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HeC

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### D.1.1.a Quality Assurance Guidelines (updating at month 28)

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#### Health-e-Child Consortium

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## 1 Abbreviations

CRF	Case Report Form
QA	Quality Assurance
QAG	Quality Assurance Guideline
PM	Project Management
PNB	Project Netboard
DoW	Description of Work

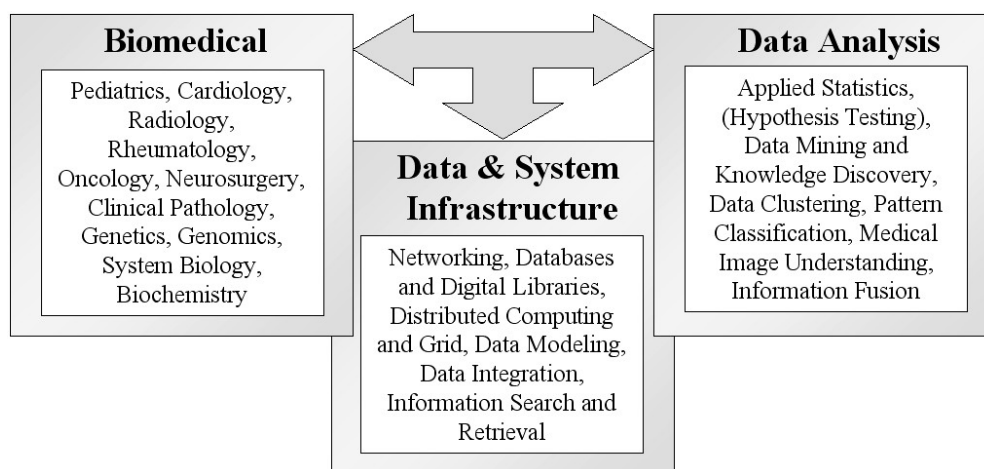
## 0 Short description

The present document has been updated and revised, as planned in the Description of Work Addendum 1 for Phase II of the HeC project.

Following the EC indications in the Consensus report of March 18th 2008 (“Establish a quality assurance scheme for all biological data which is incorporated in the modelling and database”) a particular attention has been given to the Quality Clinical Guidelines and more precise rules to enforce the Quality control of data have been established by the Clinical Coordinator.

## 0 Aim of the Document

**The Health-e-Child Consortium** understands the fundamental importance of integration of research to achieving its overall goals, which requires the Project to be able to leverage and extract new knowledge from several different scientific disciplines. The integration of competences from the Biomedical, Data Analysis, and Data and Systems Infrastructure domains - shown in the diagram below - will create significant management challenges.



The task of extracting and sharing the results, and integrating them into a larger picture, is complex, and can only be dealt with through an effective structure. For this reason the Project has planned for proper integration in all of its work packages, management bodies, committees and boards.

These Quality Assurance Guidelines establish the approach to quality procedures to be followed by the HeC project. They aim to ensure that the results and deliverables of the project are of high quality and meet the specifications set out in the DoW. They will therefore be used by all partners, and particularly by WP leaders and all members of the Consortium responsible for approving the work (IPR Committee, Scientific Committee, Ethical and Legal Review Committee).

This document is designed to give guidance on quality planning, achieving, testing, and refining in the different areas of the project – mainly IT algorithmic research, clinical research, and project management. Although the three areas are closely linked together the requirements and standard procedures are in many respects different. Therefore the document is split into the three main chapters: “4 Quality Assurance Guidelines for Information Technology”, “5 Quality Assurance Guidelines for Clinical Research and Practice”, and “6 Quality Assurance Guidelines for Project Management”.

These guidelines recognise that, with the diversity of the participating project partners, many different quality assurance and control systems are already in place - the guidelines do not, therefore, seek to override existing procedures. The QAG define the minimum requirements to be followed during the project execution phases.

In large parts the document consists of references to existing quality systems. There is no intention to develop and establish a completely new quality framework.

## 0 Quality Assurance Guidelines for Information Technology

The complete development chain from requirements collection to the installation of the prototype software at the end users, i.e. clinicians, has to be controlled and managed from a quality point of view. Therefore all partners are required to follow their internal procedures to ensure the high quality goals of the HeC project. On the other hand it is very difficult to implement a common unified framework within the consortium because of the (different) already existing quality frameworks. Therefore this document provides the users with a minimal set of tasks to be followed during all work package activities in the IT areas.

The procedural steps for the IT part of the project consist of:

- Requirements collection and analysis,
- Design of the software,
- Development of the software,
- Testing of the modules and integration test, and
- Deployment of the software prototype.

### 0.0 Requirements

The IT participants of the project recognize the importance of requirements analysis and documentation in successful software development and end-user satisfaction. To this end, a work package has been formed which is dedicated to the analysis and documentation of users' requirements and in which all IT teams participate. The successful completion of this work package (first 6 months) in itself is a quality measure, which paves the way for further development by distributed teams creating a coherent application, meeting the needs of the end-users. Further quality assurances are that on the one hand development teams observe the documented requirements and on the other that a review process allows for the evolution of the requirements documents to cater for changes during the project lifetime.

### 0.0 Design

Collaborative software development requires that the ideas behind developed program code are well documented. This facilitates maintainability, testing, requirements validation and most importantly integration of software components. The IT partners shall adhere to the practice that the design of software components will be documented, especially of those features which are interaction points between components, like APIs. Again, the guidelines for assurance are partly built in our Description of Work via deliverable design documents. We do not require – and the diversity of the project hardly allows for – that all teams follow a uniform design paradigm, but best design practices shall be guaranteed and supervised by work package leaders.

### 0.0 Development

All the IT participants have substantial expertise and experience with the software development process and all the institutes maintain their own development guidelines which are of high standard and are best suited to each institute's main profile: academic or enterprise. It is the responsibility of the workpackage leaders to synchronize and to supervise the adherence to commonly agreed development practices. Standard principles like full version control, attempt to minimize the number of different programming languages

and runtime environments used, modular development, early testing, following a coding standard, adhering to release cycles, etc... will apply.

## **0.0 Testing**

The IT developers will follow a standard multi-tier testing plan. Within developer groups, unit testing will be performed parallel to development and a work package level integration testing plan will be in place. This will be the foundation for successful integration testing across the work packages, which will follow the release cycles.

## **0.0 Deployment**

The last phase of the process will be the deployment of the completely integrated software modules. This phase is planned and well defined in activity 7 - work package 14 "System Integration – Deployment of the data management system and Grid gateway" of the DoW.

## 5 Quality Assurance Guidelines for Clinical Research and Practice

### 0.0 Clinical data acquisition

Acquisition or collection of clinical trial data can be achieved through various methods that may include, but are not limited to, any of the following: paper or electronic medical records, paper forms completed at a site, interactive voice response systems, local electronic data capture systems, or central web based systems.

There is arguably no more important document than the instrument that is used to acquire the data from the clinical trial with the exception of the protocol, which specifies the conduct of that clinical trial. The quality of the data collected relies first and foremost on the quality of that instrument. No matter how much time and effort go into conducting the clinical trial, if the correct data points were not collected, a meaningful analysis may not be possible. It follows, therefore, that the design, development and quality assurance of such an instrument must be given the utmost attention.

The ICH guidelines on Good clinical practice (GCP) use the term 'Case report form' or 'CRF' to refer to these systems. No matter what CRF is utilized, the quality and integrity of the data is of primary importance. The following recommendations are meant to assist in the design, development and quality assurance of the CRF such that the data collected will meet the highest standards.

The following is meant to highlight some of the most important points to consider during the design process.

### 0.0 Minimum Standards

Design the CRF to collect the data specified by the protocol.

Document the process for CRF design, development, approval and version control.

Make the CRF available at the clinical site prior to enrollment of a subject.

Document training of clinical site personnel on the protocol, CRF completion instructions and data submittal procedures prior to enrollment of a subject.

### 0.0 Best Practices

Design the CRF along with protocol to assure collection of only those data the protocol specifies.

Keep questions, prompts and instructions clear and concise.

Design the CRF to follow the data flow from the perspective of the person completing it, taking into account the flow of study procedures and typical organization of data in a medical record.

Avoid referential and redundant data points within the CRF whenever possible. If redundant data collection is used to assess data validity, the measurements should be obtained through independent means.

Design the CRF with the primary safety and efficacy endpoints in mind as the main goal of data collection.

Establish and maintain a library of standard forms.

Make the CRF available for review at the clinical site prior to approval.

Use NCR (no carbon required) paper or other means to assure exact replicas of paper collection tools.

### 0.0.0. Paediatric heart diseases

The Paediatric Cardiology Unit follows the international standards and guidelines established for the proper management of paediatric heart diseases.

A diagnostic coding system for paediatric heart diseases has been selected; the diagnostic coding system for paediatric heart disease selected for the Health-e-Child project is the “European Paediatric Cardiac Code” by the Coding Committee of the Association for European Paediatric Cardiology ([http://www.aepc.org/aepc/nid/European\\_Paediatric\\_Cardiac\\_Coding](http://www.aepc.org/aepc/nid/European_Paediatric_Cardiac_Coding)).

The Association for European Paediatric Cardiology (AEPC), was founded in Lyon in 1963 and has subsequently created a network of specialists working in the same field encountering similar problems. The mission of AEPC is to promote the knowledge of the normal and diseased heart and circulation and exchange of knowledge and continuous education.

Over the years, nine working groups have been set up within this Association to bring together workers with similar interests in order to facilitate collaborative research, such as collaboration with paediatric cardiac surgeons, adult cardiologists and other scientists in closely related fields.

AEPC and its Working Groups aim to enhance collaboration amongst members for scientific research and professional development and to maintain high standards of professional practice. The Ordinary Members of AEPC originate from 32 countries in Europe, and each country is represented within the Association by an elected National Delegate.

An Annual Meeting and a Teaching Course are organised by the AEPC in the third week of May in collaboration with one of the member countries. Additional symposia and courses are usually a part of the annual meetings.

These meetings, courses, symposia are evaluated by EBAC (European Board for Accreditation in Cardiology) for continuous medical educational. EBAC is a joint board of ESC, UEMS-Cardiology Section and AEPC. Newsletters are sent regularly to all the members and are also available on the AEPC website and published in the journal "Cardiology in the Young". "Cardiology in the Young" is an international journal dedicated to paediatric cardiology and congenital cardiac malformations in adults, produced by Cambridge University Press. It is published 6 times per year and comes with two to three supplements per year, one of which is the abstracts book of the annual AEPC meeting.

The Italian Society of Paediatric Cardiology (SICP) is the national reference for producing guidelines and protocols and for promoting and exchanging knowledge on paediatric heart diseases (<http://www.sicped.it>).

A paediatric case report form dedicated for collecting data of patients that are going to be inserted in the Health-e-Child project has been created for the purpose. This case report covers different aspects (clinical, laboratory, genetic, etc.) from the first contact with the patient and continues even in successive follow up visits according to each case needs.

The protocol on paediatric heart diseases is ongoing between the three Centres taking part in to the project. An Imaging protocol to standardize the imaging approach for Magnetic Resonance Imaging and Ultrasound will also be prepared.

The project will be conducted according to Good Clinical Practice. Good Clinical Practice is a standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials (EU Good Clinical Practice Directive - Brussels: European Commission, 2004).

### **0.0.0. Paediatric brain tumours**

The Gaslini brain tumour and DNA banks on brain tumours are organised in accordance with international standard and protocols including privacy and informed consent rules. The tissue and DNA/RNA banks are shared with the Pathology Unit and the Neurosurgery laboratory. Histological diagnosis and classification of CNS tumours follows the recommendations of WHO organisation (Kleiues P et al. Pathology and genetics of tumours of the nervous system. Lyon: International Agency for research on Cancer (IARC) Press, 2000). The working group on brain tumours refers to the criteria defined by the International Society of Paediatric Oncology (SIOP) for pre- and post-operative evaluation and staging systems. The organisation of trials and working groups on specific diseases is very similar to the one on rheumatic disease: an international coordinator; national coordinators; data collected at national level are referred to the international coordinator and are checked many times at many levels. Histological diagnoses are double checked through a central review policy. (References: Gloser A. Et al. A standardised strategy for qualitative assessment of brain tumour survivors treated with clinical trials in childhood. Int J Cancer 1999, S 12: 77-82; Gnekow AK. Recommendations of the brain tumour subcommittee for the reporting trials. Med. Pediatr Oncol 1995; 24:104-108).

For Childhood Brain Tumours there is also an international agreement on how to organize data (SIOP). Each country has a national and an international coordinator, so that data are exchanged and checked, thus assuring quality. A new protocol is being prepared specifically for HeC, which will be finished by the end of May. As this is an evolving field, not all aspects are yet covered by the international standards.

To summarize, starting from standard and accepted protocols used for childhood gliomas, criteria to collect data (improve the protocol) will be better defined, according to the quality assurance methodology applied in clinical research.

### **0.0.0. Paediatric rheumatic diseases**

Juvenile Idiopathic Arthritis is a very heterogeneous condition lumping together all forms of childhood-onset chronic arthritis of unknown origin. The JIA classification used routinely in a clinical setting is the "International League Association for Rheumatology" (ILAR) classification of JIA that includes seven different groups of JIA. For each of the seven different categories definitions, exclusion criteria and descriptors are reported (1).

Internationally approved Case Report Form (CRF) to collect clinical data will be used in this project. These CRF are disease specific and have already been used in International trials according to the ICH guidelines on good clinical practice (GCP).

Clinical assessment of the patients is based on standardized and validated measures of disease activity and joint and system damage.

Considerable work has been conducted in JIA in the past 15 years to develop new measures, in an effort to better define the overall outcome for JIA children (2). The process of developing and validating disease specific measures have been well established (3). This process entails a series of steps including item generation, item reduction, item presentation and scaling, and assessing reliability, validity, and responsiveness.

The validation of these instruments has been possible through multi-centered, multi-national and collaborative trials/studies; in this respect a significant contribution has been provided by the initiative of the Pediatric Rheumatology InterNational Trials Organisation ([www.pediatric-rheumatology.printo.it](http://www.pediatric-rheumatology.printo.it)). PRINTO was founded in 1996 and includes 47 countries with more than 180 centers world wide. PRINTO is composed of academic, clinical centers actively engaged in the care of children with Pediatric Rheumatic Disease. The first effort conducted by PRINTO was to develop a standardized core set of measures and a definition of improvement for the evaluation of response to therapy in JRA. This led to the publication of the preliminary definition of improvement for JIA (4;5). This definition has been adopted by the Food and Drug Administration (FDA) as primary outcome for all clinical trials involving children with JIA, and officially recognized as ACR paediatric 30 definition of improvement (6).

PRINTO has members from several nations with different languages and cultures. One problem was therefore to have common instruments to measure functional ability and quality of life translated into the different languages and validated in the different cultures. PRINTO has been able to cross culturally adapt and validate 2 childhood questionnaires, the first called Childhood Health Assessment Questionnaire (CHAQ) for functional ability assessment, and the second called Child Health Questionnaire (CHQ) for the health related quality of life assessment. The project led to the enrollment of 6,644 subjects (3,235 patients with JIA, while 3,409 were healthy children) with the validated version of the CHAQ and CHQ now available for 32 different countries (7;8). The CHAQ is now the functional assessment tool used for all trials in JIA.

The Juvenile Arthritis Damage Index (JADI) is a clinical measure that reflects the overall biological outcome of JIA. The instrument's validation of the JADI showed that this instrument exhibits good reliability, construct validity, and discriminative ability and is therefore a valid instrument for the assessment of long-term damage in patients with JIA, in the context of both clinical management and research settings (9).

An Imaging Protocol with the procedures for standardization of image techniques has been prepared. The MRI sequences included the OMERACT (Outcome Measures in Rheumatology Clinical Trials) recommended MRI core set of sequences (10). Validated assessment methods for conventional radiography are also available (11).

This kind of project requires that a substantial amount of personal data, including genetic information, are collected from the participants and shared across the network. The project will be carried out in accordance with the applicable European and National data privacy protection laws and regulations.

Biological samples will be collected and stored in the biobank of each of the centres taking part in the project, according to Local and European laws or guidelines.

IGG's Biobank follows the guidelines proposed by the Italian Society of Human Genetic (SIGU) together with Telethon Foundation.

## 0.0 Clinical Data Quality assurance

### 0.0.0. General Rules

The enrolled patients must strictly adhere to the diagnosis chosen for the project. Only complete data sets can be used for the creation of the disease models (i.e.: all data that have been planned for each patient must be present). Data must be collected according to agreed protocols and forms which are contained in D9.1 and follow the outline set out again in the DOW III. Instrument data must be computer readable and the concerning servers must be accessible by the HeC platform. Selected data must be concurrent, according to protocols. Genetic data can be collected anytime. Automatic Data Preprocessing (for noisy, outliers, and missing data) must be implemented. Incomplete data may be collected according to specific and agreed upon purposes. Two patients per pathology, per group, per trimester should be checked for appropriateness and completeness by peer review or by a central reviewer.

### 0.0.0. Cardiology

The cardiology study includes patients with Secundum Atrial Septal Defect (ASD II), Partial Anomalous Pulmonary Venous Drainage (PAPVD), and post-op Tetralogy of Fallot (TF p/o) with or without transannular patch enlargement of the RVOT (no conduit). Clinical data including environmental, familial, history, etc. are collected for every patient. The data are entered in apposite forms directly in electronic format or copied afterwards. Imaging must follow the agreed upon protocols. The collected data must be concurrent and, possibly, collected in the same day. Only if the patient's conditions are stable, clinical, laboratory data and imaging may be collected within a few days (max. 1 week). For cardio-pulmonary exercise test and Holter a 2 months interval is still tolerated.

### 0.0.0. Rheumatology

Clinical information, including demographic data, information on disease (JIA subtype, duration, etc), laboratory parameters and therapy (previous and ongoing) have to be collected. Clinical parameters reflecting disease activity and damage are collected using international validated clinical instruments and recorded on appositely devised case report form (see attachment).

All clinical and laboratory evaluations, and imaging procedures, have to be performed on the same day, with the possible exception of conventional radiography. Conventional radiographs do not need to be repeated if appropriate radiographic image, obtained no more than 3 months before study enrolment, exist so to avoid unnecessary radiation exposure.

Ultrasonography may precede or follow MRI by a few days only if no therapeutic modification has been performed during this time-lag between the two imaging procedures.

In order to compare the results of imaging investigations among the centres involved in the project the imaging procedures have to be performed according to standardized protocols (see attachment). Standardization of imaging procedures is considered crucial for post processing analysis, especially in order to allow a quantitative evaluation of disease activity or damage findings in JIA.

### 0.0.0. Neuro-Oncology

Multidisciplinary team for treatment of brain tumours in children consisting of paediatric neurosurgery, neuroradiology, pathology and neuro-oncology.

A case load of at least 30 new cases of CNS tumour per year.

Imaging (CT and MRI) is made available for central review.

A complete pre-operative staging procedure according to the International Society of Pediatric Oncology's (ISPO) brain tumours sub committee is followed.

Neuropathological review of histology by national or international peers.

Paraffin tumour tissue for further detailed neuropathological studies is available if required.

Frozen tumour tissue is available for gene expression studies according to the criteria defined by the protocols.

### 0.0.0. Common aspects for genetic quality control.

**General criteria** for quality control in molecular genetic tests by *DNA* sequencing, applied to studies on **congenital heart defects and Idiopathic Juvenile Arthritis**. *RNA* extraction, *cRNA* preparation for Microarray analysis applied to studies on the **Brain Tumour** project, in particular on children with Gliomas

- **Personnel qualification:** personnel devoted to carrying out molecular genetic tests on patients with congenital heart defects and Idiopathic Juvenile Arthritis have post doctoral degree (Specialization in the Italian System) in Medical Genetics, and a student in Medical Genetics Residency and a post doctoral fellow is carrying out studies on Brain Tumour.  
All these personnel are holding a contract officially recognized by the Institution (G. Gaslini Institute). Personnel has received specific training in molecular genetics and has long lasting experience in application to diagnostic genetic testing.
- **Laboratory technical qualification:** the laboratory is fully equipped to perform the entire procedure and utilizes regular evaluation of internal control measures of the protocols and instruments. In particular, the protocols for *DNA* and *RNA* extractions, specificity of *PCR* amplification and quality of sequencing are periodically checked on reference samples.
- **Equipment:** *PCR* thermal cyclers and automated sequencers are regularly checked and subjected to maintenance programs.

### Specific criteria:

- Specific Criteria for quality control in molecular genetic tests by *DNA* sequencing applied to studies on **congenital heart defects and Idiopathic Juvenile Arthritis**

- **Genotyping protocols:** for each gene on which either mutations or polymorphisms are searched for, *PCR* primer sets, *PCR* amplification conditions, sequencing primers and conditions are established and deposited in standardized written protocols.

Sequencing has to be done in two directions (forward and backward) for all amplification products to have confirmation of sequence variants.

**This applies to**

- *TBX5* gene, for mutation screening
  - *GATA4* gene, for mutation screening
  - *NKX2.5* gene, for mutation screening
  - *Osteopontin* gene, for polymorphisms genotyping
  - *Periostin* gene, for polymorphisms genotyping
- **Specific quality controls:** for each gene on which either mutations or polymorphisms are searched for, reference samples with known sequence and/or polymorphic allele genotype are available and periodically checked.
- Specific criteria for quality control in molecular genetic tests by *cRNA* preparation for microarray analysis Gene-Chip U133 Plus 2.0 array (Affymetrix) applied to studies on the **Brain Tumour**

Processing of tumor tissues and isolation of total *RNA* that will be used for microarray analysis.

During the processing, sections are prepared in order to perform histological and immunohistochemical staining to confirm the tumor cell content of at least 80%.

Initially the Total *RNA* is treated with *Dnase I* and, subsequently, purified.

The *RNA* is quantified and then the integrity is assessed on the Agilent 2100 Bioanalyzer.

The *cDNA* synthesis is then performed using a One-Cycle *cDNA* Synthesis kit (Affymetrix) followed by a clean-up protocol.

Then *cRNA* preparation will be done according the Affymetrix protocol using a biotinylated nucleotide analog/ribonucleotide mix.

Finally a step of clean-up, a quantification and at the end a fragmentation process of the *cRNA* will produce small fragment sizes, that will be used for the hybridization procedure on human Gene-Chip U133 Plus 2.0 array (Affymetrix).

- **Specific quality controls:** for each *RNA* preparation are assessed on the Agilent 2100 Bioanalyzer.
- **Use of standardized methods by different laboratories:** the above standardized procedures are available for use in laboratories which carry out tests with the same procedures.
  - **Reference samples for different laboratories:** reference samples with known sequence and/or polymorphic allele genotype are available for controls in laboratories which carry out tests on the same genes.



The “Quality Assurance and Proficiency Testing for Molecular Genetic Testing: Summary Report of a Survey of 18 OECD Member Countries”, OECD (2005) can be considered as a reference for the subject.

## 6 Quality Assurance Guidelines for Project Management

Quality planning is an integral part of management planning. The quality of the Project Management of HeC is assured by the following components

- Management structure
- Project planning
- Project controlling and reporting
- Deliverables quality (scientific validation)
- Risk control

### 0.0 Management structure

The Health-e-Child management structure is as follows:

- The **Governing Board** (chaired by Alok Gupta, Siemens, and consisting of one Representative per Partner) is the Consortium's main decision-making and arbitration body.
- The **Executive Board** (chaired by the Joerg Freund, Siemens) is an intermediate decision making body that makes proposals for decisions to be taken by the *Governing Board*, implements decisions, reports to the *Governing Board* on how decisions have been implemented, interacts with the *Project Management Team* and with *Advisory and Assessment Committees* (the *IPR Committee*, *Scientific Committee*, and *Ethical and Legal Review Committee*). Additionally it will ensure that from a legal and ethical point of view results are in line with European regulation and standards.
- The **Project Management Team** (chaired by Edwin Morley-Fletcher, Lynkeus, and consisting of all the WP leaders, plus one representative of partners who do not have the responsibility of a workpackage) is responsible for: monitoring the planned progress of the activities; technical co-ordination and supervision; checking the financial consistency of the Project; evaluating the need for new contractors; supporting the Project Coordinator in interfacing with the European Commission; drafting and validating the project deliverables to be submitted to the Commission; responding to requests for information from the general external community.
- The **Management Support Team** (consisting of the project secretariat led by Lynkeus, and one representative from each partner) has the following responsibilities: handling administrative, legal, financial aspects of the Project; supporting the Project Coordinator in preparing project deliverables; preparing administrative and financial reports for the *Executive Board*; implementing the secretariat tasks for the *Governing Board* and for the *Executive Board*; ensuring communication platforms for project participants including document exchange, teleconferences, email and reporting infrastructure; organizing and reporting on general project meetings and circulating agendas and minutes.
- In addition, the Health-e-Child project has a **Scientific Committee**, an **Ethical and Legal Committee** and an **Intellectual Property Right Committee**. As reported in the D1.1 Self Assessment plan "The Scientific Committee (SC) will organize a Scientific Project Review about 1-2 months before the annual Technical Review (EC review). Following the scientific review, the SC will produce a set of documents assessing the current scientific status of the project".

The Project Management team (PMT) will seek to control five variables:

Time - The amount of time required to complete the project. Typically broken down for analytical purposes into the time required to complete the components of the project, which

is then further broken down into the time required to complete each task contributing to the completion of each component.

**Cost** - Calculated from the time variable. Cost to develop an internal project is time multiplied by the cost of the team members involved. When hiring an independent consultant for a project, cost will typically be determined by the consultant or firm's hourly rate multiplied by an estimated time to complete.

**Quality** - The amount of time put into individual tasks determines the overall quality of the project. Some tasks may require a given amount of time to complete adequately, but given more time could be completed exceptionally well. Over the course of a large project, quality can have a significant impact on time and cost (or vice versa).

**Scope** - Requirements specified for the end result. The overall definition of what the project is supposed to accomplish, and a specific description of what the end result should be or accomplish.

**Risk** - Potential points of failure. Most risks or potential failures can be overcome or resolved, given enough time and resources. Of course, theoretically risk can also be negative, meaning that on principle also opportunities, for completing the project faster than expected, could also arise while tackling the different milestones.

Obviously quality in PMT influences and is influenced by time and cost of the project tasks. PMT is also responsible for the quality management in the different work packages.

## 0.0 Project planning

Within the HeC project, Quality Assurance is focused on achieving an ongoing implementation activity aimed at facilitating a common understanding and agreement of key project issues such as the formulation of user requirements, the definition of project objectives, roles and responsibilities, critical success factors, risks, constraints and organisational impact, etc.

In particular, the following list includes the main quality assurance components taken into account in the project planning processes.

- Defined roles and responsibilities: identification of the roles having responsibility, accountability, and authority within the scope of the process.
- Minimum documentation requirements for the project have been established and archived for use and updating with the Communication platform.
- Common standards and processes for use in development of the project are being identified and benchmarked.
- Attention to QA aspects has been important in preparing and reviewing the project's development plan, standards, and procedures.
- Measures for tracking project progress and project quality have been indicated through the reporting mechanisms available within the PM platform and the self assessment plan.
- Planned work project reviews, along with roles and responsibilities are being constantly updated.
- Functional configuration audit, to ensure deliverables match requirements and are consistent and ready for delivery at the end of the project
- Timing and content of planned management reviews have been identified and are being addressed.
- Provision of necessary documentation for post-project review of the project is being ensured by the use of the PM and Communication platforms.
- Demonstration activities for testing results are planned.

- All the partners of the project are aware of the roles, responsibility, authority, and value of the project.
- Deviations from the project's plan are being communicated to the project management team and effectively addressed.
- Management is notified when deviations and/or delays are not being addressed.
- Periodic reports of all ongoing activities are being provided to the project management team and highlighted relevant quality aspects are being gathered and reported.
- WP leaders will review the QA activities on a regular basis.
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## 0.0 Project Controlling and Reporting

The Health-e-Child Consortium makes use of Project NetBoard (PNB), a professional Internet-based collaborative tool for time effective and cost efficient management of projects supported by the European Commission.

PNB allows the Consortium to meet the professional management standards required by an Integrated Project. PNB is organised according to the standard project Road Map, thus offering facilities for the execution, control and re-planning monthly cycle of the project.

Users may have different access rights to input to the system task reports, time sheets, expenses, and other relevant data. PNB enables effective and efficient co-operation between the Consortium members for all phases of the project life thanks to different operational modules.

The Consortium uses two modules:

1) The Activities management and reporting module, is used for the periodic monitoring of the tasks, the work packages, the activities, the monthly time sheets and the stepwise elaboration of the periodic activity reports. This module offers specific functions to monitor the project such as closing or delaying tasks, submitting deliverables, registering milestones, updating the risk spreadsheet, moving to the next project month, etc. It is also the place to register the actors in the project, fill in the pre-prepared time sheets - or upload an institution's own time sheets - and monitor partners' monthly workloads and actual contributions to the project.

Some alert functions provide useful warnings when work plan deadlines are not adhered to, and email warnings are prepared, to be sent by the manager to partners if needed. The events which will be further listed in the periodic activity reports can be declared in this module and all meetings - agenda, minutes, attendance - can be managed consistently. The module also greatly facilitates the preparation of periodic reports and the final report.

2) The Financial follow-up and accounting module allows the processing of all financial matters, at the level of individual partners and the building up of periodic management reports, financial statements and financial reports. It is possible to control the pre-financing and consolidated payments from the Commission and the reimbursement to the partners taking into account their respective cost models, labour costs and other expenses.

As a financial observatory of the project, actual costs can be compared with the provisional budget per partner, per activity and per expenses categories at managerial level. Data

inputs are in Euro or in national currencies. The stepwise elaboration of the Financial Statements - Forms C - of each partner is facilitated so as to avoid common mistakes and inconsistencies while enabling an easy monitoring of the project financial strategy by the Project Management Team and the Co-ordinator.

PNB helps to generate all the required documents to build up and follow up the project according to the Commission's rules including the Commission's specific paper forms, electronic files and import/export formats.

Although reasonably intuitive, the instrument requires some training to get fully acquainted with the facilities and functionalities offered. The PM Team organises training sessions for all partners and continuous assistance by phone and by mail. Also available is an on-line help documentation describing what it is essential to know about the Commission's requirements and procedures applied to IP Projects, with reference to the "Guides for proposers" and the "Guide to financial issues" issued by the Commission.

The Management of the Consortium has decided to issue and to update guidelines on the use of the PNB platform, editing of task reports, risk assessment, input of efforts and expenses. All partners are requested to update information on a monthly base.

## 0.0 Deliverables quality (scientific validation)

The Self assessment Plan, first deliverable of HeC at month 1 of the project, can be considered as a first step towards deliverables quality. Both the Work package Leaders (WPLs) and the Scientific Committee Chair have been involved in defining modes and characteristics for a self-assessment of the HeC project. It is the WPLs' common belief that the Self Assessment plan must be considered as a dynamic process, undergoing appropriate updating every year in order to validate/modify the chosen indicators, and taking account of the SC yearly evaluation. The re-definition of the Self-Assessment indicators may therefore represent a deliverable at the end of each Reporting period.

As a first input, each WPL was requested to clarify the main objectives each WP aims to achieve. They then provided a description of the measurement processes/methodologies which have been adopted. Finally, and on the basis of the previous inputs, a series of correlated indicators for measuring the outcomes of the various WP activities has been defined, associating them, as much as possible, to task-level details with an approximate numerical indication of the allowed threshold limits related to each WP objective.

More recently, the Project management has proposed that a first draft of any deliverable should be uploaded three weeks after the end of the month specified for delivery, in order to let all the partners have a thorough look and possibly suggest amendments.

## 0.0 Risk

The risks that may potentially affect the Health-e-Child project are continuously monitored in order to elaborate the corresponding contingency plans. The *Executive Board* of the project will specifically address risk issues at each meeting. All Consortium Partners are concerned with **risk detection**. When a risk is detected, it is reported to the WP Manager concerned, who assesses the risk. Risks that are serious, affecting the critical path of the project, are

further reported to the Project Coordinator. In each WP monthly report, risks must be evaluated by the WP leader, together with their possible impact and the required action. Risk analysis can be recorded on the PNB platform

The risks are estimated using a numeric scale from 1 to 3, where 3 represents a risk that is almost certain on the likelihood scale, or a risk that is very serious, affecting the critical path of the project, on the risk impact scale.

Each identified risk will have an owner who is responsible for its risk mitigation, monitoring and reporting. In addition, the risk owner proposes preventive and corrective treatment, consisting of suitable actions to reduce the severity and probability of occurrence of the risk.

As stated in the DOW, the analysis of the activities to be carried out in the Health-e-Child Project lists some risks potentially threatening the achievement of project goals. A preliminary list of potential risks is presented below. The results from this analysis will be monitored and updated during the overall lifetime of the project.

**Data privacy, security, and legal requirements.** The requirements related to data privacy and security must be reconciled with applicable legislation in different countries. This risk must be managed very early at the start of the project, with the assistance of the *Ethical and Legal Review Committee*. (Estimated risk level: 2)

**Consortium heterogeneity.** The Health-e-Child project brings together clinicians and scientists with very diverse expertise and background, which makes the project management particularly challenging. The integration of the project team presents a risk that will be constantly monitored. The Project Coordinator will have a very important role in establishing an open communication channel between the clinical and computer science world, between the traditional clinical practitioners and the genomic researchers. (Estimated risk level: 2)

**Underestimation of the required effort.** This risk is handled by the WP Managers monitoring the planned versus actual effort required by each task. Indicators and statistics will be included in the periodic progress reports to the Project Coordinator (Estimated risk level: 1).

**Resource phase-in difficulties.** The Health-e-Child Project requires very skilled people to implement its challenging goals. The amount of time needed to train new personnel to work on the project will be defined and considered as part of the staffing plan (Estimated risk level: 1).

**Turn over of key-personnel.** This risk is managed by standardising the way of working across the various teams and by defining a backup policy, so that in case of unexpected departure, remaining personnel can temporarily compensate for the absent ones, while waiting for a permanent replacement (Estimated risk level: 1).

**Mismatch between the Health-e-Child requirements and the capabilities of the Grid framework.** The capability of the EGEE framework to satisfy the Grid requirements of Health-e-Child will impact heavily on the development of its middleware components. This risk is handled by close collaboration with the EGEE development team. CERN will coordinate the interaction between the two projects. (Estimated risk level: 2)

**Poor network infrastructure in hospitals.** To manage this risk it is important that the progress of the early benchmarks is monitored, and that they are achieved. In any case where poor connectivity is detected, partners will be asked to take necessary steps to improve it. This requirement will be explicitly addressed in a written agreement between partners concerned (Estimated risk level: 2)



## 7 Templates, Guidelines, Checklists

Templates produced  
MS PowerPoint template  
Agenda  
Minutes of Meeting  
Progress report  
Quarterly report

Guidelines provided  
Communication platform  
Project Management platform  
Self assessment benchmarking

Checklists used  
Action Item List  
Change requests for communication platform