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Preliminary Plan for the Use and Dissemination of Foreground

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PU	Public	
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ABSTRACT:

During the CHIC project dissemination activities play a key role in the promotion of the widespread awareness as well as strong cooperation and exchange with research communities inside and outside of the EU.
The main target of dissemination activities is to inform all relevant target groups about the project results and the implications that these results might have for clinical, industrial and societal users as well as for the research community. They will also aim for increasing awareness among other target groups, namely “all stakeholders” in general, the scientific community, industry, clinical practice and the public at large.

This document summarises the CHIC dissemination strategic plan (the communication model, the target groups, the dissemination channels and the associated responsibilities, the dissemination outputs of the first two years), the IPR management strategy (exploitation of foreground and IPR ownership issues, software licensing strategy), the expected exploitable projects outputs (clinical outputs, technological and software outputs, modelling outputs) and the exploitation plans, both individual and of the consortium. An innovation questionnaire proposed by the CHIC consortium has been filled in by the CHIC partners in order to collect the individual exploitation plans. There will be two updates to this first version of the PUDF as the CHIC project progresses (D12.4 in M36 and D12.5 in M48).

[1] **R**=Report, **P**=Prototype, **D**=Demonstrator, **O**=Other

[2] **PU**=Public, **PP**=Restricted to other programme participants (including the Commission Services), **RE**=Restricted to a group specified by the consortium (including the Commission Services), **CO**=Confidential, only for members of the consortium (including the Commission Services)

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Contents

1 Executive Summary

During the CHIC project, dissemination activities play a key role in the promotion of the widespread awareness as well as strong cooperation and exchange with research communities inside and outside of the EU.
The main target of dissemination activities is to inform all relevant target groups about the project results and the implications that these results might have for clinical, industrial and societal users as well as for the research community. They will also aim for increasing awareness among other target groups, namely “all stakeholders” in general, the scientific community, industry, clinical practice and the public at large.

This document summarises the CHIC dissemination strategic plan (the communication model, the target groups, the dissemination channels and the associated responsibilities, the dissemination outputs of the first two years), the IPR management strategy (exploitation of foreground and IPR ownership issues, software licensing strategy), the expected exploitable projects outputs (clinical outputs, technological and software outputs, modelling outputs) and the exploitation plans, both individual and of the consortium. An innovation questionnaire proposed by the CHIC consortium has been filled in by the several partners in order to collect the individual exploitation plans.

This document is a living document, and, as part of the dissemination activities will be updated and adapted according to the achieved technical and scientific results. The dissemination outputs will be collected and reported annually to the EC services.

Introduction

1.1 Purpose of this document

This document is part of the WP12 activities whose objectives are to coordinate the dissemination and exploitation of the CHIC outputs to target groups, to establish relationships and seek synergies with other projects or initiatives, and to coordinate training activities.

The previous deliverables D12.1 [1] and D12.2 [2] form the basis for the activities to be performed in the next years by the consortium. The purpose of these documents is to provide the description of the CHIC dissemination plan and the tools needed to support their dissemination efforts. Information on the events carried out will be collected annually from partners and will be then reported together with deviations or additions to the plan in the annual periodic reports and in the updated versions of the Plan for the Use and Dissemination of Foreground (PUDF).

This deliverable, as output of Tasks 12.1 (Dissemination activities) and 12.2 (Exploitation and IPR issues), aims

- at providing a vision of the strategy the CHIC consortium is going to put in place in order to increase awareness and promote the use of its scientific and technical results to the major stakeholders;
- to report the project outputs in terms of clinical results, software and models;
- to report the exploitation plans and activities, both individual and of the consortium. An innovation questionnaire proposed by the CHIC consortium has been filled in by the CHIC partners in order to collect the individual exploitation plans.

1.2 Structure of the deliverable

The document is organized as follows:

- Section 2 provides a summary and update of the CHIC dissemination plan presented in D12.1.
- Section 3 contains a description of the dissemination strategy and model chosen for the CHIC project, and its main components;
- Section 4 describes the IPR management strategy, in particular the exploitation of foreground and IPR ownership issues and the software licensing strategy;
- Section 5 provides the description of the expected exploitable project outputs: clinical outputs, technological and software outputs and modelling outputs;
- Section 6 reports the exploitation plans, both individual and of the consortium.

2 Dissemination

2.1 Dissemination plan update

A detailed dissemination plan was defined and presented in D12.1. In this section, we provide a summary of the main concepts associated to dissemination plan and updates occurred in the first two years of the project. The next section will report in summary the outcome of the first two years of dissemination activities.

The overall target of the CHIC dissemination strategy is to spread awareness about the project outputs to specific target groups that are directly or indirectly involved in the cancer modelling and its clinical translation, as well as the VPH modelling community as a whole, since a number of the technologies developed within the project will be of general use for any biomedical research on cancer.

As described in D12.1, the definition of a specific communication model, like the one in CHIC, implies the identification of the main characteristics for each of the composing elements:

1- the information *source*, which produces the message,
2- the *content*, which encodes the message into signals,
3- the *channel*, to which signals are adapted for transmission,
4- the *receiver*, which 'decodes' (reconstructs) the message from the signal.

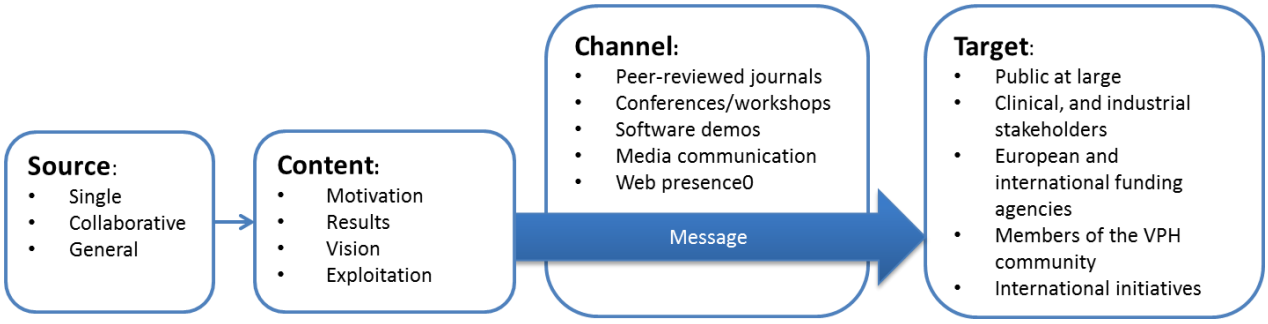

Figure 1: CHIC dissemination model overview

The *source* of all material, information, and results for dissemination purposes are the CHIC consortium members from all the technical/scientific WPs in the project. More precisely, we have classified the sources of dissemination into three types:

1. *Single*: the source is a single partner disseminating the results achieved by its institution;
2. *Collaborative*: the source is a group of partners working together in the same work package (WP) or jointly on specific research objectives;
3. *General*: the source is the all consortium.

Different *target* groups for dissemination activities were identified in the very early stages of the project, and they include stakeholders in research, scientific, clinical or industrial fields, who will be continuously informed about the intermediate and final results of the project. The identification of the target groups was based on the type and level of the involvement in the project (internal, connected, or external). For each of the groups, an analytical description is provided together with the stakeholders already identified as part of each group. Specific names and references have been added where contact has been already established. See Table 1 for all details.

Target group	Description	Stakeholders
Internal	It includes all institutions or associations, which are part of the CHIC project effort. Even if each of them has access to specific information and material, it is important to make sure that all the results and the activities of the project are well known. Awareness is important for cross-fertilization among WPs and partners' activities, increase synergies and capitalise on each other results. The specificity of the target and of the content (i.e. information with access restricted to the consortium) will require the use of specific channels (i.e. private mailing lists).	• CHIC consortium • Institutional observers (departments involved) • CHIC external advisory board: ○ D. Ingram, Professor of Health Informatics and Director of the Centre for Health Informatics and Multiprofessional Education, University College London, UK ○ M. Akay, Professor of Biomedical Engineering, University of Houston, Texas, USA and IEEE Press Series Editor for the IEEE Press Series in Biomedical Engineering ○ F. Meunier, Director General of the European Organisation for Research and Treatment of Cancer (EORTC) ○ T. Jackson, Professor of Mathematics at the University of Michigan, USA; Senior editor of Cancer Research ○ Y. Nikolksy, Chief Executive Officer GeneGo (a Thomson Reuters company)
Connected	It includes all stakeholders that might already have some connection with the CHIC activities but not actively be part of them. This group needs to access public information from CHIC but they can be provided with more technical and scientific details than the general public.	• EC community and related services • Media/journalist • Specialised media • Political stakeholders • Potential users • Related projects from the VPH: ○ p-medicine ○ VPH-Share ○ dr Therapat ○ iManageCancer ○ myhealthavatar ○ VPH-PRISM ○ Go-Smart
External	This group is composed of stakeholders who are completely external to the project activities. Some of these groups most probably have not heard of CHIC before or might not have any technical or clinical background. They should receive general information on the project, written in an easily understandable way with more emphasis on the impact and the vision of the project than on its technical aspects.	• Individual researchers • Research institution or universities • Scientific communities or associations ○ National Cancer Institute, Division of Cancer Biology ○ European Clinical Research Infrastructures Network (ECRIN) ○ The European Platform for Patients Organisations Science & Industry (EPPOSI) ○ The Meg Jones Crain Cancer charity (brainstrust) ○ International Confederation of Childhood Cancer Patient Organisation ○ IEEE ○ VPH-Institute • Clinicians/Patients • Industries ○ Pharmaceuticals ○ Healthcare service providers ○ Others • Public at large

Table 1: CHIC target groups

The *content* of the message to be disseminated has been classified into four different categories:

a) *Motivation*: to inform the taxpayers and their representatives on how the CHIC project uses the money received and the impact its results might have on the citizens.

b) *Results*: with the scope to disseminate the fundamental research and scientific results of the CHIC project toward academic, industrial and clinical researchers so as to contribute to the collective knowledge building.

c) *Vision*: results of the CHIC project in a strategic development perspective toward clinical, industrial, and societal stakeholders. It takes place when the research results compose possible and plausible strategic scenarios that are worth to be known by key stakeholders in order to plan future developments and investments.

d) *Exploitation*: message aimed at driving an effective social, clinical and industrial exploitation of the project results so to be able to create a sustainability plan for the developed tools and services after the end of the project.

The *channels* used to convey the message to the target groups are different according not only to the target group but also to the type of information to be disseminated.

A range of different dissemination channels and tools are being used to ensure the highest visibility of the project progress and its results. In general,

- Scientific and technical results are disseminated via peer-reviewed papers or specialised conferences.
- For software results, apart from technological and scientific results above, demonstrations are organised both for specific groups of stakeholders in conjunction to bigger events (such as conferences) and the organisation of instructional courses on the developed infrastructure within major worldwide events will be evaluated.
- General tools: the consortium will exploit a well-established set of dissemination processes, which includes web presence and media material preparation.
- Web presence: a strong and highly visible web presence has been set up from the very beginning of the project.

The dissemination tools can be grouped according to the type of dissemination activities they are used for, as it is shown in the following table (Table 2).

Type of content	Channel	Examples	Target group
Motivation, Results, Vision, Exploitation	Oral	Presentation on external scientific conferences/exhibitions/ workshops, project conference, summer schools/ workshop/meeting/briefing, report, face-to-face communication	Connected, External
Results, Exploitation	Demo	Webinar, e-based consultancies, online video tutorials	Internal, Connected
Results, Vision, Exploitation	Print	Report, scientific article on peer-reviewed journals, set of promotional materials (fact sheet, flyer, leaflet, brochure, posters, roll outs), information package	Internal, Connected, External
Motivation, Results, Vision	Web content	Project website, links/presence to/in other websites, e-newsletter, mailing list, e-bulletin, e-form of a set of promotional materials, information database, test versions of CHIC tools and services on public website	Internal, Connected, External

Motivation, Vision	Media (generalist and specialised)	Press-release, interviews, panel discussion, project video	Connected, External

Table 2: Overview of CHIC dissemination tools and activities Type of activity

2.2 CHIC dissemination channels update

The general channels, to be used during the project in relationship to the target groups and type of content, have been presented already in D12.1. In this section, we provide more information on some of the most relevant channels and on their set-up.

As part of the paper-based written communication, the general public is being addressed with promotional material that is part of the dissemination kit (D12.2) and that it is kept up to date periodically, while the technical and scientific results are be mostly presented in article and papers published on peer-reviewed journals (some of which are accessible via the CHIC public website; www.chic-vph.eu) and in news-entries on the CHIC website.

The CHIC partners have identified a number of clinical and research journals which they are already targeting to publish the scientific outputs of the project. This list is by no means exhaustive as other opportunities might appear in the future but it aims to provide a first overview of the targets that have been identified for the scientific publications (Table 3).

The journals are listed in alphabetical order and with the associated Impact Factor to show the high impact of the dissemination activities planned by the consortium.

Journal name	Impact factor
ACM Transactions	1.4
Acta Oncologica	2.8
Briefings in Bioinformatics	5.3
British Journal of Cancer	5.1
BMC Bioinformatics	3.0
BMC Medical Informatics and Decision Making	1.6
Bulletin of Mathematical Biology	2.0
Cancer	5.2
Cancer Research	8.6
Computers and Mathematics with Applications	1.9
European Urology	10.4
Future Generation Computer Systems	1.8
IEEE Journal of Biomedical and Health Informatics	2.3
Interface, A Journal of the Royal Society	4.9
International Journal of Multiscale Computational Engineering	0.7
International Journal of Radiation Oncology Biology Physics	4.7
Journal of Biomedical Informatics	2.1
Journal of Clinical Oncology	18.0
Journal of Computational Science	n/a
Journal of Mathematical Biology	2.3
Journal of Neuro-Oncology	3.1

Journal of Pathology	7.5
Journal of Theoretical Biology	2.3
Klinische Pädiatrie	1.9
Lancet	39.0
La radiologia medica	1.4
Mathematical Biosciences	1.8
Medical Physics	2.9
Neoplasia	5.5
Pediatric Blood and Cancer	2.3
Philosophical Transanction of the Royal Society A	3.1
PLoS Computational Biology	4.8
PLOS ONE	3.7
Prostate	3.8
Radiotherapy and Oncology	4.4
Radiation Research	2.6
Strahlentherapie und Onkologie	4.1
Tumori	0.9
Urology	2.4

Table 3: List of peer-reviewed journals which might be selected for publishing the CHIC scientific results

The CHIC partners are also actively presenting the project results to the research and the clinical communities by participating in the most relevant conference (as reported in the next section on the first two years activities).

A list of events of interest for the project partners has been defined.

- Annual Conference of Pediatric Oncology (SIPO: International Society of Pediatric Oncology)
- Bi-annual conference of German Society of Pediatric Oncology
- Annual meeting of the Society for Mathematical Biology (http://www.smb.org/meetings/annual.shtml)
- European Conference on Mathematical and Theoretical Biology, Atlanta (USA), June 30-July 3 2015 (http://math.gsu.edu/~smb/)
- Workshops associated with the MBI with emphasis on cancer and its environment
- Ohio State University, MBI Emphasis Year on Cancer and Its Environment 2014-2015 (http://mbi.osu.edu/2014-15/scientific2014-15.html)
- British Applied Mathematics Colloquium (annual applied maths meeting in UK)
- Annual meeting of the National Cancer Research Institute (UK-based meeting on cancer)
- Annual meeting of the American Association for Cancer Research
- International Conference on Computational Science
- European Complex Systems Conference
- European Association of Urology
- European Society for Radiotherapy and Oncology
- Annual International Conference of the IEEE Engineering in Medicine and Biology Society
- IEEE International Conference on BioInformatics and BioEngineering
- Symposium of Mechanisms and Models of Cancer (http://www.salk.edu/MechModels2013/index.php)
- European Cancer Congress

- International Conference and Exhibition on Biochemical and Molecular Engineering

2.3 Dissemination process update

According to the dissemination types described above, the identified stakeholders have been classified into three main target groups. A special set of appropriate dissemination methods/tools and benefits from the dissemination activities to be applied have been already summed up in Table 2.

In order to be effective in performing these activities and in their reporting to the EC services, responsibilities in coordinating the activities have been identified together with a formal reporting process. Both of these aspects are described in more detail in the next sections.

As the channels and target groups of the CHIC project are many, it has been decided that some of the partners be responsible for guiding the specific dissemination (as reposted in Table 4). This does not mean, however, that the other partners are excluded or not contributing to the dissemination project activities.

Target group	Stakeholders	Channel	Partner in charge
External	Political	Web content (website, newsletters) Paper (promo material)	USAAR, KULeuven
External	General public	Web content (website, newsletters) Paper (promo material)	USAAR, KULeuven
Connected	European Commission	Web content (website, newsletter) Paper (promo material)	Project Management team (Eurice, ICCS)
Connected	Institutional observers	Web content Paper Oral	All partners
Connected	Users	Oral (conferences and summer schools) Web content Paper	USAAR, KULeuven, BED, ICCS
External	VPH community	Oral Web content Paper	USFD, UCL, ICCS, FORTH, UOXF, CINECA, BED
External	Healthcare ICT	Oral Web content Paper	Philips, FORTH, UCL, BED, USFD, CUSTODIX, CINECA, BED, ICCS
External	Mathematical modelling	Oral Web content Paper	ICCS, UPENN, BED

Table 4: Main partners' responsibilities in the dissemination process

2.4 Dissemination results after year 2

A list of the events and contributions from the different partners for the second year of the project (among other things):

- Eurice provided assistance to the coordinator, ICCS, in the organization of the 6th IARWISOCI Workshop, which was at the same time the first of two larger CHIC workshops. ICCS has also participated to the VPH2014 conference in Trondheim, Norway.
- LUH presented two talks on “Legal and ethical aspects of in silico based medicine” and “IPR issues in multiscale modelling” at the 6th IARWISOCI Workshop. It also actively participates at the EHR4CR First European Hospital Conference and 23rd EICAR Annual Conference.
- Presentation of the CHIC project by ICCS at the 7th World Congress on Biomechanics, Boston US, 6-11 July 2014 (invited talk).
- K. Duan and D. Tartarini presented poster describing CHIC Project with the focus on Hypermodelling Infrastructure at the Insigneo Showcase 2014 on the 07/05/2014. The focus of the Showcase was on the impact achieved through collaboration with industrial and clinical partners. The event was attended by high profile guests including key representatives from industry, the health and research sector, and important funding bodies. Additionally, the leaflets describing Project CHIC were disseminated during this event.
- Oral Presentations about The CHIC Hypermodelling Framework in Cancer Research developed in WP7 was given on the 11/09/2014 by Dr Daniele Tartarini at the VPH2014 Conference in Trondheim, Norway. It was focused on the CHIC technological framework that through the CHIC Portal will allow the clinicians to investigate the clinical questions related to cancer disease and personal patients’ data. Researchers will be allowed to create hypermodel workflows involving datasets and models from repositories and execute them on the CHIC Hypermodelling Framework.
- CUSTODIX prepared and submitted a paper for the CHIC Workshop (3-4 November) and the EICAR conference (17-18 November).
- USAAR: active participation in an IT workshop on tools/services for clinical trials that was organized by ECRIN at the 26-27 May 2014 in Düsseldorf. Moreover, a talk was given at SIB/SystemsX.ch Summer School, June 22-27, 2014 in the Swiss Alps, Hotel Victoria in Kandersteg. This was a combined effort of p-medicine ad CHIC.
- UNITO: Ilaria Stura presented a talk at MPDE14 Conference at University of Turin, Italy. She also presented an e-poster at the VPH 2014 Conference in Trondheim, Norway and a she made a presentation on Modeling Prostate cancer within CHIC at the Congress “Prostate carcinoma: reports from Eureka studies”. Domenico Gabriele presents an observational, multicentric, retrospective study on prostate cancer treated by radical prostatectomy called EUREKA-1 at the same congress.

For this reporting period, UPENN listed a total of 8 dissemination activities of CHIC supported research, among them invited lectures/talks, conference presentations and activities directed at media publicity. KU Leuven has collected a total of 12 oral presentations at international conferences. A detailed description of these dissemination and publication activities is provided in Tables 6-7.

ICCS submitted for peer-reviewed journal publication the following manuscript:

- Georgios Stamatakos and Stavroula Giatili, “An Explicit Numerical Treatment of the Three-Dimensional Boundary Conditions Imposed by the Skull on an Inhomogeneous Diffusion-Reaction Tri-scale Model of Glioblastoma Multiforme Tumour Growth and Invasion into the Brain. Clinical Validation Considerations”, submitted to the journal Bulletin of Mathematical Biology.

Five articles, to which ICCS and various other CHIC partners contributed, were submitted for peer-reviewing to the 6th IARWISOCI - The CHIC Project Workshop, 3-4 Nov, Athens, Greece. These articles are listed in Table 5.

Twenty-fourth other papers, including those by partners FORTH, UNITO, UPENN, CUSTODIX, KU Leuven, UOXF, UBERN, USAAR, UCL and TEI-C were published in scientific journals and conference proceedings. A detailed overview of these publications is provided in Table 5.

Title of Publication	Contact Person	Involved Institutions	Reference	Category	Publication Date	Co-Authors	Status
Legal and Ethical Aspects of In Silico Medicine	Iheanyi Nwankwo	LUH	2014 6 th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation. DOI: 10.1109/IARWISOCI.2014.7034647	Peer-reviewed publication	10/03/2015	Marc Stauch, Alan Dahi, and Nikolaus Forgo	Published (Pending consent)
Intellectual Property Rights Issues in Multiscale Cancer Modeling	Iryna Lishchuk	LUH	2014 6 th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation	Peer-reviewed publication	10/03/2015	Marc Stauch and Nikolaus Forgo	Published (Pending consent)
A multicenter retrospective study on irradiated prostate cancer: preliminary report	Domenico Gabriele	UNITO	Abstract in Anticancer research 2014 : 34	Peer-reviewed publication	2014	Gabriele P, Ruo Redda MG, Garibaldi M, Cattari G, Garibaldi E, Guiot C	Published
Piedmont multi center retrospective study on operated prostate cancer: first report	Domenico Gabriele	UNITO	Abstract in Anticancer research 2014 : 34	Peer-reviewed publication	2014	Gontero P, Terrone C, Porpoglia F, Muto G, Guiot C	Published
Computational Horizons In Cancer (CHIC): Developing Meta- and Hyper-Multiscale Models and Repositories for In Silico Oncology - a Brief Technical Outline of the Project.	G.Stamatakos	BED, CINECA, CUSTODIX, FORTH, ICCS, KU Leuven, LUH, PHILIPS, TEI-C, UBERN, UCL, UNITO, UOXF, UPENN, USAAR, USFD	Proc. 2014 6th Int. Adv. Res. Workshop on In Silico Oncology and Cancer Investigation - The CHIC Project Workshop (IARWISOCI) (open-access version)	Conference proceedings	01/02/2015	G.Stamatakos, D. Dionysiou, F. Misichroni, N. Graf, S. van Gool, R. Bohle, F. Dong, M. Viceconti, K. Marias, V. Sakkalis, N. Forgo, R. Radhakrishnan, H. Byrne, C. Guiot, P. Buechler, E. Neri, A. Bucur, B. de Bono, D. Testi, M. Tsiknakis	Published (Pending consent)

Incorporating Data Protection in In Silico Research: A case of CHIC	Elias Neri	CUSTODIX	2014 6 th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation, DOI: 10.1109/IARWISOCI.2014.7034643	Peer-reviewed publication	10/03/2015	Wouter Dhaeze	Published (Pending consent)
Computational Delineation of Tyrosyl-Substrate Recognition and Catalytic Landscapes by the Epidermal Growth Factor Receptor Tyrosine Kinase Domain	Yingting Liu	UPENN	Molecular Biosystems doi: http://dx.doi.org/10.1039/c3mb70620f	Peer-reviewed publication	28.04.2014	Ravi Radhakrishnan	Published (Pending consent)
Mesoscale computational methods for membrane bilayer remodelling by curvature inducing proteins	N. Ramakrishnan	UPENN	Physics Reports 543, DOI: 10.1016/j.physrep.2014.05.001	Peer-reviewed publication	28.04.2014	P. B. Sunil Kumar, Ravi Radhakrishnan	Published (Pending consent)
Dendritic cell vaccination for glioblastoma multiforme: review with focus on predictive factors for treatment response	J Dejaegher	KU Leuven	Immuno Targets and Therapy. Doi: http://dx.doi.org/10.2147/ITT.S40121	Peer-reviewed publication	13.03.2014	S Van Gool; S De Vleeschouwer	Published (Pending consent)
Integrative functional assessment of ALK mutations for therapeutic stratification in neuroblastoma	Ravi Radhakrishnan	UPENN	Cancer Cell	Peer-reviewed publication	n.d.	D. Weiser, S. Bressler, P. J. Huwe, R. Radhakrishnan, M. A. Lemmon, Y. Mosse	Submitted
In silico profiling of activating mutations in cancer	Ravi Radhakrishnan	UPENN	Integrative Biology	Peer-reviewed publication	n.d.	Jordan E	Submitted
An Explicit Numerical Treatment of the Three-Dimensional Boundary Conditions Imposed by the Skull on an Inhomogeneous Diffusion-	Georgios Stamatakos	ICCS	Bulletin of Mathematical Biology	Peer-reviewed publication	n.d.	Giatili S	Submitted

Reaction Tri-scale Model of Glioblastoma Multiforme Tumour Growth and Invasion into the Brain. Clinical Validation Considerations.							
Multiscale Computational Models in Physical Systems Biology of Intracellular Trafficking	Ravi Radhakrishnan	UPENN	IET Syst. Biol. 8 (5)	Peer-reviewed publication	October 2014	Tourdot RW, Bradley RP, Ramakrishnan M	Published
Defining the Free Energy Landscape of Curvature Inducing Proteins on Membrane Bilayers	Ravi Radhakrishnan	UPENN	Phys. Rev. E 90, 022717	Peer-reviewed publication	25 August 2014	Tourdot RW, Ramakrishnan M	Published
Machine learning predictions of cancer driver mutations	E. Joe Jordan	UPENN	IEEE Proceedings of the 6th International Advanced Research Workshop on In-Silico Oncology and Cancer investigation	Conference proceedings	n.d.	Radhakrishnan R.	In press
Exploring the competition between proliferative and invasive cancer phenotypes in a continuous spatial model	Kostas Marias	FORTH	PLoS One 8 (8)	Peer-reviewed publication	08/08/2014	Tzamali E, Grekas G, Sakkalis V	Published (Open Access)
Enabling multiscale modeling in systems medicine	Georgios Stamatakos	ICCS, UOXF	Genome Medicine 6:21	Peer-reviewed publication	2014	Wolkenhauer O, Auffray C, Brass O, Clairambault J, Deutsch A, Drasdo D, Gervasio F, Preziosi L, Byrne H, et al.	Published
The Virtual Skeleton Database - An open access repository for biomedical research and collaboration	M Kistler	UBERN	Journal of Medical Internet Research. doi:10.2196/jmir.2930	Peer-reviewed publication	13.11.2013	S Bonaretti, M Pfahrer R Niklaus, P Büchler	Published (Pending consent)
High-throughput mutagenesis reveals functional determinants	Ravi Radhakrishnan	UPENN	Nucleic Acids Research 42 (15)	Peer-reviewed publication	26 July 2014	Gajula KS, Huwe PJ, Mo CY, Crawford DJ, Stiver JT, Kohli RM	Published (Open Access)

for DNA targeting by Activation-Induced Cytidine							
Molecular modeling of ErbB4/HER4 kinase in the context of the HER4 signaling network helps rationalize the effects of clinically identified HER4 somatic mutations on the cell phenotype	Shannon E. Telesco	UPENN	Biotechnology Journal. 10.1002/biot.201300022	Peer-reviewed publication	06.11.2013	Raj Vadigepalli, Ravi Radhakrishnan	Published (Pending consent)
A Hybrid Model for Multimodal Brain Tumor Segmentation	Raphael Meier	UBERN	Stegan Bauer, Johannes Slotboom, Roland Wiest, Mauricio Reyes	Conference proceedings	22.09.2013	Miccai 2013 Workshop on Brain Tumor Segmentation	Published
Multiscale Cancer Modeling and In Silico Oncology: Emerging Computational Frontiers in Basic and Translational Cancer Research	Georgios Stamatakos, Norbert Graf, Ravi Radhakrishnan	ICCS, UPENN, USAAR	Journal of Bioengineering and Biomedical Sciences	Peer-reviewed publication	25.05.2013		Published
Computational Methodology for Mechanistic Profiling of Kinase Domain Mutations in Cancers	R. Radhakrishnan	UPENN	Proceedings of the IEEE, 5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation	Peer-reviewed publication	01.01.2013	P. J. Huwe	Published (Pending consent)
In Silico Oncology: Exploiting Clinical Studies to Clinically Adapt and Validate Multiscale Oncosimulators	G. Stamatakos	FORTH, ICCS, USAAR	In Silico Oncology. doi: 10.1109/EMBC.2013.6610806	Peer-reviewed publication	01.01.2013	D Dionysiou, A Lunzer, R Belleman, E Kolokotroni, E Georgiadi, M Erdt, J Pukacki, S Rueping, S Giatili, A d'Onofrio, S Sfakianakis, K Marias, C Desmedt, M Tsiknakis, and N Graf	Published (Pending consent)
Functional tissue units and their primary tissue motifs in multi-scale physiology	Bernard de Bono	UCL	Biomed Semant, vol. 4, no. 1. doi:10.1186/2041-1480-4-22	Peer-reviewed publication	01/01/2013	P. Grenon, R. Baldock, P. Hunter	Published (Pending consent)

The Technologically Integrated Oncosimulator: Combining Multiscale Cancer Modeling with Information Technology in the In Silico Oncology Context	G. Stamatakos	FORTH, ICCS, TEI-C, USAAR	IEEE J. Biomed Health Inform. doi: 10.1109/JBHI.2013.2284276	Peer-reviewed publication	01/05/2014	Dionysiou D, Lunzer A, Belleman R, Kolokotroni E, Georgiadi E, Erdt M, Pukacki J, Rueping S, Giatili S, Donofrio A, Sfakianakis S, Marias K, Desmedt C, Tsiknakis M, Graf N.	Published (Pending consent)
A Model of Tumor Growth Coupling a Cellular Biomodel with Biomechanical Simulations	Farhad Rikhtegar	ICCS-UBERN	In Silico Oncology and Cancer Investigation (IARWISOCI), 2014 6th International Advanced Research Workshop on	Conference proceedings	4/11/2014	Eleni Kolokotroni, Georgios Stamatakos and Philippe Buchler	Published (Pending consent)

Table 5: List of the CHIC publications

Title	Type	Main leader	Reference	Date
CHIC project featured in The Parliament Magazine	Online article	ICCS	Link: http://www.vph-institute.org/news/chic-project-featured-in-the-parliament-magazine.html	05 May 2014
Computational Horizons in Cancer	Newspaper/Magazine Article	ICCS	Link to an online issue of The Parliament Magazine, Issue 389: http://viewer.zmags.com/publication/6eced2e8#/6eced2e8/36	28 April 2014
Grantee presentation to the Multiscale Modeling Consortium of the Inter Agency Modeling Group	Video	UPENN	https://www.youtube.com/watch?v=ttNG86de3ps	2014
Video introducing Physics Reports article in the author's own words	Video	UPENN	http://audioslides.elsevier.com/getvideo.aspx?doi=10.1016/j.physrep.2014.05.001	2014

Table 6: List of the CHIC press activities and other media

Title	Type	Main leader/participants	Event	Venue	Date
Prostate carcinoma: reports from Eureka studies (CHIC project)	Conference	UNITO, CINECA, ICCS, USAAR	Prostate carcinoma: reports from Eureka studies congress. Oral presentations made by Simone Bnà (CINECA), Georgios Stamatakos (ICCS), Norbert Graf (USAAR),	Candiolo, Turin, Italy	28 March 2015

			Domenico Gabriele , Caterina Guiot and Ilaria Stura (UNITO)		
Towards the mathematical principles of the natural philosophy of living matter: In Silico Oncology/ In Silico Medicine	Workshop	ICCS	6th IARWISOCI –The CHIC Project Workshop	Athens, Greece	3-4 November 2014
Computational Horizons in Cancer: Developing Meta- and Hyper-Multiscale Models and Repositories for In-Silico Oncology – A Brief Technical Outline of the project	Workshop	ICCS, USAAR, KULeuven, BED, USFD, FORTH, LUH, UPENN, UOXF, UNITO, UBERN, Custodix, PHILIPS, UCL, CINECA, TEI-C	6th IARWISOCI –The CHIC Project Workshop	Athens, Greece	3-4 November 2014
A Modular Semantic Infrastructure Layout for the Management of Hypermodel-Pertinent Metadata in the Context of In Silico Oncology	Workshop	ICCS	6th IARWISOCI –The CHIC Project Workshop	Athens, Greece	3-4 November 2014
Modelling Glioblastoma Growth and Inhomogeneous Tumour Invasion with Explicitly Numerically Treated Neumann Boundary Conditions	Workshop	ICCS	6th IARWISOCI –The CHIC Project Workshop	Athens, Greece	3-4 November 2014
A Brownian Motion Based Mathematical Analysis as a Potential Basis for Modelling the Extent of Infiltration of Glioma Cells into the Surrounding Normal Brain Tissue	Workshop	ICCS	6th IARWISOCI –The CHIC Project Workshop	Athens, Greece	3-4 November 2014
Legal and ethical aspects of in silico based medicine	Workshop	LUH	6th IARWISOCI –The CHIC Project Workshop	Athens, Greece	3-4 November 2014
IPR issues in multiscale modelling	Workshop	LUH	6th IARWISOCI –The CHIC Project Workshop	Athens, Greece	3-4 November 2014
Keynote lecture on Data Protection Reform	Conference	LUH	Leopoldina Symposium „Keimbahnmutationen bei krebskranken Kindern“	Freiburg, Germany	26 September 2014
The Importance of Data Sharing and Data Protection'	Conference	LUH	SIOPE-ENCCA conference 2014	Brussels, Belgium	18 September 2014
Multiscale modelling of cancer (workshop session)	Conference	ICCS	VPH2014	Trondheim, Norway	11 September 2014
In silico Neuro-Oncology: Simulating glioma growth and inhomogeneous invasion under explicitly treated	Conference	ICCS	VPH2014	Trondheim, Norway	11 September 2014

Neumann boundary conditions					
A Generalized Model of Tumor Growth and Response to Treatment using the PUN approach (poster)	Conference	UNITO	VPH2014	Trondheim, Norway	11 September 2014
The VPH Hypermodelling Framework for cancer research	Conference	USFD, CINECA	VPH2014	Trondheim, Norway	11 September 2014
A Two-Clones Model of Tumor Growth and its Response to Treatment	Conference	UNITO	MPDS14 Conference	Turin, Italy	29 August 2014
Nomination to Best Msc thesis work – Automatic Multimodal Brain Tumor Segmentation	Conference	UBERN	SSBE 2014 Annual Meeting	Zurich, Switzerland	27-28 August 2014
Cancer cell patterns emerging from agent based movement (poster presentation)	Summer School	FORTH	Spatiotemporal modelling and simulation of biology systems: Biology in Cyber Space	Dresden, Germany	02-09 August 2014
Patient-specific Semi-supervised Learning for Postoperative Brain Tumor Segmentation	Summer School	UBERN	Medical Imaging Summer School (MISS) 2014	Favignana, Italy	28 July - 01 August 2014
Invited lecture: What is the role of in silico modelling and simulation to help translate pre-clinical data into the design of human clinical trials	Conference	UPENN	Tumor Models Summit	Boston, MA, USA	21-23 July 2014
In Silico Oncology: A generic platform for clinically driven and oriented cancer hypermodeling. The Hypermodel Based Oncosimulator	Conference	ICCS	7th World Congress of Biomechanics	Boston, MA, USA	6-11 July 2014
Computational Challenges in Multiscale Modelling	Conference (Podium discussion)	USFD	7th World Congress of Biomechanics	Boston, MA, USA	6-11 July 2014
ApiNATOMY: The Generation of Interactive CircuitBoard Views of Complex Physiology Knowledge	Conference	UCL	4th International Conference on Complex Systems and Applications (ICCSA 2014)	Le Havre, France	23-26 June 2014
Data modeling and simulations. Do they pave the way to personalized medicine?	Workshop	USAAR	SIB/Systems X.ch Summer School	Kandersteg, Switzerland	22-27 June 2014
Piedmont multicenter retrospective study on operated prostate cancer: first report	Congress/conference	UNITO	24th Annual Meeting of the Italian Society of Uro-Oncology (SIUro)	Bologna, Italy	22-24 June 2014

Data collection for models validation: application to prostate cancer - clinical aspects	Conference	UNITO	IEEE-EMBS International Conferences on Biomedical and Health Informatics (BHI)	Valencia, Spain	1-4 June 2014
IT Challenges for innovative Clinical Trials	Workshop	USAAR	IT workshop on tools/services for clinical trials	Düsseldorf, Germany	26-27 May 2014
Participation in Training School	Workshop	UNITO	ESTRO School of Radiotherapy and Oncology: Basic Clinical Radiobiology	Istanbul, Turkey	25-29 May 2014
Data Protection reform	Invited Lecture	LUH	Datenschutzforum	Berlin, Germany	15 May 2014
Computational medicine: Current and Future prospects	Conference	FORTH	eHealth Forum 2014	Athens, Greece	12-14 May 2014
Participation in training event	Workshop	CINECA, USFD	VPHHF development training	Bologna, Italy	11-16 May 2014
Presentation of the CHIC project on a special leaflet	Showcase event	USFD	Insigneo Institute first anniversary showcase event1	Sheffield, UK	08 May 2014
Poster presentation of CHIC	Showcase event	USFD	Insigneo Institute first anniversary showcase event1	Sheffield, UK	08 May 2014
Presentation of the CHIC project	Workshop	USFD	Collaborations Workshop 2014 (CW14) - software in your reproducible research	Oxford, UK	26 April 2014
Data protection issues in ehealth projects	Conference	LUH	EHR4CR First European Hospital Conference	Brussels, Belgium	9 April 2014
Providing a Network of Trust in Processing Health Data for Research	Conference	LUH	23rd EICAR Annual Conference	Frankfurt	17-18 Nov. 2014
Threats of Data Protection Regulation	General Assembly	LUH	ENCCA General Assembly	Brussels	16 Jan. 2015
Rechtsfragen der personalisierten Medizin		LUH	Paul Fritsche Stiftung, Universität des Saarlands	Homburg	29 Jan. 2015
Data Protection and Clinical Data in Pediatric Research and Treatment	Video lecture	LUH	International Childhood Cancer Awareness Day Event in the European Parliament		03 Feb 2015
Data Protection and Data Security: A Lawyer's View on Personal Clinical Information	Winter School	LUH	Fourth Winter School Ethics and Neuroscience, Bernstein Center for Computational Neuroscience Berlin, Berlin School of Mind and Brain	Berlin	23 Feb. 2015
Computational Methods in Cancer Research	Workshop	USFD	Computational Methods in Cancer Research Workshop	Edge Conference Centre in	10.10.2013

				Sheffield	
Innovations in Healthcare Industry Open Day	Workshop	USFD	Presentation of the CHIC project at the "Innovations in Healthcare Industry Open Day".	INSIGNEO, Sheffield	06.03.2014
6 th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation – The CHIC Project Workshop	Workshop	USFD	Daniele Tartarini from USFD team discussed with WP6 partners the adoption of a Hypermodelling language and the technical solutions to decouple tightly coupled models	NTUA University of Athens, Athens, Greece	02.11.2014
The VPH Hypermodelling Framework for Cancer Multiscale Models in the Clinical Practice	Conference	USFD	Oral Presentations about The CHIC Hypermodelling Framework in Cancer Research	Crowne Plaza, Athens, Greece	02.11.2014
Brain Tumor Segmentation Challenge, MICCAI 2013, Nagoya, Japan	One-day challenge	UBERN	One-day challenge where algorithms for brain tumor segmentation are evaluated and compared. Out of 10 teams, UBERN obtained second place in this competition.	Nagoya, Japan	22.09.2013
11 th HGG-IMMUNO-Meeting	Conference	KU Leuven	The HGG-IMMUNO-Meeting is an annual meeting where international research groups and clinicians who perform experimental and clinical research on immunotherapy are invited to share knowledge and experiences. The clinical research by KU Leuven on immunotherapy will provide the input data of glioblastoma for CHIC (Task 3.2).	Leuven	21.10.2013
An update of immunotherapy translational research program at KU Leuven	Conference	KU Leuven	Presentation by Prof. Van Gool on the conference "8 Rostock symposium on tumor immunology in pediatrics" organised by Carl-Friedrich Classen, Pediatric oncology, University Rostock.	Rostock, Germany	14.02.2014
Immunotherapy for brain tumors: an update	Conference	KU Leuven	Presentation by Prof. Van Gool at "SIOPE-BTG High grade glioma working group meeting", organised by Christof Kramm, Pediatric oncology, University of Göttingen	Göttingen, Germany	27.02.2014
Immuntherapie bei Hirntumoren des Kindes- und Jugendalters	Conference	KU Leuven	Presentation by Prof. Van Gool at "HIT-TAGUNG", organised by Prof. Gudrun Fleisschack, Pediatric oncology, University Essen.	Essen, Germany	28.03.2014
Long-term survival data in patients with glioblastoma and relapsed malignant glioma after tumor	Conference	KU Leuven	Presented on 'Annual scientific meeting of the Belgian Society of Neurosurgery' by Dr. Joost Dejaegher.	Brussels, Belgium	29.03.2014

vaccination: is the paradigm slowly shifting?					
Immunotherapy for children and adults with malignant glioma: the Leuven experience	Conference	KU Leuven	Presentation by Prof. Van Gool at the Johannes Wesling Klinikum Minden, 23th GPHO Arbeitstagung Experimentelle Neuroonkologie, organised by Prof. Bernhard Erdlenbruch, at Minden, Germany	Minden, Germany	26.04.2014
Immunotherapy for malignant glioma: preclinical research and clinical research	Conference	KU Leuven	Presentation by Prof. Van Gool at the conference "Oncobiology - genes and tumoral microenvironment" at the Medical Sciences Faculty, Nova University, organised by Prof. José Luis Passos Coelho and Prof. Doutora Ana Felix, at Lisbon, Portugal	Lisbon, Portugal	09.05.2014
Immunotherapy for malignant glioma: preclinical research and clinical research	Conference	KU Leuven	Presentation by Prof. Van Gool at the 30th National Congress of Neurosurgery, organised by the Portuguese Neurosurgical Society by Dr. Miguel Casimiro, at Lisbon, Portugal	Lisbon, Portugal	30.05.2014
Immunotherapy for malignant glioma: preclinical research and clinical experience	Conference	KU Leuven	Presentation by Prof. Van Gool at the "Internal lab meeting seeking for collaboration on oncolytic virus research" organised by Prof. Alan Melcher, Medical Oncology, at Leeds, UK	Leeds, UK	16.06.2014
Immunotherapy for relapsed malignant glioma in children	Conference	KU Leuven	Presentation by Prof. Van Gool at the ISPNO conference at Singapore	Singapor	28.06.2014
Dendritic Cell Vaccination for Glioblastoma Multiforme	Conference	KU Leuven	Skype-presentation by Prof. Van Gool to the “6th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation (IARWISOCI) - The CHIC Project Worskhop”	Athens, Greece	04.11.2014
Dendritic cell therapy in brain cancer	Conference	KU Leuven	Presentation by Prof. Van Gool at the “VII congresso nacional associacao portuguesa neuro oncologia” organised by Associacao portuguesa neuro oncologia	Lisbon, Portugal	21.11.2014
Complex Mathematics Against Cancer	Press releases	EX		Athens, Greece	10.04.2013
A Novel Cancer (Related) Project	Press releases	EX			
New Horizons in Cancer Treatment	Press releases	EX			
CHIC Poster	Posters	EURICE			01.04.2013

CHIC Flyer	Flyers	EURICE			01.04.2013
Optimising cancer treatment through in-silico oncology	Web sites/App	EURICE	Article about the CHIC Kick-Off Meeting on the Eurice company website.		28.05.2013
Incorporating Data Protection in In Silico Research: A case of CHIC (publication)	Conference	CUSTODIX	Elias Neri Presented "Incorporating Data Protection in In Silico Research: A case of CHIC" at the "6 th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation"	Athens, Greece	03.11.2014
Providing a Network of Trust in Processing Health Data for Research	Conference	CUSTODIX	23rd EICAR ANNUAL CONFERENCE Trust and Transparency in IT Security	Frankfurt, Germany	18.11.2014

Table 7: List of the CHIC workshops and conferences

3 IPR management

3.1 IPR Management strategy

Management of IPR for exploitation of the Project Foreground is regulated in the Grant Agreement (EC-GA), the Consortium Agreement (CA) and, in more detail, by the Memorandum of Understanding on Disposal of Intellectual Property Rights in CHIC (referred to as "CHIC IPR MoU" or "MoU").

The CHIC IPR MoU was elaborated by LUH on the basis of a legal analysis of IPR surrounding the project which was carried out in the framework of Deliverable D.4.3, Section 5 (date of submission: 31.05.2014). The legal analysis under D.4.3 revealed that certain practical scenarios characteristic for the modelling nature of the project are not always fully covered by the default rules set out in the FP7 EC-GA (Annex II) and provisions of the Consortium Agreement. In order to clarify management of IPR in CHIC and fill in the legal gaps, rules on IPR management in the project which should supplement the existing provisions of EC-GA and CA were provided in the MoU. The MoU along with its 5 attachments was attached to D.4.3 as Appendix 5. The MoU in its initial version was provided to consideration of the CHIC consortium partners in July 2014. The partners negotiated and agreed on the rules on exercise and management of their IPR in the project foreground in MoU Version (MoU v3) on the 6th of March 2015. As of the data of submission of this deliverable the MoU is currently in the administrative process of being signed by the CHIC consortium members and is expected to be finalized by the end of April 2015. The MoU supplements the provisions of EC-GA and CA with respect to IPR and introduces and/or clarifies rules on IPR management both at the stage of project implementation and exploitation of project results. In particular, the MoU covers such issues as: sharing and exercise of rights in composite works (Cl. 3.2, in particular applicable to hyper-models (WP6) and visualisation toolkit (WP9); IPR management in works contributed to the Project by sub-contractors (Cl.2.1); software licensing and license compatibility issues (Cls.3.1, 4.5); compliance with license terms (Cl.4.6); access to the source code for the end users (Cl. 4.4).

The essential aspects of IPR management for exploitation which were agreed by the parties in the MoU are considered in the following paragraphs.

3.2 Exploitation of Foreground and IPR ownership issues

Exploitation of project foreground closely inter-relates with the IPR ownership issues. The right to exploit a work belongs to exclusive rights of the right holder. It is the right holder only who has the exclusive power and authority to decide on exploitation of his work and exercise of his rights. Where a project partner (individually or jointly referred to as a "Party" or "Parties" in the CA) develops its foreground individually and owns all IPR in it on individual basis, this partner may decide on IPR management strategy on its own, subject, however, to the rules of EC-GA and CA. However, if more than one partner develop a project foreground jointly or combine their contributions for exploitation as a composite work (for example, for the purposes of higher functionality or market coverage), the contributing partners share the IPR in the foreground generated and need to agree on exercise of their IPR by themselves[3]. Otherwise neither of the partners may exploit the common foreground on its own, or exploitation will be subject to the risk of being challenged by another co-owner claiming copyright infringement and damages (D.4.3, Section 5.2.2).

During the legal analysis under D.4.3 the types of works which are being developed in the project were investigated and the ownership types applicable to such works were distinguished. In particular the following ownership types are characteristic for the project foreground: individual, joint and composite ownership. The legal terms on exercise and management of IPR in works of different

[3] EC DG Enterprise, co-financed within the fifth framework programme of the European Community, IPR-Helpdesk, Joint Ownership in Intellectual Property Rights.

ownership types vary. A brief characteristic of these ownership types and project works to which these ownership types apply is provided below.

a) Individual ownership: this is applicable to works developed by one partner; the developing partner owns all IPR in the work alone (Art.8.1 CA)

b) Joint ownership: this is applicable to works developed by more than one CHIC consortium member where the contribution of each of the partners is inseparable from the whole work and non-exploitable on its own; the contributing CHIC partners own all IPR in their joint work jointly (Art. 8.2 CA).

c) Composite ownership: this scenario is applicable to works compiled from contributions of more than one partner where the contribution of each of the partners is identifiable and exploitable as a work on its own but assembled into a collective whole to be used as a whole; the contributing partners' own rights in the composite work as co-owners (Cl.3.2 MoU).

3.2.1 Exploitation of IPR in individual Foreground

Exploitation of IPR in works which reside in individual ownership of one partner is regulated by Art.8.1 CA. According to Art.8.1 CA a partner who generated its foreground by itself owns all IPR in its work as an individual owner. Individual ownership may apply to software or a model which is exploitable on its own and which one partner developed individually. This partner, acting as an individual owner under Art.8.1 CA, owns all IPR in its work alone. An individual owner may exploit and exercise its rights in the work at its own discretion, subject however to the regulations of EC-GA and CA. In particular, it applies to assignment of rights and exclusive licensing.

Transfer of Foreground is regulated by Art. 8.3 CA and Art. II 27 EC-GA. Accordingly, an individual owner may not transfer (alienate or assign) its rights in a foreground to a third party unless all consortium partners have been duly notified and have expressed no objection to the transfer (Art. 8.3 CA). If transfer of the foreground is to take place to a third party not associated with the FP7 Programme, objection may come on part of the European Commission (Art. II. 27.4 EC-GA). In this case, the transfer shall not take place unless appropriate safeguards satisfy the Commission and it agrees to the transfer in writing.

Also, exclusive licensing of the foreground is subject to the rules of CA. Accordingly, the licensing partner will need to pass on its obligation to grant access rights to such foreground to the "exclusive" licensee up to 12 months after the project ends (Art. 9.4.3 CA). Hence, quasi-exclusive licensing is an option, meaning that the "exclusive" licensee will then inherit the obligation to grant access rights to the project partners up to 12 months after the project ends. On the other hand, the CHIC partners may also waive their access rights in order to allow the licensing partner to grant exclusive license. What the partners need to take into account by waiving their rights is that (a) the foreground concerned must be completed and identified and (b) the waiver must be not more than necessary for the exclusive license to be granted (e.g. territorial scope, application field, modes of use, etc.)[4].

According to the data on the foreground which the partners develop in the project, the major part of the foreground resides is individual ownership of individual partners.

3.2.2 Exploitation of IPR in Joint Foreground

Exploitation of foreground which is developed by several partners jointly is covered by Art. 8.2 CA. Accordingly, if more than one CHIC partner develop a project result/output together in a way that

[4] EC, FP7, Guide to Intellectual Property Rules for FP7 projects, Version 3, available at: http://ec.europa.eu/research/participants/data/ref/fp7/89593/ipr_en.pdf.

contribution of each partner is indivisible from the whole and non-exploitable on its own, then according to Art.8.2 CA the contributing partners own all rights in their work jointly. Exploitation and licensing of works in joint ownership is regulated by Art. 8.2 Paragraph 2 CA. Hence, each joint owner may license the joint work on non-exclusive basis without obtaining consent from, accounting to or paying compensation to other joint owners, unless the joint owners agree otherwise. Hence, the joint owners have a choice either to exploit their joint work under the default rule provided by the CA, or may agree on another exploitation strategy by themselves. For instance, the joint owners may choose license models, define license terms, define allocation of revenues and territorial scope of licensing, etc. by agreement. It must be noted, that certain terms, such as division of market shares or setting the prices, may be subject to restrictions of the competition law[5]. Rules of the EC-GA and CA on transfer of foreground and exclusive licensing, considered above, apply to transfer of joint foreground as well.

According to the current state of the project work, there is only one component which meets the criteria of joint work under the CA so far. It is the VPH-HF tool which USFD and CINECA generate in WP7 jointly. Until USFD and CINECA have agreed on exercise of their rights by themselves, the default rule set by Art. 8.2 CA applies. Accordingly, when the VPH-HF tool is ready for exploitation, each joint owner, i.e. CINECA and USFD, may license it on non-exclusive basis without accounting to or paying compensation to each other.

3.2.3 Exploitation of IPR in Composite Foreground

The legal analysis of D.4.3 revealed that some categories of project foreground and exercise of rights in such foreground are not covered by the rules of the CA (D.4.3, Section 5.2). This category of works comprises composite works. Most notably, the hyper-models, which constitute the target of in silico oncology modelling under the Project (WP6) can qualify as composite works in terms of copyright; exploitation and exercise of IPR in hyper-models have not been regulated within the legal framework of the project so far. The same applies to the Image Processing and Visualization toolkit which BED, ICCS, UBERN and FORTH develop within WP9.

A hyper-model (or composite model or integrative model) is defined as a model that emerges from the composition and orchestration of multiple hypomodels, each one of which is capable of simulating a specific entity or phenomenon[6]. Having such substance a hyper-model qualifies as a composite work in terms of copyright law (D.4.3, Section 5.2). Exploitation of composite works and exercise of rights in composite works is not covered by the provisions of EC-GA and CA.

The CHIC partners have indicated their intent to agree on exploitation and management of their IPR in composite works in the MoU. The MoU rules on composite ownership (Cl.3.2) will apply to the works generated under WP6 “Cancer Model and Hypermodel Design”, WP7 “Hypermodelling infrastructure”, WP 9 “Image Processing and Visualization”. The partners who collaborate in these WPs and contribute their individual works into composite works will agree to be co-owners and share the rights in such works according to the contribution of each. Each contributing partner and its contribution into the composite work shall be recognised (Cl.3.2 paragraph 2). Also a partner who designs the hyper-modelling strategy of selecting and/or arranging models in a hyper-model in an original creative way will be a co-owner of the hyper-model in question and has a right to be recognised (Cl.3.2 paragraph 4). In terms of hyper-modelling the right to be recognised will be realised by technical means. The modelling partners in CHIC may provide information on authorship and ownership in model/hyper-model/hyper-model design in the metadata applying to the

[5] Commission Regulation (EU) No 316/2014 of 21 March 2014 on the application of Article 101(3) of the Treaty on the Functioning of the European Union to categories of technology transfer agreements (Text with EEA relevance), 28.3.2014, EN, Official Journal of the European Union, L 93/17.

[6] CHIC Deliverable No. 7.1, Hypermodelling specifications, submission date: 30.06.2014, Section 3.4.3, p.12.

model/hyper-model in question while uploading the model/hyper-model to the CHIC model repository (WP8).

It is essential that composite ownership does not affect and does not prevent the contributing CHIC partners from exploiting their individual contributions and exercising their rights in such contributions independently (Cl.3.2 paragraph 3). This rule provides a way to assemble constituent models of a hyper-model ABC into a hyper-model BCD without infringing copyright of the partners B and C in the hyper-model ABC (on condition that the partners B and C allow their models to be assembled and used in the hyper-model BCD).

As regards exploitation and management of IPR in composite ownership, the MoU does not contain any default rules for exploitation and/or licensing of composite works (as provided for licensing of joint works by Art.8.2 paragraph 2 CA). The MoU leaves it to the contributing partners to agree on the rules on IPR management by themselves. However, the MoU explicitly makes it into the obligation of the partners who wish to exploit their contributions as a composite whole to agree on the ownership shares, exercise of rights, sharing of revenues, protection measures and the division of related costs in advance (Cl.3.2 paragraph 5). The default rule on exploitation of composite works applies to the hyper-models only, where the partners contributing to a hyper-model shall have the same rights as joint owners enjoy under Art. 8.2 paragraph 2 CA, unless they agree otherwise. This means, that each co-owner of a hyper-model in question will have the right to license the hyper-model on non-exclusive basis without any accounting to or compensating the other co-owners. The partners willing to contribute their works for exploitation as composite works will need to record these works in Attachment 5 to the MoU.

Considering that exploitation of works in composite or joint ownership requires agreement of all co-owners, the CHIC partners who develop software jointly or combine their software packages into a composite, will also need to agree the software license under which they intend to release their software into exploitation (Cl. 3.1 MoU). Software licensing strategies available for the partners to choose are discussed below.

3.2.4 Exploitation of Foreground with third party contributions

In view of the plan to invite external modelers into the modelling work under the project from M38, the management of IPR in such third party contributions is also resolved in the MoU (Cl. 2.1). A partner who commissions development of works for its foreground to a sub-contractor will need to procure the rights in such constituent works by a written agreement. The scope of rights which the partner will need to procure shall allow that partner to exploit and license their foreground as they see fit and entitle that partner to grant access rights to its foreground to the other project partners in the scope, as provided by section 9 of the CHIC CA. These rights may be acquired via a license agreement with the right to sub-license or via assignment of rights to the project partners.

3.3 Software licensing strategy

3.3.1 Software licensing and copyright ownership issues

The right to exploit and license software belongs to the exclusive rights of the copyright holder. As discussed in D.4.3, Section 5.4, in order to have a right to exploit and license software a partner needs to have a status of the copyright holder in the meaning of Article 2 Paragraph 3 Software Directive[7]. Legal issues surrounding ownership in software copyright - who owns copyright in software - were considered in D.4.3, Section 5.4.

[7] Directive 2009/24/EC of 23 April 2009 on the legal protection of computer programs, L 111/16 EN Official Journal of the European Union 5.5.2009.

A partner who is an individual owner of software copyright has the exclusive right to exploit the software and license their software to third parties in the scope, under the terms and in modes as they see fit[8]. Partners who share the rights in software as joint owners each have a right to license software on non-exclusive basis as provided to the joint owners under Art. 8.2 Paragraph 2 CA, unless the joint owners agree otherwise. The partners who share copyright in software as co-owners of composite works will need to agree the licensing strategy by themselves (Cl. 3.2 MoU). Procurement of the rights should be negotiated by the respective partner on an individual basis. The scope of rights outlined above should be sufficient so as to allow the project partner to exploit their foreground and to allow other consortium members to realize their access rights.

By exploitation and licensing of software regulations of the CA on grant of access rights (Section 9 CA), transfer of foreground (Art. 8.3 CA), confidentiality clauses (Section 10) and other provisions which may be relevant for exploitation need to be observed.

3.3.2 Software license models

The license models, which are typical for software licensing and which the partners may consider for exploitation of their software, are the following: proprietary license, open source license, dual licensing, software as a service. The legal issues surrounding each of these license models are discussed in more detail below.

a) Classic proprietary license

The proprietary license is a traditional form of licensing software into the end use. A proprietary license usually authorizes the use of software for which it was intended in exchange for royalties. Beyond running of the program very few actions are authorized. Among such actions are: the right to make a back-up copy (which is granted to the lawful user by the Software Directive irrespective whether this right is provided by the contract[9]) and the right to modify software for error correction (which is also provided to the user by the Software Directive but may be regulated in the contract[10]). In proprietary licensing software is usually provided in compiled object form. The source code is kept closed and may be accessed through reverse engineering only and in the scope only as necessary for interoperability and within the strict boundaries set for this by the law[11].

The traditional software license deals with such matters as:

- To whom the license is granted;
- License type: exclusive or non-exclusive (normally non-exclusive license is granted; exclusive licensing is also subject to the obligation to grant Access Rights up to 12 months after the Project ends which the Party will need to pass on to the exclusive licensee, Section 9 CA);
- The equipment and territorial scope or location where software may be used;
- The field and modes of use to which the software may be put;
- Whether the source or object code is provided (usually only object code is supplied, source code may be made accessible under the escrow agreement);

8 Article 4 Software Directive.

9 Article 5 para 2 Software Directive.

10 Article 5 para 1 Software Directive.

11 Article 6 Software Directive.

- Whether the licensee is allowed to sub-license and transfer its rights (usually these rights are not provided);
- The duration of license: it may be fixed or indefinite (subject to termination in cases of license breach and insolvency);
- Confidentiality (if the licensor seeks to protect the software as a trade secret);
- Exemption clause (dealing with exclusion or restriction of liability)[12].

Proprietary licensing may be an appropriate license model for the CHIC partners who intend to commercialize their software and seek to protect their source code from unnecessary disclosure.

Protection of the source code from disclosure was potentially put at risk by the rules of the CA dealing with access rights for use and sublicensing software to the end users (Art. 9.8.4.2.2 CA). According to the CA these Access Rights for Use shall include the right to provide the source code to the end users for the purposes of error correction and maintenance. For protecting the source code from unnecessary exposure, the CHIC partners are to agree that the partner who grants access rights to its software to another partner may request this partner not to supply the source code to the end-user until the user proves that without the source code maintenance or error correction of the software is technically or legally impossible (Cl.4.4 MoU).

b) Open source licensing

Open source licensing is another license model which the CHIC partners may consider for release of their software into exploitation. Release of project works under open source licenses and use of open source tools in the project works is foreseen and allowed for the project by Art. 9.8.6 CA. Usually, open source licenses provide such scope of rights which allows not only to run the program as intended (as the case by proprietary licensing is), but are tailored for use of the program in further software development. The rights to copy, modify and distribute the original software and modified versions are normally included, subject to the license terms, however. Open source licensing benefits software development community and allows software to be used, modified and upgraded in further research projects. Open source licensing may be considered as an appropriate license model for the partners who intend to use and develop or release their software into use and development in further research projects.

There are about 70 open source licenses available for use[13]. However, the choice of license may be complicated by several aspects. First, the license conditions should meet interests of the partner and the license conditions of different licenses vary. Copyright licenses, such as Apache v2, BSD or MIT contain rather flexible license terms, allowing the code to be used both in proprietary and open source software, and do not require that source version of the code be disclosed[14]. On the other hand, copyleft licenses, like GNU GPL and Mozilla Public License usually require that the software which links or uses the program licensed under these licenses be also released under the same license[15]. Choice of license is even more complicated when GPL licensed program is used. When a project component is developed with the use of a GPL program, there may be no alternative than to release that component under GPL as well[16]. Second, license terms are often incompatible in some

[12] D.Rowland, U.Kohl, A. Charlesworth, Information Technology Law, 4. Edition, 2012, p. 401.

13 Open Source Initiative, Open Source Licenses, available at: http://opensource.org/licenses

[14] A.St. Laurent, Understanding Open Source and Free Software Licensing, 2004, p. 14.

[15] Ibid, p. 34.

[16] Ibid, p. 174.

respect[17]. Combining programs with incompatible license terms in one piece of software may result in loss of rights to use those programs and deprive the developing party of the legal means to realize and defend its own software copyrights[18]. Considerations on software licensing were provided in more detail in D.4.3, Section 5.6.

Against this background, choice of license for software components developed in open source software development model requires legal due diligence. Such questions as: the methods of software development (from scratch or open source software development model), what licenses apply to the software tools used (e.g. GPL, Apache, BSD, etc.), mode of use (e.g. linking, merger of the codes, etc.), whether a partner agrees to release its components as "open source" and, if yes, under what license need to be analyzed. In order to perform the legal analysis LUH will need to collect these data from the project partners. The data collection is planned to begin in May 2015.

By use and release of project software open source, the regulations of CA on controlled license terms (Art. 9.8.6) need to be observed. The CA provides that a partner who intends to release its project results/output under "Controlled license terms" in the meaning of Art.9.8.1 CA should request approval by the rest of the CHIC consortium. The CA provides that such request shall enable the CHIC partners to assess the effect of such licensing on their access rights, however, it does not specify what data the request must contain. This issue is clarified in the MoU and the data which need to be stated on the request are specified in Attachment 4.

The issue of license incompatibility, characteristic for open source software development model, is also addressed in the MoU (Cl.3.1, 4.6 MoU). Each partner who develops software individually (Cl. 4.6) and the partners who develop software together (Cl. 3.1 MoU) need to comply with the license terms and ensure that they develop and release project software in a way that license incompatibility issues do not arise. The issue of liability in joint or composite software is solved following the rule of CA (Art. 5.1 CA). When several partners develop software together the partner who puts such software into use is entirely and solely liable for its use and non-infringement of third party rights.

c) Dual licensing

The holder of copyright in the source code of a computer program, like any other copyright holder, has a right to license his rights in software to different licensees under different license terms[19]. Therefore, it is possible for the partner/s who hold software copyright to pursue this license option and license the same software under proprietary fee-based license as well as under "open source" license (based on the legal analysis to be done by the LUH). For example, a partner may choose to commercialize software and license it in object code under proprietary royalty based license to pharmaceutical industry. At the same time the same partner may license the same software in source code under royalty-free open source license into further research projects.

d) Software as a service

Another license model available for the partners is to provide software into use as a service (SaaS). This model means that the software does not need to be provided to and installed on the user's machine. Instead, the service provider hosts software on its server and provides software into use from the server via the network and the user is able to utilize it via internet.

Providing software as a service requires from software provider the following actions, namely to:

[17] Rowland, supra, p. 420.

[18] Laurent, supra, p.151.

19 Rowland, supra, p. 421.

- host software packages on its server, that otherwise would be based on the user's machine or server;
- provide access to the software via network, such as via VPN, a dedicated line, or over the internet through which the user could log on to the server and run the software;
- manage the licensing process;
- manage and maintain a standardized version of software, including upgrades, bug fixes;
- provide service on a subscription basis, such as per use or on a monthly/annual fee basis[20].

Such questions as whether the user may only run the software or also have a right to make back-up copies or reverse engineer the software; whether access is provided to the object code only or whether the user is entitled to request the source code as well constitute the points which need to be addressed in the licensing policy. The choice of a license which would be suitable for this license model and would safeguard the interests of a partner who chooses this model will depend, as in the case of choosing an open source license, on technical and legal issues underlying software development. Here options will be presented by LUH in D4.3.2 (M42)on the basis of further legal analysis and experiences with other European projects. Legal advice on component licenses for cloud computing was provided by LUH in the FP7 Project Optimis, D7.2.1.3 – Cloud Legal Guidelines: Technical Implementation of Legal Requirements, Exploitation of the Toolkit in Use Cases and Component Licenses[21].

3.4 Conclusions

As of the current stage of project implementation the essential rules of IPR management for exploitation are to be subject to agreement by the CHIC partners in the CHIC IPR MoU. Such aspects as: managing of IPR in works contributed to the project by third party modelers, copyright ownership issues and exercise of rights in individual, joint and composite ownership, exploitation of composite works and hyper-models, in particular, legal issues characteristic for development and licensing software open source, which are substantial for exploitation of Project results, are addressed and resolved in the MoU. Choice of software license models for the project components requires additional legal analysis and will be considered in due course.

[20] Rowland, supra, pp. 427-428.

[21] Optimis: Optimized Infrastructure Services, EU FP7 Project, Downloads, Deliverables, available at: http://www.optimis-project.eu/sites/default/files/content-files/document/d7213-cloud-legal-guidelines.pdf (16.03.2015).

4 Expected exploitable projects outputs – Foreground

4.1 Clinical outputs

In the first 2 years of the CHIC project there will be no clinical output.

At the moment software is under development for automatic rendering of nephroblastoma and glioblastoma. This software will also be included in DrEye and part of the workflow is being used in the clinical setting of the nephroblastoma scenario. After validation of this workflow this will be a clinical output at the end of the project. ObTiMA is further developed to be integrated into the workflow for data submission to the platform. At the end of the CHIC project, ObTiMA will serve as a clinical trial management software.

In the glioblastoma multiforme scenario, CHIC is expected to determine predictive factors for the efficacy of immunotherapy as part of the multimodal treatment for GBM patients. The need for prediction about which patient would benefit from such a treatment is valuable, as the production of the vaccines requires adequate manufacturing practice facilities and is labour-intensive for specialized technicians, and thus demanding a lot of resources.

Mainly, new know-how and software will serve the (scientific and public) community. CHIC is expected to provide important analytical knowledge through the cancer hypermodels to be developed that could support and foster immunotherapy as a treatment option for those patients who would really benefit from such treatment. The data generated through CHIC will form the first step towards integrated patient profiling in order to predict the efficacy of the treatment.

ObTiMA will be integrated for data collection and management. In the future, ObTiMA/STaRC could serve as a data server for other clinical trials.

4.2 Technological/software outputs

The overall CHIC platform jointly developed by FORTH, ICCS, USFD, BED, CUSTODIX, UCL, UBERN, CINECA, and accessed through the CHIC portal is to be exploited by both the consortium and the wider scientific and technological community in order to make use of the various functionalities provided by the various components or component systems developed by the CHIC project.

4.2.1 Model/tool repository, In silico trial repository

ICCS has undertaken the development of the model/tool repository which aims at providing user friendly and efficient storage, retrieval, updating and overall handling of models, including hypomodels, hypermodels and tools, being developed or to be developed by the CHIC modelling partners as well as the broader cancer modelling community.

ICCS has also undertaken the development of the in silico trial repository providing the same functionalities as above regarding in silico simulations/experiments/trials/results.

4.2.2 Clinical data repository

The data provided by the clinical partners are stored in the clinical data repository. This database system was built as a research collaboration tool where the all the CHIC partners can search relevant datasets to conduct their research. The system allows storing structured information on the patients, links to relevant datasets, which enable researchers to browse, organize and share their data with their peers. Although developed in the CHIC context, the software framework is generic and could be used in various contexts where storage of clinical information is required.

4.2.3 Hypermodelling framework – VPH-HF

CINECA and USFD will deliver the VPH-HF platform as an open source product. It will be released following the best practices in computational science and engineering development with emphasis on reproducibility. A public online Web service (e.g. Github.com) is used to host VPH-HF source code and provides the necessary tools for concurrent versioning systems, collaborative software development, continuous integration, user communications and bug reporting. Documentation and installation packages will be provided and released to the public to enable free test of the VPH-HF.

4.2.4 Technical tools

FORTH develops a number of technical tools and components that are expected to be exploitable:

- **Private cloud infrastructure.** In the context of CHIC a private cloud infrastructure has been deployed and is already fully utilized. The technical details of this technological platform have been described in the CHIC deliverable D5.3.
- **DrEye.** In the context of project CHIC, FORTH provided its Dr Eye application and the appropriate API to develop plugins for it, in order to serve its role as the integrator platform for the imaging tools developed by the partners of WP9. Dr Eye and the imaging tools developed in WP9 will contain the CHIC Image Processing Toolkit. Dr Eye is a flexible and easy-to-use DICOM viewer and editor for quick and precise identification and delineation of tumors in medical images. Its design is clinically driven and it is a result of FORTH's long involvement in European projects, initially developed in the context of Contra Cancrum, then in TUMOR, p-medicine and now in CHIC.
- **Hypermodelling editor.** The hypermodelling editor is the user-friendly environment for the construction of syntactically and semantically valid, multiscale hypermodels. Its target end-users, therefore, consist of mathematical modellers, computational biologists, clinicians, and other research communities and stakeholders.
- **Data Upload Tool.** The CHIC Data Upload Tool is the end user desktop application for pseudonymizing and distributing clinical and image data sets and making them available in the CHIC platform.
- **Models.** FORTH provides two state-of-the-art models that can be used as core components of a hypermodel describing the spatiotemporal evolution of tumour growth and its microenvironment. These models are specifically designed to account for polyclonal cell populations reflecting tumor extensive heterogeneity. Such models provide the possibility to investigate the constant interplay between the environment and the specific characteristics of phenotypes that should be taken into account for the prediction of tumor evolution, morphology and effective treatment. In addition, FORTH provides one sub-cellular model that describes the aberrant metabolism of cancer cells at genome scale incorporating gene expression data into well-developed constrained-based methods. This model offers true patient personalization and plays a supportive but vital role in the contraction of the fully exploitable lung hypermodel.

4.2.5 Semantic/metadata services

In order to facilitate interoperability of, and semantic reasoning over, CHIC metadata, UCL has developed a number of software systems and associated APIs, collectively referred to as RICORDO.

The three main systems are:
OWLKB, a semantic reasoning engine which allows semantically sophisticated queries over a background knowledgebase, including realtime creation of so-called "composite terms" (for example, if the background knowledgebase has terms for "blood" and "aorta", but not "blood in aorta",

OWLKB can be used to generate a semantically-meaningful term for "blood in aorta" from the two constituent terms).
LOLS, or Local Ontology Lookup Service, a lightweight server/API for translating between International Resource Identifier (IRI) and human-readable label. This tool allows quick lookup of ontology terms based on human-friendly search strings, and conversely. Its API is designed for easy integration into other partners' projects.
RDFStore, a template system to facilitate queries over bulk CHIC metadata. RDFStore acts as an intermediary in front of a 3rd-party triplestore. It allows SPARQL-experts to create templates using SPARQL (a query language for linked metadata) once, and then those templates can be used by the end-user indefinitely, without the end-user having to know anything about SPARQL.
UCL has developed a syntax known as UCL syntax, which is an extension of so-called Manchester syntax, to improve the ease with which complex ontological expressions can be written. Classically, in order to write a complex ontological expression, such as "blood in aorta", the end-user would need to individually search for IRIs of the individual terms ("blood" and "aorta"), in practice this means switching back and forth between different windows or browser tabs, quite a lot of unnecessary work for our end-users. UCL syntax removes the need for those intermediate steps. This development included nontrivial work on the problem of dealing with ambiguity in a knowledgebase comprised of multiple reference ontologies (e.g., if two ontologies contain rival terms with the same human-readable label, how to proceed).

4.2.6 CHIC Security Tools and Services

1) The CHIC project is secured by a security framework, the CHIC Security Tools and Services. This framework is made up of a set of components dealing with authentication, authorisation and auditing (as defined in D4.3.1). Authentication and identity management components are:
    a) The **Identity and Access Management Site** (IAM) is responsible for user enrolment and management. IAM allows (virtual) organisations, attributes and roles to be assigned to users. These are then used through access rules defined in the authorisation policies to give the user access to restricted resources.
    b) The **Identity Provider** (IdP) is responsible for the authentication of users who access CHIC services through a browser. It provides identity assertions, which identify the user, to all CHIC Web Sites.
    c) The **Secure Token Service** (STS) is responsible for the authentication of users who access CHIC Web Services (through a non-browser client). It provides identity assertions to all CHIC Web Services.
2) Authorisation components
    a) The **Policy Decision Point** (PDP) is the entity which takes authorisation decisions. A PDP accepts authorisation requests.
    b) The **Policy Administration Point** (PAP) is the endpoint responsible for managing policies. The PAP provides the PDP with all policies required to produce an authorisation decision. The PAP has management services through which authorisation policies can be defined.
    c) The **Policy Information Point** (PIP) provides the PDP with the needed information (attributes) to take an authorisation decision. Most resource and subject attributes are already provided through an authorisation request. If the PDP needs an attribute that was not provided, this can be obtained through the PIP.

d) A **Policy Enforcement Point** (PEP) is a component which integrates the authorisation services with application code. The PEP is responsible for creating the authorisation request and sends it to the PDP.

3) Audit Service
4) Security gateway/proxy
5) Integration modules and extensions
   a) Various integration modules are available within CHIC to integrate JAVA, PHP and .NET applications into the security
   b) Extensions (e.g. Liferay).

4.2.7 CHIC Pseudonymisation Tools

4.2.7.1 CATS (Custodix Anonymisation Tool Services)

CATS (Custodix Anonymisation Tool Services) (as defined in D4.3.1) is a set of tools and services responsible for the de-identification of data files. It consists of the CATS Engine, CATS Privacy Profile Store, CATS Data Upload Interfaces, CATS Upload Client and CATS Server.

The CATS Engine de-identifies a data file based on a set of pre-configured transformation rules (privacy profiles). The privacy profiles that need to be executed on a data file are matched based on the data file's mime type and schema. The CATS Engine can currently process XML, CSV, DICOM, CEL, plain text, PDF and WORD documents. Other data formats can be added as needed through engine extensions.

Key privacy transformation rules include:

- Scan for and replace patient identifying data by pseudonyms.
- Clear patient identifying data.
- Encrypt (parts of) the pseudonymised result file.
- Generalise sensitive indirect identifying data (e.g. replace age by age groups such as 40-50).
- Make visit dates relative to the patient data of birth and randomise that date.
- Remove identifying information from embedded free text.

The CATS Engine downloads the privacy profiles it needs from the CATS Privacy Profile Store. CATS provides a browser interface through which privacy profiles can be uploaded. Privacy profiles are XML files and can be edited through the standalone tool CAT (Custodix Anonymisation Tool).

The CATS Server is a web frontend and REST/SOAP web service endpoint which glues together the CATS engine, privacy profile store and upload interfaces. Data files uploaded to the CATS server are processed through the embedded engine by downloading profiles from the embedded privacy profile stores. Processed files are then uploaded by CATS to a backend data repository.

The CATS Upload Client is a client application with embedded CATS engine, responsible for the client side pseudonymisation and upload of data files to the CATS Server. The CATS Upload Client is not the standard CHIC upload tool, but it can be used if data formats need to be processed and uploaded which are not supported by the CHIC Upload Tool. The CATS Upload Client supports any of the data formats supported by the CATS Engine.

4.2.7.2 CHIC Data Upload Tool

The CHIC Data Upload Tool with embedded CATS engine can be used by a source/hospital to pseudonymise a data file (first round) and upload it through CATS (responsible for the second round) into the CHIC data repository.

Currently CSV and DICOM are supported. Other file formats can be added as needed. The big advantage of the Data Upload Tool compared to the CATS Upload Client is the graphical user interface through which data files can be reviewed before uploading them. This allows the data source to verify whether a file is pseudonymised correctly.

4.2.7.3 PIMS (Patient Identity Management System)

PIMS indexes patients through common characteristics such as names, former names (e.g. maiden name), date and place of birth and other identifying information. From a data protection perspective it has to be pointed out that this approach requires the transfer of personal data of the patient to a third party holding the common PIMS database. Such a transfer of personal data requires a legal basis, which will have to be the patients´ prior informed consent, since the data protection law does not allow for the creation of a comprehensive patient identity management database for various hospitals.

A client (e.g. CATS) using PIMS should ideally encrypt all identifying information. However, due to the nature of cryptographic algorithms, very similar attributes (e.g. typos) will be transformed to different encrypted values. For this PIMS allows matching of encrypted data through Q-grams and bloom filters. It is important to keep in mind that there is still a risk of re-identification when using encrypted attributes. Through statistical or frequency analysis techniques, re-identification of (parts of) encrypted attributes can still be achieved.

4.3 Modelling outputs

A considerable number of component models (hypomodels), hypermodels and hypermodelling strategies developed by the CHIC modelling partners are to be provided for reuse by both the CHIC and the extra-CHIC cancer modelling community. Each modelling entity includes a formal description, the corresponding executable, as well as useful additional information. The three major CHIC hypermodel demonstrators to be provided to the wider research community are the following: 1) the lung cancer hypermodel-based Oncosimulator, 2) the nephroblastoma hypermodel-based Oncosimulator, and 3) the glioblastoma hypermodel-based Oncosimulator. All these hypermodels are primarily based on multiscale and multilevel mechanistic models of tumour growth and response to treatment. Additional statistical models are being developed for the glioblastoma Oncosimulator. Further models (including hypo- and hypermodels) addressing other cancer types such as prostate cancer and colon cancer, as well as other treatment and treatment combinations, are being developed and will also be made usable by the wider community.

5 Exploitation plans

5.1 Innovation questionnaire

In tables 8-16 we report the answers to the questions of the CHIC innovation questionnaire provided by the members of the consortium. The innovation questionnaire was jointly developed by CINECA and Eurice and was handed out to the CHIC consortium not long after the start of the project. The aim of this questionnaire is to provide an overview of the exploitation plans of the consortium members. Not all CHIC partners have yet provided their completed innovation questionnaire, but an update of tables 8-16 will be included in the next iterations of the PUDF (D12.4, M36)

Institution	**What is your main motivation to participate in this project? What will be your main benefit/added value?**	**Which are the main expected project result(s) that you will contribute to? (e.g. know-how, database, patentable invention…)**
USFD	Further develop the VPH Hypermodelling Framework into a solid general-purpose solution for multiscale modelling.	Know-how on multiscale modelling, software development.
UBERN	1. Improve our techniques for glioma segmentation and incorporation of non-imaging information to improve planning and patient follow-up 2. Collaboration with research teams, which enables multi-scale modeling 3. Access to clinical data	Know-how, access to longitudinal datasets, operational environment to run combined mathematical models
USAAR	The main motivation is to develop new knowledge out of heterogeneous data of patients with cancer. The development of tools and models to simulate cancer growth and response to treatment is most important to find new therapeutic options. These tools and models should be used as decision support tools after validation and certification. This will be most likely as the project is driven by clinical requests. In addition the developed legal and ethical framework will be a milestone in translational research helping the scientific community to use data of patients legally correct.	The main expected project results will be the oncosimulator for nephroblastoma as a decision support tool, using the heterogeneous clinical, imaging and molecular data to predict response to treatment. In addition a tool will be developed for automatic rendering of nephroblastoma. It is he intention to also develop a database with anonymized nephroblastoma images that can be used by the scientific community.
CUSTODIX	1. Further development of our tools based on real requirements from the field. 2. Keep in touch with key medical research leaders.	Operational environment
KU LEUVEN	Modeling patients to predict efficacy of immunotherapy as part of multimodal treatment for patients with primary diagnosis of GBM.	Data sampling from the clinical scenario's resulting in the determination of predictive factors for the outcome with immunotherapy.
LUH	To ensure the ethical, data protection and data security compliance of the project under EU law. The value is to have a product that takes care of privacy by design	Design of data protection and IT-related IPR management framework; academic publications; input influencing European legislative process
UNITO	A good opportunity to join other researchers and finalize our efforts to a more performing result in the field of	Certainly the collection of database and the proposal of model algorithms.

	tumor modeling.	
ICCS	My main motivation to participate in the project is to contribute to both the development of in silico oncology and in the broader sense in silico medicine related hypermodels and the development of a technological infrastructure that would facilitate and semi-automate this endeavour. My benefit will be the strengthening of the potential of the Oncosimulator as a personalized multiscale clinical decision support (CDS) system via the development and integration of cancer models (hypomodels and hypermodels).	The development of several cancer models (hypomodels and hypermodels), a generic cancer hypermodelling architecture, the development of hypermodelling infrastructure, related know how, data and model repositories, contribution to the clinical adaptation and partial clinical validation of the hypermodels.
PHILIPS	Gain knowledge from joint collaborative work with organizations with complementary expertise. Re-use some of the CHIC designs and software components as proof of concept to show relevant functionality.	Know-how, data and model repositories.
FORTH	Our main motivation is to contribute to the advancement of computational oncology and the realization of a fully functional hypermodelling platform, visualization tools and multiscale models.	Technological platform; visualization tools; multiscale models; hypermodelling editing envrionment.
CINECA	Develop an execution framework which can be used by scientists to run their multiscale hypermodels.	Know-how of software development of web services for execution of multiscale hypermodels.

Table 8: Answers to the first and second questions of the CHIC innovation questionnaire

Institution	Which quality has the expected result?												
	My result(s) will represent/be part of a…								My result(s) will contribute to the development of…				My result (s) will…
	product innovation (commercial)	process innovation (commercial)	new service (commercial)	new service (public)	new product (public, open-source or freeware)	new method (academic)	scientific breakthrough	other (please specify)	technical standards	EU regulations/directives	international regulations	other (please specify)	be part of a PhD thesis
USFD					X	X			X				
UBERN					X	X			X		X		
USAAR				X	X		X		X			Clinical Decision support tools	X
CUSTODIX	X		X						X			New treatment modality	X
KU LEUVEN				X		X	X						

LUH						X		development of data protection and IT-related IPR framework for multi institution research		X	X		
UNITO				X	X	X						Clinical Decision tools	
ICCS				X	X	X	X	Academic, Educational	X	X	X		X
PHILIPS	X		X						X				
FORTH				X	X	X	X		X				
CINECA				X	X				X				

Table 9: Answers to the third question of the CHIC innovation questionnaire

Institution	Where in the innovation chain will your result(s) be located?						
	Expected stage of development of my result(s) at end of project:						
	Scientific and/or Technical knowledge (Basic research)	Guidelines, methodologies, technical drawings	Software source code	Experimental development stage (laboratory prototype)	Prototype/demonstrator available for testing	Results of demonstration trials available	Other (please specify):
USFD	X		X		X		
UBERN	X	X	X		X		
USAAR	X				X	X	
CUSTODIX	X				X		
KU LEUVEN	X	X		X			
LUH							Publications contributing to on-going academic legal debate
UNITO	X		X				
ICCS	X	X	X		X	X	
PHILIPS	X	X	X				
FORTH	X	X	X		X		
CINECA			X		X		

Table 10: Answers to the fourth question of the CHIC innovation questionnaire

Institution	What are your plans for securing Intellectual Property Rights (IPR) results?						
	My plans for securing results:						
	Publication of know-how	Keep know-how confidential ('Secret know-how')	Patent application	Registered design	Trademark applications	Copyrights	Other (please specify):
USFD	X					X	

UBERN	X		X				
USAAR	X						
CUSTODIX	X	X				X	
KU LEUVEN	X						
LUH	X					X	
UNITO			X				
ICCS	X						
PHILIPS			X				
FORTH	X					X	
CINECA	X					X	

Table 11: Answers to the fifth question of the CHIC innovation questionnaire

Institution	**Which parties are involved in the generation of your results?**					
	Parties involved in the generation of my results:					
	Only myself and my group members	Other individuals at my institution	Other consortium partners	Please specify (Other consortium partners):	Other partners from outside of the consortium	Please specify (Other partners from outside of the consortium):
USFD			X	All partners of WP7		
UBERN		X	X	WP8, WP6, WP9		
USAAR		X	X	All partners		
CUSTODIX						
KU LEUVEN	X					
LUH			X	CUSTODIX		
UNITO					X	Clinical Partners
ICCS	X		X	Most of the consortium members		
PHILIPS			X	ICCS, FORTH		
FORTH	X		X			
CINECA			X	All partners of WP7		

Table 12: Answers to the sixth question of the CHIC innovation questionnaire

Institution	**For results with potential for commercial application:**						
	When will commercialization be possible?				Commercialization partners		
	during the project	Please specify the expected starting time point:	within 3 years after the project	later than 3 years after the project	Are all expected commercialization partners part of the consortium?	If not, what is the strategy to contact them (how, when, by whom)?	Please specify:
USFD				X			(Too distant to respond)
UBERN			X		NO		Direct contact to R&D dept.
USAAR			X		NO		Pharmaceutical industry needs to be contacted by the coordinator as soon as possible in the project

CUSTODIX	X	unknown	X		YES		
KU LEUVEN							
LUH							
UNITO			X				
ICCS			X	X	NO		The general assembly of the CHIC project is entitled to decide on this matter
PHILIPS				X			
FORTH		X			YES		
CINECA				X			Too early to answer

Table 13: Answers to the seventh question of the CHIC innovation questionnaire

Institution	**Which role(s) do you see for yourself in the commercialization of your result(s) (if applicable)?**								
	My role(s) in the commercialization of my result(s):						For results with potential for commercial application…		
	Developing and selling own products/services	Developing and selling products/services by starting up a spin-off company	Making a cooperation agreement	Selling IP rights	Selling the (IP based) business	Licensing IP rights (out-licensing)	I am aware of other departments in my institution to be involved when it comes to commercialization and IP protection	I know/am aware of the individuals to contact at my institution when it comes to commercialization and IP protection.	I am aware of/will familiarize myself with the licensing policy of my institution
USFD		X	X			X	YES	YES	YES
UBERN			X			X		YES	
USAAR			X				YES	YES	YES
CUSTODIX	X		X				NO	YES	YES
KU LEUVEN									
LUH									
UNITO			X						YES
ICCS			X			X	NO	NO	YES
PHILIPS	X						YES	YES	YES
FORTH		X	X			X	YES	NO	YES
CINECA	X		X			X	YES	YES	YES

Table 14: Answers to the eighth question of the CHIC innovation questionnaire

Institution	**For results with potential for public release:**								
	Which will be associated licence to your result?					Which are the license types for the libraries/components used to build your result?			
	BSD/Apache	LGPL	GPL	Proprietary	Other (please specify)	BSD/Apache	LGPL	GPL	Proprietary (please specify)
USFD	Probable					X	X		

UBERN	X					X			
USAAR					unknown				unknown
CUSTODIX				X		X			Own license
KU LEUVEN					Scientific publications				
LUH									
UNITO									
ICCS	X			X	Freeware	X	X		Matlab
PHILIPS	X					X			
FORTH	X	X		X		X	X		
CINECA						X	X		

Table 15: Answers to the ninth question of the CHIC innovation questionnaire

Institution	**For results primarily aimed at scientific publication:**											
	When do I expect the first results to be published?				Expected type of publications			Expected co-authors		With regards to scientific publication…		
	during the project	Please specify the expected starting time point:	within 3 years after the project	later than 3 years after the project	only peer-reviewed publications	peer-reviewed publications in parts	no peer-reviewed publications	Are all expected co-authors part of the consortium?	Are there any additional co-authors?	I am aware of my contractual obligation to do my best to publish open access	I will assess open access possibilities for each publication of my result(s) and will discuss this issue with my co-authors	I am aware that the open access status for all of my publications resulting from this project will be documented and communicated to the European Commission.
USFD	X	YR3-YR4			X			YES		YES	YES	YES
UBERN	X	2014			X			NO		YES	YES	YES
USAAR	X	18 month			X			NO	YES	YES	YES	YES
CUSTODIX	X	unknown						YES	NO	YES	YES	YES
KU LEUVEN	X		X	X	X	X	X	NO	YES	YES	YES	YES
LUH	X	Around PM36				X		YES	NO		YES	
UNITO	X	2014			X				YES	YES		
ICCS	X	First year				X		YES		YES	YES	YES
PHILIPS	X	PM36			X			YES	NO	YES	YES	YES
FORTH	X	2015	X		X	X	X	NO	YES	YES	YES	YES
CINECA	X				X	X	X	YES	NO	YES	YES	YES

Table 16: Answers to the tenth question of the CHIC innovation questionnaire

5.2 Project exploitation plans

Sustainability:

Following lengthy discussions in collaboration with several partner projects of CHIC, such as p-medicine and My Health Avatar, the scenario of establishing an independent organization for the sustainability of the outcome of several related EC-funded projects, called StaRC (Study Trial and Research Centre), proposed by USAAR (Prof. N. Graf) and supported by several partners appears to be a realistic sustenance channel. Such an entity could ensure the working order and usability of the major outcomes of the CHIC project. A thorough investigation of the various aspects of this scenario is to take place during the last year of the CHIC project.

ICCS also explores plans to sustain several components and outcomes of the CHIC project, including the model and in silico trial repositories, by providing access to the wider community after the end of the CHIC lifetime.

5.2.1 Clinical outputs

The clinical output as described in section 5.1 will be exploited using several channels:

- Presenting the nephroblastoma scenario at clinical meetings and conferences (e.g.: SIOP-RTSG group [Renal Tumor Study Group of the International society of Paediatric Oncology] SIOP-RTSG 2015 in Stockholm; ECCO [European Cancer Organization] ECCO 2015 in Vienna)
- Summer School held in Schloss Dagstuhl, Germany from the 7th to the 9th of September 2015
- Advertising ObTiMA via STaRC. STaRC will be a legal entity founded under p-medicine and will serve as an exploitation channel of results coming from CHIC
- Writing papers in peer-reviewed scientific journals
- Sharing experience with tools developed in CHIC with other departments of the university
- Presentation (oral, poster) in scientific meetings
- When approved, implementation in new clinical trials

The potential impact of the exploitation of the clinical outputs can be relevant. Adequately clinically adapted, validated and certified versions of the models (hypo- and hypermodels) and the corresponding clinical decision support systems (CDS) could result in extension of life expectancy of cancer patients, a better quality of life, and decrease of the associated financial and societal burden.

5.2.2 Technological/software outputs

5.2.2.1 Clinical data repository

Exploitation

Several exploitation options will be investigated for the clinical data repository. The first direction is to exploit the system as a collaboration tool for clinical trials performed at different locations. The benefit for clinician involved in collaborative research projects is that they have better control on what they share and with whom. Additionally, the dataset does not leave the hospital/data provider before being reviewed and anonymized.

Another exploitation option is the development of centralized repository for medical images. Statistical shape analysis techniques are very popular in the medical imaging community and results can be transferred to companies active in implant design or imaging. A large data collection of medical images would major issue of the techniques, which is the very large number of dataset required to build a valid model. This constrain is even more critical when pathological situations are

concerned. In the same direction, this platform could be used to propose open challenges such as image segmentation competition. On one hand open challenge stimulates research by providing a common set of data to compare new developments with existing benchmarks. In addition, proposing challenges is a great way to attract researcher, process available data and promote the system. .

Sustainability/maintenance plans

From an organisational perspective, the development and maintenance of this database system will be supported in the future by a non-profit foundation. The foundation name Si-CAS is based in Delémont (Switzerland) aims at becoming a support platform providing know-how and services in biomedical engineering. One of the core competences is linked to medical image analysis and modelling, including statistical shape modelling.

5.2.2.2 Model/tool repository, In silico trial repository

Exploitation

- Can be exploited as a source of various software components for the development of Clinical Decision Support (CDS) systems.
- Can be exploited as a trustable and convenient storage and model handling environment for additional cancer models. Additionally, the repositories could be extended in order to accommodate other disease or physiological models.

Impact

- A high impact on the physiological, pathological and medical research software infrastructure is expected due to both the complexity of the problems addressed and the advanced multipurpose functionalities of the components and systems being developed.
- Technologies being developed and/or integrated within the framework of the CHIC project are expected to boost the European biomedical software industry and contribute to its leading role in the emergent in silico oncology and in silico medicine domain.

5.2.2.3 Hypermodeling execution framework – VPH-HF

USFD, collaboration with the other partners involved in WP7 is producing a software framework (VPH-HF) to orchestrate the execution of hypermodels. It interacts with the components of the other partners to provide in a secure cloud-based infrastructure a set of user-friendly services for clinicians through a web interface: clinical data analysis/visualisation tools, clinical model/data repositories with semantic annotation and search functions, hypermodelling editor to compose new hypermodels to answer specific clinical questions on patient data or to generate new *in silico* trials.

USFD is delivering the software framework VPH-HF to support the orchestration and execution of hypermodels that process patient clinical data. It is embedding cutting edge research methodologies that aim to change the current technical standard. The underlying principle is that the research outcomes have to create value for the society, the SMEs and ultimately the patients and taxpayer. Therefore VPH-HF will be licensed under a BSD like license with open source code to be European software for the Europeans. This philosophy guarantees from one side a stronger commitment to deliver high quality software engineering products that can set the standard for good practices in computational science. On the other side European citizens and SMEs can freely access the source code of VPH-HF as a learning reference or a starting point to extend and provide more software services. In both cases the impact in European society will be substantial as translational knowledge and exploitable product. The aim is to build a substantial academic computational science community around VPH-HF such that its maintenance and extension will be the result of a self-supported collective interest and effort – this would be an interesting innovative measure of success. Furthermore VPH-HF is developed following the best practices in computational science reproducibility and releasing it open source will provide a concrete example in this direction.

The main impact of CHIC/VPH-HF development will come from the unique combination of skills developed during the project consortium collaboration. The VPH-HF platform will be able to be exploited beyond the end of the CHIC project both from clinical cancer research stakeholders and other simulation based research scenarios based on multiscale models. In fact the VPH-HF his designed to be modular, extensible and customisable with reasonable effort. This will be source of exploitation value that could be generated through services sale, consultancy or an ad-hoc spin-off company.

5.2.2.4 Technical tools

As we described in paragraph 5.2 there are a number of technical tools and components developed in the context of CHIC by FORTH which are exploitable either as independent tools or as parts or in conjunction with other components.

- **Private cloud infrastructure.**
    - Exploitation.
      The private cloud infrastructure can be exploited in various ways, due to the diverse functionalities that it offers. It provides resource pooling, virtualization, scalability and elasticity in utilizing computational resources and as such it provides the basis for transforming FORTH's own data centre facilities which on its own constitutes an ongoing exploitation plan. It can be utilized in future research projects, since there is a trend in moving applications and services in the cloud (Software as a Service) as well as utilising its computational and storage capabilities in big data computing in the biomedical domain. It can also be exploited as a service, both to research and academic context or for commercial purposes, via a spin-off company targeting to niche markets.
    - Sustainability.
      The private cloud infrastructure has been built by harnessing, in a great extent, already available resources. On this ground, the cloud infrastructure is expected to provide us a return on investment since it will diminish operational costs that were already present.
    - Impact.
      The impact of the cloud infrastructure has already been acknowledged, both to the research and to the commercial environment, due to the functionality that it offers. We expect that it will enhance the productivity of our group, it will provide better utilization of our computational resources and it will provide ground for possible collaboration with other groups in future research projects.
- **DrEye.**
    - Exploitation.
      DrEye is an open access, flexible and easy to use platform, for intuitive annotation and segmentation of tumor regions. Its clinically driven development followed an open modular architecture focusing on plug-in components. DrEye's main advantage is that the user can quickly and accurately delineate complex areas in medical images in contrast with other platforms that do not facilitate the delineation of areas with complicated shapes. Additionally, multiple labels can be set to allow the user to annotate and manage many different areas of interest in each selected slide. The close collaboration with clinicians in designing the platform has ensured that it can be effectively used in the clinical setting. DrEye allows computational "in-silico" models of cancer growth and simulation of therapy response to be easily plugged in,

in order to provide a future integrated platform for modelling assisted therapy decision making.

- Sustainability.
  The support for the continuation of the development of the DrEye Medical Imaging platform will largely come from own resources and the participation of FORTH in relevant subsequent research projects. DrEye is regularly maintained according to feedback received by a number of regular users from different clinical settings. Its functionality is expanding according to clinical needs that arise from existing and new users.
- Impact.
  Due to its wide field of usage and its proven extensibility, DrEye continues its successful path in the communities of radiologists and imaging medical experts. With the updates that will implement in the context of the CHIC project and the extension of its communication functionalities with the clinical trial system of CHIC, its profile will become even more appealing to the stakeholders.

- **Hypermodelling editor.**
  - Exploitation.
    The hypermodelling editor is the user-friendly environment for the construction of syntactically and semantically valid, multiscale hypermodels. Its target end-users therefore consist of mathematical modellers, computational biologists, clinicians, and other research communities and stakeholders. To engage these communities and strengthen the collaboration, the Editor will be offered as open source software but also in a “software as a service” (SaaS) delivery model. The involvement of key end users and relevant communities is crucial in order to get feedback and guarantee the Editor’s sustainability so dissemination of its objectives and features will be pursued through publications, involvement in future research projects, and demonstrations in suitable workshops and conferences.
  - Sustainability.
    The support for the continuation of the development of the Hypermodelling Editor will largely come from own resources and the participation of FORTH is relevant subsequent research projects. The provision of the Editor as an open source software provides opportunities for its sustainability, assuming that the critical mass of the user community contributing to its development (i.e. by submitting ideas, bug reports, fixes, etc.) has been gathered.
  - Impact.
    The Hypermodelling Editor is expected to have a positive impact on the computational modelling community and its activities. The Editor is expected to be of great value as a user friendly, web based graphical environment for supporting the researcher in the full cycle of experimentation/exploration, design, publication, execution and monitoring of complex integrative computational models.

- **Data Upload Tool.**
  - Exploitation.
    The CHIC Data Upload Tool is the end user desktop application for pseudonymizing and distributing clinical and image data sets and making them available in the CHIC platform. Due to the dependencies on the security framework and the rest of the CHIC architectural components this tool cannot be exploited as is in isolation. Nevertheless, the majority of the end user visible functionality and its usability

features can be repackaged and distributed separately, following an open source software development model.

- Sustainability.
  The data upload tool will be maintained after the end of the project by the adaptation and reuse in follow-up projects.
- Impact.
  Despite its narrow set of objectives (pseudonymizing and uploading data sets) this tool aims to be valuable for the CHIC partners and end users. Outside of the CHIC project its impact will likely be limited, depending on its repurpose as a general upload tool in other research infrastructures.

- **Models.**
  - FORTH provides in total three models that greatly assist in the prediction of tumor evolution, morphology and effective treatment. These models are going to be part of the model repository and will be exploited accordingly.

5.2.2.5 Semantic-metadata services

UCL's RICORDO systems have been designed with well-documented APIs intended to ease usage in other partners' software packages. Other CHIC partners can exploit this work by using the APIs to seamlessly integrate sophisticated semantic/metadata operations into their own software. By adopting semantic best practices, CHIC ensures high interoperability of its metadata, as well as making its metadata compatible with all kinds of automated reasoning / knowledge discovery software.

RICORDO is inherently sustainable/maintainable, because of the way it constructs its core knowledgebase from open source ontologies. These open source ontologies are maintained by experts in their respective fields, and only a minimum of effort is needed to incorporate these ontology updates into the RICORDO instance running on CHIC hardware (in practice, it is not even necessary to incorporate such updates immediately on their release: regular updates every couple months or so should be more than adequate, based on the already mature status of the reference ontologies in question).

CHIC is optimistic that the semantic metadata best-practices it has committed itself to will have a significant impact on medical research in general. We hope CHIC will prove the utility of having its data so interoperable and reasoner-friendly and thereby provide a precedent for future projects.

5.2.2.6 CHIC security tools and services

Evolving software from research outcome to a marketable product requires a lot of investment. Custodix feels that the research, proof-of-concepts and definition of a unique selling proposition are not sufficiently matured yet to be able to attract the investments needed to commercialize all of the security components. Therefore, at this point in time, the security components are mainly used in combination with existing products (e.g. CATS, PIMS) and will be promoted as security integration layer in projects where Custodix acts as system integrator. This allows the security components to mature with respect to applicability, robustness and performance in real world situations. The innovations brought by the approach to authentication, authorization and audit will be further promoted to the biomedical community (who needs the advanced features not found elsewhere) through research projects in which Custodix is already engaged. Introducing this technology in (commercial) one-off projects and to research infrastructures in which industrial partners play a significant role (e.g., EMIF, which is a project under the Innovative Medicines Initiative, which is a large public-private partnership between the European pharmaceutical industry and the EU

Commission) further allows Custodix to identify which competitive advantages are truly valued by the market, i.e., the advanced security feature set, the integration capabilities (also with legacy solutions) or the fact that authentication, authorization and audit is integrated.

5.2.2.7 CHIC Pseudonymisation Tools

CATS and PIMS are both long term Custodix products. In parallel to the research versions commercial grade spin-offs of CATS and PIMS are exploited and continuously maintained.

5.2.3 Modelling outputs

Exploitation

- Can be exploited as a model source for the development of Clinical Decision Support (CDS) systems, following the necessary clinical adaptation, validation and certification processes.
- Models (hypo- and hypermodels) can also be used in order to support basic biomedical research in the generic setting, including a deeper and more quantitative understanding of the various natural phenomena which constitute physiology, disease and disease response to treatment. Certain hypomodels related to cancer can also be used in order to construct hypermodels for physiological and pathological mechanisms encountered in physiology and pathology outside the domain of cancer.

Impact

- See 6.2.1
- Models being developed and/or integrated within the framework of the CHIC project are expected to boost the European biomedical software industry.
- Due to the vast scientific, technological and clinical scope and depth of the CHIC project a great impact on the academic educational procedure is expected in the form of (post) graduate courses, laboratory classes, as well as the shaping and advancement of new scientific domains such as in silico oncology and in silico medicine is expected.

5.3 Individual exploitation plans

USAAR-KU Leuven exploitation plans

The own foreground of USAAR and KU Leuven will be exploited using the same channels as for the clinical output described under 6.2.1

ICCS exploitation plans

ICCS plans to use most of the components and systems being developed by CHIC in the context of future research endeavours within the intercontinental level by taking into account all pertinent legal and ethical restrictions. Eventual future EC funded projects constitute primary targets of such a strategy.

Since ICCS is the research hub of the School of Electrical and Computer Engineering (SECE) of the National Technical University of Athens (NTUA), several forms of the CHIC outcome will serve as the starting point for the conduction of new doctoral theses and post-doctoral research.

In SECE-NTUA the globally first post-graduate course dedicated to multiscale cancer modelling and in silico medicine was designed and taught by the CHIC coordinator, Research Prof. G. Stamatakos. (http://chic-vph.eu/highlights/details/article/first-postgraduate-course-on-in-silico-medicine/, http://www.vph-institute.org/news/new-postgraduate-subject-on-multiscale-cancer-modelling-and-

in-silico-medicine-mscm-ism.html). Within this context the entire outcome of the CHIC project will also serve as an academic educational platform.

USFD-CINECA exploitation plans

VPH-HF is a collaborative product developed starting from a previous result achieved during the VPH-OP EC project. The aim is to exploit the final release of VPH-HF developed in CHIC as a customisable platform for the execution of multiscale models to simulate physical phenomena and healthcare systems in different scenarios. The ideal way to exploit the value built in this framework is to sell services/consultancy and customised solutions through a spin-off company. A more detailed plan will be developed, with the agreement of the CHIC consortium, in a later stage closer to the end of the CHIC project.

FORTH exploitation plans

FORTH is planning to also individually exploit some of the developed CHIC technologies first by sustaining them after the end of the project for as long as is possible with own sources. At the same time it will continue the development of the tools by seeking opportunities for new collaborations with organizations for which the tool could be useful or within the context of future projects.

FORTH will also contact Medical University Schools in Greece for evaluating and using the DrEye tool in a scenario where a professor could ask the students to annotate DICOM images and perform a number of post-processing tasks using powerful CHIC technologies. In parallel, FORTH will attempt to further evaluate and promote the tools also in Greek hospital networks by licensing them for clinical sites. To this end, FORTH and in particular the computational medicine laboratory is coupled with the Center for eHealth Applications and Services (CEHA) which develops and deploys professional IT software for the healthcare sector providing integrated and qualitative tools and solutions. CEHA has expressed its initial interest to assess the possibility of commercialization of some of these products.

Moreover, FORTH will seek opportunities to re-use and/or expand its CHIC tools to current or future research projects.

UCL exploitation plans

The RICORDO suite, which UCL developed to handle CHIC's metadata and knowledgebase, are widely applicable outside of CHIC, and UCL is optimistic about sharing these benefits with other research projects as well.

TEI-C exploitation plans

TEI - C is mainly involved in WP5 which focuses on the definition of the architecture for subsequent implementation and integration. The architecture specification will provide the software architecture design patterns to effectively guide and support the construction of a coherent and consistent system. Particular emphasis will be given to the definition of appropriate interfaces among the modules to enable interoperability. As a result the foreground knowledge that will be generated by TEI-C - through its participation in these highly demanding activities - will be used in updating the relevant courses that Prof. Tsiknakis teaches at TEI-C, which include a) modeling and simulation of biomedical systems, and b) Advanced topics in eHealth and mHealth systems and services

CUSTODIX exploitation plans

Custodix' core business is securing sensitive data. Since its founding, Custodix has always focused on the life sciences sector where the need for data protection is clear. For this the company provides a variety of services and products, such as Trusted Third Party data collection services, de-identification tools, data privacy consultancy, etc.

Within the CHIC project, Custodix is responsible for providing the tools to ensure data protection compliance (such as the security infrastructure and the CHIC de-identification services). Two aspects of the CHIC work are important for exploitation by Custodix. First of all, within the project, research is

continued on the de-identification tools: CATS and PIMS, which contributes to their continuous improvement.

Secondly, the CHIC project is one of the projects in which Custodix has been able to further research its ideas on improving the integration of security in service oriented IT environments (with high requirement with respect to data protection). The goal of this work is to design a unified solution to identity provision, access management and audit, which allows building highly secure IT systems without compromising on development complexity and end-user usability. Custodix believes such a solution has commercial value.

Although the different components of the framework (identity manager, security proxy, access management components, audit services, etc) are envisaged to be marketable in a wide range of domains, the initial focus for exploitation will be the health and clinical domain (where the majority of the Custodix commercial activity resides). The high level of security that the framework aims to bring through its exceptional features (e.g. credential delegation) is expected to be a differentiator in this domain (cf. sensitive medical data).

The rationale behind this approach is the following. It has been understood for already quite some time that collaboration and sharing of clinical data is becoming key to the further advancement of medicine. Trying to find the perfect solution to enable this sharing has therefor been a prominent topic in life sciences IT. Originally the general sentiment was that monolith IT systems would encompass the needed functionality. However, the long time to market, the high maintenance cost (even when one needs only one component the complete system needs to be set up and maintained) and the fact that uniform solutions can't fit the wide range of differentiating requirements has caused researchers and clinicians to look to other solutions. In a rather recent wave of pragmatism, different (isolated) tools are built each tackling a specific sub-problem. Many people faced with the challenge to build more complex clinical application environments are thus now turning towards a "pick and choose" strategy for composing their toolset.

The task that does remain is proper integration of these tools. Next to the obvious functional integration aspect (e.g. exchange of data between tools), the importance of security should not be underestimated. The possible impact on usability and manageability is huge. Imagine daily usage of several tools for which one needs to remember different usernames and passwords (or even use different tokens), imagine that sharing rights needs to be reconfigured in every separate tool (and kept in sync), etc. In practice, security encompasses a substantial part of the system integration work in environments in which data protection is important. A framework that offers the required security functionality at low implementation complexity and integrates (out of the box) with commonly used tools will clearly have a competitive advantage.

In this context, the participation in CHIC not only serves in defining technical specifications and developing the technological components for the security framework, but also to validate if the framework accommodates for all needs of researchers, clinicians, system integrators and compliance officers.

Custodix' exploitation strategy with respect to this security framework already resulted in the spinning-off a commercial version of the Identity Management Service (IdM) (with a reduced feature-set compared to the research work done in the project). This IdM is promoted as an integration tool in the clinical domain in order to find out whether a strategy towards system integration specifically in this domain will pay off. The subsequent result will determine the prioritization of the further development of the security tools or a possible repositioning of the framework.

It goes without saying that with respect to system integration Custodix is complementary to the other CHIC partners, and thus open to any form of commercial cooperation.

UBERN exploitation plans

The software BraTumIA has been released to the scientific community and since last May over 150 download requests have been processed. The software has been clinically evaluated at the local hospital in Bern and will be employed as comparison basis for future developments. Namely, the software will be extended to include longitudinal analysis as well as analysis of low-grade gliomas. In addition, the software's core components will be refactored to enable reutilization of the technologies to other diseases of the central nervous system.

6 Conclusions

This document describes the output of the activities carried out so far in WP12; in particular, it provides a detailed definition of the strategic dissemination plan, which includes the identification of the target groups and the dissemination channels to be used, the projects outputs and the exploitation activities.

In particular, for the target groups, an effort has been made during the first year not only to define their overall categories but also to identify the stakeholders who are part of them. This has allowed the consortium to start addressing them from the very beginning of the project. For the dissemination channels, we identified the relevant peer-reviewed journals and conferences for the presentation of the scientific outputs of the project and to the web content.

An important part of the document has been dedicated to the IPR management strategy both at the stage of Project implementation and exploitation of Project results. In particular, the following issues are covered: sharing and exercise of rights in composite works, IPR management in works contributed to the Project by sub-contractors, software licensing and license compatibility issues, compliance with license terms and access to the source code for the end users.

Another important section is dedicated to the CHIC project results in terms of clinical results, software and mathematical/computational model and to the exploitation plans of the consortium and of the individual members. An innovation questionnaire proposed by the CHIC consortium has been filled in by the several partners in order to collect the individual exploitation plans.

7 References

[1] D12.1 - Dissemination Plan

[2] D12.2 - Dissemination Kit available

Appendix 1 – Abbreviations and acronyms

WP	Work Package
MoU	Memorandum of Understanding
IPR	Intellectual Property Rights
EC	European Commission
GA	Grant Agreement
CA	Consortium Agreement
CDS	Clinical Decision Support
GBM	GlioBlastoma Multiforme
GNU	GNU's not UNIX
GPL	General Public License
LGPL	Lesser General Public License
BSD	Berkeley Software Distribution
STaRC	Study Trial and Research Centre