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Personalized Health Certification Procedure White Paper

Project Coordinator	Dr Harald Reiter Philips Technologie GmbH Forschungslaboratorien Aachen (DE)		
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Author	**Company**	**e-mail**
Eirini Lekka	AUTH	lekka@med.auth.gr
Harald Reiter	PHILIPS	harald.reiter@philips.com
Jean Luprano	CSEM	Jean.LUPRANO@csem.ch
Reinhard Hammerschmidt	empirica	reinhard.hammerschmidt@empirica.com
Nikos Maglaveras	AUTH	nicmag@med.auth.gr

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Abbreviations

AAL	Ambient Assisted Living
API	Application Programming interface
CE	Conformité Européenne
CAD	Coronary Artery Disease
DICOM	Digital Imaging and Communications in Medicine
EHR	Electronic Health Record
FDA	Food and Drug Administration
HF	Heart Failure
HL7	Health level Seven
HRN	Health Reporting Network
IF	Interface
IHE	Integrating the Healthcare Enterprise
IP	Internet Protocol address
ISO	International Organization for Standardization
IT	Information Technology
LAN	Local Area Network
MDD	Medical Devices Directive
PAN	Personal Area Network
PHS	Personal Health Systems
WAN	Wide Area Network

1 Executive Summary

Personal Health Systems (PHS) offer individualization of interventions aimed to prevent and/or treat diseases. Starting from simple telemonitoring they have advanced to closed loop solutions integrating care at home with professional care in the hospital. They combine a) ubiquitous, unobtrusive, pervasive biodata acquisition, processing, and management, b) intelligent processing of multilevel medical and environmental information in order to derive important new insights about individual's health status, and c) biofeedback mechanisms either from health professionals or directly from the devices to the individuals, assisting in disease prevention, treatment and lifestyle management. For such complex systems expectations on quality assurance and interoperability are evident. However, since PHS are still in their infancy, there is no established certification framework. The HeartCycle project aiming to develop a closed loop PHS for the health monitoring and management of patients with cardiovascular disease, contributes to the development of such a framework. As a research project, HeartCycle does not include certification in its objectives. However, it has conformed to all standards that will lead to certifiable products and has identified relevant gaps and stakeholders recommendations that can contribute to the development of a PHS certification framework.

Based on the collective HeartCycle experience the current paper presents an overview of **current certification procedures** for PHS, identifies **major gaps** and draws **recommendations.**

CE certification is a prerequisite for marketing PHS products in Europe and similar procedures exist worldwide (FDA in United States). It addresses safety issues for both medical devices and software. Continua Design Guidelines are recommended to ensure interconnection of devices. There is high need of clinical validation standards addressing the quality of medical devices as well as the interpretation of measurements produced by intelligent processing modules. Interoperability should advance beyond interconnection of devices to aspects such as standardization of objective and subjective measurements, and guidance for development of interoperable applications such as behavior management and patient empowerment.

2 Introduction

2.1 Scope

The white paper aims to contribute to the development of trustworthy Personal Health Systems that offer high quality health services to the citizens. Driven from the HeartCycle experience, the paper intends to identify current certification procedures relevant to innovative PHS solutions and to draw recommendations that can contribute to the development of a certification framework for PHS.

Currently, certification procedures cover specific aspects of a Personal Health System. Specifically, in order to market PHS in Europe, they should be certified to ensure patient safety and should carry the CE mark. In addition, the Continua Alliance has created a product certification logo program with a consumer recognisable logo signifying the use of proven connectivity standards thus ensuring some level of interoperability. Clearly there is high need to develop additional certification programmes addressing broad interoperability among different products and devices and ensuring the quality of the services offered by the PHS.

While this white paper addresses the HeartCycle use cases, its findings and recommendations can be extended to other PHS having similar level of complexity and architecture.

The paper addresses the following goals:

- To present an overview of **current certification procedures** for PHS,
- To propose **recommendations drawn from the HeartCycle experience** that can contribute to the development of a certification framework for PHS.

The document can be used as reference by developers of PHS who intend to develop closed-loop PHS. Potential customers of PHS such as healthcare authorities can also use this paper to become aware of the certification requirements they can pose to the vendors. Finally, this paper can assist to the efforts of existing certification bodies (e.g. CONTINUA alliance) and of the PHS industry for the development of additional certification procedures that will produce interoperable PHS ensuring patient safety and high quality healthcare services.

2.2 Document Structure

Following the Executive Summary and Introduction the document presents a brief overview of the functionality of PHS, its main components as well as a broad view of the stakeholders' expectations for certification. Chapter 4 presents current certification programs, and Chapter 5 presents recommendations on standards to be used during PHS developments as well as gaps and recommendations on clinical validation standards and interoperability. The document ends with Conclusions.

2.3 Definitions and Terms

Certification is a labeling process by which a third party gives written assurance that the system meets the requirements of a standard.

Directive: An order or instruction, especially one issued by a central authority. An EU (European Union) directive is a legislative act of the European Union which requires member states to achieve a particular result without dictating the means of achieving that result. It can be distinguished from regulations which are self-executing and do not require any implementing measures

Validation consists of the steps necessary to perform the conformance testing by using an official test suite in a prescribed manner

3 Need of Certification for Personal Health Systems

3.1 Personal Health Systems

Personal Health Systems (PHS) are an emerging concept reflecting the most innovative vision of how advanced technologies can be used in healthcare. Following the definition from the PHS2020 project [1]:

Personal Health Systems (PHS) assist in the provision of continuous, quality controlled, and personalized health services to empowered individuals regardless of location.
They consist of:

a) Ambient and/or body (wearable, portable or implantable) devices, which acquire, monitor and communicate physiological parameters and other health related context of an individual (e.g. vital body signs, biochemical markers, activity, emotional and social state, environment);

b) Intelligent processing of the acquired information and coupling of it with expert biomedical knowledge to derive important new insights about individual's health status;

c) Active feedback based on such new insights, either from health professionals or directly from the devices to the individuals, assisting in diagnosis, treatment and rehabilitation as well as in disease prevention and lifestyle management.

PHS adopt the aforementioned technologies to provide health monitoring, disease management and ambient assisted living (AAL) expected to offer continuity of care, improve patients' quality of life, and rationalize healthcare costs [2].

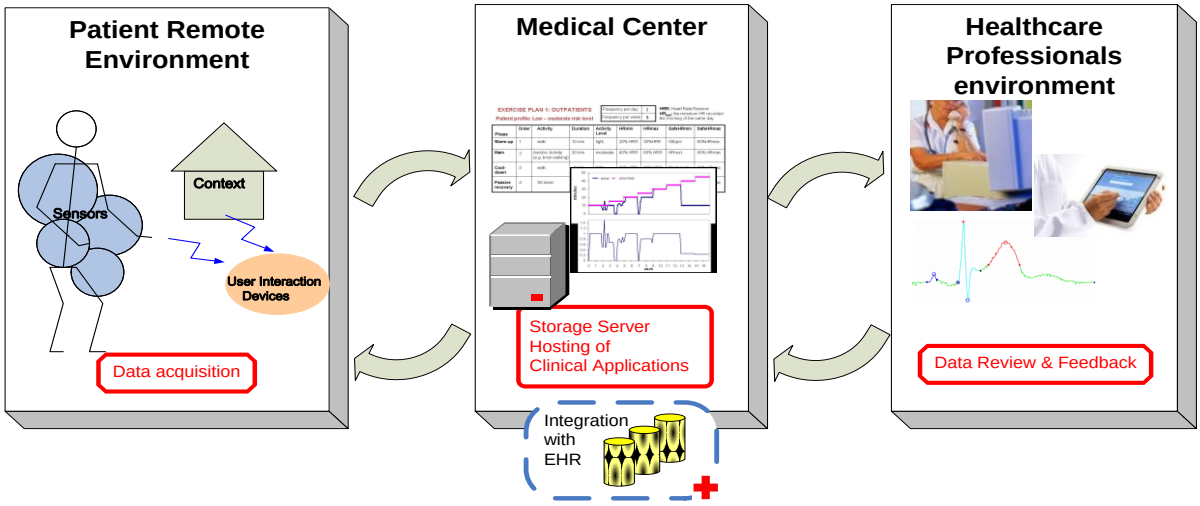

Figure 1 PHS overview

PHS usually span across three sites illustrated at Figure 1. At the patient remote environment, sensor devices record vital signals and together with other context information they are transmitted to user interaction devices. User interaction devices (smart phones, PCs, TV set-top-boxes, standard phones) host patient-friendly applications that support the users for their daily disease management. They also provide communication software that transmits the collected data to a backend server at a medical center. The medical center also hosts clinical applications that enable healthcare professionals to review the data provided by patients. Data processing may occur either at the site of acquisition (e.g. with on-body electronics) or at the medical centre. Processing and analysis must take into account the

established medical knowledge and professional expertise where appropriate. The processed and analysed data are then communicated between various actors, in a loop that is from patient/individual to medical centre, from medical centre that analyses the acquired data to doctor/hospital and then and back to the patient/individual from either directly through the data acquisition and/or data processing systems itself or through the doctor or the medical centre (e.g. in the form of personalised feedback and guidance to the patient, adjusted treatment via closed loop therapy, control of therapy devices).

3.2 PHS Devices and Processes

Devices together with a number of processes are required to offer the PHS functionality that has briefly been presented. A part of the processes is responsible for collecting information about vital signs (Sensing and Parameter Extraction), while a part is collecting information on how the patient is feeling and his behaviour. This input is analysed (Multi Parameter Analysis) together with the care plan in order to identify trends, possible risks, etc related to patient's condition. The outcome of the analysis, especially deviations from the proposed care plan, is input for a decision making process (Decision Support) about the required patient feedback and involvement of a professional caregiver. When it comes to feedback, there are two categories of processes. One for providing feedback to the patient (Patient Feedback and Patient Feedback UI) and another for input from professionals (Assessment UI and Professional Assessment) allowing him to take direct actions towards the patient (e.g. invite him/her for a consultation at his office), or provide suggestions for changes in the patients care plan [11].

Devices	Processes
Patient ▪ Sensor devices ▪ User interaction devices (smart phone, PC, TV, etc) **Medical Center** ▪ Storage and application servers **Healthcare Professional** ▪ Assessment device (e.g. PC)	▪ Sensing and Parameter Extraction ▪ Subjective measurements and Context ▪ Multi Parameter Analysis ▪ Decision Support ▪ Professional Assessment ▪ Patient Feedback

Table 1 Devices and processes of PHS

3.3 PHS Stakeholders

It is clear that PHS integrate various components offering different types of functionalities. From hardware sensor devices, to intelligent processing software modules, all components are involved to patient health monitoring and disease management, and there may be unforeseen consequences when they malfunction.

The need on mechanisms or processes to ensure overall system performance is evident. All parts of the loop, health status measurement, analysis, treatment management, and patient feedback should properly function**.** Furthermore, as PHS implementations integrate components from many different vendors, the system should allow interconnection to commercial devices and software. Healthcare professionals should be able to choose sensors that best fit patients' health needs and patients should be able to choose interaction devices according to their personal preferences. Full market exploitation and utilization of PHS requires certification processes ensuring stakeholders that their requirements on critical issues such as **patient safety**, **high quality services** and **interoperability** are satisfied. **Individual components** such as devices (sensors, medical devices, user interaction devices) and software (communications, DSS, UI) should adhere to respective industry standards and should be certified accordingly.

The European Coordination Committee of the Radiological, Electromedical and Healthcare IT Industry (COCIR) has reported on certification expectations of primary and secondary stakeholders for Health IT products [3]. In the HeartCycle project, healthcare professionals and vendors have also provided their expectations for certification for PHS offering health monitoring and disease management applications [12].

The table below summarizes the results.

Stakeholder	Expectations
Care Providers	Assure **proven clinical utility** addressed by the specific application
	Want to receive the product with the **interoperability** capabilities that were promised.
Patients	Have **safety concerns** (e.g. for devices) and expect high quality of care.
	Have **privacy and security** concerns for health data.
Healthcare Authorities	Improve the **quality** and reduce the cost of patient care by proactively promoting the adoption of these products or by means of regulation
	Need products with proven clinical utility and assurance of expected benefits
Vendors	Need a **harmonized and stable market** and easy, cost efficient market access in order to provide affordable and high quality solutions.
	Promote the adoption of such products in the care delivery process by means of **incentives related to certification**
Standard Development Organizations	Foster the **development and deployment of standards**

Table 2 Expectations for the certification for healthcare IT products

4 Current Certification Processes

4.1 Patient Safety: Medical Device Certification

4.1.1 CE Marking

PHS need to carry the CE mark in order to be released to the European market. CE marking is a mandatory requirement for selling all products that it applies to into EU Countries. It implies that the product has been subject to all applicable evaluation and assessment procedure(s) as defined by the CE directives.

CE Marking through the symbol CE stands for "Conformité Européenne" which is French for "European Conformity". When the symbol is affixed to a product it is the manufacturer's declaration that the product conforms to the essential requirements of all European directives. The essential requirements would include Safety, public health, Electromagnetic Compatibility, and consumer protection, among other things.

CE marking is not a quality symbol. It only indicates that the product conforms to the directives set forth by the EU. It is not an indicator of the overall quality of the product.

There are three European CE marking directives that specifically apply to medical devices manufacturers:

- The Medical Devices Directive (MDD) applies to all general medical devices not covered by the Active Implantable Medical Devices Directive or the In Vitro Diagnostics Directive.
- The Active Implantable Medical Devices Directive (AIMDD) applies to all active devices and related accessories intended to be permanently implanted in humans.
- The In Vitro Diagnostics Directive (IVDD) applies to all devices and kits used away from the patient to make a diagnosis of patient medical conditions.

4.1.2 The Medical Devices Directive (MDD: 2007/47/EC)

Directive 2007/47/EC defines a medical device as:

"any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings. Devices are to be used for the purpose of:

- *Diagnosis, prevention, monitoring, treatment or alleviation of disease.*
- *Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap.*
- *Investigation, replacement or modification of the anatomy or of a physiological process*
- *Control of conception*

This includes devices that do not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means."

The Medical Devices Directive is concerned with all medical devices, from sterile gants to electronic monitoring equipment and complex MRI-scanners.

Based on this definition, a Personal Health System as a whole falls in the definition of a Medical Device and should be CE certified as a Medical Device to be marketed in Europe. Instructions for CE certifications have been included in ANNEX 1.

Medical devices are classified according to 2 criteria, the level of invasiveness, and the accompanying level of risk to the patient.

	Class I	Class IIa & IIb	Class III
Description	Non-invasive low risk (electric/electronic) equipment or devices without a monitoring function (e.g. external patient support products)	Non-invasive or short time invasive equipment or intensive patient skin contact or administration of body fluids or medicinal fluids or gases (e.g. electro-medical devices)	Devices with high risk and invasive devices (e.g. cardiovascular catheters)
CE certification Procedure	The so-called manufacturers' declaration is applicable and no involvement of any certified or notified body is required. Most Class I equipment is not invasive at all, and should not administer anything to the patient, no medicines nor energy	Class II equipment (and up) requires the involvement of a Notified Body that will approve customers documentation and/or Quality management System (QMS)	In addition to the procedures for Class II: a detailed design dossier is required

Table 3 Classification of medical devices and overview of CE certification procedures

Examples of Standards required to obtain CE marking:

- ISO 14155, Clinical investigation of medical devices for human subjects — Good clinical practice
- ISO 14971, Medical devices – Application of risk management to medical devices
- MDD 2007/47/EC, Council Directive concerning Medical Devices
- ISO 13485, Quality management systems – Medical devices – System requirements for regulatory purposes
- ISO 60601-1-1, Medical electrical equipment – Part 1-1: General requirements for safety – Collateral standard: Safety requirements for medical electrical systems
- ISO 60601-1-2, Medical electrical equipment – Part 1-1: General requirements for safety – Collateral standard: Electromagnetic compatibility – Requirements and tests
- ISO 60601-1-4, Medical electrical equipment, Part 1-4, General requirements for safety – Collateral standard: Programmable electrical medical devices
- IEC 62304, International standard for software design in medical products

For product certification worldwide the relevant regulatory and quality management programmes are listed below:

Region/Country	Certification Programme
Europe	CE marking
USA	FDA 510k Third -Party Review Program
Australia	Australia – EU CAB
Japan	Japan PAL
Hong Kong	Hong Kong Conformity Assessment Body (CAB)
Canada	Health Canada CMDCAS

Table 4 Certification programmes worldwide

4.1.3 Medical device software

Until recently, software was not formally classified as a medical product by the Medical Devices Directive. With the new medical device directive (MDD: 2007/47/EC) software intended for use by the manufacturer for medical purposes (whether integral with a device or as a stand-alone product) is now classified as a medical device and should adhere to the IEC 6234 standard. IEC 62304 is a well considered, logical standard for developing safety critical and high reliability software for medical devices. This is good news for the safety of patients, but also for the manufacturers themselves, as the standard establishes a more level playing field. In addition, as IEC 62304 is a harmonised standard that has been adopted internationally, it tends to equalise quality expectations between Europe and the United States.

4.2 Interoperability: Continua Health Alliance Certification

There have been significant efforts targeting technical interoperability aspects in the eHealth sector. Standards such as HL7 [4] (Health Level Seven) and DICOM [5] (Digital Imaging and Communications in Medicine), and initiatives such as IHE [6] (Integrating the Healthcare Enterprise) and Continua Health Alliance [7], play an important role in addressing interoperability aspects. In the current document we focus in Continua Health Alliance that addresses PHS interoperability and which has adopted IHE and HL7 standards.

4.2.1 Introduction

The Continua Health Alliance [7] is a non-profit, open industry alliance of healthcare and technology companies in the world joining together in collaboration to improve the quality of personal healthcare. Through the efforts of a collaborative industry organization, Continua aims at enabling a personal health eco-system where many diverse vendors can combine their products into new value propositions with significant health benefits for people worldwide.

Continua has identified the following barriers in making a personal health eco-system reality:

- Technical

    - Data interoperability lacking
    - Interoperable platform components lacking
- Regulatory
    - Safety and efficiency regulations restrict development of multi-vendor solutions
- Financial
    - Economic value of new models of care difficult to demonstrate
    - Difficult to get the business model right

The Continua Health Alliance addresses these barriers through the following activities.

- *Design Guidelines:* enable interoperable sensors, telehealth platforms, and health & wellness services.
- *Certification & Logo:* create a consumer recognizable logo signifying the promise of interoperability with other certified products.
- *Health & Safety Regulations:* work with regulatory agencies to safely and effectively manage diverse vendor solutions.
- *Reimbursement:* work with leaders in the healthcare industries to develop new ways of addressing the costs of providing personal telehealth systems.

The Continua design guidelines specify requirements for the connectivity interfaces of devices in a PHS. They specify how to use existing standards to build interoperable personal health care solutions. It is worth noting that Continua design guidelines are about the **connectivity interfaces only**. They refer to the network transport, messaging layer and data format to be used. Continua design guidelines **do not address management services, sensing techniques, parameter extraction techniques**, etc. These guidelines were specifically written for device manufacturers that intend to go through the Continua Certification process with their devices, for companies that integrate Continua devices in systems and subsystems, and for test labs that certify compliance to Continua specifications. Having a Continua Certified product ensures some level of interoperability and can be used as an incentive from the vendors to successfully market their product (see **Table 2**).
The Continua Certification process is provided at http://www.continuaalliance.org/products/cert-process.html

4.2.2 Continua Design Guidelines

The Continua Reference Architecture [8], [9] defines three kinds of elements:

- Components: models logical entities, such as services.
- Devices: models physical entities. Each device can host one or more components.
- Interfaces: define the communication between components. Interfaces between components hosted by different devices are called ‘network interfaces’, while those between components hosted by the same device are called ‘application programming interfaces (APIs)’.

Depending on the interfaces implemented, devices are classified as:

- Application hosting device: device, such as a personal computer, cell phone, or monitoring hub.
- PAN devices: either a sensor or an actuator.
- LAN device: aggregates and shares (though a network) the bound PAN devices’ information (this is often referred to as a proxy function). A LAN device can also implement sensor and actuator functionality directly.

- WAN device: implements a managed-network-based service, using IP communication capabilities (such as xDSL, DOCSIS, GPRS, EDGE)
- HRN device: implements a health-care record.

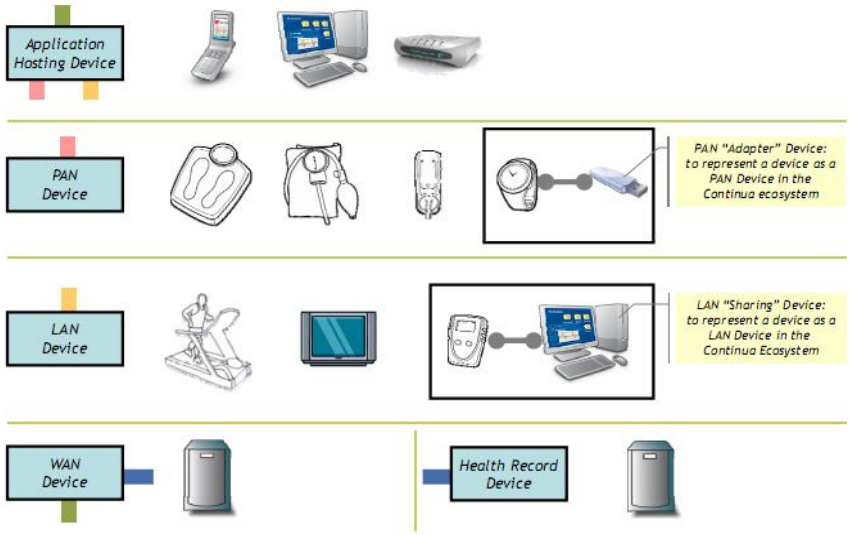

Figure 2 Devices (source: Continua Health Alliance)

The connectivity interfaces offered by a device determine to which other device it can be connected. In other words there are some topology constraints based on the connectivity interfaces of a device. The Continua Reference Topology (see Figure 3) shows that a Peripheral Area Network (PAN) device can be connected to an application hosting device and the latter can be connected to a Wide Area Network (WAN) device.

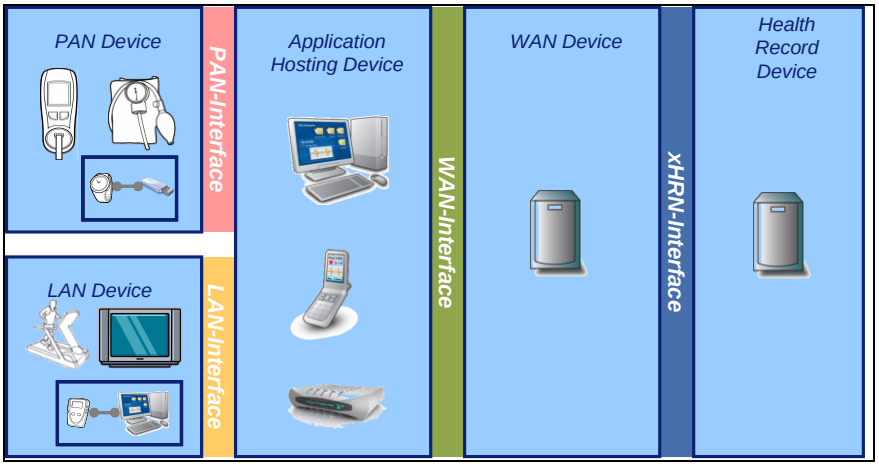

Figure 3 Reference topology (source: Continua Health Alliance)

The network interfaces are at the center of Continua's interoperability goals and are the crux of the test and certification targets for candidate devices.

Two versions of guidelines for the network interfaces have been issued so far:

Version 1 Guidelines (February, 2009): In this initial version of the Continua guidelines, the scope covers guidelines for the PAN-IF (wired and standard wireless) and HRN-IF.

Version 1.5 Guidelines (September, 2010): In this version of the Continua guidelines, the scope covers guidelines for the PAN-IF (wired and standard wireless), LAN-IF (sensor LAN), WAN-IF (data upload) and HRN-IF.

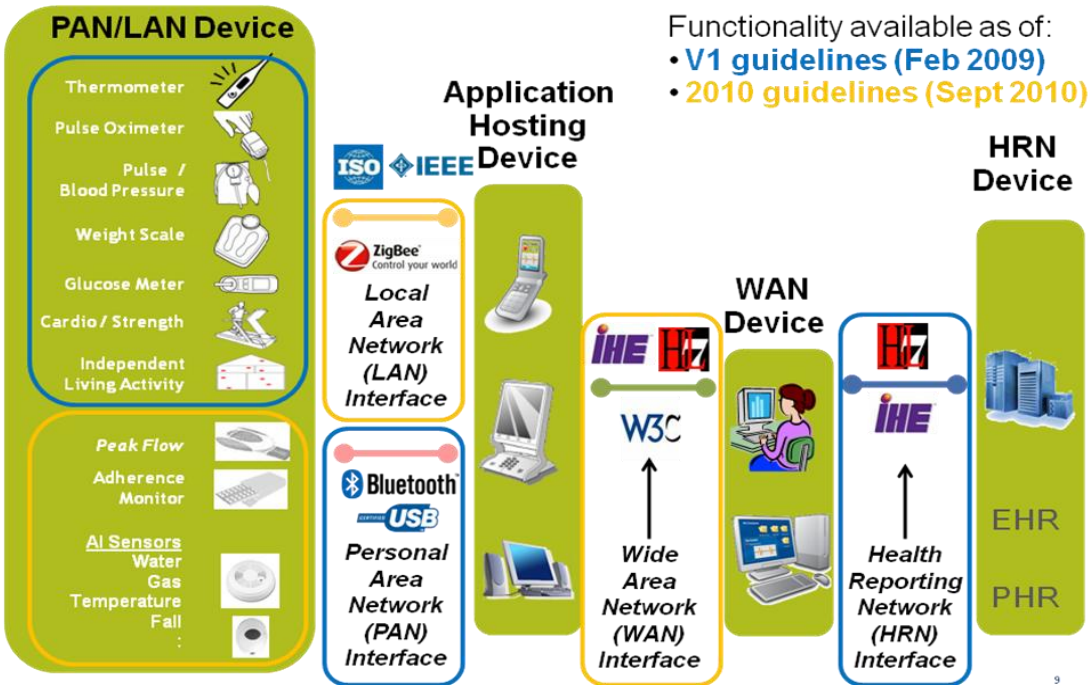

Figure 4 Continua interfaces and standards

As shown in Figure 4, CONTINUA has adopted proven connectivity standards. A recent addition has been the definition of the WAN-IF interface for IHE compatibility [10].

Integrating the Healthcare Enterprise (IHE) is an initiative by healthcare professionals that aims to contribute to cross-institutional data exchange. The IHE Patient Care Device (IHE-PCD) deals with all clinical settings, life-critical applications, and chronic disease diagnosis and treatment (acute/intensive care, surgery, implants, physician offices, and home care). It focuses on device safety and integrating data into Electronic Medical Records/Electronic Health Records and Personal Health Records. IHE-PCD defines use case-bounded “Profiles” to describe clinical “transactions” that involve “actors” (e.g. entities like the sending device and the receiving hospital information system). This allows systems that are independently developed, but adhere to the IHE-PCD “Profile,” to interoperate without individual customized configuration. The Continua WAN-IF interfaces have adopted the IHE-PCD profiles, thus promoting interoperability with hospital EHRs.

With regards to security, Continua has worked to ensure that the Design Guidelines support the development of secure systems.

Continua members may download the Version 2010 Design Guidelines and Version One Design Guidelines for free.

4.3 Other Healthcare Systems' Certification Initiatives

4.3.1 EuroRec – Integration with EHR

In view of interoperability with and potential integration into EHR systems, two initiatives of EuroRec (http://www.eurorec.org/), should be mentioned: Q-REC and EHR-QTN.

EuroRec is an independent not-for-profit organisation, promoting in Europe the use of high quality Electronic Health Record systems (EHRs). As the European certification body, it also supports EHRs quality labelling and defining functional and other criteria. These have been elaborated within the Q-REC project, “European Quality Labelling and Certification of Electronic Health Record systems (EHRs)", a Specific Support Action, co-funded by the European Framework Programme.

The Institute is currently drawing up a plan, together with DG "Enterprise", to implement the process of Quality Labelling of EHR systems in the European Union.

The Institute aims as part of its business plan to generate the full confidence of all stakeholders in Europe, healthcare provider policy/decision makers, clinicians and other end users, systems developers and vendors, and citizens/patients, in the reliability of these services. This is being supported by EHR-QTN, a Thematic Network project that prepares the health community across Europe for systematic and comparable quality assurance and certification of eHealth products.

Moreover, the EuroRec EHR Quality Seal has been introduced (http://www.eurorec.org/services/seal/index.cfm). Its main objective is to initiate a process of harmonisation between EHR systems, favouring in Europe cross-border interoperability of those systems. It is not the intention of the EuroRec Seals to replace existing (e.g. national) certification initiatives (which can be/are supported by ProRec centres or EuroRec locally). In this stage, the seal is to be considered as a mechanism to avoid re-certification of EHR systems (i.e. systems already certified by other certification instances in EU member states using criteria compliant with the EuroRec ones). The content of the EuroRec Seal will evolve over time and encompass other criteria as well (e.g. functional ones and content-related ones).

4.3.2 Eucomed – Ethical standards

Besides technical and functional certification, compliance to ethical standards and principles is being promoted and certified by Eucomed, the European Medical Technology Industry Association (http://www.eucomed.be). Eucomed has developed educational and training programmes in the so called “Code of Ethical Business Practice” (http://www.eucomed.be/ethics.aspx).

The Code of Ethical Business Practice is intended to provide ethical standards and principals within Europe for the medical technology industry. It is not intended to supplant or supersede national laws or regulations or other professional or other business codes which may apply to its members.

Eucomed represents 4500 designers, manufacturers and suppliers of medical technology used in the diagnosis, prevention, treatment and amelioration of disease and disability. Eucomed members include national trade and pan-European product associations and internationally active manufacturers of all types of medical technology. The mission of Eucomed is to improve patient and clinician access to modern, innovative and reliable medical technology.

5 Towards a Certification Framework for PHS

5.1 The HeartCycle Case

The functionality of the first PHS systems was focused in remote monitoring of vital signals through sensor devices, therefore, certification requirements and procedures addressed the safety of the patients using these devices. With a wide range of such devices becoming available, the need for device interoperability emerged and relevant certification initiatives addressed intercommunication of such devices. As development now has advanced to closed loop solutions integrating care at home with professional care in the hospital PHS have moved beyond simple monitoring into diagnosis and treatment.

The HeartCycle project is a paradigm of a closed-loop PHS for health monitoring and disease management that offers personalised interventions to patients with heart failure and coronary heart disease. The system consists of two loops (Figure 5). An inner home-based loop directly interacts with the patient in his daily life, giving feedback, motivation and help, and an outer loop involves medical professionals, maintaining a personalised care plan for optimal therapy.

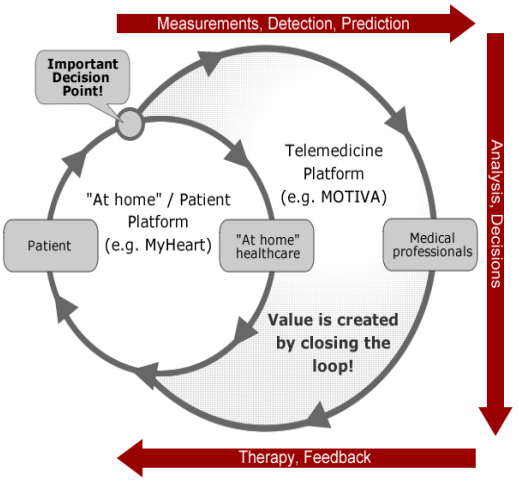

Figure 5 HeartCycle: A Closed Loop PHS

HeartCycle develops two closed-loop systems aiming to help patients become engaged in their care and to motivate them to follow their treatment plan:

i) The “Heart Failure Management” system: it uses the commercial MOTIVA communication platform as the backend system, communicating with telemonitoring devices. MOTIVA is already a product from Philips Medical Systems.

ii) “Guided exercise” for patients with Coronary Artery Disease (CAD): consists of the IMAGE integrated sensing device that interfaces a number of sensors and a personal digital assistant (PDA).

Prototypes of these systems will be validated through trials. In addition, as part of the project’s research line, Assessment Case is also being developed. In Assessment Case we do not have an integrated system but a set of distinct modules supporting highly innovative use cases addressing patient’s compliance, education and motivation aiming to enhance patient-professional encounter.

As a research project, HeartCycle does not involve the certification process in its timeframe. However, it has conformed to all standards that will lead to certifiable products and has identified relevant gaps and stakeholders recommendations that can contribute to the development of a PHS certification framework. HeartCycle outcomes can contribute to the development of a certification framework for PHS as follows:

5.2 Gaps and Recommendations on Clinical Validation Standards

Healthcare professionals will use PHS if their clinical utility is demonstrated. The ultimate evidence of the clinical utility of an intervention is demonstration that it improves outcomes. This could be improving the efficiency of uptake and maintenance of therapy, improving patient well-being, reducing morbid events or prolonging life. Randomised clinical trials demonstrating improved outcome with the use of PHS would prove the clinical utility of such systems and promote their adoption by healthcare professionals. However, such a validation would require the existence of clinical validation standards.

A. Evaluation health management applications of PHS requires reference standards. Specifically, there is no established knowledge on the effect of life style choices and medication on clinical variables assessed by monitoring sensors. Since telemonitoring systems are still in their infancy and have not been used for health management, there is no relevant data or established knowledge available. For example it is not known how medication dosage changes are expected to affect daily blood pressure measurements. . Such information is needed to distinguish disease progression from background variability and a) enable healthcare professionals to correctly interpret the readings of PHS and use them efficiently, and b) provide the basis for reliable decision support tools.

Recommendation: Research is required to assess the the **effects of the methods** proposed by PHS (e.g. life style choices and drug therapy) **on clinical variables** assessed by monitoring sensors. The HeartCycle trials work towards the assessment of the effects of lifestyle and medication on clinical variables assessed by sensors for patients with Heart Failure.

B. Healthcare professionals will use PHS if the medical devices provide accurate measurements. For the comparison, golden standards are required. However gold standards are not always available or they could be less accurate than the new device.

Recommendation: Identify the golden standards to use as reference for the validation of accuracy of medical devices.

C. Healthcare professionals will use PHS if the medical devices ensure **reproducibility** and **sensitivity to change**

Reproducibility usually requires patients to have multiple comparative tests. Sensor should also be able to detect changes, and measure the magnitude of change, in other words be well calibrated. Recommendation: Acceptance criteria for reproducibility tests and sensitivity to change should be identified.

D. Clinical trials should be designed to verify the new methods for disease management implemented by PHS applications. In the context of these trials, the devices that are used on human subjects, should fulfil safety, risk and performance requirements according to the applicable standards (listed in Table 5). The clinical trial protocols have to be accepted by ethics committees and the patients participating to the trials have to be informed and have to sign an informed consent.

In addition to the verification of the PHS clinical utility, clinical trials represent an important step towards the certification of the devices. Since the devices are intended to be used in a specific way according to the PHS application, one has first to prove the methods and then the device will need to be clinically tried, on a larger number of patients and for longer periods, to verify their effectiveness and suitability for their intended use, in order to get the CE approval.

5.3 Standards during PHS Development

It is evident that in a new emerging and complex field, such as PHS, there are very limited certification procedures currently in place (presented chapter 4). However, standards and guidelines from the Healthcare and ICT domain apply in the development and validation of PHS and could be adopted in future certification initiatives [11], [12], [13].

	Standards applying for PHS
Medical Devices	In addition to the standards listed in 4.1.2 **ISO 9919** international standard for Medical electrical equipment and particular requirements for the basic safety and essential performance of pulse oximeter equipment for medical use. **ISO 13485:2003** specifies requirements for a quality management system where an organization needs to demonstrate its ability to provide medical devices and related services that consistently meet customer requirements and regulatory requirements applicable to medical devices and related services. **ISO 14155** This standard addresses the clinical validation of a medical device that has been certified.
Communication of Devices	Continua Design Guidelines v1.5
Communication of Software	Continua Design Guidelines v1.5
Care Plans	Care plans should be defined in close collaboration with medical experts and in line with the guidelines of established clinical associations. In the case of HeartCycle addressing patients with Heart Failure and Coronary Artery Disease the guidelines of the European Society of Cardiology (2005 updated) have been followed
Conduct of Clinical Trials	EU regulations that apply: ICH E6 document: Guideline for Good Clinical Practice is the scientific guideline from the ICH (International Conference on Harmonisation for Technical Requirements for Registration of Pharmaceuticals for Human Use) that must be taken into account. EU Directive (2001/20/EC): Directive across 25 members that accomplishes ICH-GCP (International Conference on Harmonisation - Good Clinical Practice). EU Directive (2005/28/EC): European Commission directive regarding investigational medicinal devices for human use.

Table 5 Recommended standards for PHS development

5.4 Gaps and Recommendations for Interoperability Certification

While conformance to Continua Design Guidelines ensures interconnectivity of devices, there are many other aspects of interoperability that should be ensured in order to allow medical professionals to choose the components that best fit to the needs of their patient. Certification of broad interoperability would constitute an important incentive to be used for product promotion.

As PHS move to health management, the solutions offered by different systems on behaviour management should be interoperable with monitoring solutions offered by different devices. A number of similar issues are identified in the list below.

Gaps in interoperability
End to End Interoperability: Ensure that the PHS product consists of interoperable devices and software and is interoperable with EHR systems
Secure Data Transfer: Ensure security during data transfer between interoperable components
Interoperable subjective and objective measurements: Ensure that the output of sensor devices is in standardised formats Ensure that subjective patient input is in standardised formats Ensure that the output of software modules is in standardised formats. For example, Decision Support tools should be able to interface and accept input from different Multi Parameter Analysis tools.
Interoperable modules for disease management: Ensure interoperability of behavior management and patient empowerment applications so that they can be embedded in different PHS For example, medically related educational content (as in reminders and behavior management) should be provided in standardized formats so that it can be adapted delivered through different PHS solutions
Recommendations
Continua Design Guidelines (for the Communication Interfaces): Stop adding more alternatives for uploading measurements and shift towards maintenance (fixing bugs) and support for the adoption of the current standards and compliance with the guidelines
Work towards the interoperability of approved use cases for remote health management (behavior management, patient empowerment

Table 6 Gaps and Recommendations for Interoperability of PHS

6 Conclusion

Driven by the HeartCycle experience the current paper presents an overview of **current certification procedures** for PHS, identifies **major gaps** and draws **recommendations.**

CE certification is a prerequisite for marketing PHS products in Europe and similar procedures exist worldwide (FDA in United States). It addresses safety issues for both medical devices and software. Continua Design Guidelines are recommended to ensure interconnection of devices. There is high need of clinical validation standards addressing the quality of medical devices as well as the interpretation of measurements produced by intelligent processing modules. Interoperability should advance beyond interconnection of devices to aspects such as standardization of objective and subjective measurements, and guidance for development of interoperable applications such as behavior management and patient empowerment.

7 References

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ANNEX I

CE normal certification procedure based on the directive MDD: 93/42/EC

Conformity assessment procedures

1. In the case of devices falling within Class III, other than devices which are custom-made or intended for clinical investigations, the manufacturer shall, in order to affix the CE marking, either:

(a) follow the procedure relating to the EC declaration of conformity set out in Annex II (full quality assurance); or

(b) follow the procedure relating to the EC type-examination set out in Annex III, coupled with:

(i) the procedure relating to the EC verification set out in Annex IV;

or

(ii) the procedure relating to the EC declaration of conformity set out in Annex V (production quality assurance).

2. In the case of devices falling within Class IIa, other than devices which are custom-made or intended for clinical investigations, the manufacturer shall, in order to affix the CE marking, follow the procedure relating to the EC declaration of conformity set out in

Annex VII, coupled with either:

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(a) the procedure relating to the EC verification set out in Annex IV; or

(b) the procedure relating to the EC declaration of conformity set out in Annex V (production quality assurance); or

(c) the procedure relating to the EC declaration of conformity set out in Annex VI (product quality assurance).

Instead of applying these procedures, the manufacturer may also follow the procedure referred to in paragraph 3 (a).

3. In the case of devices falling within Class IIb, other than devices which are custom-made or intended for clinical investigations, the manufacturer shall, in order to affix the CE marking, either:

(a) follow the procedure relating to the EC declaration of conformity set out in Annex II (full quality assurance); in this case, point 4 of Annex II is not applicable; or

(b) follow the procedure relating to the EC type-examination set out in Annex III, coupled with:

(i) the procedure relating to the EC verification set out in Annex IV; or

(ii) the procedure relating to the EC declaration of conformity set out in Annex V (production quality assurance); or

(iii) the procedure relating to the EC declaration of conformity set out in Annex VI (product quality assurance).

4. The Commission shall, no later than five years from the date of implementation of this Directive, submit a report to the Council on the operation of the provisions referred to in Article 10 (1), Article 15 (1), in particular in respect of Class I and Class IIa devices, and on the operation of the provisions referred to in Annex II, Section 4.3 second and third subparagraphs and in Annex III, Section 5 second and third subparagraphs to this Directive, accompanied, if necessary, by appropriate proposals.

5. In the case of devices falling within Class I, other than devices which are custom-made or intended for clinical investigations, the manufacturer shall, in order to affix the CE marking, follow the procedure referred to in Annex VII and draw up the EC declaration of conformity required before placing the device on the market.

6. In the case of custom-made devices, the manufacturer shall follow the procedure referred to in Annex VIII and draw up the statement set out in that Annex before placing each device on the market.

Member States may require that the manufacturer shall submit to the competent authority a list of such devices which have been put into service in their territory.

7. During the conformity assessment procedure for a device, the manufacturer and/or the notified body shall take account of the results of any assessment and verification operations which, where appropriate, have been carried out in accordance with this Directive at an intermediate stage of manufacture.

8. The manufacturer may instruct his authorized representative to initiate the procedures provided for in Annexes III, IV, VII and VIII.

9. Where the conformity assessment procedure involves the intervention of a notified body, the manufacturer, or his authorized representative, may apply to a body of his choice within the framework of the tasks for which the body has been notified.

10. The notified body may require, where duly justified, any information or data, which is necessary for establishing and maintaining the attestation of conformity in view of the chosen procedure.

11. Decisions taken by the notified bodies in accordance with Annexes II, III, V and VI shall be valid for a maximum of five years and may be extended on application, made at a time agreed in the contract signed by both parties for further periods of a maximum length of five years.

12. The records and correspondence relating to the procedures referred to in paragraphs 1 to 6 shall be in an official language of the Member State in which the procedures are carried out and/or in another Community language acceptable to the notified body.

13. By derogation from paragraphs 1 to 6, the competent authorities may authorize, on duly justified request, the placing on the market and putting into service, within the territory of the Member State concerned, of individual devices for which the procedures referred to in paragraphs 1 to 6 have not been carried out and the use of which is in the interest of protection of health.

14. The measures designed to amend non-essential elements of this Directive, by supplementing it, relating to the means by which, in the light of technical progress and considering the intended users of the devices concerned, the information laid down in Annex I Section 13.1 may be set out, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 7(3).