

**Deliverable No. D7.101**

**Hypermodels: definitions**

Grant Agreement No.: 600841

Deliverable No.: D7.101

Deliverable Name: Hypermodels: definitions

Contractual Submission Date: NA

Actual Submission Date: 21/05/2014

|  |
| --- |
| **Dissemination Level** |
| **INT** | Internal, non-contractual document. Do not redistribute outside the consortium |  |

|  |
| --- |
| ***COVER AND CONTROL PAGE OF DOCUMENT*** |
| Project Acronym: | **CHIC** |
| Project Full Name: | Computational Horizons In Cancer (CHIC): Developing Meta- and Hyper-Multiscale Models and Repositories for In Silico Oncology |
| Deliverable No.: | D7.101 |
| Document name: | Hypermodelling - definitions |
| Nature (R, P, D, O)[[1]](#footnote-1) | Internal, non contractual |
| Dissemination Level (PU, PP, RE, CO)[[2]](#footnote-2) | Internal, consortium only |
| Version: | 3 |
| Actual Submission Date: | 21/05/2014 |
| Editor:Institution:E-Mail: | Marco VicecontiUSFDm.viceconti@sheffield.ac.uk |

|  |
| --- |
| **ABSTRACT:**This deliverable, internal and non-contractual, aims to provide an agreed set of definitions that will be used consistently through out the consortium. |

|  |
| --- |
| **KEYWORD LIST:**Definitions, hypermodel |

*The research leading to these results has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement no 600841.*

*The author is solely responsible for its content, it does not represent the opinion of the European Community and the Community is not responsible for any use that might be made of data appearing therein.*

|  |
| --- |
| ***MODIFICATION CONTROL*** |
| **Version** | **Date** | **Status** | **Author** |
| 1 | 15/11/2013 | Draft | Partner USFD created first draft |
| 2 | 27/3/2014 | Draft | Partner ICCS and USAAR added glossary. |
| 3 | 23/4/2014 | Draft | Addition partners CIN and USSAR |

**List of contributors**

All WP leaders:

|  |  |  |
| --- | --- | --- |
| WP02 | User Needs and Requirements | Graf Norbert |
| WP03 | Clinical and Translational Science Scenarios | Van Gool Stefaan |
| WP04 | Legal and Ethical Framework | Forgó Nikolaus |
| WP05 | IT Architecture | Tsiknakis Manolis |
| WP06 | Cancer Models and Hypermodel Design | Stamatakos Georgios |
| WP07 | Hypermodelling infrastructure | Viceconti Marco |
| WP08 | Model and Data Repositories | Stamatakos Georgios |
| WP09 | Image Processing and Visualization | Dong Feng |
| WP10 | Integrated Platform | Marias Kostas |
| WP11 | Clinical Adaptation and Validation | Graf Norbert |
| WP12 | Dissemination and Exploitation | Testi Debora |

Contents

1 Executive Summary 5

2 Introduction 6

2.1 Purpose of this document 6

2.2 General definitions 6

3 Models and hypermodels definitions 8

3.1 Scientific Models 8

3.2 Models, metamodels, hypomodels, and hypermodels 8

3.3 Archival and publishing 9

4 Clinical definitions 10

5 Ethical and Legal definitions 11

# Executive Summary

*In silico* medicine is young, emerging technological domain. As such it uses a large number of neologisms, terms that do not exist in the common language, that are used to indicate fairly specific technical details. Typically, every research group use a different set of terms, with overlaps, redundancies, and some time lack of consistency and precision. This internal deliverable is an attempt to consolidate the terminology, at least within the CHIC consortium, in order to increase the efficacy in the communication and reduce misinterpretations.

# Introduction

## Purpose of this document

The scope of this document is to reach consensus within the consortium for a set of terms, and of related definitions, that should be used consistently throughout the project, including all documentation, reports, deliverables, and user interfaces.

## General definitions

### In silico medicine

In silico is an expression used to mean "performed on computer or via computer simulation." The phrase was coined in 1989 as an analogy to the Latin phrases in vivo, in vitro, and in situ, which are commonly used in biology and refer to experiments done in living organisms, outside of living organisms, and where they are found in nature, respectively.

<http://en.wikipedia.org/wiki/In_silico>

### Virtual Physiological Human (VPH)

The Virtual Physiological Human (VPH) is a methodological and technological framework that, once established, will enable collaborative investigation of the human body as a single complex system. The collective framework will make it possible to share resources and observations formed by institutions and organizations creating disparate, but integrated computer models of the mechanical, physical and biochemical functions of a living human body.

 <http://en.wikipedia.org/wiki/Virtual_Physiological_Human>

### The VPH research agenda

After seven years of research based on the original VPH Research Roadmap elaborated by the STEP consortium (http://www.europhysiome.org/), 67 public and private institutions started a no profit organisation called the VPH Institute, to coordinate and sustain the VPH research agenda at national, European, and international level. Under the general heading of in silico medicine that appeared in the first document on the next European research framework, Horizon 2020, the VPH Institute proposed three grand challenges for the development of the VPH: the Digital Patient, In silico Clinical Trials, and Personal Health Forecasting.

<http://www.europhysiome.org/roadmap>

<http://ec.europa.eu/research/horizon2020/pdf/contributions/post/international_organisations/vph_institute.pdf#view=fit&pagemode=none>

#### Digital Patient

The Digital Patient is the challenge to make directly usable to the clinical specialists the VPH technologies. An ever-increasing wealth of information is collected by health professionals. At the same time, predictive models of physiological systems are evolving rapidly. Many human diseases are complex, long-term and interconnected with other conditions, making their management difficult. The aim of the Digital Patient initiative is to develop an integrative approach to health prediction using patient-specific information and predictive models.

<http://www.digital-patient.net/>

#### In Silico Clinical Trials

In silico clinical trials are the challenge to make directly usable to the health industry the VPH technologies, for the development of new health products, including medical devices, surgical instrumentation, pharmacological products, tissue engineering products, etc. The original idea was proposed roughly at the same as the VPH, but only recently it became evident that VPH mechanistic models can be used within stochastic frameworks to simulate entire populations of synthetic individuals.

<http://insigneo.org/research/avicenna-a-strategy-for-in-silico-clinical-trials/>

#### Personal Health Forecasting

What we propose is to develop personalised VPH models (integrative predictive models) that constantly update to respond to all the data transmitted by personal health systems, wearable sensors, ambient assisted living technologies, mobility monitors, etc. and predict how specific aspects of our health will evolve in a near or not-so-near future. Such models should account for chronic diseases, recurrent prescriptions, or specific disabilities and could be further personalised with clinical data such as medical imaging, biomedical instrumentation, biomarkers, etc.

# Models and hypermodels definitions

## Scientific Models

In this context we can define **scientific models** as: “finalized cognitive constructs of finite complexity that idealize an infinitely complex portion of reality through idealizations that contribute to the achievement of knowledge on that portion of reality that is objective, shareable, reliable and verifiable” (Viceconti M 2011 A tentative taxonomy for predictive models in relation to their falsifiability. Philos Transact A Math Phys Eng Sci 369(1954):4149-61).

## Models, metamodels, hypomodels, and hypermodels

We define a **computer model** as a computer program that implements a scientific model, so that when executed according to a given set of control instructions (control inputs) computes certain quantities (data outputs) on the basis of a set of initial quantities (data inputs), and asset of execution logs (control outputs).

In the CHIC hypermodelling framework:

* Every computer model is exposed through a wrapper that standardise the control flow syntax. Thus all control inputs and all control outputs are provided according to a unique semantics; the wrapper is responsible of translating the hypermodelling framework standard control syntax in the program-specific control syntax that each computer model requires.
* Every data input and every data output are made available on a sandbox local to the computer program in the format that the computer program requires/produce. The storage services are responsible for managing the replication between the local storage sandbox and the remote central storage, and for translating the data to and form the format required by the central storage.

We define a **metamodel** the semantic description of a computer model. The “Minimal Information Required In the Annotation of Models” (MIRIAM, <http://co.mbine.org/standards/miriam>) provides a set of general guidelines for the annotation of computational models in Biology[[3]](#footnote-3). In CHIC we define that, at a minimal level, the “metamodel” description should include some descriptive information, such as:

* Model Title,
* Description,
* Creator(s)/Author(s)
* Publication information
* “See also”/”More info” references
* Important dates (e.g. creation date, publication date)
* Validation information (verification, pre-clinical accuracy, etc.)
* License and terms of use information

We observe nature, and we notice recurrences. We develop causal knowledge, first by induction, associating the current observable states to predicted future states, and then by inferring why such causal relation exists, recognising some fundamental principles, and then by deduction derive from these principles mechanistic explanations of the observations.

A **hypermodel** is the composition and orchestration of multiple **hypomodels** (single models either scientific or computer ones):

* **Component hypomodels** capture the existing knowledge about a portion of the process, typically at a characteristic space-time scale.
* **Relation hypomodels** define how certain properties predicted by one hypomodel transform within the set of idealisations used to build another hypomodel that takes such properties as input.

It should be noted that a hypermodel could be re-used as a hypomodel in another more complex hypermodel. This poses some potential issues from a terminology point of view.

Hypomodel and model will be used most of the time as synonyms.

## Archival and publishing

In CHIC there two main digital resources: data and models. In relation to their archival and publishing, some definitions can be provided:

* Resource
	+ Data: factual information, whether observed or predicted.
		- Observed: generated through observation, measurement, etc.
		- Predicted: generated through speculative reasoning informed by existing knowledge
	+ Hypomodel: speculative information that represent the existing knowledge.
		- Phenomenological: models capture predominantly knowledge generated inductively, by analysis of available data. Relies on implicit idealisations such as regularity, smoothness, etc.
		- Mechanistic: models that capture predominantly knowledge generated deductively. Relies in explicit idealisations.
	+ Hypermodel: structural representation on a hypomodels’ orchestration
	+ Metamodel: semantic representation of a model, or hypermodel

# Clinical definitions

**Cancer** or malignant neoplasm is a group of diseases that is characterized by unregulated cell growth, invasion in surrounding tissue and building metastasis by spreading through the lymphatic system or through blood. More than 200 different cancers are known in humans. The International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3)[[4]](#footnote-4) represents a multi-axial classification of the site, morphology, behaviour, and grading of neoplasms.

The **aetiology of cancer** is complex and only partially understood. The **hallmarks of cancer** are described by Hanahan and Weinberg[[5]](#footnote-5) (see also D2.2, chapter 2.3). Cancer can affect people of all ages, but the risk of developing cancer increases with age. Some cancer types are typically for children.

Signs and symptoms of cancer are broad and often uncharacteristic. Suspicion of cancer arises from clinical symptoms, screening tests, laboratory and medical imaging. But only histology can proof cancer. Today molecular biology of cancer and the interaction with the host are important research topics.

**Treatment** of cancer is based on surgery, chemotherapy, irradiation and nowadays also targeted therapy. **Targeted therapy** describes a treatment option, where small molecules interact with tumor specific receptors. A typical example is Imatinib (Glivec®) for the treatment of Chronic Myelocytic Leukemia (CML).

Treatment of cancer should always be done within a **clinical trial**.

**Clinical trials** are research studies that involve people. They are the final step in a long process that begins with research in a lab and animal testing. Many treatments used today are the result of past clinical trials. In cancer, clinical trials are designed to answer questions about new ways to treat cancer, to diagnose cancer, to prevent cancer and to manage symptoms of cancer or side effects from its treatment.

The National Cancer Institute (NCI) provides a comprehensive cancer database that contains a summary of a wide range of cancer topics:

* [**http://www.cancer.gov/cancertopics/pdq**](http://www.cancer.gov/cancertopics/pdq)

The Physician Data Query (PDQ) contains the NCI Dictionary of cancer terms:

* [**http://www.cancer.gov/cancertopics/pdq/cancerdatabase**](http://www.cancer.gov/cancertopics/pdq/cancerdatabase)

All relevant clinical definitions can be found in these databases. A detailed description of clinical definitions in this document is therefore not justified to ovoid a selection bias.

# Ethical and Legal definitions

Personal data

Personal data means any information relating to an identified or identifiable natural person ('data subject'). An identifiable person is one who can be identified, directly or indirectly, in particular by reference to an identification number or to one or more factors specific to his/her physical, physiological, mental, economic, cultural or social identity.[[6]](#footnote-6) Therefore a set of data collected under a certain number or sign “patient xxx”, “tissue YYY” can be personal data, if the patient concerned can still be identified by other means than his/her name.

Sensitive (personal data)/Special categories of data

Sensitive personal data are personal data revealing racial or ethnic origin, political opinions, religious or philosophical beliefs, trade-union membership, and data concerning health (including genomic data) or sex life.[[7]](#footnote-7) The processing of sensitive data is prima facie prohibited under European data protection law, but allowed with the data subject’s express informed consent or within the scope of certain exceptions explicitly stated by the national laws of the Member State.

Anonymous data / Rendering anonymous

Rendering data anonymous means to modify personal data in a way that the information concerning personal or material circumstances can no longer be identified, or this is only possible with a disproportionate amount of time, expense and labour. Data that have been anonymised are no longer “personal data” in the legal sense. In CHIC, where the technical, legal, and organisational measures taken to secure the data, including the contractual agreements, are adhered to, it will take a disproportionate amount of time, expense and labour to attribute the data to an identified individual. Accordingly the data processed within the CHIC infrastructure shall be regarded as **(de facto)** **anonymous data**.

**Data controller**

The data controller is the natural or legal person who alone, or jointly with others, determines the purposes and means of the processing of personal data. The data controller is liable for the legality of the processing and the fulfilment of the obligations towards the national data protection authority and the patients. The hospitals/investigators participating in the CHIC project (data providers) are data controllers with regard to the collection of Patient Data and their transmission to CHIC, whereas the CDP is the data controller with regard to the data stored in the CHIC infrastructure. Finally the CHIC end-users are in the position of data controllers with the obligation to ensure full confidentiality and security of the data they receive from the CHIC infrastructure and repositories.

Technical and organisational measures (for data security)

Organisational measures, together with technical measures, are means of ensuring an appropriate level of security of the data processing, taking into account the state of the art and the costs of their implementation relative to the risks inherent in the processing and the nature of the data to be protected. These measures shall be taken to prevent accidental loss, destruction or alteration of, or damage to, personal data and against unauthorized or unlawful processing of personal data in particular where the processing involves the transmission of data over a network, and against all other unlawful forms of processing. Appropriate organisational measures to ensure the confidentiality, integrity and accuracy of processed data should include inter alia: control of the entrance to installations; control of data media; memory control; control of utilization; access control; control of communication; control of data introduction; control and securing of data transmission; and availability control.

**Trusted Third Party**

The Trusted Third Party in CHIC is an independent security authority, which holds the pseudonymisation key (cross table) needed to link the double-encrypted CHIC data set to the initial de-identified data sets provided by the data providers. The involvement of the TTP guarantees that a CHIC data set can only be linked back to the original patient by the data provider institution treating the patient, in the exceptional circumstances where it is required, in the compelling interests of that patient / data subject, to contact him/her.

Informed Consent

Informed consent means any express indication of data subject´s wishes, expressing his/her agreement to data relating to him/her being processed, provided that he/she has sufficient information about the purposes of the processing, the data or categories of data concerned, the recipient of the data, and the name and address of the controller and of his/her legal representative if any. The consent must be freely given and specific, and may be withdrawn by the subject at any time. If the subject is incapable of a free decision or domestic laws do not permit the subject to act on his/her own behalf, consent is required of the person recognised as legally entitled to act in the interest of the data subject or of an authority or any person or body provided for by law (legal representative).

Center for Data Protection (CDP)

The CDP means the central data protection authority of the CHIC infrastructure, which agrees to receive from the healthcare organisations/hospitals (data providers) data intended for processing in accordance with the terms of the Data Provider Agreement. The CDP guarantees privacy within the CHIC infrastructure and repositories.

**Software**

Software means sequences of instructions to carry out a process in, or convertible into, a form executable by a computer and fixed in any tangible medium of expression[[8]](#footnote-8). A further synonym used for Software is a computer program, or a program for short.

**Source Code**

Source Code means software in human readable form normally used to make modifications to the same, including, but not limited to, comments and procedural code such as job control language and scripts to control compilation and installation[[9]](#footnote-9).

**Object Code**

Object Code means software in machine-readable, compiled and/or executable form, including, but not limited to, byte code form and in form of machine-readable libraries used for linking procedures and functions to other software[[10]](#footnote-10).

**Application Programming Interface**

Application Programming Interface means the application programming interface materials and related documentation containing all data and information to allow skilled Software developers to create Software interfaces that interface or interact with other specified Software[[11]](#footnote-11).

**Open source software**

Open source software means software distributed under the license which complies with the [Open Source Definition](http://opensource.org/osd) (<http://opensource.org/osd>).

**Intellectual Property Rights (IPR)**

IPR means all rights resulting from copyright protection, related rights, design rights, patent rights, plant variety rights, rights of creators of topographies of semiconductor products), similar forms of protections (e.g. sui generis right for databases) and unprotected know-how (e.g. confidential material)[[12]](#footnote-12).

**Author**

Author means the natural person or group of natural persons who has created the program or, where the legislation of the Member State permits, the legal person designated as the rightholder under that legislation[[13]](#footnote-13)

**Copyright**

Copyright means the rights of authors in their literary and artistic works, protected by copyright law[[14]](#footnote-14).

**Copyright law**

Copyright law means all relevant legislation and/or case law in the states making up the European Economic Area or, as the case may be, the United States for the protection of the rights of authors in their literary and artistic works[[15]](#footnote-15).

**Software license (License)**

Software license means the conditions under which the Author permits the rights in the software protected by copyright to be exercised[[16]](#footnote-16).

Appendix 1 – Hypermodelling glossary

|  |  |
| --- | --- |
| Term | Definition |
| **Adaptor** | A piece of software that adapts the output of a hypomodel so as to be possible to be merged with the (potentially adapted) output of another hypomodel via a merger and give rise to a new hypermodel (probably following an additional adaptation of the joined output of the two hypomodels). |
| **Orchestration Choreography** | In the context of Service-Oriented Architectures (SOA) the two terms indicate the coordinate execution of multiple services. Different authors use the two terms differently (see <http://www.infoq.com/news/2008/09/Orchestration>). However, in cases like our where the execution of the services is coordinate centrally (autocratic), the term *orchestration* is preferred.  |
| **Component model** | An alias for hypomodel.  |
| **Composite model** | An alias for hypermodel. |
| **Digital patient** | The Digital Patient is the challenge to make the VPH technologies directly usable to clinical specialists. Health professionals collect an ever-increasing wealth of information. At the same time, predictive models of physiological systems are evolving rapidly. Many human diseases are complex, long-term and interconnected with other conditions, making their management difficult. The aim of the Digital Patient initiative is to develop an integrative approach to health prediction using patient-specific information and predictive models. <http://www.digital-patient.net/> |
| **Component hypomodel** | It captures the existing knowledge about a portion of the process, typically at a characteristic space-time scale. |
| **Computer model** | A computer program that implements a scientific model, so that when executed according to a given set of control instructions (control inputs), it computes certain quantities (data outputs) on the basis of a set of initial quantities (data inputs), and asset of execution logs (control outputs). |
| **Data** | Factual information, whether observed or predicted.* + Observed: generated through observation, measurement, etc.
	+ Predicted: generated through speculative reasoning informed by existing knowledge.
 |
| **Digital resource** | May refer to either Data or Models. |
| **Elementary model** | An alias for hypomodel. |
| **Folksonomy** | A system of classification derived from the practice and method of collaboratively creating and translating tags to annotate and categorize content; this practice is also known as collaborative tagging, social classification, social indexing, and social tagging. |
| **Fundamental science architecture** | The architecture of a hypermodel seen from the fundamental or basic science perspective. |
| **Fundamental science strategy** | A high level plan to achieve one or more goals under conditions of uncertainty seen from the fundamental science perspective. |
| **Generic Stub** | The “Component Model Generic Stub”, or Generic Stub for short, is a template that all the models that participate in the CHIC system should comply with in order to be effectively integrated with the rest of the platform. |
| **Hypermodel** | 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. The hypermodel can simulate an entity or phenomenon that may be more complex than the ones simulated by each separate simpler model. |
| **Hypermodel editor** | A portal that provides appropriate tools for the design of new hypermodels  |
| **Hypermodelling**  | The developing of hypermodels |
| **Hypermodelling Framework** | The software layer that facilitates the development of hypermodels and allows their execution |
| **Hypermodelling infrastructure** | The technological infrastructure that facilitates the development of hypermodels and allows their execution |
| **Hypomodel** | A model that captures the existing knowledge about a portion of the process, typically at a characteristic space-time scale and that simulate a simpler entity or phenomenon compared to a model or a hypermodel. |
| **Integrative model** | An alias for hypermodel. |
| **In Silico Clinical Trials** | In silico clinical trials are the challenge to make the VPH technologies directly usable to the health industry, for the development of new health products, including medical devices, surgical instrumentation, pharmacological products, tissue engineering products, etc. <http://insigneo.org/research/avicenna-a-strategy-for-in-silico-clinical-trials/> |
| **In silico medicine** | In silico is an expression used to mean "performed on computer or via computer simulation." The phrase was coined in 1989 as an analogy to the Latin phrases in vivo, in vitro, and in situ, which are commonly used in biology and refer to experiments done in living organisms, outside of living organisms, and where they are found in nature, respectively. <http://en.wikipedia.org/wiki/In_silico>  |
| **Linker** | A piece of software inserted between the outputs of two hypomodels so as to allow the construction of a hypermodel. The linker consists generally of adaptors and a merger. |
| **Meta-hypermodel** | The semantic description of a hypermodel.  |
| **Meta-hypomodel** | The semantic description of a hypomodel. |
| **Meta-model** | The semantic description of a computer model. In CHIC we define that, at a minimal level, the “metamodel” description should include some descriptive information, such as:* Model Title,
* Description,
* Creator(s)/Author(s)
* Publication information
* “See also”/”More info” references
* Important dates (e.g. creation date, publication date)
* Validation information (verification, pre-clinical accuracy, etc.)
* License and terms of use information

<http://co.mbine.org/standards/miriam> |
| **Model** | A mathematical or computational construct incorporating speculative information that represents the existing knowledge. Computational implementation of such a model is capable of virtually regenerating an entity or phenomenon. |
| **Ontology**  | In computer science and information science, an ontology formally represents knowledge as a set of concepts within a domain, using a shared vocabulary to denote the types, properties and interrelationships of those concepts. |
| **Personal Health Forecasting** | The development of personalised VPH models (integrative predictive models) that constantly update to respond to all the data transmitted by personal health systems, wearable sensors, ambient assisted living technologies, mobility monitors, etc. and predict how specific aspects of our health will evolve in a near or not-so-near future.  |
| **Relational hypomodel** | Defines how certain properties predicted by one hypomodel is transformed to provide the input to another hypomodel. Alias for Merger. |
| **Strategy** | A high level plan to achieve one or more goals under conditions of uncertainty. |
| **Technological architecture** | The architecture of a hypermodel seen from the technological perspective. |
| **Technological strategy** | A high level plan to achieve one or more goals under conditions of uncertainty seen from the technological perspective. |
| **Virtual Physiological Human (VPH)** | A methodological and technological framework that will enable collaborative investigation of the human body as a single complex system. The collective framework will make it possible to share resources and observations formed by institutions and organizations creating disparate, but integrated computer models of the mechanical, physical and biochemical functions of a living human body. <http://en.wikipedia.org/wiki/Virtual_Physiological_Human>  |
| **The VPH research agenda** | After seven years of research based on the original VPH Research Roadmap elaborated by the STEP consortium, 67 public and private institutions started a no profit organisation called the VPH Institute, to coordinate and sustain the VPH research agenda at national, European, and international level. Under the general heading of in silico medicine that appeared in the first document on the next European research framework, Horizon 2020, the VPH Institute proposed three grand challenges for the development of the VPH: the Digital Patient, In silico Clinical Trials, and Personal Health Forecasting. <http://www.europhysiome.org/roadmap> <http://ec.europa.eu/research/horizon2020/pdf/contributions/post/international_organisations/vph_institute.pdf#view=fit&pagemode=none>  |
| **Wrapper** | Software layer that “wraps” an existing model implementation and provides the integration layer so that the model can become one hypomodel of an hypermodel. This implies translation of the control flow, and management of the data flow. |
| *3DCRT* | 3D Conformal Radiation Therapy |
| *ADC* | Apparent Diffusion Coefficient |
| *ATRA* | All-trans-retinoic acid |
| *BAC* | Binding Affinity Calculator |
| *BBB* | Blood-Brain Barrier |
| *BP* | Blood perfusion |
| *CD* | Cell density  |
| *CDISC-ODM* | Clinical Data Interchange Standards Consortium - Operational Data Model |
| *CT* | Computerized Tomography |
| *CTLA-4* | Cytotoxic T-Lymphocyte Antigen 4 |
| *DCE* | Dynamic Contrast Enhanced |
| *DC(i/m)* | (Immature/Mature) Dendritic Cell(s) |
| *DCE-MRI* | Dynamic Contrast-Enhanced - Magnetic Resonance Imaging |
| *DCm-HGG-L* | mature Dendritric Cells loaded with Lysate from the High Grade Glioma |
| *dMRI* | Diffusion weighted Magnetic Resonance Imaging |
| *DSC-MRI* | Dynamic Susceptibility Contrast - Magnetic Resonance Imaging |
| *DWI* | Diffusion weighted imaging |
| *ECE* | Extra-Capsular Extension |
| *EORTC* | European Organisation for Research and Treatment of Cancer |
| *FACS* | Fluorescence-Activated Cell Sorting |
| *FLAIR* | FLuid Attenuated Inversion Recovery |
| *FMH* | Fertigkeitenskala Münster Heidelberg |
| *GARP* | Glycoprotein A Repetitions Predominant |
| *GBM* | Glioblastoma Multiforme |
| *GCP* | Good Clinical Practice |
| *GE-EPI* | Grade Echo – Echo-Planar Imaging |
| *HGG(-L)* | (Lysate of) High Grade Glioma |
| *HGPIN* | High-Grade Prostate Intra-epithelial neoplasia |
| *IGRT* | Image Guided Radiation Therapy |
| *IDH1* | Isocitrate DeHydrogenase 1 |
| *IFNγ* | Interferon gamma |
| *IMRT* | Intensity Modulated Radiation Therapy |
| *KPS* | Karnofsky Performance Scale |
| *KWS* | ‘Klinisch Werk Station’ Clinical Working Station |
| *LIE* | Linear interaction energy |
| *LOH* | Loss of heterozygosity |
| *LOI* | Loss of imprinting |
| *MD* | Molecular dynamics |
| *MGMT* | Methyl-Guanine Methyl-Transferase |
| *MM* | Molecular mechanisms or molecular mechanics |
| *MMSE* | Mini-Mental State Examination |
| *MM-TR* | Molecular mechanisms of treatment response |
| *MRI* | Magnetic Resonance Imaging |
| *NK(T)-cells* | Natural Killer (T)-cells |
| *NSCLC* | Non-Small-Cell-Lung-Cancer |
| *ObTiMA* | Ontology based Trial Management Application |
| *PBMC* | Peripheral Blood Mononuclear Cell(s) |
| *PBSA* | Poisson-Boltzmann surface area |
| *PET* | Positron Emission Tomography |
| *PFS (6m)* | Progression Free Survival (at 6 months) |
| *PSA* | Prostatic Specific Antigen |
| *qPCR* | Quantitative Polymerase Chain Reaction |
| *RP* | Radical Prostatectomy |
| *RPA* | Recursive Partitioning Analysis |
| *RPC* | Remote Procedure Call |
| *RT* | Radiation Therapy |
| *SaaS* | Software as a Service |
| *SOA* | Service Oriented Architecture |
| *SOAP* | Simple Object Access Protocol |
| *STITCH* | Search tool for interactions of chemicals |
| *TI* | Thermodynamic integration |
| *Treg-cells* | Regulatory T-cells |
| *TSG* | Tumor suppressor gene |
| *TTD* | Therapeutic Target Database |
| *TTP* | Trusted Third Party |
| *UDDI* | Universal Description, Discovery and Integration |
| *URI* | Uniform resource identifier |
| *WAGR* | Wilms Tumor, Aniridia, Urogenital malformations, Retardation |
| *WHO* | World Health Organisation |
| *WSDL* | Web Services Description Language |

1. **R**=Report, **P**=Prototype, **D**=Demonstrator, **O**=Other [↑](#footnote-ref-1)
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) [↑](#footnote-ref-2)
3. Nicolas Le Novère et al., “Minimum Information Requested in the Annotation of Biochemical Models (MIRIAM),” *Nat Biotech* 23, no. 12 (December 2005): 1509–1515, doi:10.1038/nbt1156. [↑](#footnote-ref-3)
4. <http://www.who.int/classifications/icd/adaptations/oncology/en/> [↑](#footnote-ref-4)
5. Hanahan D, Weinberg RA: Hallmarks of cancer: the next generation. Cell 144:646–674, 2011 [↑](#footnote-ref-5)
6. Art. 2 (a) Data Protection Directive (95/46/EC) [↑](#footnote-ref-6)
7. Art. 8 Data Protection Directive (95/46/EC) [↑](#footnote-ref-7)
8. Article 1.2 CA. [↑](#footnote-ref-8)
9. Article 9.8.1 CA. [↑](#footnote-ref-9)
10. Article 9.8.1 CA. [↑](#footnote-ref-10)
11. Id. [↑](#footnote-ref-11)
12. Guide to Intellectual Property Rules for FP7 projects, available at: <http://ec.europa.eu/research/participants/data/ref/fp7/89593/ipr_en.pdf> [↑](#footnote-ref-12)
13. Article 2 Directive 2009/24/EC of 23 April 2009 on the legal protection of computer programs (Software Directive). [↑](#footnote-ref-13)
14. Preamble Berne Convention, available at: http://www.wipo.int/treaties/en/text.jsp?file\_id=283698. [↑](#footnote-ref-14)
15. Id., Article 1. [↑](#footnote-ref-15)
16. Article 11 bis Berne Convention. [↑](#footnote-ref-16)