Grant Agreement no. 287596

d-LIVER

ICT-enabled, cellular artificial liver system incorporating personalized patient management and support

INSTRUMENT: Collaborative Project (Integrating Project)

OBJECTIVE: ICT-2011.5.1

Final Report

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1. Final Publishable Summary Report

Executive Summary

The d-LIVER project originates from clinical needs and applies a scenario driven development methodology in response to FP7 ICT Objective ICT-2011.5.1: Personal Health Systems. This emphasizes research that aims for disease management and also targets rehabilitation and treatment at the point of need with a focus on specific diseases and in particular the requirement to address the need for ICT enabled artificial liver systems to facilitate detoxification as remote transient therapy at the point of need, offering continuous care from hospital to home settings, as stated in Target Outcome a3) Liver Failure.

There is a clear, unmet need for an ICT-enabled bio-artificial liver (BAL) in combination with liver patient management and support systems with associated monitoring and control for the remote management of patients with chronic liver disease outside the hospital. The overall goal of the project is to provide safe and cost-effective systems for continuous, context-aware, multi-parametric monitoring of both patient and BAL system parameters in order to: enhance the quality of medical treatment and management; improve the quality of life for patients; reduce the incidence and duration of hospitalization and consequently reduce the health economic burden of chronic liver disease. d-LIVER will facilitate improved treatment whilst enabling patients to spend more time at home under constant, albeit remote, medical supervision.

The d-LIVER system concept is illustrated in Figure 1. Central to this concept is the pursuit of more efficient bio-artificial liver support devices, with significant detoxification capability and synthetic metabolic activity, as well as high biocompatibility and safety. These systems will be capable of constantly communicating the status of both the patient and the BAL remotely to central clinical services, in a secure and confidential manner, such that patient monitoring is continuous and intervention can be both swift and beneficial.

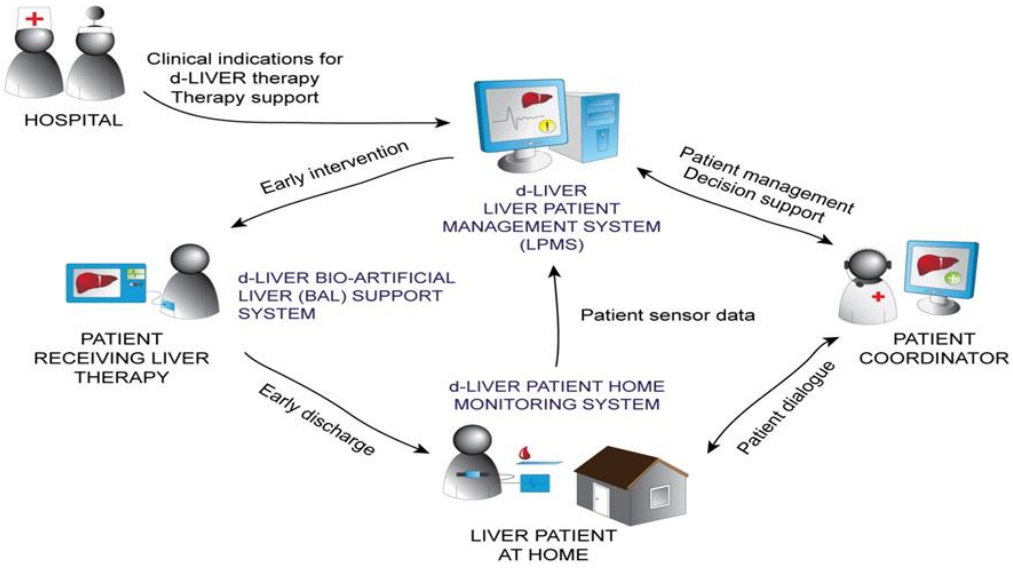

Figure 1: The d-LIVER system concept.

The d-LIVER project is application-orientated and based on four inter-linked scenarios, defined by clinicians, which drive ICT and sensor technology development in order to meet exactly the needs for continuous clinical support, monitoring and therapy of liver patients at the point of need from hospital to home settings. These scenarios are:

- Chronic liver failure
- Chronic cholestatic itch
- Bridging therapy before liver transplantation
- Acute liver failure

On the basis of these scenarios, a full set of both physical and biochemical parameters have been defined in d-LIVER which will be required to be measured either at regular intervals (patient status monitoring) or continuously (BAL efficacy monitoring). Each scenario has its own most appropriate sub-set of these essential parameters which will be required to be measured and communicated with the ICT LPMS. Monitoring is fundamentally focused on five main branches:

1. Indication/ decision/ timing/ planning for bio-artificial liver support sessions
2. Basic remote monitoring during d-LIVER bio-artificial liver support therapy
3. Evaluation of therapy success after liver support / detoxification
4. Remote monitoring of patient liver function/ toxin level/ general condition until the indication for the next session
5. Actual recommendations for patients at home regarding personal life-style and behaviour based on patient data monitored by the LPMS

Summary description of project context and objectives

The specific overall objectives of d-LIVER are to:

- Define the clinical requirements for patient management and bio-artificial liver unit operation in the chosen clinical scenarios **(Month 7)**
- Develop wearable sensing technologies for remote continuous monitoring of patient physical status **(Month 32)**
- Develop biochemical sensor technologies for accurate analytical measurements of patient blood biochemistry and bio-artificial liver unit quality parameters **(Month 32)**
- Produce model bio-artificial liver unit based on primary human or porcine hepatocytes integrated with multi-parametric sensor systems and closed loop control **(Month 36)**
- Develop instrumentation hardware platforms **(Month 36)**
- Develop Liver Patient Management System (LPMS) and integrate with hardware platform **(Month 40)**
- Clinically evaluate d-LIVER system for use at Point-of-Need in a clinical environment according to the defined scenarios **(Month 42)**
- Develop and evaluate clinically high risk bio-artificial liver technology **(Month 42)**
- Encompass innovation management ensuring exploitation of the developed technology **(Month 48)**
- Promote wide sectoral and geographical dissemination of the project results **(Continuous)**
- Integrate multidisciplinary education, training and skills development with research activities **(Continuous)**

More detailed objectives for each Workpackage are described below.

WP1: Clinical application scenarios and validation

WP1 was planned to have a vital role both at the beginning and end of the project. In the initial stages it was important to deal with the definition, requirements and algorithms of the clinical application scenarios from the clinician's side and also from the technology development and end-user/patient perspectives. Subsequently, in the latter stages WP1 was responsible for the multi-modal evaluation of the d-LIVER systems (clinical performance, impact on management, quality of life and health-economic issues) either in the home or a simulated home environment.

WP2: System design and medical device regulatory requirements

The objectives of WP2 were to:

- Express the vision and mission of the d-LIVER concept in terms of a set of system requirements specifications and target system specifications
- Establish an overview of project design input affecting the design
- Establish the regulatory requirements essential for the d-LIVER devices
- Establish a framework for effective work collaboration among the project partners by generating a well-defined, easy to understand, description of system components and interfaces
- Establish a basis for minimizing potential technical risks and hazards

WP3: Sensor development

The main objective of WP3 was to develop biochemical and physical sensors for the monitoring of patient parameters and the bio-artificial liver support unit (in conjunction with WP5). These measurements were developed in accordance with the parameters defined in the d-LIVER scenarios. The sensors developed monitored biochemical (e.g. electrolytes, small molecules, clotting) or physiological parameters (e.g. heart rate, skin body temperature, blood pressure).

The biochemical sensor platforms were designed to be incorporated into the microfluidic cartridge developed in WP4 and also provided to WP5 for possible re-engineering for integration into the bio artificial liver support unit's functional monitoring system. Software and signal processing requirements were fed into WP6. The biochemical sensors for continuous monitoring of the status of the progenitor cells were transferred to WP4.

WP4: Microfluidics, packaging and integration

The sensors and measurement protocols provided by WP3 for the various parameters were transferred into designs for microfluidic cartridges. The sensors were packaged into the fluidic cartridge which had suitable mechanical, optical, fluidic and electrical interfaces to the instrument developed in WP6. Sensor performance within the integrated cartridges was evaluated in comparison with unpackaged sensor systems and the overall functionality of the cartridge tested with the instrument.

WP5: Development and monitoring of Bio-artificial Liver Support Unit

The objectives of WP5 were as follows:

- Specify the requirements of the sensor system and bio-artificial liver support unit to enable the monitoring and control of cell culture and cell culture conditions
- Integration of sensors for ammonia, cell viability and cell density in the bio-artificial liver support unit and development of strategies for the prediction of critical condition of cell culture
- Development of test systems for the quality control of cells before using the cells for the bio-artificial liver support unit
- Investigation of correlation between on-line measurements of cell impedance spectra and off-line measurements of e.g. albumin or glucose consumption/lactate production
- Development of methods for deducing the efficacy of the detoxification session from impedance spectra measured on-line
- Closed-loop control of cell culture conditions based on integrated sensors performing on-line measurements
- Development of bio-artificial liver support unit for proof of concept and evaluation in a clinical setting (technical validity, efficiency and clinical outcome)

WP6: Instrumentation platforms

The objective of WP6 was to build the instrumentation platforms that would service the requirements of d-LIVER. These included three different systems as follows:

- Instrument for use with the blood biochemistry microfluidic cartridges developed in WP4
- Logging device for continuous collection of physiological patient parameters (i.e. heart rate, blood pressure, skin temperature, and human kinetics) from wearable sensors developed in WP3
- Instrumentation to interface with the sensor systems incorporated within the bio-artificial liver developed in WP5

WP7: Communications, Patient Management and Decision Support

WP7 aimed to deliver an advanced web-based information system for the management of patients with a chronic liver condition in ambulatory and home settings in combination with the d-LIVER patient monitoring and bio-artificial liver support system. In addition, it provided the overall communication and security framework for the d-LIVER platform with a particular focus on interoperable and open solutions as well as on patient safety and privacy. An innovative ontology based Liver Patient Management and Decision Support System (LPMS) was developed that enabled intelligent real-time monitoring of liver patients at home, the surveillance of liver support sessions, therapy and intervention planning, triaging, alert and emergency management. The embedded decision support component could guide healthcare professionals through the different therapy phases of patients with liver failure and provided support to therapy decisions and possible interventions based upon disease-specific personalisable treatment plans in combination with editable semantic decision rules, which trigger actions and interventions in response to incoming monitoring information.

WP8: Progenitor cells for bio-artificial liver

The objectives of WP8 were to:

- Optimise purification of human pancreatic hepatocyte progenitors, archive and characterise progenitor function
- Characterise trans-differentiation of human pancreatic hepatocyte progenitors and assess hepatic function *in vitro*
- Test the human pancreatic hepatocyte progenitor seeded extracorporeal liver device using “toxic” model plasma (human plasma modified to mimic the characteristics of plasma seen in liver failure)
- Obtain regulatory approval for a “proof-of-concept” clinical study to test the human pancreatic hepatocyte progenitor seeded extracorporeal liver device in patients
- Perform a “proof-of-concept” clinical study to evaluate the human pancreatic hepatocyte progenitor seeded extracorporeal liver device in practice

WP9: Dissemination, training and exploitation plans

The objectives of WP9 were to disseminate the results of d-LIVER, establish a project website, identify and manage the intellectual property developed, and ensure that suitable exploitation plans are drawn up. Furthermore, d-LIVER consortium partners exchanged researchers for hands-on and lecture style training and short- and long-term secondments/exchanges, in order to broaden their skills across technical disciplines. Training needs of academic and research organisations, industry and healthcare providers were to be identified, new material was to be developed to address market and societal needs and training delivered across Europe.

WP10: Consortium Management

The objective of this WP was the overall management of the project, including:

- Establishment of management committees and guidelines for their operation
- Establishment of technical and financial reporting guidelines
- Establishment of structures for execution of committee/co-ordination group tasks
- Provision of financial and technical monitoring and reporting
- Administration of Consortium Agreement
- Delivery of all necessary reports including periodic and final project reports

Description of the main S&T results/foregrounds

WP1: Clinical application scenarios and validation

WP1 was the clinical driver for the whole of the d-LIVER project. It is essential that technology development in the medical diagnostics, monitoring and management fields is driven by real clinical need rather than by technology push. WP1 therefore initially defined the clinical needs for patient monitoring and created a mutual understanding of d-LIVER systems between technology developers and clinicians such that the required technical specifications for the different system components could be elucidated.

From the outset WP1 investigated a number of objective and subjective factors which could be affected by successful technology development and implementation into different European healthcare systems. This included an assessment of patient quality of life at home, economic burden of chronic liver failure and the definition of suitable indication and outcome variables. These studies were carried out in 3 clinical centres in the UK, Germany and Italy, and the regional differences were reported in public deliverables available on the project website.

The final clinical evaluation studies to be carried out using the sensor, instrumentation and information technologies developed in technical Workpackages were designed well in advance and local ethics approval obtained for each individual study in good time. These evaluations included:

- Wearable device (functionality, usability, patient perception)
- Electronic number connection test for cognitive function (comparison with standard method and patient acceptability)
- Home monitoring and management of encephalopathy (HoME) study using LPMS from WP7 (cognitive function, changes to drug regimen, patient acceptability of tablet-based App, comparison with standard care)
- Overall d-LIVER system including Blood Biochemistry Instrument and LPMS (multi-centre, patient acceptability, ease of use)
- Biochemical sensor measurements of patient samples and comparison with hospital laboratory results (correlation, agreement, method interchangeability, effect on clinical decision making)
- Bioartificial liver support unit (detoxification of liver patient serum using progenitor cells in clinical grade BAL)

WP2: System design and medical device regulatory requirements

The overall goal of WP2 was to address components, functionalities and requirements of the d-LIVER systems and to provide direction for the detailed implementation and evaluation to be carried out in other technical Workpackages, thus establishing a shared understanding among the different fields of competence within the d-LIVER project and communication and information flow between the partners across the different enabling Workpackages. The Workpackage thus facilitated the description of different terms, components and their interfaces in more detail and provided a definition of the overall d-LIVER system goals and technical requirements, based on the clinical medical device regulatory requirements elucidated in Workpackage 1. The main objective was to translate the vision and mission of the d-LIVER concept into workable formats, by providing detailed information concerning the technical and system level implementation plan and creating a top-level view of the systems to be developed.

WP3: Sensor development

The objective of WP3 was to develop physical and biochemical sensors for the monitoring of patient parameters at home. The sensors developed were designed to monitor a defined set of biochemical parameters (electrolytes, biomolecules and blood clotting) and physiological parameters (heart rate, skin temperature and blood pressure) which would be the most effective in remote monitoring and management of patients with chronic liver disease. At the outset of the project there were initially 11 parameters in total: albumin, bilirubin, creatinine, ammonia, bile acids, sodium, potassium, clotting time, heart rate, temperature and blood pressure.

The biochemical and physical sensors were characterized and their performance was compared with the requirements of the d-LIVER project. At the end of the first year, 8 individual sensors out of the 11 were operational and 6 met the project requirements.

Strategies for some sensors were then reviewed to make them operational and work on other sensors focused on integrateability and further characterization. Front-end electronic board and signal processing required for the cartridge readout was also developed. At the end of second year, the decision was made to remove ammonia and bile acids sensors from the d-LIVER blood biochemistry cartridge (BBC) and to choose an optical configuration for the clotting time sensor. Work then focused on the integration of the 6 sensors that were finally integrated in the BBC and the 3 in wearable device (see WP6). For the 6 biochemical sensors in the cartridge, all are now operational under "in cartridge" conditions and have undergone clinical comparative analysis using 150 patient samples with excellent correlation with hospital laboratory referee methods in most cases.

WP4: Microfluidics, packaging and integration

Workpackage 4 was dedicated to the design and manufacture of the integrated sensor microfluidic cartridges required by d-LIVER as well as the fluidic evaluation of these devices. An iterative chip development programme was instigated which allowed initial designs to be tested using milling procedures prior to locking down designs and proceeding to produce larger numbers of cartridges by injection moulding for the analytical and clinical evaluation studies. Within WP4 a microfluidic cartridge for the blood biochemistry instrument was developed and for that purpose, suitable polymer materials as well as potential coatings were identified within the first few months of the project. Important issues such as biocompatibility and haemocompatibility were assessed and care was taken to ensure that these materials were compliant with safety regulations and directives for medical devices on the basis of, the international standard ISO 10993 and the guidelines of Unites States Pharmacopeia Class VI. Suitable polymer materials for the fluidic devices were identified with regard to processability and performance and polycarbonate proved to be the most favourable for use. Specifically, micromilling, injection moulding, solvent bonding and γ-sterilization could be applied to this material and, in addition, certain types of polycarbonate are optically transparent – an important issue for the clotting time sensor developed in WP3.

The final BBC developed and manufactured is shown in Figure 2. This was designed to measure six blood parameters (clotting time, Na^+, K^+, bilirubin, albumin, and creatinine) at home on a daily basis. From the viewpoint of the patient, the use of the BBC should be as easy as possible within the home environment and with no accidental harm to the patient. For these reasons, the fundamental design rule was the minimization of the volume of blood to be provided to the BBC by the patient, such that a standard finger prick technique could be used. The developed cartridge consisted of two components; the microfluidic cartridge which housed all of the sensors and a reservoir chip which contained any reagents or solutions which were required to realise the sensor-based measurements in blood. Whole blood (20µl) was drawn into the cartridge by capillary forces and was then separated to release the serum component. Serum was

then diluted 1:5 on-chip and flowed sequentially over the sensors. One patent application on the BBC was submitted a second one is under preparation by patent attorneys.

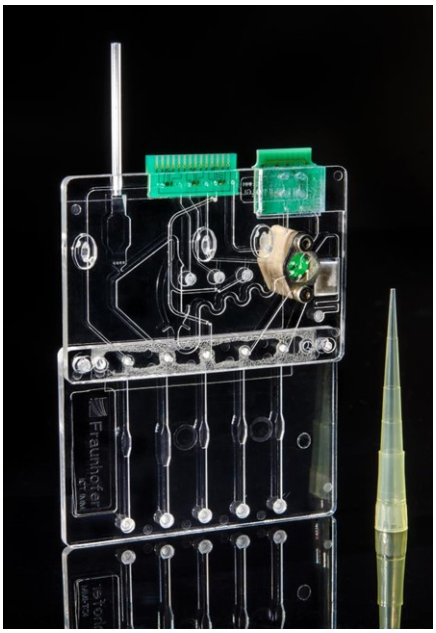

Figure 2: Final fully-assembled Blood Biochemistry Cartridge. The two components of the cartridge assembled automatically when the BBC is placed in the blood biochemistry instrument (see WP6). The sensor PCBs (green) are at the top of the image.

WP5: Development and monitoring of Bioartificial Liver Support Unit

WP5 focused on development of a bioreactor technology that addresses the cellular needs of 3D tissue density conditions in a highly physiological environment. An approach was taken which was designed to cultivate human or porcine liver cells within a four-compartment hollow fibre-based bioreactor which exhibited a controlled 3D perfusion environment – the d-LIVER "Bioartificial Liver Support Unit" (BAL). This complex four-compartment bioreactor technology would allow enhanced mass-exchange by counter-current flow perfusion, as well as integral, decentralized oxygenation through gas-permeable capillary membranes (that facilitate long-term culture and storage, in contrast to whole organs which cannot be stored for long periods in a viable state). Thus, this construction would enable close-to-physiological nutrient and oxygen supply to the cells cultured in the extra-capillary space. An important aspect of the technology development was automation of culture and cell viability monitoring using closed-loop control.

WP5 defined the requirements of the multi-parametric sensor system which would be employed for continuous monitoring of cell viability within the BAL. Concepts for the integration of the different sensors were developed and initially realized in 8ml bioreactors. This included sensors for control of perfusion conditions in the BAL (temperature, system pressures, pH and oxygen), mass flow meters for control of gas flow rates, and sensors for assessment of cell viability and functionality (impedance, ammonia). Sensors were successfully integrated and tested in culture experiments. The results showed that changes in cell behaviour could be graded into different states dependent on the toxin concentration. Measures and procedures for cell recovery or culture termination could then be undertaken dependent on the actual state of the bioreactor culture.

These sensor systems were up-scaled in the final year of the project to provide a clinical grade BAL which was then tested successfully using the hepatocyte-like progenitor cells developed in WP8.

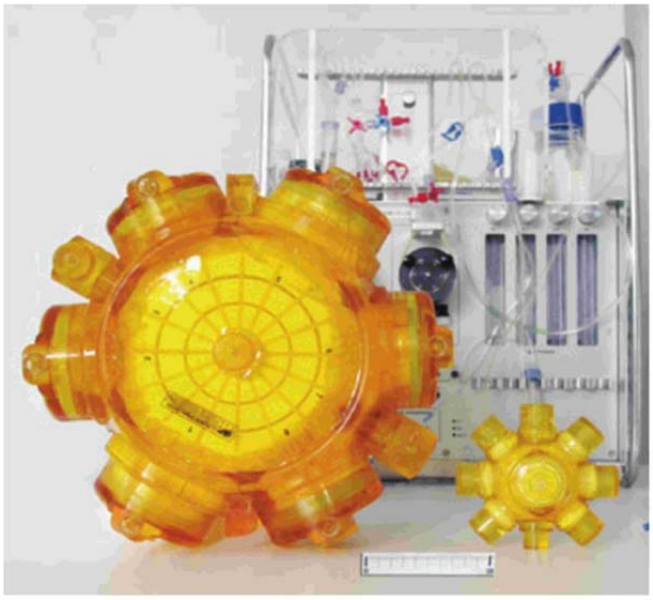

Figure 3: *Bio-artificial liver support system (BAL) showing clinical grade 800ml bioreactor and an 8ml bioreactor for laboratory research.*

WP6: Instrumentation platforms

The objectives of this Workpackage were to develop and build the instrumentation platforms that would serve the requirements of d-LIVER as optimized prototypes for clinical evaluation. One of the key requirements in WP6 was to develop an instrument for the home-care setting that could perform a panel of biochemical analyses from a single finger-prick sample of blood – the so-called Blood Biochemistry Instrument (BBI). Due to the requirement that the BBI be ultimately used by liver patients at home, it had to be simple and easy to use. The only interfaces with the user are a power plug, an on/off button, an Ethernet socket, a Wi-Fi link and a touchscreen. The BBI instrument design included housing, power management, control unit with dedicated software and user interface, electronics allowing controlling all the interfaces with dedicated firmware, and communication aspects. The instrument (Figure 4) was able to host and assemble the BBC (see WP4) which, in turn, housed the sensors developed by WP3. The BBI was designed to control actuators interfacing with the microfluidic cartridge, to perform the driving of the blood sample in the cartridge, to process the signal outputs from the sensors and to then transmit the results wirelessly to the Liver Patient Management System (LPMS) developed in WP7.

Figure 4: Blood Biochemistry Instrument with BBC in place. The action of closing the cover over the BBC automatically assembled both of the cartridge components.

A second element of instrumentation development in WP6 was the development of wearable physiological sensors which are intended to worn on the body to continually measure parameters such as temperature, activity, heart rate and blood pressure where the different sensor functionalities are integrated into one single unit which can transmit data via a Bluetooth Health Device Profile (HDP) to the d-LIVER Personal Health Manager (PHM) which was developed in WP7. As shown in Figure 5, the wearable device consists of an electronic compartment which has an on/off button on the front and two LEDs on upper edge to indicate the status, and a connector slot for the on-body electrodes. On the back side are two push buttons to attach the belt the compartment was designed to be splash protective and could be gently swiped with a soft cloth with water or disinfection agent.

Figure 5: d-LIVER Wearable Device.

WP7: Communications, Patient Management and Decision Support

At the outset of the project it was the aim that WP7 would deliver an advanced web-based information system – the d-LIVER "Liver Patient Management System" (LPMS) – for the monitoring and management of patients with chronic liver conditions in ambulatory and home settings. In addition, it set out to provide the overall communication and security framework for

the d-LIVER platforms with a particular focus on interoperable and open solutions as well as on patient safety and privacy. WP7 analysed the main use case scenarios (see WP1) and specified, developed and delivered the communication and security framework via continuous validation cycles. Furthermore WP7 was designed to develop, in collaboration with the d-LIVER clinical centres, models for decision support and therapy outcome prediction for chronic liver disease patients.

As a major outcome, the LPMS was iteratively developed in response to formal standards to meet patient safety requirements of the planned clinical evaluation studies, resulting in the production of LPMS 3.0. LPMS 3.0 is a laboratory prototype at Technology Readiness Level 4 to 5, which can be utilized to remotely monitor patients and to support the management of complications in patients with chronic liver failure at home; in particular patients with encephalopathy, ascites and cholestatic itch through a telemonitoring solution adapted for liver diseases in combination with a decision support system that guides patients and doctors through the treatment of these complications. As such, this system controls and adapts the dosage of specific drugs with or without confirmation by the physician according to up-to-date health data obtained from the patient. Of relevance is the fact that LPMS communicates with devices according to Continua Health Alliance standards by using the Device Manager. This facilitates the deployment of the system and general purpose monitoring devices, bought by the patients, will be able to interoperate with the LPMS. The Device Manager does not only integrate Continua Health Alliance devices but also is able to integrate non-Continua devices, such as the BBI.

WP8: Progenitor cells for bioartificial liver

The inclusion of WP8 in d-LIVER was important as a programme of "high-risk, high reward" research designed to characterize trans-differentiation of human pancreatic hepatocyte progenitors and to assess hepatic function *in vitro* in the experimental and clinical grade bioartificial liver support units (BALs) developed by WP5.

There is currently considerable effort directed towards generating human hepatocytes from stem cells since these would have both basic science (e.g. drug metabolism and toxicity screening) and clinical (e.g. incorporation into bio-artificial liver devices) applications. However, embryonic stem cells and induced pluripotent stem cells have so far failed in their ability to generate cells with comparable function to human hepatocytes *in vitro* or, at the very least, require efficient (i.e. viral-mediated) forced over-expression of liver transcription factors. One alternative to using stem cells as a source for hepatocytes, is to use progenitor cells. Prior to d-LIVER commencing it had been shown that a rat pancreatic progenitor "B-13" cells appear to be the only cells capable of differentiation into hepatocytes in a highly cost-effective manner, requiring the addition of a simple glucocorticoid hormone treatment. In WP8 the target was to investigate the possibility of generating a cost-effective human equivalent cell line capable of being readily expanded in a simple culture system and converted into functional hepatocytes using a simple regulatory switch. In a major development in the area this goal was achieved and the human equivalent cells shown to be metabolically functional in a clinical grade bioreactor (WP5). A patent application was submitted regarding these cells and their use. The successful outcome of this "high-risk, high reward" Workpackage could therefore have enormous societal benefit by the production of a viable, effective, economical, high quality source of human hepatocytes derived from progenitor cells in sufficient quantity for exploitation in bio-artificial liver devices.

Potential impact and the main dissemination activities and exploitation of results

Potential Impact

The specific project impacts are discussed in detail below. However, in general, these can be summarised as follows:

- Reduced hospitalisation and improved disease management and treatment at the point of need, through more precise assessment of health status.
- Improved quality of life for liver patients.
- Economic benefits for health systems without compromising quality of care.
- Reinforced leadership and innovation of the industry in the area of Personal Health Systems and medical devices.
- Improved links and interaction between patients and doctors facilitating more active participation of patients in care processes.
- More effective bioartificial liver support as a result of having a viable, effective, economical, high quality source of human hepatocytes.
- Demonstrated potential for spin-offs with protected IP through several patent applications.

The liver is a complex organ with various vital functions in synthesis, detoxification and regulation; its failure therefore constitutes a life-threatening condition. Liver failure can either occur without preceding liver disease (acute liver failure), or as decompensation of a chronic liver-related illness.

The only long-term therapy in most cases is orthotopic liver transplantation, unless the liver is able to regenerate. Many patients, especially those who are not listed for high urgency transplantation, may not survive until a suitable donor organ is available, since donor organs are rare. In other cases, contraindications do not permit liver transplantation.

d-LIVER has fundamentally advanced an ICT-enabled system to remotely monitor and manage liver patients in their home, such that patient monitoring is continuous and intervention can be both swift and beneficial, leading to improved patient health and survival along with a significant enhancement of patient quality of life.

The innovative liver patient management system (LPMS) supplied with the sensor and instrumentation systems could lead to a completely new dimension of home care for the patient and a concomitant reduction in morbidity and mortality. The management and therapy of patients with chronic liver disease will thus be taken to a new level. As such, this system can control and adapt the dosage of specific drugs with or without confirmation by the physician according to up-to-date health data obtained from the patient. The LPMS can also alert the patient and the hospital when additional interventions or the next liver support session are required. Complications can be prevented by this strategy and costs conclusively reduced when the patient does not need to be admitted to the hospital.

Potentially, this could also be supplemented by the innovative and functioning bio-artificial liver system based on human progenitor cells which have been developed. This possibility would have an enormous impact on the bio-artificial liver field. Furthermore, it is envisaged that the progenitor cells would have exploitable opportunities in drug discovery, screening and toxicity studies in the pharmaceutical industry.

The success of d-LIVER will enhance the quality of healthcare at a European level and will improve European competitiveness in medical device technology.

Dissemination

Within the first 6 months of the project, a project website www.d-liver.eu was established and this has been maintained throughout the course of the project. The website contains the following public pages:

- A home page describing the aims of the project and hosting project vision, execution and technology development videos
- A partner page with specific links to their relevant websites
- A deliverables page containing any publicly available deliverables and reports
- Pages with specific information for patients and for healthcare professionals – in English, German and Italian
- An events page, detailing events where d-LIVER will be, or has been, presented together with copies of any presentations

In addition, a secure Virtual Research Environment and Filestore were created which contain all confidential deliverable reports, the publication clearance procedures and IPR. Finally, a Twitter account was created and maintained which provided immediate announcements on d-LIVER and related activities.

The dissemination activities in d-LIVER achieved their goals in various ways; by collecting, collating and managing the information developed during the project, by disseminating the information as widely as possible via the production and distribution of press releases, newsletters, project flyers and technology updates throughout the course of the project. More specifically, these goals have been achieved through the organisation of Showcase Workshops in conjunction with a strong presence at major Trade Fairs and exhibitions such as AACC, MedTec, Mobile World Congress and Korea Eureka Day as well as a number of presentations and posters at major international conferences e.g. EASL and BASL and publication of articles in high quality scientific journals. As part of these activities an assessment of a Business Development Framework, including a Freedom to Operate analysis, has allowed the production of the Final Exploitation Plan and Technology Roadmap for the future commercialization of d-LIVER results.

The concepts and ideas behind the d-LIVER project have also been disseminated on a broader level to general audiences through video interviews about d-LIVER which are available on the project website, Futuris and YouTube. Finally, news articles were published on the Futuris and Cordis websites and in national and local newspapers describing the concepts behind the project and its vision for the future of remote monitoring and management of chronic liver disease.

Exploitation

The d-LIVER systems can be viewed as disruptive technologies which could confer new breakthroughs in the world of information-enabled monitoring and management tools. As a consequence it was of particular importance to the project to undertake a coordinated effort to understand the marketplace, the barriers to entry and the competitive position, with the ultimate aim of producing a confidential d-LIVER Final Exploitation Plan and Technology Roadmap. IP protection has been continued for critical components of the systems, including aspects of a Freedom to Operate analysis in line with recommendations at both the systems and component levels. In order to carry this out effectively, d-LIVER needed to:

- Investigate how d-LIVER could impact the management of chronic liver disease and improve patient quality of life
- Assess how d-LIVER could address the economic burden of chronic liver disease
- Determine the most appropriate methods for commercial exploitation from the laboratory, through to remote management and therapy at the point of need
- Investigate market potential in the targeted clinical application area and for applications outside the area investigated in the project, bearing in mind that the d-LIVER approach might be regarded as a series of platform technologies

The Final Exploitation Plan was prepared which contained an overview of the potential for d-LIVER monitoring and bioartificial liver support systems, along with details on the category drivers and competitors. Some of the main issues that need to be overcome were discussed and potential business models presented. Final commercialization recommendations were included and these, along with details of exploitation plans, were presented to the European Commission at the final Technical Review.

Address of the project public website

The address of the project website is www.d-liver.eu. The website will remain active for at least 2 years after the end of the project.

2. Use and Dissemination of Foreground

Section A (public)

The table below lists all of the scientific (peer reviewed) publications relating to the foreground of the project, starting with the most important ones.

TEMPLATE A1: LIST OF SCIENTIFIC (PEER REVIEWED) PUBLICATIONS, STARTING WITH THE MOST IMPORTANT ONES

No.	Title	Main author	Title of the periodical or the series	Number, date or frequency	Publisher	Place of publication	Year of publication	Relevant pages	Permanent identifiers[1] (if available)	Is/Will open access[2] provided to this publication?
1	Adult human exocrine pancreas differentiation to hepatocytes – potential source of a human hepatocyte progenitor for use in toxicology research		Toxicology Research				2013		http://dx.doi.org/10.1039/C2TX20061A	Yes
2	The B 13 hepatocyte progenitor cell resists pluripotency induction and differentiation to non-hepatocyte cells		Toxicology Research				2013		http://dx.doi.org/10.1039/C3TX50030F	Yes
3	Utility of B-13 Progenitor-Derived Hepatocytes in Hepatotoxicity and Genotoxicity Studies		Toxicological Sciences				2013		http://dx.doi.org/10.1093/toxsci/kft258	Yes
4	Health related quality of life in people with advanced chronic liver disease		J. Hepatology				2014		http://dx.doi.org/10.1016/j.jhep.2014.06.034	Yes
5	Enzymatic liver function capacity correlates with disease severity of patients with liver cirrhosis: A		Digestive Diseases and Sciences				2014		http://dx.doi.org/10.1007/s10620-014-3250-z	No

[1] A permanent identifier should be a persistent link to the published version full text if open access or abstract if article is pay per view) or to the final manuscript accepted for publication (link to article in repository).

[2] Open Access is defined as free of charge access for anyone via Internet. Please answer "yes" if the open access to the publication is already established and also if the embargo period for open access is not yet over but you intend to establish open access afterwards.

	study with the LiMAx test									
6	A novel personal health system with integrated decision support and guidance for the management of chronic liver disease		Proc. 25th European Medical Informatics Conference (MIE2014), Studies in Health Technology and Informatics	205	IOS Press		2014	83-87	http://dx.doi.org/10.3233/978-1-61499-432-9-83	Yes
7	Progenitor-derived hepatocyte-like (B-13/H) cells metabolise 1' hydroxyestragole to a genotoxic species – An animal donor-free in vitro screen for phase II activated genotoxins		Toxicology Letters				2014		http://dx.doi.org/10.1016/j.toxlet.2014.06.204	No
8	Improving expression levels of transporters in progenitor-derived hepatocyte-like (B-13/H) cells		Toxicology Letters				2014		http://dx.doi.org/10.1016/j.toxlet.2014.06.499	No
9	Co-culture of B-13 hepatocyte progenitors with liver myofibroblasts promotes progenitor WNT signalling repression in response to glucocorticoids and enhances their transdifferentiation towards hepatocyte-like cells		Toxicology Letters				2014		http://dx.doi.org/10.1016/j.toxlet.2014.06.488	No
10	The glucocorticoid-dependent conversion of the B-13 progenitor cell into hepatocyte-like (B-13/H) cells is dependent on a short exposure to glucocorticoid and epigenetic alterations		Toxicology Letters				2014		http://dx.doi.org/10.1016/j.toxlet.2014.06.495	No
11	Predictors of quality of life in patients evaluated for liver transplantation		Clinical Transplantation				2014		http://dx.doi.org/10.1111/ctr.12426	No
12	Prognostic value of enzymatic liver function for the estimation of short-term survival of liver transplant candidates: a		Transplant International				2014		http://dx.doi.org/10.1111/tri.12441	No

	prospective study with the LiMAx test									
13	An expandable donor-free supply of functional hepatocytes for Toxicology		Toxicology Research				2015		http://dx.doi.org/10.1039/C4TX00214H	No

The table below lists all of the other dissemination activities (publications, conferences, workshops, web sites/applications, press releases, flyers, articles published in the popular press, videos, media briefings, presentations, exhibitions, thesis, interviews, films, TV clips, posters).

TEMPLATE A2: LIST OF DISSEMINATION ACTIVITIES

No.	Type of activities[3]	Main leader	Title	Date/Period	Place	Type of audience[4]	Size of audience	Countries addressed
1	*Web*	*iXscient*	*Project website (www.d-liver.eu)*	*1st October 2011 to date*	-	*General public*	-	Worldwide
2	Other	UNEW	Public consultation and dissemination organised by LIVErNORTH	Continuous	Newcastle, UK	General public, patient support groups	-	UK
3	Other	UNEW	Lecture to Medical Biotechnology module of Biomedical Sciences degree	3/12/11	Newcastle, UK	Higher education	100	UK
4	Other	UNEW	Lecture to MRes module Nanomaterials in Healthcare	12/12/11	Newcastle, UK	Higher education	20	UK
5	Press	FhG-IBMT	d-LIVER press release	16/2/12	-	General public	-	Germany
6	Flyer	4M2C	d-LIVER project flyer	11/6/12	-	General public	-	Worldwide
7	Oral presentation at the 18th World MicroMachine Summit	4M2C	Discussion of "d-LIVER activities"	23-26/4/12	Hsinchu, Taiwan	Scientific community	100	Worldwide
8	Oral presentation at the Biotest Wilsede-Workshop für experimentelle und klinische Lebertransplantation und Hepatologie	Charité	d-LIVER - Ein neuartiges Behandlungskonzept für Patienten mit chronischer Lebererkrankung	21-23/6/12	Kiel, Germany	Clinicians	50	Germany
9	Oral presentation at COMS 2012 conference	4M2C	d-LIVER FP7 project	24-27/6/12	Tønsberg, Vestvold, Norway	Scientific community, industry	300	Worldwide
10	Seminar at Integrative Toxicology Training Partnership meeting	UNEW	Progenitor cells as a source for hepatocytes	28/6/12	Rutland, UK	Scientific community	36	UK

[3] A drop down list allows choosing the dissemination activity: publications, conferences, workshops, web, press releases, flyers, articles published in the popular press, videos, media briefings, presentations, exhibitions, thesis, interviews, films, TV clips, posters, Other.

[4] A drop down list allows choosing the type of public: Scientific Community (higher education, Research), Industry, Civil Society, Policy makers, Medias, Other ('multiple choices' is possible).

11	Oral presentation at the 24th International Congress of The Transplantation Society	Charité	d-LIVER - A new approach for bridging therapy to transplantation of the chronic liver failure patient	18/7/12	Berlin, Germany	Scientific community, clinicians	-	Worldwide
12	Poster presentation at the 24th International Congress of The Transplantation Society	Charité	d-LIVER - A new approach for bridging therapy to transplantation of the chronic liver failure patient	18/7/12	Berlin, Germany	Scientific community, clinicians	-	Worldwide
13	Poster presentation at XVII Trobada Transfronterera de sensors i biosensors	URV	d-LIVER biosensors	20-21/9/12	Tarragona, Spain	Scientific community	100	Spain
14	Oral presentation at EC Proposer's Day	FhG-IBMT	d-LIVER overview	26-27/9/12	Warsaw, Poland	Scientific community	100	Europe
15	Oral presentation and discussion at Iran Nano Forum	4M2C	d-LIVER activities	6/10/12	Tehran, Iran	Scientific community	200	Worldwide
16	Oral presentation and discussion at Ikerlan workshop	4M2C	d-LIVER activities	18/10/12	Mondragon, Spain	Scientific community	12	Spain
17	Poster presentation at The Liver Meeting 2012 – 63rd Annual Meeting of the American Association for the Study of Liver Disease	Charité	A potential solution for outpatient management of chronic liver failure	8/11/12	Boston, USA	Clinicians	-	Worldwide
18	Oral presentation and discussion at ETP MINAM workshop	4M2C	d-LIVER activities	8-9/11/12	Brussels, Belgium	Scientific community, industry	60	Europe
19	Seminar at Edinburgh University	UNEW	Stem cells	9/11/12	Edinburgh, UK	Scientific community	20	UK
20	Oral presentation in bilateral meetings in the scope of the Healthcare Brokerage Event, MEDICA 2012	AT4	d-LIVER overview	14-17/11/12	Düsseldorf, Germany	Industry	12	Worldwide
21	Closed workshop on Stem Cells in Drug Discovery and Development	UNEW	d-LIVER activities	21-23/1/13	Newcastle, UK	Scientific community	30	UK, India
22	Booth display and presentation at the Mobile World Congress	AT4	d-LIVER overview	25-28/2/13	Barcelona, Spain	Industry	50+	Worldwide
23	Poster presentation at the 48th Annual Meeting of the European Association for the Study of the Liver (EASL)	UNEW, Charité	-	24-28/4/13	Amsterdam, The Netherlands	Clinicians	1000	Worldwide
24	Interviews given to CONSOLIDER project	UNEW, Charité, iXscient	Civil society participation in research	28/5/13	-	General public	-	Europe
25	Press	SINTEF	d-LIVER press release	June 2013	Oslo, Norway	General public	-	Norway
26	Poster presentation at the Gordon Research	CEA-	Blood clotting sensor	9-14/6/13	Lucca, Italy	Scientific	170	Worldwide

	Conference (GRC)	LETI				community		
27	Web press release	SINTEF	An artificial liver stationed at the hospital can help people with chronic liver failure to live longer, better lives	15/6/13	Oslo, Norway	General public	-	Scandinavia
28	Oral presentation at the LETI Innovation days	CEA-LETI	Ionic sensors	25-28/6/13	Grenoble, France	Scientific community	300	Europe
29	Oral presentation at Bath University	UNEW	Adenoviral-liver transcription factors	20/8/13	Bath, UK	Scientific community, clinicians	-	UK
30	Oral presentation at COMS 2013 conference	4M2C	d-LIVER FP7 project	25-28/8/13	Enschede, The Netherlands	Scientific community, industry	350	Worldwide
31	Detailed d-LIVER project profile produced and published for ePractice.eu	UNEW	d-LIVER: ICT-enabled, cellular artificial liver system incorporating personalized patient management and support	30/8/13	-	General public	-	Europe
32	Seminar at MRC Toxicology Unit, Leicester University	UNEW	Molecular and cellular responses in liver cell injury	25/9/13	Leicester, UK	Scientific community	50	UK
33	Two oral presentations and poster at MicroNanoBioSystems (MNBS) EC Concertation meeting and EPoSS event	4M2C	-	24-27/9/13	Cork, Ireland	Scientific community	180	Europe
34	1st d-LIVER video	UNEW	d-LIVER clinical need	4/10/13	Newcastle, UK	General public	-	Worldwide
35	Presentation at Continua Alliance webinar	AT4	Continua Ensemble Connector, a practical application of IT for Health Information Exchange	12-14/10/13	-	Scientific community	-	Worldwide
36	Article in Gemini – SINTEF popular press magazine	SINTEF	Artificial liver support for the chronically ill	October 2013	-	Scientific community	7900	Worldwide
37	Seminar at King Saud University	UNEW	Progenitor cells	11/12/13	Riyadh, Saudi Arabia	Scientific community	100	Saudi Arabia
38	Presentation at IVAM meeting	4M2C	d-LIVER overview	16/12/13	Dortmund, Germany	Scientific community	10	Germany
39	Oral presentation at the 30th Annual Meeting of the German Association for the Study of the Liver (GASL)	UNEW, Charité, SCS	Dexamethasone induced hepatic differentiation of rat pancreatic progenitor cells (B-13) in a 3D multicompartment bioreactor system	24-25/1/14	Tübingen, Germany	Clinicians	250	Germany
40	Booth display and presentation at the Mobile	AT4	d-LIVER overview	24-26/2/14	Barcelona, Spain	Industry	5000+	Worldwide

	World Congress							
41	Poster presentation at the 49th Annual Meeting of the European Association for the Study of the Liver (EASL)	UNEW	Resource use associated with hepatic encephalopathy in patients with liver disease	11/4/14	London, UK	Clinicians	9000	Worldwide
42	Oral presentation at IEEE EMBS BHI2014 Conference	SINTEF	Development of a wearable multisensor device enabling continuous monitoring of vital signs and activity	2/6/14	Valencia, Spain	Scientific community	30	Worldwide
43	Oral presentation at Norwegian Association for Automation Annual Conference for Health and Medical Technology	SINTEF	d-LIVER overview	12/6/14	Norway	Scientific community	50	Norway
44	Poster presentation at the British Society of Gastroenterology Annual General Meeting	UNEW	Development And Validation Of The Newcastle Patient Reported Ascites Measure	16-19/6/14	Manchester, UK	Clinicians	4000	Worldwide
45	Poster presentation at the British Society of Gastroenterology Annual General Meeting	UNEW	Associations Between Healthcare Resource Utilisation And Health-related Quality Of Life In Cirrhosis	16-19/6/14	Manchester, UK	Clinicians	4000	Worldwide
46	Press	FhG-IBMT	Fraunhofer press release about d-LIVER results	1/7/14	-	General public	-	Worldwide
47	Oral presentation at the 25th European Medical Informatics Conference (MIE2014)	FhG-IBMT	A novel personal health system with integrated decision support and guidance for the management of chronic liver disease	1/9/14	Istanbul, Turkey	Scientific community	-	Worldwide
48	Oral presentation at the 16th Symposium of the International Society for Hepatic Encephalopathy and Nitrogen metabolism (ISHEN)	UNEW	Outcome measures in HE: health economics in clinical trials	13/9/14	Ascot, UK	Scientific, community, clinicians	100	Worldwide
49	Poster presentation at the British Association for the Study of the Liver (BASL) Annual Meeting	UNEW	Health Related Quality of Life of Patients with Previous Overt HE Compared to Age and Sex Matched Cirrhotic Controls	15-17/9/14	Newcastle, UK	Clinicians	600	Europe
50	Oral presentation at the 41st Annual Congress of the European Society for Artificial Organs (ESAO)	Various	Integration of multi-parametric sensor systems in bioartificial liver support system	17-20/9/14	Rome, Italy	Scientific community, clinicians	500	Worldwide
51	E-mail survey to members of the European Association for the Study of the Liver (EASL)	UNEW	Opinions of health professionals on d-LIVER	September 2014	-	Clinicians	500	Europe
52	Oral presentation at the Entwicklerforum Medizinelektronik 2014	FhG-IBMT	Eine prozessorientierte Telemedizinplattform zum	8-9/10/14	Munich, Germany	Scientific community	200	Germany

			Management von Patienten mit chronischen Lebererkrankungen					
53	Poster presentation at the 23rd annual meeting of the German Transplantation Society	Charité	Lebensqualität von Patienten mit chronischer Lebererkrankung auf der Transplantation-swarteliste – Verbesserung des Patientenmanagement	16-18/10/14	Mannheim, Germany	Clinicians	300	Germany
54	Euronews video on d LIVER published on Futuris website	Various	d-LIVER overview	3/11/14	-	General public	-	Europe
55	Article accompanying Euronews video published on Cordis	Various	d-LIVER overview	4/11/14	-	Scientific community, General public	-	Europe
56	Interview	ICH	Malattie del fegato, nasce d LIVER: Live longer, live better	25/11/14	Milan, Italy	Scientific community, clinicians	-	Italy
57	2nd stage d-LIVER video	UNEW	d-LIVER technology	4/12/14	-	General public	-	Europe
58	Article in MINA-NEWS	CEA-LETI	Ionic sensors	December 2014	Grenoble, France	Scientific community	-	France
59	Article in “Les défis du CEA”	CEA-LETI	d-LIVER overview	February 2015	Grenoble, France	Scientific community	-	France
60	Booth display and presentation at the Mobile World Congress	AT4	d-LIVER overview	2-5/3/15	Barcelona, Spain	Industry	-	Worldwide
61	d-LIVER instrument exhibited at the German Biosensor Symposium	FhG-ICT-IMM	-	13/3/15	Munich, Germany	Scientific community, industry	250	Germany
62	Invited talk at “Sensors in Medicine 2015”	URV	Sensors for Monitoring of Liver and Kidney Function	22-24/3/15	London, UK	Scientific community, clinicians, industry	-	Europe
63	d-LIVER instrument and fluidic cartridges exhibited at MedTec 2015	FhG-ICT-IMM	-	21-23/4/15	Stuttgart, Germany	Scientific community, industry	-	Worldwide
64	Flyer	4M2C	Updated d-LIVER project flyer	5/5/15	-	General public	-	Worldwide
65	Workshop	Various	d-LIVER Showcase Workshop	27/5/15	Milan, Italy	Scientific community, industry	49	Europe
66	Video by the UK National Institute for Health Research (NIHR)	UNEW	-	6/6/15	-	Scientific community,	-	UK

						industry		
67	Demonstration and display of wearable device during SINTEF 65 year anniversary day	SINTEF	-	11/6/15	Oslo, Norway	Scientific community	1600	Norway

3. Report on Social Implications

A General Information *(completed automatically when **Grant Agreement number** is entered.*

Grant Agreement Number:	287596
Title of Project:	ICT-enabled, cellular artificial liver system incorporating personalized patient management and support
Name and Title of Coordinator:	Prof. Calum McNeil, Newcastle University

B Ethics

1. Did your project undergo an Ethics Review (and/or Screening)? • If Yes: have you described the progress of compliance with the relevant Ethics Review/Screening Requirements in the frame of the periodic/final project reports? Special Reminder: the progress of compliance with the Ethics Review/Screening Requirements should be described in the Period/Final Project Reports under the Section 3.2.2 *'Work Progress and Achievements'*	***YES*** ***YES***
2. Please indicate whether your project involved any of the following issues (tick box) :	
RESEARCH ON HUMANS	
• Did the project involve children?	
• Did the project involve patients?	✓
• Did the project involve persons not able to give consent?	
• Did the project involve adult healthy volunteers?	
• Did the project involve Human genetic material?	
• Did the project involve Human biological samples?	✓
• Did the project involve Human data collection?	✓
RESEARCH ON HUMAN EMBRYO/FOETUS	
• Did the project involve Human Embryos?	
• Did the project involve Human Foetal Tissue / Cells?	
• Did the project involve Human Embryonic Stem Cells (hESCs)?	
• Did the project on human Embryonic Stem Cells involve cells in culture?	
• Did the project on human Embryonic Stem Cells involve the derivation of cells from Embryos?	
PRIVACY	
• Did the project involve processing of genetic information or personal data (e.g. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction)?	
• Did the project involve tracking the location or observation of people?	
RESEARCH ON ANIMALS	
• Did the project involve research on animals?	
• Were those animals transgenic small laboratory animals?	
• Were those animals transgenic farm animals?	
• Were those animals cloned farm animals?	
• Were those animals non-human primates?	
RESEARCH INVOLVING DEVELOPING COUNTRIES	
• Did the project involve the use of local resources (genetic, animal, plant etc)?	
• Was the project of benefit to local community (capacity building, access to healthcare, education tc..)?	
DUAL USE	
• Research having direct military use	
• Research having the potential for terrorist abuse	

C Workforce Statistics

3. Workforce statistics for the project: Please indicate in the table below the number of people who worked on the project (on a headcount basis).

Type of Position	Number of Women	Number of Men
Scientific Coordinator	1	3
Work package leaders	1	9
Experienced researchers (i.e. PhD holders)	14	33
PhD Students	2	4
Other	21	33

4. How many additional researchers (in companies and universities) were recruited specifically for this project?	17
Of which, indicate the number of men:	10

D Gender Aspects

5. Did you carry out specific Gender Equality Actions under the project?

○ Yes
● No

6. Which of the following actions did you carry out and how effective were they?

		Not at all effective				Very effective
❑	Design and implement an equal opportunity policy	○	○	○	○	●
❑	Set targets to achieve a gender balance in the workforce	○	○	○	○	○
❑	Organise conferences and workshops on gender	○	○	○	○	○
❑	Actions to improve work-life balance	○	○	○	○	○
○	Other:					

7. Was there a gender dimension associated with the research content – i.e. wherever people were the focus of the research as, for example, consumers, users, patients or in trials, was the issue of gender considered and addressed?

● Yes- please specify

Statistical analyses in clinical studies included gender.

○ No

E Synergies with Science Education

8. Did your project involve working with students and/or school pupils (e.g. open days, participation in science festivals and events, prizes/competitions or joint projects)?

● Yes- please specify

Several partners organised events targeted at students and school pupils.

○ No

9. Did the project generate any science education material (e.g. kits, websites, explanatory booklets, DVDs)?

● Yes- please specify

Education materials for patients and healthcare professionals were placed on the project website. Educational video material has also been made available through YouTube.

○ No

F Interdisciplinarity

10. Which disciplines (see list below) are involved in your project?

Main discipline[5]: 3.2

Associated discipline[5]: 1.1

Associated discipline[5]: 2.2

G Engaging with Civil society and policy makers

11a Did your project engage with societal actors beyond the research community? *(if 'No', go to Question 14)*

● Yes
○ No

11b If yes, did you engage with citizens (citizens' panels / juries) or organised civil society (NGOs, patients' groups etc.)?

○ No
○ Yes- in determining what research should be performed
○ Yes - in implementing the research
● Yes, in communicating /disseminating / using the results of the project

[5] Insert number from list below (Frascati Manual).

11c In doing so, did your project involve actors whose role is mainly to organise the dialogue with citizens and organised civil society (e.g. professional mediator; communication company, science museums)?	○ ●	Yes No

12. Did you engage with government / public bodies or policy makers (including international organisations)

○	No
○	Yes- in framing the research agenda
○	Yes - in implementing the research agenda
●	Yes, in communicating /disseminating / using the results of the project

13a Will the project generate outputs (expertise or scientific advice) which could be used by policy makers?

○	Yes – as a **primary** objective (please indicate areas below- multiple answers possible)
●	Yes – as a **secondary** objective (please indicate areas below - multiple answer possible)
○	No

13b If Yes, in which fields?

Agriculture		Energy		Human rights	
Audiovisual and Media		Enlargement		Information Society	
Budget		Enterprise		Institutional affairs	
Competition		Environment		Internal Market	
Consumers		External Relations		Justice, freedom and security	
Culture		External Trade		Public Health	✓
Customs		Fisheries and Maritime Affairs		Regional Policy	
Development Economic and Monetary Affairs		Food Safety		Research and Innovation	✓
Education, Training, Youth		Foreign and Security Policy		Space	
Employment and Social Affairs		Fraud		Taxation	
		Humanitarian aid		Transport	

13c If Yes, at which level?

- ○ Local / regional levels
- ○ National level
- ● European level
- ○ International level

H Use and dissemination

14. How many Articles were published/accepted for publication in peer-reviewed journals?	**13**
To how many of these is open access[6] provided?	
How many of these are published in open access journals?	**5**
How many of these are published in open repositories?	**0**
To how many of these is open access not provided?	**8**
Please check all applicable reasons for not providing open access:	
✓ publisher's licensing agreement would not permit publishing in a repository ❑ no suitable repository available ✓ no suitable open access journal available ✓ no funds available to publish in an open access journal ❑ lack of time and resources ❑ lack of information on open access ❑ other[7]: ……	

15. How many new patent applications ('priority filings') have been made? *("Technologically unique": multiple applications for the same invention in different jurisdictions should be counted as just one application of grant).*		**7**
16. Indicate how many of the following Intellectual Property Rights were applied for (give number in each box).	Trademark	**0**
	Registered design	**0**
	Other	**0**
17. How many spin-off companies were created / are planned as a direct result of the project?		**Too early to say**
Indicate the approximate number of additional jobs in these companies:		

18. Please indicate whether your project has a potential impact on employment, in comparison with the situation before your project:

✓	Increase in employment, or	✓	In small & medium-sized enterprises
✓	Safeguard employment, or	✓	In large companies
❑	Decrease in employment,	❑	None of the above / not relevant to the project
❑	Difficult to estimate / not possible to quantify		

19. For your project partnership please estimate the employment effect resulting directly from your participation in Full Time Equivalent (*FTE = one person working fulltime for a year*) jobs: Difficult to estimate / not possible to quantify	*Indicate figure:* **91**

[6] Open Access is defined as free of charge access for anyone via Internet.
[7] For instance: classification for security project.

I Media and Communication to the general public

20. As part of the project, were any of the beneficiaries professionals in communication or media relations?

○ Yes ● No

21. As part of the project, have any beneficiaries received professional media / communication training / advice to improve communication with the general public?

● Yes ○ No

22 Which of the following have been used to communicate information about your project to the general public, or have resulted from your project?

✓	Press Release	✓	Coverage in specialist press
❑	Media briefing	✓	Coverage in general (non-specialist) press
✓	TV coverage / report	✓	Coverage in national press
✓	Radio coverage / report	❑	Coverage in international press
✓	Brochures /posters / flyers	✓	Website for the general public / internet
✓	DVD /Film /Multimedia	❑	Event targeting general public (festival, conference, exhibition, science café)

23 In which languages are the information products for the general public produced?

✓	Language of the coordinator		English, German, Italian
✓	Other language(s)		

***Question F-10*:** Classification of Scientific Disciplines according to the Frascati Manual 2002 (Proposed Standard Practice for Surveys on Research and Experimental Development, OECD 2002):

FIELDS OF SCIENCE AND TECHNOLOGY

1. NATURAL SCIENCES

1.1 Mathematics and computer sciences [mathematics and other allied fields: computer sciences and other allied subjects (software development only; hardware development should be classified in the engineering fields)]

1.2 Physical sciences (astronomy and space sciences, physics and other allied subjects)

1.3 Chemical sciences (chemistry, other allied subjects)

1.4 Earth and related environmental sciences (geology, geophysics, mineralogy, physical geography and other geosciences, meteorology and other atmospheric sciences including climatic research, oceanography, vulcanology, palaeoecology, other allied sciences)

1.5 Biological sciences (biology, botany, bacteriology, microbiology, zoology, entomology, genetics, biochemistry, biophysics, other allied sciences, excluding clinical and veterinary sciences)

2 ENGINEERING AND TECHNOLOGY

2.1 Civil engineering (architecture engineering, building science and engineering, construction engineering, municipal and structural engineering and other allied subjects)

2.2 Electrical engineering, electronics [electrical engineering, electronics, communication engineering and systems, computer engineering (hardware only) and other allied subjects]

2.3. Other engineering sciences (such as chemical, aeronautical and space, mechanical, metallurgical and materials engineering, and their specialised subdivisions; forest products; applied sciences such as geodesy, industrial chemistry, etc.; the science and technology of food production; specialised

technologies of interdisciplinary fields, e.g. systems analysis, metallurgy, mining, textile technology and other applied subjects)

3. MEDICAL SCIENCES

3.1 Basic medicine (anatomy, cytology, physiology, genetics, pharmacy, pharmacology, toxicology, immunology and immunohaematology, clinical chemistry, clinical microbiology, pathology)

3.2 Clinical medicine (anaesthesiology, paediatrics, obstetrics and gynaecology, internal medicine, surgery, dentistry, neurology, psychiatry, radiology, therapeutics, otorhinolaryngology, ophthalmology)

3.3 Health sciences (public health services, social medicine, hygiene, nursing, epidemiology)

4. AGRICULTURAL SCIENCES

4.1 Agriculture, forestry, fisheries and allied sciences (agronomy, animal husbandry, fisheries, forestry, horticulture, other allied subjects)

4.2 Veterinary medicine

5. SOCIAL SCIENCES

5.1 Psychology

5.2 Economics

5.3 Educational sciences (education and training and other allied subjects)

5.4 Other social sciences [anthropology (social and cultural) and ethnology, demography, geography (human, economic and social), town and country planning, management, law, linguistics, political sciences, sociology, organisation and methods, miscellaneous social sciences and interdisciplinary , methodological and historical S1T activities relating to subjects in this group. Physical anthropology, physical geography and psychophysiology should normally be classified with the natural sciences].

6. HUMANITIES

6.1 History (history, prehistory and history, together with auxiliary historical disciplines such as archaeology, numismatics, palaeography, genealogy, etc.)

6.2 Languages and literature (ancient and modern)

6.3 Other humanities [philosophy (including the history of science and technology) arts, history of art, art criticism, painting, sculpture, musicology, dramatic art excluding artistic "research" of any kind, religion, theology, other fields and subjects pertaining to the humanities, methodological, historical and other S1T activities relating to the subjects in this group]