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
Gra+ nt 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. 2, from 01/04/2014 to 31/03/2015
Place of review meeting:	Brussels
Date of review meeting:	08/07/2015
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 THIRD review of the project covering the 13-24 month period, assessing the project's progress and the adherence to suggestions made at previous reviews.

During the period the project work has been focused on technical and research issues. All the planned deliverables have been produced, with good quality, though almost all with slight delays. The progress report of the period is very detailed, work has been reported per work package, contribution of each partner has been clearly envisaged per work package and task, resource usage is almost as planned, no big deviations. However, a consolidated view on the work done and progress made, remains unclear in the report.

Very good results have been achieved with CHIC technical architecture and platform components and with the security framework development. Two demonstrations during the review showed that the technical infrastructure has been developed and is functioning, however, there is not yet medical or biological content and the user interface is still rather naïve. This was also evident in the first evaluation results (deliverable D11.2). From now on, there is a clear and urgent need to focus on integration of the developed components and on clinical adaptation of the models and tools and to collect evidence on their usefulness and usability. This was already asked by the reviewers in 2014 review.

As the project stands now it has workflows, toolkits, databases, a private cloud, a good legal understanding and framework and a good clinical understanding of the models to be tried out, but no significant integration between the two areas. What is needed urgently now is to test the overall concept by getting to a "black box" demonstrator for the targeted clinician.

Many deliverables have been released on due date, although both the mean and the average delay of the deliverables is about 2 months. The project stated that these - almost systematic - delays have not created any serious issues but, going forwards, there is a concern that significant problems could result if the reasons are systemic. The deliverables are of good quality and the presentations at the review were very detailed. It turned out that the agenda

proposed was over ambitious resulting in significant delays during the day in spite of an effort made by presenters to present very rapidly.

Activity on exploitation still remains at an early stage and this must be corrected urgently.

Resources consumption and costs reported are globally consistent with work performed and delivered results. Some readjustments of effort (also) between partners were made with good reasons and good results.

Partners all seem committed but the objective stated at the last review that the technical effort was "driven" by the clinical requirements, was not convincingly demonstrated.

As in the previous review, the demonstrations of the platforms were basic and mostly illustrative of the technical advances of the project. The user interface does not seem to be developed with the ultimate end-user in mind. The key for the project to reach its goals is to have convincing demonstrators, showing ***clear clinical relevance*** to the targeted clinicians, within months now.

Data protection and IPR issues have now been adequately and extensively addressed with an IPR agreement signed between all partners. The legal partner provided a very convincing reply to one of the most important recommendations of the previous review. A Memorandum of Understanding has been signed by all partners, which is an achievement worth mentioning.

The project management is of good quality. However, the project activities appear still too much focusing on individual work packages and too fragmented for an IP. The project coordination needs to put more focus on the consolidation and integration of the results achieved in the different work packages, and the ultimate clinical relevance of the CHIC project.

There has been a significant improvement into the consideration of the necessary ultimate evaluation of the potential tools in a clinical setting, i.e. Clinical Trials and adherence to GCP.

In summary, the project makes good progress in individual work packages but the overall integration is planned for very late in the project and this poses significant risks for the overall impact of CHIC.

A monitoring review of the progress would be useful in 6 months to ensure that the clinical-orientation has been applied.

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 previous review recommended that a *clear and explicit* Gantt chart documenting which services are available to the clinicians, when and from where was provided. As such, it has not been presented. The one provided during the Review lacked enough detail to be of help in *clarifying the clinical relevance of the final integration.*

- 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, it has not been demonstrated up to date.
- 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. This has not convincingly been demonstrated.
- Recruitment issues at FORTH have been clarified.
- A contingency plan should be devised in case a clinical significant disruptive development occurs during hypermodelling of each cancer scenario. This has still not been convincingly demonstrated.

Comment [PN1]: I would like to add this comment, as they have not explicitly mentioned standards in their work yet.

As a summary, the major concerns on the work done during the period are related to 1) the clinical relevance of the achievements and 2) evaluation and validation of the models, tools and the CHIC platform and to the clinical usability, usefulness and acceptability of the tools and environment by the clinical users – the ***clinical relevance*** of the work done. Additionally, consolidated presentation of the work done was not evident in the deliverables and review presentations.

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.

A change in focus of the future project work needs to be implemented, from technical and research-orientation, to clinical-orientation.

The following changes are recommended to be implemented:

1. The key word for the future work should be **integration** – integration of models, hypermodels, tools and components into a usable, reliable, valid and ***useful clinical environment.***
2. Focus on the consolidated approach of the CHIC environment and on collecting evidence on its validity, usability and usefulness in the clinical practice. It would be good to nominate a ***clinical integrator***, a clinician (from the consortium), to support the coordinator and technical integrator and to enable better integration of the technical and clinical work.
3. Accelerate to the extreme the development - under the direction of the clinical partners - of at least one clinically-oriented packaged demonstrator to be used for getting CHIC "sold" to the community, result must be available within months
4. Downscale the project scope; focus on the 3 cancer types, no additions or extensions. For the demo session during the next review, the consortium needs to prepare realistic clinical scenarios to demonstrate the added value of the developed computational environment.
5. Emphasize clinical usability and user interface in the next evaluation workshop
6. Use the external advisory committee to review the detailed plans for integration now to be developed
7. Reorganise the evaluation and validation activities:
    - Validate the models and hypermodels: their validity, correctness, coverage, consistency etc,

- Evaluate the tools, components and the CHIC environment: functionality, performance, reliability, security etc,
- Evaluate from the ***clinical users perspective***: usability, usefulness, acceptance, sustainability etc.
- Make a detailed planning with good internal milestones (and metric) to be able to follow progress in integration over the coming months, including a list of decisions to be taken and when with precise calendar dates. Include extra resources for coordination and management
- The previous recommendation of ultimately designing a Randomised Clinical Trials for each type of cancer still applies, 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.
- A contingency plan should be devised in case a clinical significant disruptive development occurs during hypermodelling of each cancer scenario, as was recommended in previous review

To implement this change the consortium is asked to prepare a practical step-by-step plan how to continue the project work to achieve a clinically relevant, validated and evaluated CHIC environment for clinicians working in the cancer domain. This plan should be presented for the reviewers for acceptance and a monitoring review of the progress would be useful in 6 months to ensure that the clinical-orientation has been applied.

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 is on schedule and has globally achieved the objectives set in the DoW. The results delivered up to now are of expected scientific level and quality.

The objectives of the reporting period have been principally achieved; very good progress and results in the technical and security aspects; however in the clinical aspects the achievements are minor.

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 work-packages have progressed as expected and delivered their results. Although significant delays observed in the completion of many deliverables the management report indicates that there will be no significant impact on the project schedule. It is to be noticed that FORTH is now fully operational and even has uptake unforeseen work on its own resources.

WP1: Project Management. The project management is of good quality. All the work packages are progressing according to the plan and the engagement and the motivation of the research partners is high. Part of this work package was also the development and signing process of the CHIC Memorandum of Understanding (MoU), which will be an addition to the CHIC Consortium Agreement.

Resource usage is almost as planned, no big deviations. Recruitment issues have been solved by hiring less experienced persons, therefore the number of person months has grown but the budget is as planned. Advisory board has not been actively involved in the project coordination and management.

Quite a number of deliverables were delayed (average and mean both about 2 months). There was no summary reporting of the replies by the project consortium to the recommendations from the last review. Some seemed not to have been addressed.

The External Advisory Committee did not meet.

WP2: User Needs and Requirements. The focus was on the further development and documentation of requirements for hypermodels beyond the domain of cancer, the collection of imaging and molecular data, the further development and refinement of scenarios and use

cases by the clinical partners. Interaction and collaboration with the p-medicine project continued.

User needs and requirements: Reuse of extended hypermodels studied for other domains. General requirements presented, it is not primarily of user needs but more on the needs of other domains and various modelling perspectives and levels (D2.3)

Only deliverable planned for this period was D2.3 about the possibility of using the CHIC approach for other domains than cancer. It is recommended to focus on the three cancer domains originally selected

Collection of clinical, imaging and molecular data continued, scenarios and use cases were further developed and refined. An integrative framework for combining the state-of-the-art knowledge in structural biology and machine learning, in order to delineate mechanisms and relationships in cancer genomes was provided.

WP3: Clinical and Translational Science Scenarios. The work package was concerned with the exploitation of Wilms tumor and lung cancer patients' multiscale data, the definition of the specific multiscale data to be provided for glioblastoma modelling, the further development of the ontology-based clinical trial managing system ObTiMA to collect data also for glioblastoma.

A major part of the activity was devoted to the definition and collection of data in view of modelling various types of cancer (glioblastoma, nephroblastoma, non-small cell lung cancer and prostate cancer for patients treated by radical surgery or radiotherapy).
The ontology-based clinical trial management system ObTiMA was further developed. Case report forms were established and significant data set for the 3 types of cancer were collected and introduced into ObTiMA.

WP4: Legal and Ethical Framework. The work package advances very well. The first iteration of the data protection and copyright framework was completed and an Intellectual Property Rights (IPR) memorandum of understanding was developed. A mapping of the data evaluation and privacy profile for the transfer of data to the CHIC research environment was also produced.

An Intellectual Property Rights (IPR) Memorandum of Understanding has been signed by all partners, and agreements on data protection were reached.

Excellent work and report

WP5: IT Architecture. The work package completed the final stage of the initial version of the CHIC technical architecture. The second phase of the integration of the single-sign-on security mechanism into the model/tool repository and the *in-silico* trial repository has been initiated. The final version of the security guidelines and an initial version of security tools have been produced.. A black-box testing of the new integrated authentication module for VPH-HF (Virtual Physiological Human – Hypermodelling Framework) version alpha 0.2 has been passed.

IT architecture: CHIC technical IT architecture has been defined (D5.1.1.1) and it covers functionality, information, deployment and security views. The reference architecture has not been documented. Security guidelines and initial version of security tools update has been produced (D5.2) and techniques to build the cloud infrastructure available to the community

(D5.3). Various open source cloud models have been compared and openStack selected for implementation of the CHIC private cloud. Good progress. Interplay between the IT architecture and the clinical models is not yet made explicit.

A decision was taken to give up to convert the private cloud service to a public one was made after legal advice, which is seen as an excellent decision.

Good progress overall.

WP6: Cancer Models and Hypermodel Design. The work package continued further research on the development and validation of cancer hypomodels and related hypermodelling strategies. For instance, an alternative mathematical approach to the phenomenon of glioblastoma invasion to surrounding tissues based on the Brownian motion was developed and published; advanced numerical checking and exploration of an existing model of non-small cell lung cancer response to treatment was performed; new components of vasculature growth with a focus on the interaction with the tumour growth component model have been formulated.

Lots of activities regarding the methodology for the realization and validation strategy of hypermodelling have been conducted. At the same time, the implementation and experimentation of several hyper models have been started, notably regarding lung cancer, nephroblastoma and glioblastoma. Mathematical approaches regarding responses to treatment are also under investigation for a large variety of cancers. Many phenomenon related to mutation have been studied. Apparently considerable work is on-going, along multiple directions, but this reflects the organization of the WP in which several tracks are explored in parallel. The first results have been published in D6.2. and turned to demand more resources than expected.

WP7: Hypermodelling infrastructure. The focus of this work package was on the deployment of a set of hypomodels supplied by WP6 which constitutes the first CHIC exemplar lung cancer multimodeller hypermodel, the consolidation of the first version of the metadata schema used to annotate data and resources to be used in VPH-HF, the construction of an initial version of folksonomy tagging service and successful implementation and deployment of the first release of the revised VPH-HF and demonstration of test workflows on two test nodes.

Both relevant deliverables D7.1 and D7.2 were 2-3 months late. Good research work in general

Exemplar sets of hypomodels supplied by project partners including hypomodels constituting the first CHIC exemplar lung cancer model were deployed; black box hypomodels representative for initial testing and consolidation of the first version of the metadata schema used to annotate data and resources were developed. On the testing sites the first release of the revised VPH-HF was successfully implemented and deployed. Models and hypermodels with their annotation were provided for testing purposes.

A specific software program facilitating the deployment of alpha version of hypermodelling environment on a remote machine was developed and the revised architecture for the beta version ment was agreed.

WP8: Model and Data Repositories. The work package advanced very well performing the following activities: finalization of the information model and the technologies for the

model/tool and the *in silico* trial repositories, design of the back-end of the model/tool and the *in silico* trial repositories, completion of the advanced phase of the definition of the interoperable interfaces for retrieving model and hypermodel descriptions from the model/tool repository, development of components of the back-end of the model/tool and *in silico* trial repositories and deployment on the CHIC's private cloud, completion of the second phase of the integration of the single-sign-on security mechanism into the model/tool and the *in silico* trial repositories, integration of the data repository with the first version of the CHIC data protection framework.

Review has been done how p-medicine is dealing with semantic interoperability; however, the results of this review have not been documented. Progress in the development of 'HOT (Hallmarks-Ontologies-Tumor) Maps' of tumour-specific hallmark knowledge. Design of the CHIC repositories documented (D8.1), however, the validation of the repositories and maintenance of their validity is not presented. Prototype implementation of the CHIC repositories (D8.2) delivered.

Deliverable 8.1 (design of the repositories) was delayed by almost 4 months

WP9: Image Processing and Visualization. This work package developed software for the preprocessing of imaging datasets according to the needs of the CHIC hypermodel Oncosimulator. Both the timeline and CCGVIS (a 3D volume rendering software) have been internally tested. Most of the technologies have been integrated into the DrEye image processing platform.

The decision to use the DrEye tool as the single integrated imaging platform has entailed additional integration effort uptaken by FORTH. In the same way new plug-in (as automatic segmentation of tumor or rendering of tumor volume) were/will be integrated into the DrEye software. Many other developments regarding tumor imaging are also in progress.

Good presentation, no deliverables - not even before month 44 (31.1.2017)

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WP10: Integrated Platform. The work package focused on the definition of the programmatic interfaces for accessing the model repositories, the implementation of the CHIC Data Upload tool for the secure uploading of sensitive patient data to the CHIC platform, the further development of the current PhysiomeSpace encryption services with state of art encryption algorithms, initial design of the CHIC Hypermodelling Editor.

These interfaces are meant to be used by the components of the CHIC platform and also to enable interoperability with external organizations. The CHIC Data upload tool has been developed. Further development of the PhysiomeSpace encryption services and design of the CHIC Hypermodelling Editor. However, it remains open how the model validity is ensured when allowing editing
Design of the orchestration platform related components and interfaces (D10.2) and the CHIC encryption services (D10.3) delivered.

Demonstrations showed that the software work has progressed but it is difficult to assess the clinical readiness in the absence of a "packaged" clinically oriented demonstration. The "user" interface still remains to be adapted to the CHIC objectives of being usable by (research) clinicians

WP11: Clinical Adaptation and Validation. The first round of evaluation tests of the CHIC components has been completed. Cloud resources have been used for the evaluation activities

of CHIC. The first multi-modeller hypermodel of lung cancer has served as a first complete example for the fine-tuning of the CHIC infrastructure based on the corresponding multiscale clinical data. The first round of evaluation tests of the CHIC components took place in Leuven, Belgium. The organization of the first round of evaluation tests was carried out using the cloud resources of the project. This experience turned to be very positive in terms of technical knowledge earned and looks very promising for the future steps of the evaluation.

Deliverable D11.1, Evaluation and validation criteria for clinical adaptation, presents the criteria for clinical validation. The applied usability criteria differ from the well-known criteria in the scientific literature (e.g. J Nielsen, ISO9241-standard). Deliverable D11.2 reports on the first evaluation workshops round, and presents the results of the evaluation workshop.

There is a certain mismatch in the evaluation - end users, clinicians, evaluate e.g. maintenance of software, source code documentation, further development of software, interoperability etc, these are aspects that the users should not evaluate. Usability of the tools in the first workshop showed to be poor.

There should be separate evaluation questionnaires for the developers and for the users. Additionally, detailed descriptions on the tools, their use and uploading are not needed in the results report.

WP12: Dissemination and Exploitation. The work package produced a first version of the Preliminary Plan for the Use and the Dissemination of Foreground (PUDF). Training activities, most notably the CHIC Summer School 2015, have also started or are currently being organized. A clinical workshop primarily dedicated to prostate cancer was organized by the CHIC partner UNITO in Turin, where most CHIC clinical partners, modellers and the CHIC coordinator participated in it disseminating CHIC to the wider clinical community.

The project partners have been extremely active in participating to conferences and workshops and publishing scientific contributions. However, the release of D12.6 (issue 1 of the project newsletter) was been delayed by 7 months.

The project communication model has been further investigated. An innovation questionnaire regarding the exploitation of results has been circulated among the partners. The analysis of the answers allowed drafting the list of exploitable outputs and the individual partners' intentions. Participation to scientific events and publications of scientific papers has been very productive. All achievements are reported in D12.3

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).

Many deliverables have been released on due date, although both the mean and the average delay of the deliverables is about 2 months (longest delay about 7 months). The project stated that these - almost systematic - delays have not created any serious issues but, going forwards, there is a concern that significant problems could result if the reasons are systemic. All deliverables are of overall good quality, substantial and informative. All are accepted.

STATUS OF DELIVERABLES			
No.	**Title**	**Status** *(Approved/Rejected)*	**Remarks**
D2.3	Requirements for enhancing hypermodels beyond the domain of cancer	Approved	An extension of the original deadline (M18) was requested because the partners responsible for the deliverable agreed to go beyond the mentioned atomic/granular models, thereby showing common ways in reusing models in other domains. Therefore, further information from modelers had to be gathered and incorporated into the deliverable.
D5.2	Security guidelines and initial version of security tools	Approved	A first version of D5.1 was submitted in 2014. However, an updated version of D5.2 was produced after a second internal review and sent to the EC in May 2015. The updated version contains the following modifications: Updated security vocabular, updated integration tutorials, added audit Json schema Good report, but 7 months late
D5.3	Techniques to build the cloud infrastructure available to the community	Approved	Presents the methodology followed for the selection of a cloud platform considering the particular legal and ethical restrictions caused by the management of clinical and health care data and the needs for computational and storage resources to store and process these data. The document justifies how the selected platform Openstack matches the requirements above and fulfils the required functionality. The last part is a brief guide for a step-by-step installation and configuration of the platform. The methodology used is very adequate, the selection criteria are relevant and the decision taken is well argued. A very solid and convincing document..
D6.2	Cancer hypomodelling and hypermodelling strategies and initial component models	Approved	This deliverable was postponed by about 3 weeks due to its complex and multidisciplinary nature as well as due to the Christmas break. The EC officer was informed accordingly.
D7.2	First Release Hypermodelling framework deployed on test nodes	Approved	The submission of this deliverable was postponed by

			2 months and the EC was informed accordingly on 26 March 2015. The reason for this delay was an ongoing consensus process on the architectural design which had to be fully resolved before work on D7.2 could be started Late submission (2 months).
D8.1	Design of the CHIC repositories	Approved	The submission of this deliverable was postponed due to unforeseen workload at the partner in charge. After the CHIC review meeting held on the 3rd of September 2014 and the very valuable comments that we received from the reviewers during the review meeting concerning the data representation (both clinical data and models), the partners decided to wait for the official review report in order to understand more precisely the suggestions of the reviewers. In the meantime a draft version of the deliverable was circulated by email among the involved partners, so the postponement did not cause any delays on the work described in the DoW.. Late submission by almost 4 months
D8.2	Prototype implementation of the CHIC repositories	Approved	The deliverable was delayed by about 4 weeks. The request for a later submission results from the heavy workload at ICCS, one of the partners strongly involved in the writing of D8.2, that followed a recent change in staff.
D10.2	Design of the orchestration platform, related components and interfaces	Approved	An extension of the original deadline (M18) was requested because new needs related to the interfaces and the orchestration of the different components were identified during the Technical Meeting in Leuven and it was crucial to incorporate the necessary changes in the deliverable, having in mind the reviewers' recommendation on paying special attention in models and components integration. Late submission by 2 months
D10.3	The CHIC Encryption Services	Approved	Describes the functionalities, APIs and implementation of the data encryption/decryption services provided by the CHIC infrastructure (basically a symmetric-key algorithm to

			encrypt the data files and a RSA public asymmetric-key algorithm to encrypt the key). A technical and very clear document
D11.2	Report on the first evaluation workshops round	Approved	The original submission date was 30 September 2014 (M18). However, the deliverable submission was extended by about two months. The reason for the extension of the original deadline was that the CHIC consortium met for a first round of evaluations of the CHIC tools in mid-October, during the CHIC Progress Meeting in Leuven, Belgium. The corresponding report, which is D11.2, was then written after this evaluation workshop. Late submission by 2 months
D12.3	Preliminary Plan for the Use and Dissemination of Foreground	Approved	Due to the slow feedback of some of the CHIC partners, the deliverable was delayed by about 4 weeks. The EC was informed accordingly.
D12.6	Periodic Newsletters	Approved. Delivered at Review	The second issue of the CHIC newsletter is delayed by about 6 weeks, as valuable contributions to its content are missing
	CHIC Project Periodic 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 with clinical relevance.***

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

Well reported. Little variation on the man-months but significant (about 30%) under- expenditure on the manpower-cost (lower graded staff than planned)
These economies can be used now with advantage in the integration phase where extra effort should be planned both for the work and for the coordination.

Other expenditures

No specific comment. Look adequate and quite reasonable.

The resources have been used almost as planned, no big deviations. The recruitment problems have been solved. The resources have been used to achieve progress and following the principles of economy, efficiency and effectiveness. Good reports on resources and their usage were presented in the review.

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 otcome 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 worked well in administrative, financial and technical issues.

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

More emphasis should be given in management to integrate the clinical aspects with the technical development.

Therefore, the assignment of a ***clinical expert to support and advise the project coordinator*** is recommended to ensure that clinical issues are fully integrated and made visible in the project work.

By now, the advisory board has not been involved in the project work, this should be improved in the next period.

The structure and contents of deliverables reflects an effective organisation of the work within each work package.. All project documents (deliverables, periodic report, etc.) were delivered. The amount of presentation material was excessive.

A Consortium Agreement relative to IPR issues has been signed.

The recommendations made at the previous review were not explicitly summarised and the comments in some of the individual work packages suggest that they were not all considered for implementation in this period. A clear documentation of services addressing clinicians is still lacking as well as an accompanying schedule for their availability (Gantt chart).

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.

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.

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.

Exploitation activities are still at a very preliminary stage. The expectation expressed in the previous review 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 has not been fully met although the UBERN individual exploitation plan is nicely specific and realistic. The role of giving clinical demonstrations to group of clinical end-users is perhaps not explicited enough with which demonstrations to give to who when.

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..

Communication to a larger public has also been considered through the project web site, and 2 online or newspaper articles. Unfortunately, the second 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.

To implement the proposed changes, the consortium is asked to prepare a practical step-by-step plan how to continue the project work to achieve a ***clinically relevant, validated and evaluated CHIC environment for clinicians working in the cancer domain***.

This plan should be presented for the reviewers for acceptance and a monitoring review of the progress would be useful in 6 months to ensure that the clinical-orientation has been applied.

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