5th Concertation and Consultation Workshop on Micro-Nano-Bio Convergence Systems MNBS 2011,

Special topic "The Road to Commercialization"

April 5-6, 2011
Arrasate-Mondragón, Gipuzkoa (Spain)

Report

Rapporteurs: Paul Smit, Raymond Campagnolo
Contact: Andreas Lymberis (andreas.lymberis@ec.europa.eu)
Javier Bonal (Francisco.bonal-villanova@ec.europa.eu)

1. Executive Summary

The objectives of this workshop were to encourage the diffusion and exchange of information on the development of science and technology in MNBS, Micro-Nano-Bio Convergence Systems, to identify synergies and possible collaborations to tackle issues that cover the full value chain from R&D to exploitation, and to reach common understanding of the challenges and topics for further R&D. The program is in Annex I.

The focus was on the road to commercialization and addressed the question of how to transform R&D results into business opportunities, to improve the return on investment of EC funding. The workshop was the best attended ever and saw over 100 participants from across Europe, who represented all 17 running FP7 projects as well as finished FP6 projects. For the list of participants see Annex II.

The Projects covered two broad areas, i.e. miniaturized in-vitro diagnostics systems, also known as "labs-on-a-chip" or LOCs for advanced Point-Of-Care systems, and micro-systems that interact with the body such as implantable devices that support or restore body function, high precision surgical robots and targeted drug delivery systems. Such systems address broad unmet needs in healthcare, and serve fast growing markets which are estimated to be around € 16 bln, growing at 25% a year. Key note speeches were held by Andreas Lymberis, European Commission, on the MNBS program and the broader EU agenda, Jean-Philippe Leclercq, Yole Development and COWIN, on the commercialization of R&D projects, and Maria Aguirre from the Biobasque Agency on the Basque Country development in the area of micro-nano bio systems. COWIN, the coordination consortium on commercialization, which is funded as a FP7 Coordination and Support Action, held 25 one-to-one meetings in a parallel session. In addition to project progress reports, the impact of regulation and lessons learned from successful market introductions were discussed as case studies.

Progress

The projects differ widely in the risks faced in terms of technology, business development and market readiness. While in many projects technological challenges are being overcome, system integration of the many sub-modules consistently appears to pose one of the biggest technology challenges.
From a portfolio perspective, a balanced portfolio would see a mixture of risk-reward projects, ranging from low-risk, low-reward to high-risk, high-reward. Although practically all projects developed platforms that can be used for a range of applications, for successful commercialization the choice of the first product and application is crucial. For a number of projects such choices have been made. The projects currently in the portfolio can be characterized in order of increasing risk as:

- Breakthroughs on existing platforms in a mature business environment
- New–to-the-world in a mature business environment
- New-to-the-world in a new business environment

The presence of large or medium size companies obviously mitigates the risk of commercial failure, while new-to-the world concept has the highest risk and potentially the biggest reward in terms of financial success and employment. Some projects have not yet defined their first product and application and were advised to do this as soon as possible. Many projects are in the third category and will require consistent and intensive support on the road to commercialization.

For a successful and competitive industry to emerge, a variety of SME[1]s need to develop themselves along the supply value chain, and the beginning of such a development could be witnessed during the workshop. Industrial participants pointed out that they saw a lack of consistent and intense patent deposition as a major concern on the road to commercialization. Early success is achieved in the ultrasound transducer industry, where European companies have taken the lead in a new class of therapeutic transducers.

Consultation outcome

It became clear that 4 years is too short a period for a greenfield MNBS project to build a system from new concepts and have it tested and validated for the healthcare market. It was mentioned that in France funding is provided up to regulatory approval, i.e. CE marking. Stopping a successful project in the midst of its development bears a significant risk of value destruction.
As the projects develop and start-up companies are launched, it becomes clear that this fledgling industry needs to build a deeper understanding of the clinical value chain, i.e. the context is which the products are used, regulatory approval and reimbursement. System integration, sample preparation, sensitivity repetitiveness and reproducibility remain key challenges. In addition more business opportunities can be created through a process to define common and open standards.

Technologies such as Lab-On-Chip would be easier to deploy in less heavily regulated sectors than healthcare (e.g. Food, environment,); after the technology has been proven through market acceptance and revenue creation, it could be extended to healthcare.

[1] SME: Small and Medium Enterprise

2. Objectives

The 5th annual Concertation and Consultation workshop on Micro-Nano-Bio Convergence Systems, MNBS, was held in Mondragon, northern Spain, and co-organised by the European Commission and IKERLAN-IK4, a private, non-profit Technological Research Centre who also hosted the meeting. About 100 participants met to discuss the progress and outlook of this cluster of EC-funded projects. Specifically, the objectives of this workshop were:

- to encourage the diffusion and exchange of information on the development of science and technology
- to identify synergies and possible collaborations to tackle issues covering the full value chain from R&D to exploitation
- to reach common understanding of the challenges and topics for further R&D

The focus was on the road to commercialization and addressed the question of how to change R&D results into business opportunities, to improve the return on investment of EC funding.
In the workshop past FP6 and ongoing FP7 projects were presented, as well as invited contributions. The program and the list of participants can be found as Annexes I and II.

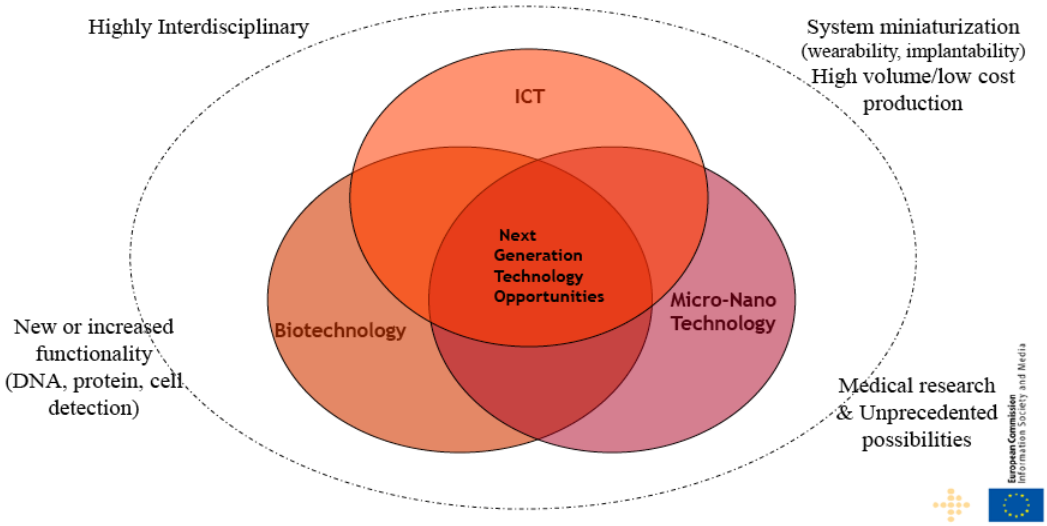
3. Introduction

The capacity to research, develop, manufacture and sell systems that employ components based on nano and micro structures with biological functionality, and are capable of ubiquitously sharing information through networks, is at the forefront of worldwide economical competition. A wave of new materials, processes and technologies is building up that enable highly integrated, miniaturized and compact systems to be engineered. The fruits of these efforts can be used in many areas, such as biomedicine, transport, telecommunications, , safety, the environment, smart textile and others.

These fast technology developments are also at the heart of the explosive growth in Life Sciences, which is leading to an ever increasing understanding of life at the sub-cellular and molecular level. By bringing these parallel developments to healthcare, ultrafast and sensitive systems can be developed to diagnose diseases with high accuracy and speed, and to support and improve body functions, or to replace lost functionality. Such systems will help to diagnose and treat the world's major and orphan diseases with better outcomes and at lower costs than previously deemed possible.. It could make a substantial contribution to bring healthcare expenditures under control and increase its productivity. At 10% of the world's GDP and growing at 6% per year governments around the world are struggling to keep healthcare equitable to their citizens.[2].

[2] Price Waterhouse Coopers, HealthCast 2020: Creating a Sustainable Future, 2006

The MNBS group aims to speed up the convergence of micro- and nano technology with the Life Sciences and accelerate the development of highly integrated diagnostic, monitoring and therapeutics devices.

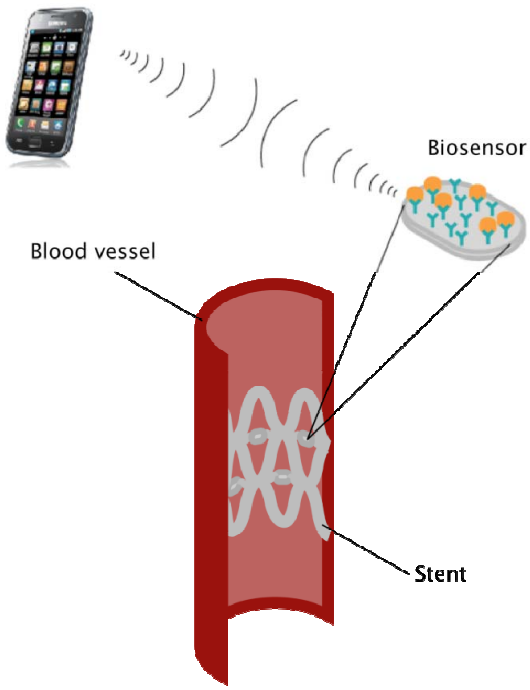


Relationship between converging knowledge areas
Source: Andreas Lymberis, European Commission

For diagnostics highly integrated, compact devices are developed, dubbed point-of-care products or POCs that incorporate lab-on-a-chip or LOC technologies, to achieve integration of the hitherto separate processes of sample preparation, separation, amplification and analysis. New therapeutic devices are envisioned that are implanted to support body functions or organs that are weakened by disease or lost through amputation, or allow high precise surgical interventions to minimize damage to surrounding tissue. Such new products could reduce the severity and mortality of the world's most severe diseases such as heart attacks and failure, stroke, cancer, neurodegenerative and infectious disease. Time critical diagnostics information can be obtained more rapidly at the point-of-care or point-of-diagnosis, and treatment monitoring with immediate feedback becomes more feasible, e.g. for bacterial or viral infections. Also, more personalized treatment becomes possible by measuring the patient's genetic predisposition to side effects and response. New monitoring devices will promote and improve patient follow up, thus addressing the limited caregiver resources, the growth in chronic diseases driven by aging and lifestyle, and healthcare's budget constraints. Such less intrusive, miniaturized and hassle free devices with enhanced patient acceptability will reduced the risk of social exclusion and improve patient support at home.

Therapeutic devices will allow surgical interventions that today are not possible or lead to serious impairment, e.g. in diseases such as prostate cancer or afflictions of the nervous systems. Other devices envisioned are implantable biochips and autonomous on-body biosensors, which allow continuous monitoring of body functions, networked to the outside world through wearable textile. Projects that are supported in the MNBS program develop:

- Robotic systems for highly precise surgery
- Neuro-interfacing implantable devices that treat phantom limb pain, restore motor functions or intervene in the cardiovascular system
- Lab-on-a-chip systems employing a variety of technologies for sample handling, separation and identification for both body fluids and food
- Improved diagnostic transducers and transponders
- Detection and identification of circulating cancer cells
- Devices for a new imaging principle
- New sensors, body area networks and biomedical informatics



Example of an ICT enabled implanted biomolecular sensor
Source: R. Campagnolo

Healthcare is one of the EU focus areas, with significant potential to contribute to higher quality of life and life expectation, as well as higher efficiency and effectiveness in the system.

4. Presentations and Discussions

4.1 Opening and welcome

On Day 1, **Javier Mendigutxia,** General Manager of IKERLAN–IK4, welcomed all participants to the town of Mondragón, and to the core of the cooperative experience represented by the Mondragón Corporation. IKERLAN-IK4 belongs to this group, which has more than 85,000 employees in both the Basque Country and worldwide, and it carries out its activity in the financial, industrial, distribution and knowledge sectors. It has a University, 3 Technology Centres and 9 Business R+D Centres. Technology transfer and to promote technology-based initiatives and businesses is the focus of IKERLAN-IK4, and it covers a broad area for developing mechanical and electrical systems, micro and nano systems and so on that enables the design of new products based on micro/nano technologies, embedded systems, etc., which are the basis for new products for the life, food and environmental sectors. Its modus operandi is that of the open

network, and it is a member of both Spanish (i.e. IK4, CIC Microgune) and international research alliances.

Andreas Lymberis, European Commission, Information and Media Directorate General, Micro & Nano Systems, explained the objectives of the MNBS program, which included an increase in and improvement of investment in R&D, convergence of research efforts, creation of pathways to bring R&D results into practice and the strengthening of the European industrial base. Added to this he emphasized the need to diffuse the research results into society. This workshop in particular was to intended to find further synergies between the projects, to identify challenges and objectives for future research, and to focus on the road to commercialization, as the question now becomes "how to turn R&D into business?". Under the MNBS umbrella, created in 2004, some 41 projects have been launched, of which 24 in FP6 and 17 in FP7, and € 171 mln has been spent up to today. MNBS is part of the EU's competitive strategy that going forward looks to improve the returns on the investments in R&D and to contribute to a strong European industrial base. Putting R&D results into practice also involves exploitation of the synergies with the EU's platforms EPOSS and Nanomedicine.

Jesus Ruano, from IKERLAN–IK4 explained that this workshop was to be different from other workshops, to that extend the participants were invited to be just that, i.e. actively and vividly participating in the discussions and questions , and in giving direction to the future development.

As part of the opening**, Jean Philippe Leclerq, Yole,** presented **COWIN, www.cowin4u.eu,** a recently established support action to enhance the value creation from FP6 and FP7 projects, and strengthen the European competitiveness in smart systems by finding "gold nuggets" in European research projects. In particular, COWIN's mission was explained to "facilitate the take-up of advanced technologies"… "in smart system worthy of investment", leading to a path to new markets and profits. In order to achieve this, COWIN works with the individual consortia and builds connections to industrial partners, customers and end-users, to bridge the gap to the market by constructing a valuable roadmap towards commercialization. New business opportunities are created with the help of an innovation stakeholders network, access to best, dedicated European initiatives and financing and through start-up and licensing activities. The institutions and companies that together are COWIN are largely complementary and cover a broad area of business, technology, market and strategy development competences. Some 91 projects have been analyzed and 51 receive active support over the last 6 months. A purpose-made, web-based platform supports a wide area of activities at no fees to beneficiaries.

On Day 2, **Maria Aguirre**, from the Biobasque Agency, gave an overview of the Basque country, its population and the broad range of activities in bio sciences and technology. The population is highly educated, the majority of the export consists of technology, and there is a longstanding tradition of cooperation between the public and private sector. Four cooperative research centres have been established which operate within the MNBS field. These centres have an advanced research infrastructure at their disposal, and close ties with the health systems have been established to allow efficient transfer of new technologies into clinical practice. A bio-bank with 22,000 DNA samples is part of the

translational research program. Technology parks and an infrastructure with capital providers and service companies stimulate the creation of new companies, to take research successes to the market. About 4 new companies are established yearly, a majority devoted to human health, where a broad research program has been put in place.

Andreas Lymberis, European Commission, discussed the funding opportunities that exist in the MNBS research program as an ICT priority area. After a start in the FP6 program with a total M€ 301 in funding over a 4 year period for a no. of industrial areas, the MNBS cluster emerged to focus on bio and health applications. MNBS brings together the fields of ICT and micro and nano technology with biotech. It has become a strong cluster, attracting significant funding while covering a variety of medical applications. The market prospects are extraordinary, forecasting a growth between 17% and 33% for the largest market segments, from an existing multi-billon € market. A review of the progress achieved over the last 4 years was given, as well as the factors affecting market adoption. In FP8 M€ 39 have been reserved for the next MNBS call, which will be asking for application-driven proposals. New items will be considered in the evaluation criteria and scoring, and the ICT Proposers' Day 2011 will take place on May 19 & 20 in Budapest, to discuss this in more detail.
FP8 will be guided by three broad objectives, i.e. Research Societal and industrial challenges,. A Green Paper has been issued for consultation by all interested parties, which discusses the EU2020 strategy and goals.

4.2 Microsystems interacting with the body

Compared to Laparoscopy, which is a mature technique today and the standard for many abdominal operations, new techniques such as Natural Orifice Transluminal Endoscopy Surgery (NOTES) and Single Port Laparoscopy (SPL) bring the potential to revolutionize the field of minimally invasive surgery. The ARAKNES project ultimate goal is to enable versatile, efficient, user friendly and safe (accurate, reliable) endoluminal surgery and single port laparoscopy by means of micro-robotics devices and advanced navigation system integration.

In 50-80% amputees, following amputation of a limb, phantom limb pain (PLP), a neuropathic pain develops in the lost limb. There are currently no effective treatments available for this kind of pain. According to recent studies, the effect of enhancing the sensory feedback related to the missed limb by electrical stimulation of nerves in human subjects, can alleviate PLP. The aim of the TIME project is to develop an innovative Human Machine Interface (HMI) that will apply multi-channel micro-stimulation to the nerve stump of an amputee volunteer to manipulate his/her phantom limb sensations, paving the way for using the neuro-modulation as a treatment for PLP.

The classical neuro-prosthetic way to alleviate paralysis after severe spinal cord injury (SCI) is based upon muscles recruitment to restore motor functions bypassing spinal neuronal circuits. NEUWalk addressed the restoration process in an entirely new approach by directly extracting motor cortex information decoding theses signals in order to drive directly spinal neuronal networks by means of an implanted neuro-stimulator through a wireless link. The NEUwalk

cortico-spinal neuro-prosthetic system, previously described, will bring new opportunities to treat more efficiently Parkinson drug resistant Disease symptoms competing with Deep Brain Stimulation.

An aortic aneurysm is a general term for any swelling of the aorta. The major concern of aortic aneurysm is the risk of rupture, which causes massive internal haemorrhage and, without prompt treatment, death occurs rapidly. The definitive treatment for an aortic aneurysm may be traditional, open surgical or minimally invasive endovascular repair (stent graft). In some cases, this stent doesn't perfectly fit the aneurysm and leakage around the graft can occur. The goal of the Heart-e-Gel project is to benefit from the Electro Active Polymer (EAP) hydrogel properties for closing, filling or sealing vessels or cavities thanks to the electrically tunable volume phase transition capabilities of EAP material.

Main achievements

- The success of the test session with expert surgeons using the first prototype and their positive feedback demonstrates the relevance of the general concept. The patented introducer associated with an industrial robot brings a high level of dexterity but lot of work remains to be done for the workspace analysis (ARAKNES).
- The ability of electrodes to activate more muscles with higher selectivity than competitive electrodes was demonstrated and a highly versatile multichannel bench-top stimulator was realized. A multi-channel connector that could be used in other prostheses was patented (TIME).
- Demonstration, in lab environment, of the impressive capacity of spinal cord electrical stimulation to promote walking function in paralyzed SCI rats (NEUwalk, recently started project).

Main challenges

- The full potential of the proposed concepts will only be achieved by overcoming the main challenges of integration of sub-systems, miniaturization of components with ultra low power consumption particularly for implantable devices and high reliability.
- A cost efficient fabrication process remains challenging in order to compete with commercially available devices (e.g. Da Vinci Surgical System, the gold standard for the ARAKNES project) but with improved functionality. More advanced micro-fabrication and micro-packaging technologies will be needed to overcome this challenge.
- Biocompatibility and long–term stability of new kind of material interacting with human tissues represent a clear challenge for smart implants.
- The ARAKNES project will require the proper convergence of endoscopic instrumentation, minimally invasive surgery, computer-assisted surgery, imaging and robotics.

Progress

- For ARAKNES, a market analysis, which monitors the competition, was conducted and a very aggressive targeted price was proposed. The patent

deposition process was still very active for system components and derivatives devices.
- Compared to last year, the TIME consortium succeeded in producing prototypes the third generation scalable electrodes mandatory for patient customization.

Take aways
- Selection of the right components can be crucial to mitigate the regulatory burden.
- Focus on biocompatibility and long term stability of new material as early as possible.
- Continuous monitoring of the business plan assumptions and cost estimates of the CE approval, management of IP rights, and updating of the competitive landscape and market development, i.e. opportunities and trends.
- A four years period is definitely too short for the development of a full implantable system or an highly innovative instrument from scratch
- By exploiting a set of components in the market of animal studies, or by integrated components in existing products, risks can be reduced and business growth generated.
- Clearly, the TIME and NEUWalk teams have common interests as they share challenges (biocompatibility, electrodes, power requirements). As proposed the last year, the opportunity to organize a meeting dedicated to autonomous implants is still there, and other project such WiserBand, Heart-e-Gel and ULTRAsponder can benefit from such an event as well.

4.3 Lab-on-a-chip

Under this heading prototype devices are being developed that aim for diagnostic systems with a small footprint and lower costs. Samples are taken from one of the body 's fluids, which can be collected at much smaller quantities than current central lab equipment require. The diagnosis can be done immediately after sample taking, in the presence of the patient and physician, and with the outcome availability in minutes rather than days. Reports on the projects LabonFoil, microFLUID, PYTHIA, Positive, SIMS and ARROW were given. Obviously, these projects are not all in the same phase and thus will differ in achievements and challenges.

Main achievements
- Working prototype modules have been built and used to analyze real samples of drugs-of-abuse. A start-up company is being set-up to commercialize the results.
- For fast prototyping and small series production femto second laser fabrication of polymer lab-on-a-chip components are found to be competitive.
- Label-free detection of bio molecules have been achieved in an integrated device.

- Alternative approaches, such as miniaturizing mass spectrometers, could yield broadband diagnostic tools.

Main Challenges

- To achieve portability and sensitivity while keeping the device price low.
- To migrate prototype biochips from special purpose fabrication to mass-production technologies as used in Si foundries requires a major redesign.
- For the integration of heterogeneous processes on monolithical substrates serious hurdles have to be overcome.
- Performance of the devices' prototypes.
- Clinical trials to prove the clinical efficacy and economic advantages of successful prototypes.
- To reconcile initial performance goals with market requirements.

Take-aways

- In the planning process early on, workflow considerations and manufacturing requirements need to be taken into account. The ease of sample taking, the toolset for doing so and injection into the device play an important role in the acceptance by clinicians and patients alike.
- Continuous competitive scouting will help to keep plans competitive.

4.4 Microsystems interacting with bacteria and cells

While bio molecules small and large reveal intricate details of sub-cellular processes, cells circulating in the body can give complementary or more specific information on organ pathologies. A number of projects therefore strive for the identification of bacteria and cells. Devices that can rapidly analyze such entities will mean breakthroughs in infectious disease and cancer diagnosis. For bacterial infection, the identification of the pathogen will enable the best therapy, i.e. bacterium-specific antibiotics. For cancer, the identification of tumour cells circulating in the blood will not only reveals the presence of disease, but could also pinpoint the affected organ. Through single cell manipulation and analysis, the accuracy of early diagnosis of disease can be improved over the analysis of the average of large collections of cells. The projects InTopSens, Miracle and PASCA deal with these challenges.

Main achievements

- A sensor has been devised that works in a continuous regime by cascading two ring resonators. Also, a novel polymer system has been devised for LOC applications that has many favourable characteristics and is compatible with standard lithography equipment for rapid prototyping and medium-scale production. This will allow a low-cost, cartridge-based solution to be developed. Through collaboration with 2 SMEs the time-to-working-prototype will be considerably

shortened. EU funding has been obtained to continue the project for another 5 years (InTopSens).

- A device has been envisioned as a LOC that aims to count and characterize occult circulating tumour cells. The choices of key components and growth processes are such that fast prototyping and production is possible, and that short-cycled iterations allow for rapid improvements (Miracle).
- The principle of isolating single cells by single-cell-printing has been proven; this approach needs only minute amounts of sample and is capable of high quality cell separation (PASCA).

Main challenges

- The identification of bacteria and cells is technically very complex as it requires the sequential steps of lysis, breaking down cells, and PCR, multiplying the bacterial, viral or circulating cells' DNA. The readout systems can be made label free, which eliminates an additional step in the readout process, or labelled when high specificity is required. While the modules could well be developed individually, integrating these into one system is a big challenge.
- Analyzing samples with a mixture of bacteria is a much more difficult problem to tackle than a single strand analysis
- Sepsis is likely one, if not the most difficult application in the field of LOCs. An educated guess that M€100 project would be required to come up with a working product, is likely to be an underestimation.
- No thorough testing of any rapid molecular system in a clinical setting has so far been achieved. However, given the widespread occurrence and high mortality of infections the impact of fast, integrated molecular systems can be expected to make a big impact, especially in high-intensity care of weakened patients.

Take-aways

- As an alternative to commercialization of the full product, IPR-protected modules and methods can be licensed.
- There is a collaboration opportunity in sample handling, purification, micro PCR and high sensitivity read-out given the huge challenges.

4.5 Microsystems for health and related initiatives

Current cancer therapy is based on systemic drug delivery (chemotherapy) through the vasculature, often in conjunction with radiation therapy or surgery. A more targeted therapy using drug loaded nanoparticules and a guiding mechanism could increase effectiveness and dramatically reduce side effects. The NANOMA project's goal is to benefit from the magnetic propulsion of ferromagnetic capsules produced by a clinical MRI system to bring the anticancer drug to the tumor cells. An appropriate design of the nanovector is needed to mix magnetic properties, drug encapsulation function and low immune system visibility.

In the field of integrated label-free bio-molecular sensing (Lab On chip), instruments for cancerous tissue detection and chemical analysis make use of different bands of the electromagnetic spectrum. Unexplored regions like the terahertz (THz) band, in between the microwave and the infrared frequency range, offer a promising alternative for enhanced analytic capabilities. The aim of the ULTRA project is to develop two low cost, reliable and power efficient new instruments based on the terahertz radiation with a very small footprint and high sensitivity. The CMOS technology and micro packaging process, developed by the ULTRA consortium, will enable low cost solutions for components fabrication and integration in case of mass production.

Only limited wireless connectivity is available in most wearable and implantable devices like hearing aids, cardiac implants, insulin wearable pumps and cochlear implants jeopardizing their integration in healthcare networks. The general trend of shrinking the size and improving the autonomy of this kind of devices could be compromised by the footprint and power consumption of present solution based on RF channels. The WiserBAN project aim is to provide a highly competitive, extremely miniaturized and power efficient wireless micro-system for Body Area Network. The WiserBAN micro device is expected to be at least an order of magnitude smaller and lower power than today's radio modules (Bluetooth). The ULTRAsponder consortium takes a different technological approach than RF to deal with the problem of communication and control of deep implanted sensors and actuators. To overcome electromagnetic attenuation in living tissues, ultrasonic waves will serve as a medium for the bidirectional data link between sensors and an external control unit on patient's skin. In addition, the ultrasound energy produced by this unit will provide power to the sensors.

ACTION-Grid, ended in May 2010, is a Specific International Cooperation Project on healthcare information systems based on Grid capabilities and Biomedical Informatics (BMI) between Latin America, the Western Balkans and the European Union (EU). Its goal is to expand previous initiatives to create a common health information infrastructure in Europe, to extend it to other regions. The project will enhance cooperation between research centres, universities, hospitals, SMEs, public entities, and others. ACTION-Grid will expand the impact of EC achievements in Grid and BMI to researchers, educators, and health practitioners' worldwide.

Main achievements

- A spin-off company Aeon Scientific (http://www.aeon-scientific.com) has been launched in January 2011 to distribute magnetic micromanipulation system for light microscopes (NANOMA).
- Patent depositions about control algorithms for endovascular steering and navigation of magnetic nanoparticules have been made (NANOMA).
- Non Linear Transmission Line and other components using standard CMOS technology were produced and Localized Surface Plasmon Resonances proved to enhanced sensitivity (ULTRA).

- For the first time, a transmitter module (3D packaging) based on CMOS lines and off-chip-antenna has been tested up to 180 GHz, and first images were taken with it (ULTRA).
- High level of dissemination activities and IP protection took place (ULTRA).
- Use-case scenarios, specifications and architecture, driven by industrial partners, have been developed (WiserBAN).
- Proof of concept of remotely powered wireless communication through ultrasonic waves has been achieved (ULTRASponder).
- Information dedicated to nanotoxicity has been efficiently mined (ACTION-Grid).

Main challenges

- Nanocapsule toxicity issues, particularly those based on Single Wall Carbon Nanotube, poses a high risk of thrombosis (NANOMA).
- Finding partners in NMR systems and long term view of the commercialization turned out to be more difficult than expected (NANOMA).
- Compatibility with low cost applications needs to be established (ULTRAsponder).
- To achieve ultra low power radio (20x -50x improvement vs. state of the art) using MEMS technology in a highly compact footprint (4 mm x 4 mm x1 mm) requiring advanced 3D packaging (50x improvement) is a struggle (WiserBAN).
- To design a miniature 2.4 GHz antenna (10x improvement) with adaptive characteristics to handle close-to-the body and in-the-body propagation is proving difficult (WiserBAN).
- Costs appear to be higher than anticipated
- To increase the bandwidth of data transmission up to 200 kbits/s is a serious challenge (ULTRAsponder).
- To limit the long term adverse effects of high ultrasound power in order to comply with FDA standards (ULTRAsponder).

Take-aways

- The check on biocompatibility of material is a must as early as possible, to avoid dead ends.
- Use-case scenarios and specifications need to be driven by experienced partners and require their strong involvement.
- Select a set of relevant applications if the technology is to be broadly applied, as for radio communication; in this case particular care must be taken for antenna propagation and power requirements for implantable devices.
- Possible side effects of data links (RF or ultrasound) need to be established early on.

5. The road to the commercialization

In this session, reports were given on case studies for Ultrasound transducers and implantable devices, the growth pains of a new diagnostic device company, the success of a SME offering microfluidics services and the intricacies of obtaining the necessary regulatory approvals, completed by a panel discussion.
A number of noteworthy points were raised during the presentations:

- Developing new technologies for existing markets reduces the product and application risk, since much is known about customer requirements, and often implementation on existing platforms is possible
    - In addition, from market research unmet needs can be quantitatively defined and technology developments can be undertaken which focus on these targeted needs
    - Examples using MEMS, Micro Electro Mechanical Systems, technology for new Ultrasound transducers and miniaturized implantable devices for cardiac resynchronization therapy were given, opening new opportunities for advanced manufacturing (integration, packaging) and bringing new, stimulating challenges for micro-systems in contact with body components
- Starting a new company based on new technology for a pressing societal need, in this case fast detection of Legionella bacteria, can prove to be very challenging, as product development often takes (much) longer and costs (much) more than expected.
- Regulatory requirements, while harmonized on European level, do not prevent national authorities to impose additional demands, and the choice of an experienced Notified Body is key to success. Also, the clinical studies required to obtain approval can quickly become stumbling blocks if not carefully designed and timed. It pays off to involve the regulatory body early on in the development process in order to design an optimal regulatory pathway.
- In the early phase of the industry, business opportunities exist for SMEs that supply one or more services or products along the value chain. Collaboration actions can accelerate industrial development.

During the panel discussion, aspects of the technology choices, the question of in-house development *vis-à-vis* outsourcing or purchasing, the important role of Intellectual Property protection, IPR, and the implications of regulatory requirements were discussed.

Recommendations

- While some of the projects have already defined a business model and end product, for many others such choices have not yet been made. This needs to be made as early as possible, as it clearly defines the focus areas of the project and helps to make the choice of partners, i.e. the make or buy decision much easier. In parallel the **regulatory approval** requirements and **clinical**

study design should to be included in the prototype's requirements list early on.

- Design for manufacturing becomes a key concern once the prototype starts to meet the design criteria and should where possible be **taken** into account from the beginning.
- For healthcare devices it may take 7 to 8 years to reach the market, which is why long term financing is so important. It was stated that in France subsidies could be made available until regulatory approval – CE marking. This seems to be the exception, and other funding sources exist such as venture capital providers, other companies, the EIB and specialized banks. While it may appear appealing to provide more subsidy to reach CE marking, this usually does not help to make companies more competitive or focused on market needs, and certainly would give un unfair advantage to companies financed with private capital.
- Increasingly companies are asked to provide the evidence that the new product not only lead to higher quality care but also lead to savings in the healthcare systems - Healthcare Technology Assessments. Although for diagnostic products no standard way to do this has yet emerged, it saves time and money later on if the clinical study for regulatory approval integrates cost data as much as feasible.
- In the medical market the **clinical, technical and financial** value of the product need to be well understood, in order to assure that the product is specified to meet the needs of the owner, end user and patient.
- For sustainable success of suppliers to a new value chain, the complete value chain needs to be developed. This can only be done by successful system suppliers or OEM[3]s, which establishes end-user markets. A healthy market needs successful value chain suppliers as well as successful OEMS.
- In addition to starting a company, **licensing** can be a good option to create value and commercializes the R&D results
- In some countries - France was explicitly mentioned – not enough attention is dedicated to protect inventions with the proper patents. Lack of creating the right IPR reduces the chance of commercialization significantly, since the basis for getting funding for start-up companies is much weaker and the opportunity for licensing disappears.
- The regulation constraints in vitro diagnostic are currently evolving. They are becoming more and more complex to manage and closer to in vivo diagnostic ones. These should be taken into account while conducting a project targeting this application field.
- In parallel, food and environmental monitoring application represent good opportunities. Consortia should consider this application field with a strong interest. Indeed the market is less concentrated than the diagnostic market which could facilitate market access, moreover the demanding is increasing. In any case the choice of business model should take into account the industrial food chain organization. It is important to define if the industry and market is concentrated or atomized and what types of companies have access to the market.

[3] OEM: Original Equipment Manufacturer

- The good collection of end users' specifications including reliability / robustness requirements, target price for consumable diagnosis devices are key factor of success

Parallel to the plenary meeting, COWIN representatives had organized 25 one-to-one first encounters with representatives from the consortia to take stock of the support needed on the road to commercialization. These meetings were reported as being helpful by the project teams (see Annex III).

6. Concertation and Cluster activities

To kick-off this part of the workshop, section 6, Javier Bonal introduced the subject, dubbed "Past and Present" and posed a number of provocative questions. In Annex IV the hand-out text is reproduced.

Concerning the organization of the MNBS workshops, the general feeling was that the Commission should stay in charge, and there was a strong sentiment to involve other stakeholders, especially from the clinical community, but also from regulation and reimbursement authorities. Some participants called for the Commission to exert more pressure on potential participants, as they thought the field had not yet reached critical mass. The Commission representatives stated in conclusion, that the cluster will be organized as it is today next year.

A heartfelt plea was made to organize the workshop adjacent to another meeting, as people felt there were too many isolated meetings and consultation workshops in NMP, ICT and Health priorities, most of which could be combined. For MNBS an option is to organize it together with the EPoSS meetings, the next one is coming up in October 2011 in Barcelona. Another idea was to have a thematic meeting, together with other activities in NMP & Health priorities.

On the continuation of the financing of LOC projects, a lively discussion took off. The opinions that were offered covered a broad range:

- Through the projects many teams had gained considerable knowledge and new skills, no show stoppers had been identified; however, repeatability and reliability remained challenging issues
- Criteria are needed for the next stage, to go beyond state–of-the-art
- The market is starting, more time is needed and involvement of end users is expected
- The term "LOC" should be changed in "Lab-in-a-product"
- The field should continue because it develops enabling technology, not products and it's still a challenge for the European industry
- The question: "Do we have a sensitivity issue" was raised, and the need for more advanced surface chemistry to achieve surface functionality; the next call (FP7 Call 8-MNBS) will emphasize this point
- The question "How integration account for the selection of a proposal " was also raised. Andreas Lymberis, explained that expert are advised to take into consideration integration innovation in the proposal which can be very innovative in this area. He also stated that each year, 20 to 25 % of experts are new experts, if they don't feel comfortable with the

proposal (out of their field of expertise) they can decline the expertise. Javier Bonal invited the attendees to become experts.

- More emphasis on the business case was mentioned, and the urge for EPoSS and VDI/VDE to continue
- The wish to get funding until CE marking was ventilated
- It was stated, that the medical market is a difficult one, and other application areas in order to gain critical mass should be looked for. The killer application may well be here, but is slow to develop due to the regulatory and reimbursement hurdles.
- The counter argument, that Healthcare is too important to ignore, and also is a socio-economic priority are for the EU, found strong backing, and it was mentioned that the pharma industry is gaining interest in LOC type of diagnosis as part of the personalized medicine trend. The drug discovery market, although much smaller, was referred to as a potential candidate for the first killer app. It was pointed out, however, that this was less likely as the pharma industry has already invested massively in standardized, automated lab equipment.

The idea of **finding high volume markets outside healthcare**, in order to apply the accumulated knowhow to healthcare once the approvals were in, met with broad sympathy. As likely candidates the food, drink and allergy markets were mentioned, although it appeared that the indigenous industry had shown little interest up till now, and environmental monitoring. In this area more involvement from the EC is needed, some believed.

Food processing, in addition to finished-food analysis could be an alternative high volume market. However, food testing will be more complex due to sample preparation requirements, so from this perspective the medical applications are to be preferred. The Fraunhofer Institutes have established a food-chain management alliance to assure stable food quality.

On the topics of **interfacing with nervous systems** and deep brain stimulation, various opinions were voiced:

- In neurology, a vast and largely unknown territory, multidisciplinary teams are needed, incl. mathematicians, to interface and interlink with neurons
- Neurophysiology knowledge will also gain from microsystems development, these fields develop in parallel, and neurophysiology constantly needs new tools. The support for projects dealing with nervous system interfaces, like Deep Brain Stimulation need to be maintained in order to broaden future applications (not restricted to Parkinson treatment) with less invasive micro-systems.
- Brain stimulation is competing with pharmaceutical drugs and traditional surgery; outside stimulation through focused electromagnetic fields have a future as well.

Related to the perceived lack of proposals on **surgery**:

- There have been submissions in other units (call related to robotics and inclusion), and it was mentioned that projects are being financed in France.
- The need for smarter tools such as lancets and other significant opportunities do exist in the field of surgery (mainly cardiac) and new ideas have emerged

for improvement, which, for the time being, employ mechatronics rather than micro systems.

Wearable micro-systems were also the subject of an exchange of opinions:

- Such systems were judged to be helpful in dealing, among other, with the challenge of the aging population, as self support and autonomy is strengthened when people can stay at home with the proper support. It would make therefore sense to include wearable technologies in MNBS topics.
- Since other ICT projects are likely to be funded in this topic as well, overlap should be minimized.

7. Consultation: future challenges - how to meet them?

The focus of this workshop is on the **road to commercialization**, and progress has been shared across a range of areas. From the two days it appears that many technological challenges have been overcome, while new ones are becoming apparent. New companies are positioning themselves to offer specialized services to projects that aim to build complete systems, and microfluidics knowhow is fast becoming a European stronghold.

Some **technology challenges** stand out among the projects, especially system integration, power supply, wireless networks, sample preparation, sensitivity and reproducibility. The challenge of reducing power supply requirements was stated as a problem of more efficient processing. Every day improvement of CMOS technology will help to overcome this challenge. The same concept can be apply for the wireless challenge, the extraordinary capabilities of nowadays wireless chip and 3D integration technologies used for the smart phone market are facilitators to overcome this challenge. As we are immersed in numerous heterogeneous (norm, coverage, encryption scheme, security, data rate and so on) and supposedly easy accessible networks, the main challenge that will emerge is now the interoperability of all these ICT capable systems.

The **market share of LOC** is also one of the major challenge to face and a large discussion took place about this topics. To increase the market share of LOC applications, it was proposed to identify a killer application and to choose novel parameters panel suited for the Lab On Chip function. Numerous other proposals were raised, like designing LOCs as upgrades for standard devices (eg. Centrifugation) or to take a microfluidic platform based development approach. Other suggestions were set like using improved software development tools for the design phase or trying to integrate LOC into existing workflow (interface)

On of the challenges pointed by the attendees was the problem of mass production, the only proposed solution was to establish a low cost high throughput cartridge manufacturing process (replication, sealing, cutting). Concretely, this means the realization of a pilot production line for validation purpose, capable of producing thousands of Lab On Chip. This line will enable extended validation of developed LOC system using low cost material. Another way to improve market share of LOC is to improve involvement of decision makers in order to influence regulatory issues. This topic is related to another proposal made by the attendees, the implementation

of quality control, this will need to investigate the availability of suitable control tools for LOC.

System integration and modularization with well-defined interfaces could mitigate the integration risks. Common, open interfaces and standards would speed up the creation of commercial sub assemblies and modules, and help to speed up the return on investment. An approach to tackle this challenge is to have the management of the interfacing dealt with by one or more experienced industrial partners and this will also promote a market driven approach (coming form my notes)

The projects that are furthest developed in time are now facing choices with respect to product specifics, clinical validity and business model. The COWIN team can be helpful to support such projects to the road to commercialization.

For a balanced European portfolio of projects one ideally would like to see a mixture of projects along the axes of risk and reward. Realizing that 4 years is too short for any greenfield medical technology project, a funding solution needs to be found to minimize risks further and to carry consortia through to at least the clinical study phase 1, i.e. safety tests on patients or clinical validation, whichever comes first. Successful finishing of this phase will make it considerably easier to find new funding.

In addition, for products to become successful, deeper understanding of the clinical value chain is needed in the consortia. In other words:

- The **context** in which the product will be operated and its usage
- The **requirements** of patients and physicians alike need to be well understood
- **Payers**, i.e. government and insurance companies need to be shown the clinical as well as the financial benefits of the products
- For LOCs , solutions need to be found to overcome possible **conflicting interest** between physicians and lab managers

Within the EU, business opportunities may lie initially with **commercial healthcare providers**, while regulators rethink the regulatory system in view of the technological possibilities and demographic challenges. Emerging economies with a pragmatic approach also offer new opportunities.

8. Recommendations

Making the business case

- While some of the projects have already defined a **business model** and end product, for many others such choices have not yet been made. This needs to be made as early as possible, as it clearly defines the focus areas of the project and helps to make the choice of partners, i.e. the make or buy decision much easier. In parallel the **regulatory approval** requirements and **clinical study** design should to be included in the prototype's requirements list early on.
- **Design for manufacturing** becomes a key concern once the prototype starts to meet the design criteria and should where possible be taken into account from the beginning.

- Developing new technologies for **existing markets** reduces the product and application risk, since much is known about customer requirements and often implementation on existing platforms is possible
- Given the long time span for healthcare devices to reach the market and the need for **long term funding**, it may seem appealing to provide more subsidy to reach e.g. CE marking. However, there is no evidence that this helps to make companies more competitive or focused on market needs. Also, it certainly would give an unfair advantage compared to companies financed with private capital.
- Regulatory requirements, while harmonized on European level, do not prevent national authorities to impose additional demands, and the choice of an **experienced Notified Body** is key to success. The clinical studies required to obtain approval can quickly become stumbling blocks if not carefully designed and timed. It pays off to involve the regulatory body early on in the development process in order to design an optimal regulatory pathway
- Increasingly companies are asked to provide the evidence that the new product not only lead to higher quality care but also lead to savings in the healthcare systems - **Healthcare Technology Assessments**. Although for diagnostic products no standard way to do this has yet emerged, it saves time and money later on if the clinical study for regulatory approval integrates cost data as much as feasible.
- In the medical market the clinical, technical and financial **value of the product** need to be well understood, in order to assure that the product is specified to meet the needs of the owner, end user and patient.
- For sustainable success of suppliers to a new value chain, the complete value chain needs to be developed. This can only be done by successful system suppliers or **OEMs**, which establish end-user markets. A healthy market needs successful value chain suppliers as well as successful OEMS.
- In addition to starting a company, **licensing** can be a good option to create value and commercializes the R&D results
- In some not enough attention is dedicated to protect inventions with the **proper patents**. Lack of creating the right IPR reduces the chance of commercialization significantly, since the basis for getting funding for start-up companies is much weaker and the opportunity for licensing disappears.
- For products to become successful, deeper understanding of the **clinical value chain** is needed in the consortia. These include the context in which the product will be operated and its usage; the requirements of patients and physicians alike; payers, i.e. government and insurance companies need to be shown the clinical as well as the financial benefits of the products; for Labs-on-a-Chip, solutions need to be found to overcome possible conflicting interest between physicians and lab managers.

Continued EU support

- Given the considerable knowledge and new skills that has been built up in the EU on Lab-on-a-chip technologies, and the emergence of start-up companies it appears the original goals of the MNBS program are being met. As this is still a fledgling industry further support is needed, especially to improve

system integration, sensitivity - advanced surface chemistry-, **repeatability and reliability**, and the design experience to achieve fit-for-the-market products.

- Realizing that **4 years is too short** for any greenfield medical technology project, a funding solution needs to be found to minimize risks further and to carry consortia through to at least the clinical study phase 1, i.e. safety tests on patients or clinical validation, whichever comes first.
- **Minimal or non-invasive surgery** is the future, and here more proposals can be actively sought. There is a strong development in image-guided , non-invasive Ultrasound based therapies, but also smart catheters under non-ionizing imaging, smarter lancets, more cardiac and brain applications appear possible.
- **Wearable micro-systems** are judged to be helpful in dealing with the challenge of the aging population, as self support and autonomy is strengthened when people can stay at home. It would make therefore sense to review the total EU support for wearable technologies, and decide which programs promise the best chance of success.
- System integration and modularization with well-defined interfaces could mitigate the integration risks. Common, **open interfaces and standards** would speed up the creation of commercial sub assemblies and modules, and help to speed up the return on investment. An approach to tackle this challenge is to have the management of the interfacing dealt with by one or more experienced industrial partners. This subject warrants an horizontal action.
- The next workshop should involve more **clinicians, regulatory and reimbursement** experts. Alternatively, every consortium could get help in setting up a dedicated workshop on design for users, patients and applications. Also, the MNBS workshop is advised to be adjacent to another meeting. One option is together with an EPoSS conference, e.g. October 2011 in Barcelona. Another idea was to have a thematic meeting, together with other activities in NMP & Health.

Annex I: Program

5 April 2011

Welcome & Opening
08.30 – 09.00 Registrations
09.00 – 09.15 Welcome speech
Javier Mendigutxia, General Manager IKERLAN-IK4
Andreas Lymberis, European Commission
Jesús Ruano, Ikerlan-IK4

09.15 – 09.45
Converging resources to support the value creation in Europe of Microsystems and Smart Miniaturized Systems research projects (COWIN).
Jean Philippe Leclerq , Yole Développement, FR

09.45 – 10.45 **Section 1: Microsystems interacting with the body**
09.45 – 10.05
Array of Robots Augmenting the KINematics of Endoluminal Surgery (ARAKNES).
Paolo Dario, Scuola Superiore Sant'Anna, IT
One to One meeting with COWIN
10.05 – 10.25
Transverse, Intrafascicular Multichannel Electrode system for induction of sensation and treatment of phantom limb pain in amputees (TIME), Winnie Jensen, Aalborg University, DK
10.25 – 10.35
Neuroprosthetic interface systems for restoring motor functions (NEUWalk).
Peter Detemple, IMM, DE
10.35 – 10.45
Microsystem integration based on electroactive polymer gels for cardiovascular applications (Heart-e-Gel), Renzo Dal Molin, Sorin CRM, FR

10.45 – 11.00 Coffee break

11.00 – 12.30 **Section 2: Lab on Chip**
11.00 – 11.20
Laboratory Skin Patches and SmartCards based on foils and compatible with a smartphone (LabOnFoil), Jesús Ruano, Ikerlan-IK4, ES
One to One meeting with COWIN
11.20 – 11.40
Micro-Fabrication of polymeric Lab-on-chip by Ultrafast lasers with Integrated optical Detection (microFLUID), Sabine Brunklaus, IMM, DE
11.40 – 12.00
Monolithically Integrated Interferometric Biochips for label-free Early Detection of Human Diseases (PYTHIA), Ioannis Raptis, IMEL NCSR 'Demokritos', GR
12:00 – 12.10

A highly integrated and sensitive PORous Silicon based lab on a chip for multiple quantitaTIVE monitoring of Food allergies at point of care (Positive), Daniel Hill, Universidad de Valencia, ES
12:10 - 12.20
Development of a Smart Integrated Miniaturised Sensor System for analytical challenges in diagnostics, industry and the environment (SIMS).
Anthony Killard , Dublin City University, IE
12:20 - 12.30
Advanced interfaced microsystems Research for analysis of Real-wOrld clinical, food, environmental and Waste Samples (ARROW), Alan Finlay, Microsaic Systems UK

12:30-15:00 **Section 3: The road to the commercialization**
12.30 – 12.50
From MEMS devices to Medical Diagnostic market. A case study: Ultrasonic Imaging Probes, An Nguyen-Dinh, Vermon SA, FR
12.50 – 13.10
From MEMS to active cardiac implantable medical devices: what does the market needs?, Alain Ripart, Sorin Group, FR

13.10 – 14.00 Lunch

Section 3: The road to the commercialization (continuation)
14.00 – 14.20
Legyon Case Study – How to bring a lab on chip device to the market., Rik Thijssen, Vitens Solutions, NL
14.20 – 14.40
Regulation as driver of innovation for medical device technologies, Christophe Amiel, Voisin Consulting, FR
14.40 – 15.00
Creating Jobs & value experiences in building a microfluidics company, Claudia Gaertner, microfluidic ChipShop GmbH, DE

15.00 – 16.00 The road to commercialization Panel Discussion
Summary of the day
Paul H. Smit, Raymond Campagnolo (Rapporteurs)

16.00 – 17.00 Visit to Ikerlan Laboratories
17.00 – 18.00 Return trip to Bilbao (Hotels) by bus

SOCIAL EVENING at the Guggenheim MUSEUM (BILBAO).
Visit: From 19:00 h to 20:00 h – Dinner: From 20:00 h to 22:00 h

6 April 2011

Welcome & Opening
08.30 – 09.00 Registrations
09.00 – 09.30
Convergence and integration at the core of the Basque BioRegion

María Aguirre, Biobasque Agency, ES
09.30 – 10.00
Future opportunities for funding MNBS research under the ICT priority
Andreas Lymberis, European Commission

10:00-10:40 Section 4: Microsystems interacting with bacteria and cells
10.00 – 10.20
A highly integrated optical sensor for point of care label free identification of pathogenic bacteria strains and their antibiotic resistance (InTopSens), Aman Russom, KTH- Royal Institute of Technology, SE
One to One meeting with COWIN
10.20 – 10.30
Magnetic Isolation and moleculaR Analysis of single Circulating & disseminated tumor cElls on chip (Miracle), Cristina de Joncheere, IMEC, BE
10.30 – 10.40
Platform for Advanced Single Cell-Manipulation and Analysis (PASCA), Peter Koltay, IMTECK, DE

10.40 – 11.00 Coffee break

11:00-12:45 Section 5: Microsystems for health and related initiatives
11.00 – 11.20
Nano-Actuators and Nano-Sensors for Medical Applications (NANOMA).
Antoine Ferreira, Ecole Nationale Supérieure d'Ingénieurs de Bourges, FR
One to One meeting with COWIN
11.20 – 11.40
Ultrafast eLectronics for Terahertz Rapid Analysis in compact lab-on-chips applications (ULTRA), Helge Bohlmann, Microtec, DE
11.40 – 11.50
Smart miniature low-power wireless microsystem for Body Area Networks (WiserBan), Vincent Peiris, CSEM,CH
11:50 – 12.10
European initiative on Grid Computing, Biomedical Informatics and Nanoinformatics (ActionGrid), Diana de la Iglesia, Universidad Politecnica de Madrid,ES
12:10 - 12.30
Towards commerzialization of lab-on-a-chip technology, Felix von Stetten, HSG-IMIT, DE
12:30 – 12:45
In vivo ULTRAsonic Transponder System for Biomedical Applications (ULTRAsponder), Caterine Dehollain, EPFL, CH

13.00 – 14.00 Lunch

14:00-16:30 Section 6: Consultation and summary
14.00 – 14:20
EPoSS MedTech Working Group position paper on Healthcare, Renzo Dal Molin, Sorin CRM, FR
14:20 - 15:30

Consultation Workshop chaired by Andreas Lymberis, Javier Bonal, European Commission
15.30 – 16.00
MNBS cluster meeting committee and 2012 event
16.00 – 16.30
Summary of the consultation and consultation workshop
Paul H. Smit, Raymond Campagnolo (Rapporteurs)
16.30 – 17.30 Return trip to Bilbao (Hotels) or Bilbao Airport by bus

Annex II: List of participants

First Name	Last Name	Organisation	Country
Maria	AGUIRRE	BioBasque Agency (SPRI)	SPAIN
María	AGUIRREGABIRIA	IKERLAN-IK4	SPAIN
Egoitz	ALDANONDO	LORTEK-IK4	SPAIN
Zulfiqur	ALI	Teesside University	UNITED KINGDOM
Rafael	AMASORRAIN	ULMA DD.CC	SPAIN
Christophe	AMIEL	VOISIN Consulting	FRANCE
Miryam	ASUNCION	CIC nanoGUNE	SPAIN
Iker	BADIOLA	INNOPROT	SPAIN
Borja	BARREDO	microLIQUID	SPAIN
Josu	BERGANZA	GAIKER-IK4	SPAIN
Helge	BOHLMANN	microTEC Ges. f. Mikrotechnologie mbH	GERMANY
Javier	BONAL	European Commission	BELGIUM
Frederic	BREUSSIN	Yole Developpement	FRANCE
Sabine	BRUNKLAUS	Institut für Mikrotechnik Mainz GmbH	GERMANY
Marcelino	CABALLERO	IKERLAN-IK4	SPAIN
Raymond	CAMPAGNOLO	CEA-LETI/DTBS	FRANCE
Carles	CANE	CNM-CSIC	SPAIN
Enrique	CASTAÑO	CIC microGUNE	SPAIN
Laszlo	CSERNAK	European Commission	BELGIUM
Francisco	CUESTA	DAS Photonics S.L.	SPAIN
Renzo	DAL MOLIN	SORIN CRM	FRANCE
Paolo	DARIO	SCULA SUPERIORE SANT'ANNA	ITALY
Cristina	DE JONCHEERE	Imec	BELGIUM
Diana	DE LA IGLESIA	Universidad Politecnica de Madrid, Biomedical Informatics Group	SPAIN
Catherine	DEHOLLAIN	Ecole Polytechnique Federale de Lausanne	SWITZERLAND
Peter	DETEMPLE	IMM	GERMANY
Jean-Louis	DIVOUX	MXM-NEUROMEDICS	FRANCE
Klaus Stefan	DRESE	Institut für Mikrotechnik Mainz GmbH	GERMANY
Anne	DUPRAZ-POISEAU	Voisin Consulting	FRANCE
Lola	ELEJALDE	Innobasque	SPAIN
Artiza	ELOSEGUI	ZABALA Innovation Consulting	SPAIN
Antoine	FERREIRA	University of Orléans	FRANCE
Alan	FINLAY	Microsaic Systems	UK
Coralie	GALLIS	CEA	FRANCE

Jaime	GARCÍA-RUPÉREZ	Nanophotonics Technology Center - Universidad Politécnica de Valencia	SPAIN
Ana	GARMENDIA	INSTITUTO INVESTIGACIÓN SANITARIA BIODONOSTIA	SPAIN
Claudia	GÄRTNER	microfluidic ChipShop	GERMANY
Wolfgang	GESSNER	VDI/VDE-IT - EPoSS	GERMANY
Aritz	GOÑI	ZABALA Innovation Consulting	SPAIN
Regis	HAMELIN	EURIPIDES - COWIN	FRANCE
Daniel	HILL	University of Valencia	SPAIN
María Eugenia	IÑURRIETA	IKERLAN-IK4	SPAIN
Maitane	IPIÑAZAR	GAIKER-IK4	SPAIN
Guillermo	IRAZOKI	IKERLAN-IK4	SPAIN
Winnie	JENSEN	Aalborg University (AAU)	DENMARK
Tony	KILLARD	Dublin City University	IRELAND
Peter	KOLTAY	IMTEK	GERMANY
Florian	LAOUENAN	IKERLAN-IK4	SPAIN
Jean-Philippe	LECLERCQ	YOLE DEVELOPPEMENT	FRANCE
Henk	LEEUWIS	LioniX BV	NETHERLANDS
Thierry	LEICHLE	LAAS-CNRS	FRANCE
Guillaume	LHERMITE	Primadiag	FRANCE
Carlos	LURI	CIC MICROGUNE	SPAIN
Andreas	LYMBERIS	European Commission	BELGIUM
Angel	MAQUIEIRA	Universidad Politécnica de Valencia	SPAIN
Iride	MARTINEZ	Policlínica Gipuzkoa	SPAIN
Amaia	MARTINEZ	AGENCIA NANOBASQUE-SPRI	SPAIN
Fernando	MARTÍNEZ	IKERLAN-IK4	SPAIN
Ana Isabel	MARTÍNEZ ESNAOLA	IKERLAN-IK4	SPAIN
Kepa	MAYORA	IKERLAN-IK4	SPAIN
Javier	MENDIGUTXIA	IKERLAN-IK4	SPAIN
Santos	MERINO	FUNDACIÓN TEKNIKER	SPAIN
Chris	MERVEILLE	IKERLAN-IK4	SPAIN
Jyrki	MOLARIUS	VTT	FINLAND
Aoife	MORRIN	Dublin City University	IRELAND
Sergio	MOYA	CIC biomaGU NE	SPAIN
Miguel	MUÑOZ	Biomedical Informatics Group - Universidad Politécnica Madrid	SPAIN
An	NGUYEN-DINH	Vermon SA	FRANCE
George	NOUNESIS	BioGenomica	GREECE
Peter	O'BRIEN	Tyndall Institute	IRELAND
Estibalitz	OCHOTECO	CIDETEC	SPAIN
Cristina	OYON	SPRI	SPAIN
Marcin	PACEK	Proteomika	SPAIN

Vincent	PEIRIS	CSEM	SWITZERLAND
Manuel M	PEREZ PEREZ	ATOS	SPAIN
Claire	PRUMMEL	CEA-Leti	FRANCE
Ioannis	RAPTIS	NCSR 'Demokritos'	GREECE
Vaidas	REPECKA	PMC-Minatech	LITHUANIA
Raúl	REYERO	IKERLAN-IK4	SPAIN
Alain	RIPART	SORIN CRM SAS	FRANCE
Jesus	RUANO-LÓPEZ	IKERLAN-IK4	SPAIN
Aman	RUSSOM	Royal Institute of Technology	SWEDEN
Aman	RUSSOM	Royal Institute of Technology	SWEDEN
Erika	SAENZ	Contract-Biotechnology.com	SPAIN
Arantxa	SANZ	Inst. for Bioengineering of Catalonia (IBEC)	SPAIN
Michael	SCHOLLES	Fraunhofer IPMS	GERMANY
Paul	SMIT	Agathellon	NETHERLANDS
Sara	SOLOZÁBAL	EBA	SPAIN
Wolfgan	STREULE	BioFluidix GmbH	GERMANY
Naiara	TELLERIA	KONIKER S.COOP.	SPAIN
Rik	THIJSSEN	Vitens	NETHERLANDS
María	TIJERO	IKERLAN-IK4	SPAIN
David	TOPHAM	Arts & Science	UNITED KINGDOM
Claude	VAUCHIER	CEA-Leti	FRANCE
Felix	VON STETTEN	HSG-IMIT	GERMANY
Rafal	WALCZAK	Wroclaw University of Technology	POLAND
Petra	WEILER	EPoSS Office, c/o VDI/VDE-IT	GERMANY
Claude	WEISBUCH	Genewave	FRANCE

Annex III: Face-to-face COWIN-MNBS projects: summary

Objectives:
- First interactions of COWIN's partners with projects' coordinator and partners
- Further discussions after a first data compilation for the projects already contacted by COWIN
- Work on commercialization action plan

Description of participants:
Number of people met with one-o-one meeting sessions: 32
Including:
- 6 companies & 17 research organizations,
- 12 project coordinators & 8 project participants.

Main motivations of participants to discuss with COWIN's partners:
- Need to get additional market data
- Need to meet with partners especially for production or clinical validation
- Identify real market needs

COWIN's actions related to the one-o-one meetings.
The first objective of COWIN's action is to support the commercial exploitation of research results. To do so, concrete data (e.g. example of tests performed and results obtained) are collected toward projects coordinators.

Indeed, for most of the projects interviewed, the proof of concept is done. To go further in the preparation of the commercial exploitation of the research results, it would be better to have the following data:
o Comparison of the technology with existing ones,
o Test of the technology on real sample,
o Validation of the manufacturability. It is important to make sure that the technology fit with production process and the identification of production partners able to produce the chip,

Main conclusions of our interactions with projects partners and coordinators at Mondragon MNBS cluster forum

FP6/FP7 projects coordinators presented very interesting concepts and technologies. However a technology does not sell by itself.
Indeed nobody buys a technology because it is a great technology but because it has a unique added value to answer a specific market need. The value of the technology will be even better if it matches with a growing and unsolved market needs.

Customers are looking for functions and solutions, VC's are looking for team and unique value proposition, and industrial companies investing in IP and licensing are looking for technology reinforcing their market positioning.
COWIN will work with FP6 and FP7 projects partners and coordinators to demonstrate the value of their technologies with market / customers perspective.

To do so, IT will work on facilitating interactions with potential customers and users. It is indeed very important to face the market at an early stage in the development to make sure that the project will fit with market needs.
It is more complex to make a complete development and when it is finalized to try to sell it to customers that we do not even know.
COWIN rather encourages projects partners and coordinators to use a stage gate approach in having a 360°C vision in their technological development. Any technical decision should be made in taking into account the key market specifications (for example cost/volume, risk of contamination, type of parameters to be tested, number of parameters etc…) and also its impact in the production process.
It was noticed that the demand from a large majority of partners and coordinators for market data, is more generic than specific. Most of time it helps researchers to feel confident in the technology. It is good but not enough for the commercial exploitation of a technology.

COWIN's job will also be to explain and educate FP6 and FP7 projects partners and coordinators on the need to find concrete market needs with specific functions and applications to enter the targeted field in a niche market. This could be part of a training session organized by COWIN.

Moreover it was noticed in the COWIN data collection process a broad range of technology for biosensing and detection. Based on the information collected, a technology portfolio is being building to encourage the re-use of advanced technologies in new projects. It is also the intention to map the different technologies developed and analyze their attractiveness for the different Life Science application field. Such portfolio will be helpful in addressing users and industrial partners to promote smart system technologies and encourage their innovation in this field.
Bringing an innovation in the Life Sciences requires a very long process. A stage gate approach to validate each step is thus encouraged.

Interactions with users and customers should be considered at a very early stage.
COWIN is currently entering in contact with Life Sciences companies to test their interest in smart systems especially why and how they could use it. The gathered inputs will be important to support projects under preparation or newly started.

On-going actions

COWIN is currently gathering data from projects coordinators interviewed and met during the event. It is a long process depending on willingness of coordinators to share information on the development status of their project. This step is time consuming but very critical since the involvement and commitment of projects partners and coordinators is key in the value creation process.
After reception of data from project coordinators, the business potential of each project will be analyzed in identifying gold nuggets to be promoted. Then, a concrete action plan to promote project's technology will be submitted to project coordinators.

Annex IV: Past and Present, Questions to Chapter 6

The Microsystems Unit of DG INFSO organized the first MNBS concertation and consultation workshop in 2007, to create a forum where projects funded by the European Commission and related to this topic could interchange experiences and identify opportunities for collaboration. The aim was to increase the return on investment in this field for the European taxpayers. Also an additional, important goal was to obtain inputs for the preparation of future work programmes. Since then, we have celebrated 4 additional workshops. In each workshop the project community have been more active and taking more ownership of the workshop. A turning point was 2010 event, hosted by the first time by one of the institutions participating in a MNBS project. This year we have continued the evolution, opening the event to finished projects and an invited group of external attendees, and increasing the ranges of activities. Also the inputs of previous workshops' were taking in consideration for the work programmes and specific topics were introduced as consequence of those inputs.
In the future we aim to maintain the same targets for the workshop and the clusters in the near future:

- to increase the return on investment in this research field for the European tax payers
- to obtain inputs for the preparation of future work programmes.

We believe these targets could be better achieved if the research community in this topic continue to increase its leadership in the organization of the workshop and in the identification of other potential activities for the clusters. For this reason we would like to discuss a no. of questions:

1. Should the EC transfer the leadership of the cluster to a committee? Should the committee be open to any interested person or only to participant in EC projects? Any volunteers?
2. Should the activities of the committee be limited to the organization of MNBS workshop or other potential activities should be explored?
3. How should we decide on the location of next year workshop, and what should be the topic for next year?
4. Is an annual workshop enough to achieve the target of the cluster? Or should some communication platform (web page or social media) be established? Would it be feasible to sustain it through the years? Any volunteers to lead this potential initiative?
5. Any additional feedback or recommendations for future improvements?
6. Should the Commission stop financing LOC projects?
7. Should the financing of project(s) in Microsystems on interfacing with the nervous system be continued, and is there a future for deep brain stimulation
8. Why are there so few proposals in Surgery?
9. Could wearable electronics help with healthy aging?

Annex V: Written feedback submitted by Participants

Participant A's Feedback

- **Q1: Should the Commission stop financing LOC projects?**

  A big majority of the project financed in the area of MNBS are in lab-on-chip for human diagnostic. Typically the project starts from cero and sensor, micro fluidic, biological assay, reader and software are developed and integrated with more or less success during the project. All the project are innovative, with new sensing principle, analytical protocols, micofluidic components, material, etcetera. Nevertheless in most the case, the project did not continue after the EC funding is finished. In somehow, it give the impression that we are moving in circle?. Is the technology mature and the problem is elsewhere in the value, chain?. If the roadblock is still technical, could it be defined precisely to be more efficient in the funding?.

- **Q2: Is there a future for MNBS for drug discovery, environment, and food and drink control?**

  All the calls have been open for Microsystems for drug discovery and food, and environment control. Nevertheless the numbers of proposals received have been very small and for obvious statistical reasons, the number of project funded haven been minimum. Why?, Is there a market?, are the Microsystems technologies the right technologies for those challenges?. If he answer to the 2 previous question is yes, could be defined precisely the research needed.

- **Q3: Should wait the financing of project in Microsystems interfacing with the nervous system until the neurophysiology is more advanced?**

  Research in neuroengineering is very attractive but for the outsider is not evident if the challenge is mainly in understating the neurophysiology or in the development of the Microsystems. If the challenge is in the neurophysiology maybe a more basic research program should be reinforced instead of this one?;

- **Q4: Is there a future for deep brain stimulation?**

  Deep brain stimulation have had at least some success treating case of Parkinson and in Epilepsy. Nevertheless given the invasive and risk of this treating, pharmacology and surgery are preferred, if they are possible. Could the deep brain stimulation become a useful tool for the medical doctor or after some few years will be a curiosity in the text books.

- **Q5: What is the role of Microsystems for surgery?**

  Minimal invasive surgery is used everyday more frequently in the normal medical practice and there is a growing interest in natural orifice surgery. These fields look very promising for the Microsystems technologies, nevertheless the number of project proposals received in this field are very limited. Why? Is there enough critical mass, scientific or industrial, in Europe?, Could be defined the research needed more precisely?

- **Q6: Could wearable Microsystems (in or on the body) help with the challenge of the aging population?**

  The European population is aging very quickly. This phenomenon is increasing the chronics and degenerative diseases and the raising the health care cost. The EC is conscious of the challenge and it analysing potential actions. One potential help could be remote monitoring using wearable Microsystems, but would those Microsystems increase or decrease the cost of the health care cost?. Could be defined the requirement of this Microsystems more precisely?

Participant B's Feedback

Q1: Should the EC stop financing research in Lab-on-Chip for human diagnostic?

The time required to reach a state at which a device could be considered a prototype to be used as a diagnostic tool is in general terms longer than 3 years. This is even more dramatic within the area of LOCs, where several different components and technologies should be combined and implemented. Perhaps, the problem is the lack of continuity of a project that has reached a level of proof of concept.

Many projects address the "technological" issues ("Typically the project starts from cero and sensor, micro fluidic, biological assay, reader and software are developed and integrated with more or less success during the project"). The "hardware" items should be reasonably available now. The problem is in the biological assay-analytical protocols side and its practical implementation. The projects should fund the application and not the "hardware" development.

- **Q2: Is there a future for MNBS for drug discovery, environment, and food and drink control?**

  There are many interesting applications of microsystems for the environment and food sectors. But in the last years the clinical and biomedical applications have been given priorities, and therefore a lot of groups have addressed their

research on this direction thus abandoning other applications. Besides, the money addressed to I+D+i from industries of food and environmental control is lower, compared with pharmaceutical industry, for example.

Food is in the headlines of every initiative dealing with new technologies and societal challenges, but it has been hardly properly taken care of in the MNBS area. For a series of reasons, some of them understandable, it has been shadowed by health related applications. More often than not, even when appearing in the headlines it is the food safety edge the one being retained. But food is more than safety; it is also quality, process control and production management. There is much to be gained in terms of knowledge and process and product consistency if smart systems are let to prove their strength there. Quality control and process control are less subjected to the regulatory restrictions that stand in this application when dealing with safety aspects. Also unlike the safety aspects, they tend to be better served by physical and chemical sensing than by biological sensing, making them more apt for on-line rather than at-line control. It is important to have this in mind and keep those non-strictly bio aspects inside MNBS to avoid dispersing and thinning out even more the food topic.

The potential of new enabling technologies are more poorly established in the food sector than in the health sector. Food industry and food researchers are not fully aware of what smart systems may bring. Their community and our community have not mixed enough yet, and after some trials there have been no continuing efforts in this direction. We advocate, if possible, for some temporary focused action in food within ICT. It could be argued that ICT should not be the only one left with the 'burden' of the lack of knowledge about this existing potential. A common approach with KBBE could be studied then (it is hard to believe that ICT-MNBS shall not pursue something in common with a topic that calls itself knowledge based bio economy!)

In the meanwhile, it would be beneficial if some specific CSA and/or food oriented research project could make it to keep the flame alive. In this sense, IPs offer the advantage of reuniting the research and the dissemination/raising awareness components. It must be noticed, though, that in addition to being less 'sexy' when compared to health, projects approaching wisely the food application may deal more with integration and adaptation of already existing technologies than with edgy research, and as a result they risk obtaining poorer marks when left to free competition.

- **Q3: Should wait the financing of project in Microsystems interfacing with the nervous system until the neurophysiology is more advanced?**

It looks like the challenge is still mainly in the neurophysiology, including the knowledge of the behavior of the interfaces between microsystems and the nervous system, but microsystems themselves may provide this knowledge.

- **Q5: What is the role of Microsystems for surgery?**

  One reason may be that the challenges seem to be more at the system level (mecatronics) than at the microsystem or "chip" level. In many cases (e.g. smart stents) flexible non standard electronics may be required.

- **Q6: Could wearable Microsystems (in or on the body) help with the challenge of the aging population?**

  In the mid term, wearable microsystems with remote monitoring will probably increase the health care cost. For the aging population, clearly the more widely controlled parameters are blood pressure and glucose concentration.

Participant C's Feedback

- **Q1: Should the EC stop financing research in Lab-on-Chip for human diagnostic?**

  I fully understand the concern. Science and Technology always takes more time to take off than expected and we should be patient. However, if we take the Gardner hype cycle model, I believe Labonachip is right on the Slope of Enlightment. We have obtained the right maturity level in terms of election of materials and fabrication processes which should not be giving for granted. It is true that microfluidic control components might need further tested under real situations. However, we have a set of components ready to be integrated to create LabonaChip based systems. We should not start from scratch anymore. This feasibility was not available before and it is the moment to take advantage of it.
  I believe that the 8th FP call regarding Labonachip must be focused on three aspects: Reinvention, Applications and Manufacturing automatisation.
  In the former case, you still need to allow basic researchers to invent new concepts born within the ICT community working on nanofluidics, digital microfluidics, new fluidic control components, materials or LOCs. But this work should be funded under one crucial condition; FP8 should ask researchers to link their innovation to a real application or social/business need. This should be done independently how peregrine or bizarre the idea is.
  In the second case (Applications), we need to take what is being developed, optimize it and apply it in applications with a close approach to the market creating a system. We should work on Validation of the systems but testing those aspects which are crucial for the success of the system. We should work on improving reproducibility, repeatability, sensitivity, specificity or cost rather than nice looking approaches of the system. Apart from the diagnostic

use, do not forget the LabonaChip potential working as a microreactor for biochemical synthesis or integrative biology.
In the third case, it is compulsory for the competitiveness of the Labonachip players to count with a manufacturing system automatic enough to deal with the whole fabrication: injection/embossing, metallization, reagent dispensing, freeze dry, surface modification, pick and place, sealing, dicing and blistering. Once again, this has to be done with an application in mind to test the performance. This is one of the most important steps that need to be funded.
How to do that? It is time for convergence. Proposals cannot be developed exclusively from ICT community. I propose to create joint calls with: Agriculture and food; Biology and medicine; Environment, and Industrial manufacture.Proposals should be chosen under a lens of pragmatism. Do we want to promote swallow research collaboration among too many partners or close collaboration between few partners with deep and long term results? If the answer is the latter one, we should promote those projects that seem more manageable and feasible with partners that have enough critical mass to deal with as many aspects as possible.

- **Q2: Is there a future for MNBS for drug discovery, environment, and food and drink control?**

In the case of food and drink control, I believe there is a potential market. The reason of the low amount of projects may lay down on the fact that food might no be as fancy as health. Besides, added value in food products is also much lower than in health making difficult to develop systems that fit in cost or attract investors. Finally, legislation and regulation seem reluctant to use new technology. However, the recent developed Labonachips, manufactured at a very low cost by injection and lamination, could be successful. It is needed a successful case to attract others to follow the same path. I believe this successful case will take place in a short term. Therefore, I think that food processing could take advantage of labonachip based systems. For example, Labonachip systems to immediately detect the freshness of the fish in big fish auctions; pathogen free eggs or monitoring food chain processes.

- **Q3: Should wait the financing of project in Microsystems interfacing with the nervous system until the neurophysiology is more advanced?**

I do not know.

- **Q4: Is there a future for deep brain stimulation?**

I do not know.

- **Q5: What is the role of Microsystems for surgery?**

The silicon micromechanical structures working as surgery are too fragile. I believe that there is room for polymer micromechanical surgery.

- **Q6: Could wearable Microsystems (in or on the body) help with the challenge of the aging population?**

In the case of wearable Microsystems, the limited types of samples make very difficult to obtain useful information. Deeper biochemical analysis needs to be done in sweet analysis as a source of disease information. I think there is no much research on that. Therefore, I think this wearable Microsystem research need to be done in collaboration with a health program (joint call?)

Participant D's Feedback

- **Q1: Should the EC stop financing research in Lab-on-Chip for human diagnostic?**

REGENE-ARRAY project aims at developing a versatile Lab-on-a-Chip (LoC) technology. The two main characteristic of this concept are:
1) the reusability of the chip by REGENERATION of active receptors;
2) its generic micro-fluidic/micro-optic analysis chip which can easily be CUSTOMIZED by third parties.

Present commercial LoC diagnostic systems are based on disposable, low cost chips. Disposables are moulded plastic chips with limited functionality. Although material and production costs of disposables are relatively low, investments to develop a disposable based system are high, which makes this model only feasible in high volume (medical) markets. Niche like applications, e.g. analysis in the food and environment sector are less suited since the development costs per application are too high to allow a reasonable price per analysis.

To address low volume markets it is required to reduce development costs and to make the chips re-usable.
REGENE-ARRAY aims to bring about a paradigm shift by the creation of a versatile and reusable Lab-on-a-Chip (LoC) biosensor platform. To appreciate the impact of this objective, one first needs to understand the character and current paradigm of disposable LoC devices.

Advantages of LoC devices
LoC devices offer many advantages over common analysis technologies since they integrate one or several (analytical) laboratory functions on a single chip of only a few square millimetres to a few square centimetres in size. These advantages are:

small size and weight → portable analysis equipment and on-site implementation

short running-time of analysis chain → on-line implementation (continuous monitoring)
tiny amounts of sample → easy handling and fast measurements
high degree of integration and automation, minimal human input → cheap and high reliability

Since the mid-1990s the trend exists to reduce the production costs per chip in order to effectively penetrate the market of analysis technologies. Currently, disposable chips made by cost-effective mass-production techniques, define the common standard in Research and Development, although the commercial LoC success stories are scarce.

Disposable vs. reusable solutions
Although disposable chips appear to be appropriate for some large-scale or monolithic segments of the market, this concept is less suited for more specialized applications. Due to the high development costs and risky investments, hardly any disposable LoC's are devised for specialized niche applications outside medical applications.

The development of the REGENE-ARRAY represents a disruptive approach to challenges in the contemporary analytical world of which the focus lies mainly on further development of disposable LoCs or traditional (bulkier) analytical methods. Unfortunately, the commercialisation of disposable analytical micro devices requires high and risky investments, which limits the application for (niche) products outside the medical analyses.

The REGENE-ARRAY will be an advantageous analysis instrument platform especially for SMEs, as the overall concept removes an essential roadblock for commercialisation of LoC. The new LoC concept reduces development costs due to its large versatility and reusability. In this way a higher added value per LoC can be achieved, which will justify investment for lower market volumes. When SMEs will take up the REGENE-ARRAY, the progress in microscale biosensors is rapidly transformed into benefits for Europe's industry into a large variety of niche markets in Food & Beverage and Environmental Water and other on-site analysis/detection requiring application fields."

The main technical roadblock clearly is the ability to regenerate in assay based detection.

- **Q2: Is there a future for MNBS for drug discovery, environment, and food and drink control?**

As is clear from the statements above: definitely yes, especially if it will be possible to use high-added value chips more than one time. A nice example is the development of an on-line analysis system for water applications at our spin-out company CapiliX in Leeuwarden, the Netherlands (see www.capilix.com).

Next to the environmental and food diagnostic/analysis application, because of our 'expensive' platform, we also are focusing on the drug discovery/development application with 'cells-on-chip'. Attractive applications and business cases are testing of drugs in living cells (functionality, side-effects) and the (pre-)selection of good-functioning genetically modified cells for biopharma production. We just started a big nationally funded R&D project on these subjects.

Participant E's Feedback

- **Q3: Should wait the financing of project in Microsystems interfacing with the nervous system until the neurophysiology is more advanced?**
- **Q4: Is there a future for deep brain stimulation?**

Let me first present myself as a neurologist and neurophysiologist with a keen interest in active implanted devices including their engineering aspects (I am teaching a course on bioinstrumentation and one on implanted devices at the engineering department of our university). My interest was of course cached by your questions about neural interface and deep brain stimulation. I have been actively involved in several European projects among which MIVIP and OPTIVIP (visual prosthesis stimulating the optic nerve) as well as SENS and IMANE (improving the interface to the peripheral nervous system). I personally coordinated the last two projects. I have served as a review expert for NEUROPROBES, a project with relatively similar topic but much larger size. It is also important to indicate that, while working at the Université Catholique de Louvain in Brussels, I was one of the founders of the spin off company Neurotech SA for which I still work as a part time advisor.

A first comment is about the economic impact of such projects, simply observing the history of Neurotech. This company is now in the last months of a CE marking procedure before to enter the market with a vagus nerve stimulator for the treatment of epilepsy. This is a fast growing market where only a single American competitor is present. Neurotech was started in 1996 and participated in the four projects mentioned above, starting with MIVIP and OPTIVIP. I can certify that without the European projects, Neurotech would not even exist. Thus, in this example, objective data about the economic impact of the projects will only be available by the end of this year and 2012. We really hope this will be a success story but it had a gestation period of 6 (the last project, IMANE, started in January 2006) to 15 years. Admittedly, this is just one example, but we really believe that the time scale needed for a proper evaluation is much longer than often anticipated and this might lead to a wrong judgement.

Neurotech is a very small company and has now a little over 10 employees. It nevertheless sets out to compete about high-tech products with a much larger player. The secret is networking with many partners in Europe. The

culture of networking and finding the right partners across Europe is a direct result of the European projects.
Collaboration with the university has proven very important. It was of course 'built in' the bird of Neurotech but fruitful collaborations have been established with several other universities as well. The main difficulty here is the difference in point of view and role in collaboration. At the university, research must take on an exploratory attitude, always ready to pay attention to unexpected results that might lead to important discoveries or completely new fields. To the contrary, industry must close its mind to side ways and focus on a well defined practical objective, using all available means to reach it. After all, the industrial investor took real risks in a project in which he believes with guarantee of success. The university and industrial attitudes are necessary and complementary. Sometimes, it seems that these differences are not well recognised in research projects when both partners are trying to adopt an inefficient intermediary point of view. This is very close to the problems of public- private partnership coordination. The worst case is when all adopt an in between position, loosing the specific value of each partner. It is much more rewarding to recognize the specificities of each, make the necessary effort for cross understanding while using each partner where he is best for.

Let us now come to the topics of brain interface and deep brain stimulation. We see this topic as a new but extremely promising endeavour for the following reasons.
The nervous system can for a large part be described as a computer handling information in an electric form. Despite the fear that the word 'electricity' sometimes induces, our brain is very much an electrical machine and electricity indeed is extremely well tolerated by the brain and the body compared to the many unknown and unexpected actions of drugs.
Electrical activity is important for the construction of the nervous system during embryogenesis and later in maintaining it in good shape. Electrical stimulation is and will probably remain an important tool across the field of revalidation even as a temporary mean for the body to heal itself.
There are already many examples of well accepted clinical applications (pacemakers, cochlear prosthesis, stimulators against pain, DBS in Parkinson, brain- computer interfaces, to name just a few).
Clearly, the many more examples that are announced are in sharp contrast with a lack of knowledge at several levels most of those treatments are still very much empiric and require more physiological knowledge
- Most of those treatments are still very much empiric and require more physiological knowledge
- We need also a better technical training of the medical professionals involved
- Taking out the 'brakes' above will clearly accelerate the development of the field.
Surgery should be presented in a realistic way. Yes it does impress people fearing the surgical invasiveness, but we see that patients quickly forget after the operation. A successful operation often gives a feeling of complete health restoration whereas medication continuously remembers the patient to

his/her state of dependence and exposes him/her to frequent chronic complications. Patients carrying an implant often describe surgery as less invasive than people think and medication is a bigger burden than expected.
Financially, implants represent a significant 'one time' expense that can easily compete on the long run with the accumulation of the recurrent payments for a drug treatment.
Nowadays, most of the existing neural implant applications are completely empiric. We do not have the necessary knowledge about the nervous system to really design new therapies. This has three consequences:
- It is very likely that today's applications are far from optimal.
- We are probably missing many useful applications
- Any trial will have an exploratory character about the brain function and not be limited to the clinical test of a therapy

In too many Micro-Nano projects, developments are seen from a strict engineering point of view (which are important of course), but the bio components is limited to biocompatibility pass or fail tests. This is incredibly primitive. The body uses a set of very sophisticated reactions to all implants (including the so-called biocompatible ones). Knowing the details of these reactions and taking them into account in the design of an implant is clearly a necessity in areas where high parallel interfaces are required (brain and vision for example). When the tissue reaction is part of the overall design, there is an important pressure on the development of new materials and nano-technologies. A better multidisciplinary interaction would cross-fertilize the different disciplines involved. By multidisciplinary, we really mean a collaboration within which each partner takes care of his own field but puts enough effort in learning about the other field to be able to grasp the problems completely. An overlap in knowledge is not a waste, it is a necessity. Sometimes it looks like everyone more or less involved in this field is writing a project to make a new DBS system. This of course is a waste. There is no need for that many designs as long as we lack the knowledge necessary to come up with a proper design. However, many teams working on one or another of the many problems identified in this application would guaranty future innovation and economic impact for the few companies involved in the production of such systems. This probably means that large collaborative projects would be more efficient if the coordination could be made simple enough to be handled by a small company.
Instruments for discovery are necessary despite the limited market for such products. Why would we accept to spend enormous amounts of money to discover a new planet and consider that collecting knowledge about our own brain is a waste? There is no market for a mars exploration system. There is only a need to explore and a hope that the developed technologies will be applied for other more lucrative purposes. Similarly, there is a need to explore the brain and it would be most unexpected that the resulting knowledge cannot be put to good use for the sake of human health. In addition, one would also have the benefits of the new technologies developed for this exploration. No knowledge is useless when the time has come for the benefits to emerge. This is the right time for the brain because man now wants to interfere with it.

Conclusions: In the frame of Lisbon Strategies, European R&D priorities are: stimulate innovation, increase economic impact and answer to major societal challenges (health, ageing population, climate change, food security and raw material rarefaction). The development of neural interfaces is clearly an answer to the first two examples of societal challenges. In addition, this topic has the power to strongly stimulate innovation and increase economic impact is expected to grow very significantly. Of course, some conditions must be taken into account, mainly the specific role of partners (perhaps with specific rules when participating in common projects), a true multidisciplinary and long (ten years or more) term views.