIC platform with the health IT environment. The project has already achieved valuable results, and their exploitation is important so that the researchers and potential users have a possibility to utilise the developed models, services and tools.

It is of utmost importance that the results of the CHIC project not be lost when the EU funding ends.

The project is exploring two possibilities (STaRC, Study Trial and Research Centre and Philips) for funding continued work but they both sound sufficiently far out in the future that - as a minimum - a **sure** method must be found to keep the project results alive or properly mothballed till such opportunities become reality. It is supposed that the Private Cloud in Forth will be kept for some time,

offering the maintenance in operation of the virtual machines, and some of the partners will continue working whereas others will have to stop when the funding stream dries up.

Recommendation: All possibilities should be explored by the project to protect the results of CHIC in a way where further development work can continue driven by the need to reach clinical validation at some point in time. All avenues to advance towards clinical validation have to be explored. The final review should have this on the agenda, including the possibilities which the Commission can see.

This recommendation assumes that the CHIC system is well defined and the final deliverable D5.1.3 is very important in this respect (as is the Integrated Clinical Research Integrated Platform (D10.5, due in month 46)

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.

- Deliverables of this partial period 4 were available from WP 2, 4, 5, 6, 7 and 8:

WP1 – Project management

Project management is still effective. Work is progressing according to schedule. Deliverables are released on time and are of excellent quality. Financial issues are well managed.

The consortium seems to have good team spirit and they are aware of their shared vision and mission. Management has been focused during the period to preparation and finalisation of Amendment with some corrective actions like changes to the management structure and bodies, removal of other cancer types except nephroblastoma, glioblastoma, lung and prostate cancer and the deletion of corresponding tasks, addition of new deliverables to monitor the project work more effectively and shifts of resources between categories and partners.

WP2 – User needs and requirements

During the last months the work was focused on the acceptance by physicians and patients when using hypermodel technology in clinical practice. A study for paediatric oncology based on a quationnaire was conducted. The findings are reported in D2.4.

The study reported has been rather restricted and preliminary and has focused only on the neproblastoma hypermodel which has been presented at conferences and discussed with participants. A questionnaire to collect feedback from broader community had been delivered via websites and other channels receiving 39 respondents. The study resulted in three points that need to be addressed: Clinical relevance of hypermodels, education and explanation of hypermodels and validation and certification of hypermodels. Also the user interface needs improvement. Mostly validation and certification of hypermodels are needed to increase the trust in hypermodels. In addition, users ask for more background information to understand the benefits of hypermodels in comparison to standard clinical care.

WP3 – Clinical and Translational science scenarios

In progress. No deliverable due.

WP4 – Legal and ethical framework

During the period, the legal and ethical basis to start early clinical validation of hypermodels has been further investigated. Options for exploitation and related IPR issues have also been refined. Outcomes are reported in D4.3.2., an excellent report.

Three mutually supporting contractual agreements: the CHIC Data Provider Agreement, signed by the clinical project partners providing patient data to the CHIC infrastructure; the CHIC End User Agreement, signed by the technical modelling partners, accessing and processing the data within CHIC; and the CHIC Trusted Third Party (TTP) Agreement have been defined. These terminate when the project finalizes, and their sustainability needs to be elaborated.

IPR issues have been elaborated with identified 22 exploitable outputs: 14 technological/software components, 7 models (including both hypo and hyper-models), and the CHIC platform as a whole. Open source licenses are under consideration for the CHIC platform- possibly in such a way that the CHIC platform shall be licensed as an aggregate and individual components go under their own licenses and the users have a possibility to use individual components within the scope permitted by each component license.

WP5 – IT architecture
D5.1.2 and D5.2.2 from this work package both demonstrated excellent knowledge and work progressing towards the work package objectives

The full documentation on the final IT architecture is in progress. A first report of the deployment view is provided in D5.1.2 in which various deployment models of the CHIC platform are considered and discussed along technical and financial perspectives.

Drawbacks and advantages of different deployments of the CHIC architecture have been elaborated. The plan is to deploy the private cloud – CHIC Platform-as-a-Service, locally CHIC platform-as-an-Application. The deliverable documents very thoroughly all potential deployment models.
(WP 10 - Integrated Platform WP 10 has to mentioned here although there were no deliverables at this review since the deliverable **D10.5 The CHIC Clinical Research Integrated Platform** will also be very important for the survival of the CHIC results beyond the end of the project.)

WP6 Cancer Models and Hypermodel Design
During the period, work focused on the engineering perspective of building hypermodels, such as standardization issues, integration, development, tuning and execution. Results of these achievements are reported in D6.3. The report describes the developed hypermodels concerning nephroblastoma, non small cell lung cancer, glioblastoma multiforme, and prostate cancer.

WP7 Hypermodelling infrastructure
The final prototype of the hypermodeling framework, including the CRAF environment was completed. The full production environment is ready to be deployed on the test sites. Results are reported in D7.4.
Deliverable describes the final release of the hypermodelling framework (VPH-HF) technology and its deployment on the CHIC production and test nodes. The hypermodelling framework design has been redesigned to be compatible with the CHIC needs.

WP8 – Models and data repositories
The 4 CHIC repositories (model and tools; clinical data; in-silico trial and semantic metadata: knowledge bases and annotations encoded in RDF) and the associated access services are completed, with users manuals and guidelines.Deliverable D8.4 Report on the final system describes the current status of the model and tool, the clinical data, the in-silico trial and the RDF CHIC Repositories as well as the user interface and the web services that expose the content are described. Good work.

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).

During the period, all deliverables where released on time. All are of very good scientific and technical quality, and are approved.

STATUS OF DELIVERABLES			
No.	**Title**	**Status** *(Approved/ Rejected)*	**Remarks**
D2.4	**How to get acceptance of hypermodels by patients and physicians**	**A**	The nephroblastoma hypermodel considered as a generic example was presented at 2 international clinical conferences dedicated to paediatric oncology. The audience included a full range of interested stakeholders both medical (physicians, medical students, patient associations, pharmaceutical companies) and non-medical (software development, training and data management companies). An online questionnaire with the objective to elicit the conditions for acceptance of hypermodels in clinical practice has been developed. However, the findings reported are still too generic and further investigations are necessary. Results emphasise the need to validate the models, to demonstrate the clinical relevance of the system and to educate/train users to understand and use the models.
D4.3.2	**Development of the data protection and copyright framework for CHIC – Second iteration**	**A**	The first part defines the legal and ethical basis to start early clinical validation of hypermodels under the perspective of usability and utility of prediction. The data protection and de-identification framework supporting the use of patient data in the context of direct clinical activity are carefully investigated and described in details. Updated data protection and security framework is presented covering patient data use for model validation and refinement, operation of syntactic de-identification process. The second part provides an update on provision of clinical data for model building and updated copyright framework including analysis of software licensing compatibility for project exploitation. It identifies the exploitable software outcomes. Suitable licensing options are proposed and IPR issues raised by exploitation are discussed. The methods and scope of protection measures for the CHIC components, repositories and clinical data are also investigated. The deliverable features a clear understanding of the issues and the approach adopted is sound and convincing.
D5.1.2	**Deployment models of the CHIC technical architecture and its private cloud**	**A**	This report depicts the deployment view of the technical architecture that considers the functional and runtime dependencies of the platform components in their operational environment. Various deployment models of the CHIC platform are considered: centralized (stand-alone installation), distributed installation and cloud-based installation (either using a private cloud – as retained for the project – or hiring services of a public cloud). All these options are briefly discussed with pros and cons regarding the envisioned usage (educational, research, clinical usage, etc.) with indications on the possible financing schemas associated to these various scenarios. The architecture of a complex software system based on a set of views and the corresponding viewpoints is described as well as the different deployments of the CHIC architecture have been elaborated A very relevant discussion explaining and justifying high level technical orientations taken in the project.
D5.2.2	**Final version of security tools and guidelines**	**A**	This document describes the security framework of the system which is now in its final version. At first the broker-based authentication (using SAML requests between the user and the invoked services) , and authorization policy is presented and further

			detailed for web sites, web services and system components. The auditing services are then comprehensively presented along a relevant approach based on the event/action/actor paradigm. The security t tools are then investigated and described in full technical details depending of the use of CHIC as a research platform or as a clinical platform. In both cases the various kinds of users are identified and the specific security functions they require are carefully considered. The last part of the document provides a comprehensive set of guidelines for ensuring a full interoperability of the platform with the exploitation site. The deliverable is sound and substantial. Technical presentations are solid; arguments are convincing and feature a deep understanding of the subject.
D6.3	**Initial standardized cancer hypermodels**	**A**	This document presents the first "standard" forms of hypermodels for the 4 types of cancer retained in the project. The hypermodels and their component hypomodels (with some common to several types of cancer) are described in full details. In each case, the integration and orchestration between the hypermodel and its component models are depicted, interaction links and parameters are fully specified. Semantic annotations of the models along the 13 perspectives previously identified are documented. The strategy and technological resources used for the development of the models (spatiotemporal approach, machine learning, statistical methods, etc.) are documented. Adaptation of the models and experimental results for particular clinical cases illustrated by concrete questions are provided. The second part of the document provides a reminder of the process to develop hypermodels (hypermodel edition and integration, semantic annotation of models, etc.) and to use and execute them for clinical research with the CRAF environment. The document is very rich and provides a deep insight in the scientific and technological achievements of the project. Obviously, the approach is successful.
D7.4	**Final hypermodelling framework deployed on test nodes**	**A**	This is a description of the final prototype deployed on the test sites (CINECA and USFD), and on the CHIC private cloud (production environment). The functional architecture and implementation of the hypermodelling framework is provided with a detailed description of the functionality and API's of each component. The integration of the HF into the CHIC platform is depicted, including dependencies and interactions with the user (hypermodel editor and CRAF environment) as well as with the system (generic stub, repositories and authentication/ authorization functions). The last sections are devoted to the deployment and execution on the pilot sites, described along two levels of abstraction: orchestration layer (components, libraries and tools ruling workflows, storage and retrieval of data) and computational/model layer (models with tools and libraries required for execution). A practical example with the execution of the nephroblastoma hypermodel is developed. This deliverable is of high technical value and the achievements reported demonstrate a fruitful integration and cooperation in the consortium, the technical choices are explained and justified
D8.4	**Report on the final system**	**A**	This is a technical description of the 4 CHIC repositories (model and tools; clinical data; in-silico trial and semantic metadata: knowledge bases and annotations encoded in RDF) and of the user interface and web services that provide access to these repositories. It addresses also the user's point of view by providing comprehensive manuals that guide and help the end-user to operate the system for their daily research and clinical activities.

			Each of the first 3 repositories above is depicted in details, with a reminder of the architectural design and data models. User interface and web services are carefully explained with nice illustrating examples, as well as integration with the semantic management services and repository, in order to ensure semantic interoperability. The last section is devoted to the organization and structure of the semantic repository built on top of the RICORDO framework and includes a very comprehensive description of the semantic services provided by the platform. In all cases, the API's to access the services are documented in full as well as the requirements and guidelines for installing the software. This deliverable is a very valuable piece of work and features achievements of high scientific and technical quality.

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.

Objectives are still relevant and achievable with the available time and resources. The value of scientific approach and methodology are demonstrated by the quality of the deliverables and by presentations given at the review meeting.

(i) project objectives are still very relevant. The project has high potential to achieve excellent impacts on the cancer modelling and treatment domains.
(ii) The objectives are achievable with the remaining project resources. However, after the project end wider exploitation and introduction of the system to clinical use requires future funding and development efforts to achieve sustainability.

The project is ambitious and its wider clinical perspectives can only be reached through a sustained effort over the coming years with appropriate funding. This is clearly indicated already in the Project Proposal and the Technical Annex, and it is a useful complement to the project in its final phases.

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.

N/A

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.

Use of resources is appropriate and consistent with the work performed. Underspending is well justified and part of the budget should remain available at the end o the project.

Therefore, it is likely to end up with a small amount of underspending. Consequently, it is recommended to the EC allow the project to spend these resources on preparing the future giving an extension of 3-6 months (whatever the project and the EC can agree on), to reach a point where the work of CHIC can be the basis for a continuation effort which will take some time before starting.

b. Deviations

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

No deviations observed.

[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.

Management (technical as well as administrative and financial) is very effective. The review was well organised, all documentation (deliverables and presentation slides) was delivered on time and is of high quality.

The project has been re-oriented to reflect the new version of the technical annex in a most effective way

b. Collaboration and communication

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

Collaboration and communication is excellent, as shown by the quality of achievements gathering contributions from many different participants.

The consortium seems to work well together; they have a good team spirit. During the reviews it has been clearly visible that all partners are committed to the project and they are aware of their shared vision and mission.

The provided evidence so far suggests that the work produced in the different work packages is in most of the cases result of a collaborative effort

The consortium demonstrates excellent cohesion and cooperation (viz. the Intellectual property MOUs in WP 4)

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 participants remain fully committed and were very reactive during the review, well committed to the project, with no signs of underperformance of lack of interest

Partners are highly skilled and very motivated towards the project goals. There is no evidence for underperforming beneficiaries.

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)?

Potential scientific impact is high, both for clinical research and for cancer treatment. The technical hypermodeling infrastructure features important progress with many potential applications beyond the healthcare domain.

Large scale hypermodeling is a real challenge and the demonstration of a scientifically feasible approach would be a decisive progress. Clinical and social consequences could also become important with time in optimizing the diagnosis and treatment of cancer diseases helping thus to improve the patient's quality of life. The developed models, tools and services offer new ways and options to study cancer processes and develop new treatments and analysis methods.

The project has excellent scientific progress and has the potential to advance further the state-of-the-art in the field. The clinical relevance of the developed modelling environment is also very convincing, but requires further clinical validation to facilitate adoption in the medical practice

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.

The research results of CHIC are promising so this should happen and the project has been most ambitious and succeeded in much of its ambition that it is really necessary to go to this next step, requiring new funding.

The effective use of results for routine clinical practice is subject to a validation process that is beyond the scope of the project. Considering the high quality of the achievements, it is recommended to use the remaining resources to start clinical validation in the frame of an extension of the project.

The consortium has prepared itself well for the exploitation of foreground but real economic impact will only come as the hypermodelling demonstrated reaches the early stages of clinical tests or, at least, widespread experimental use.

c. Dissemination

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

Significant efforts towards dissemination of the CHIC concept addressing clinicians and other main stakeholders have been engaged and dedicated workshops have been organized in the frame of international conferences, addressing a large audience of stakeholders. A first study focusing on acceptance issues is presented in D2.4, which deserves to be further developed.

The dissemination activities towards the medical community has continued at a high level of activity The project demonstrated overall excellent dissemination, supported by an impressively long list of dissemination activity e.g. journal articles and organisation and participation to conferences and workshops is reported.

e. Involvement of potential users and stakeholders

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

Potential users and stakeholders are well involved, in particular through the organisation of dedicated conferences, presentations and studies.

Re-orientation of CHIC during the current year to become more clinically guided has improved involvement of clinical and research stakeholders.

The project has therefore engaged very closely and pro-actively with the relevant research and clinical stakeholders disseminating the hypermodelling approach and working towards the elicitation of the necessary requirements for adoption in the clinical practice.

The potential uses have been involved in small number in the user acceptance testing reported in D2.4. More users and clinicians should be involved in the future for validation and clinical relevance experimentations to achieve wider feedback, and evidence on acceptability and validity

f. 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).

Not relevant for this interim review

6. OTHER ISSUES

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

Safety and security issues as well as ethical issues have been handled appropriately taking into account the relevant legislations and normative rules and other guidelines.

Names of experts:	Signatures:
Tor BLOCH	*[e-signed]*
Henry KANOUI	*[e-signed]*
Jorge MARTINEZ de HURTADO	*[e-signed]*
Pirkko NYKANEN	*[e-signed]*
Elena TSIPORKOVA	*[e-signed]*
Date: 13.12.2016	