

# NANOMEDICINE 2020

NANOMEDICINE RESEARCH AND INNOVATION IN EUROPE

Concept for a contribution  
of the ETP-Nanomedicine  
to a Public Private Part-  
nership on Health

### Disclaimer and Contact

This document has been compiled by collaborative work of many people involved in the ETP Nanomedicine and is the outcome of an in-depth discussion process that took place in the ETPN. It does not necessarily reflect any individual position or opinion of the authors but shall reflect the general state of the discussion within the Nanomedicine community.

The ETP Nanomedicine

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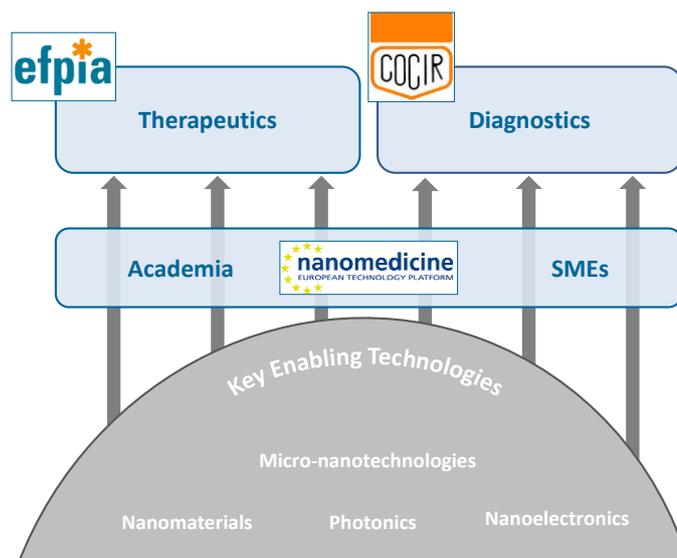
### 1. Nanomedicine in a PPP on Health

The concept for the contribution of nanomedicine can make to a Public Private Partnership (PPP) on Health is based on the three pillars of the Framework Programme Horizon 2020, which are respectively *Scientific Excellence*, *Competitive Industries* and *Better Society*. It outlines how excellent science and research in Nanotechnology can be further improved and translated from a Key Enabling Technology (KET) into new and innovative medical products to be developed for the benefit of the European economy and patients. To achieve these goals it will be necessary:

- to significantly improve the management of interaction between different academic disciplines, different industries (pharmaceutical, medical devices and diagnostics) and clinical disciplines to define and continuously update the topics for a European Strategic Research and Innovation Agenda (SRIA),
- to create and sustain a continuous R&D supply chain from inventions coming from knowledgeable SMEs or academic research to act as innovation drivers to large industry, which commercialise them and
- to set-up integrated infrastructures such as a EU-Nano Characterisation Laboratory (EU-NCL) and GMP production facilities, which will dramatically assist SMEs and/or academia to commercialise their innovations.

The European Technology Platform Nanomedicine (ETPN) has identified and is able and willing to tackle these objectives. It has a track record of networking research organisations, SMEs, and industries leading to comprehensive strategic research agendas, widely used by public funding agencies (ETPN 2006 Strategic Research Agenda, *Nanomedicine: Nanotechnology for Health*; Joint European Commission/ETPN Expert Report 2009, *Roadmaps in Nanomedicine Towards 2020 – Documents* available [on http://www.etp-nanomedicine.eu/public/press-documents/publications/etpn-publications](http://www.etp-nanomedicine.eu/public/press-documents/publications/etpn-publications)). In addition, its members have developed and published concepts for structural changes necessary to improve translation of innovations in Europe to keep production and jobs in European companies (ETPN Opinion paper (June 2010); ETPN White Paper to the Horizon 2020 (2011); ETPN's contribution to the Europe 2020 Flagship Initiative (2010) – Documents available [on http://www.etp-nanomedicine.eu/public/press-documents/publications/etpn-publications](http://www.etp-nanomedicine.eu/public/press-documents/publications/etpn-publications)).

Based on this experience, the ETPN will cooperate with health care industry organisations such as COCIR or EFPIA to bring together EU, national and private resources to create an SME based supply chain for innovative ground breaking therapeutics and diagnostics. It will focus on nanotechnology based medicine and regenerative medicine, moving EU SMEs to a position where their knowledge of development competes with the best in the US and Far East. This strengthening of the nanomedicine supply chain will support nanomedicine innovation and keep high tech jobs in Europe for the benefit both of the European economy and patients.



## 2. Strategic Research Agenda

Nanotechnology is one of the Key Enabling Technologies (KET) that has a big impact on many different medical developments in the three main areas: Therapeutics, Diagnostics/Imaging and Regenerative Medicine. Accordingly, the mapping of nanotechnology research in these areas to diseases is at the heart of the Strategic Research Agenda (SRA) in nanomedicine. The matrix shown below highlights **some** diseases that nanotechnology can address. Based on such topics specific priorities can be identified jointly by industry and the EC, to be filled by dedicated calls for proposals.

Challenges	Therapeutics	Diagnostics / Imaging	Regenerative Medicine
CVD	<ul style="list-style-type: none"> <li>▪ Implantable devices (nano surface modification)</li> <li>▪ ...</li> </ul>	<ul style="list-style-type: none"> <li>▪ Nanoparticles for theranostic approaches</li> <li>▪</li> </ul>	<ul style="list-style-type: none"> <li>▪ Intelligent bioactive materials</li> <li>▪ Stem cell mobilisation and homing at site of injury</li> </ul>
Neuro	<ul style="list-style-type: none"> <li>▪ Semi invasive nanodevices for drug delivery (for Parkinson)</li> <li>▪ Nanoformulations for crossing the BBB</li> </ul>	<ul style="list-style-type: none"> <li>▪ Image guided implantation of advanced neurostimulators</li> </ul>	<ul style="list-style-type: none"> <li>▪ Site specific delivery of neuro active molecules</li> <li>▪ Intelligent biomaterials controlling regeneration in CNS</li> </ul>
Diabetes	<ul style="list-style-type: none"> <li>▪ Insulin measurement and delivery by nano enabled devices</li> </ul>	<ul style="list-style-type: none"> <li>▪ Encapsulation and monitoring of labelled islet transplants</li> <li>▪ Whole body imaging of fat distribution with nanoparticles</li> <li>▪ Implanted non-invasive continuous glucose monitoring</li> </ul>	<ul style="list-style-type: none"> <li>▪ Functionalization of 2D and 3D materials for time and spatial release of biochemical factors for artificial pancreas</li> </ul>
Cancer	<ul style="list-style-type: none"> <li>▪ New nano formulations for targeting agents to tumours</li> <li>▪ Implantable devices for localised delivery of drugs</li> <li>▪ New therapeutic tools with physical mode of action</li> <li>▪ Monitoring of therapy efficacy</li> </ul>	<ul style="list-style-type: none"> <li>▪ Composite nano particles for monitoring of therapy</li> <li>▪ Minimal invasive endoscope / catheter for diagnostics and therapy</li> <li>▪ Nanostructured surfaces for biosensors</li> </ul>	<ul style="list-style-type: none"> <li>▪ Functionalised nanoparticles for targeted in vivo activation of hematopoietic stem cell production</li> </ul>
Inflammation	<ul style="list-style-type: none"> <li>▪ Soft nanomaterials for bone regeneration, Rheumathoid Arthritis and Crohn's disease</li> </ul>	<ul style="list-style-type: none"> <li>▪ Imaging of nanoparticle labelled white cells</li> </ul>	<ul style="list-style-type: none"> <li>▪ 3D Nanomaterials for stem cell immobilisation at site of injury</li> </ul>

The examples in the table above demonstrate the importance of “smart” nanostructured and functionalised surfaces, scaffolds and nanoparticles for new and advanced diagnostic and therapeutic treatments. Especially self-assembled and self-repairing soft nanomaterials and the “loading” of these materials with chemicals such as growth factors, drugs or biologicals, or the assembly of multi-functional nanoparticles combining imaging and drug carrier features will revolutionalise the early diagnosis of diseases and their therapy. Cancer, for example, as a major cause of death needs new therapeutic approaches, which target the disease and avoid drug resistance. Nano-delivery of drugs has and will provide new approaches to address such unmet medical needs in cancer and other diseases. In addition, many nano-features will be crucial prerequisites for implementation of personalised medicine and therapy or even treatment of chronic diseases.

However, the nanotechnologies in these treatments are developed mainly by physicists and chemists and their spin-offs, who do not know much about biology and medicine, and, even more importantly, how new technologies can be translated into medical applications nor how they can be manufactured in an industrial environment. Therefore, an organisation is needed, where different academic disciplines, different industries and clinical disciplines can discuss and work together on new technologies for improving healthcare. The ETPN has managed such interdisciplinary discussions several times, leading to SRAs for diagnostic, therapeutic and regenerative medical topics. Therefore, the research agenda for the PPP on Health agreed upon by COCIR and EFPIA should utilise the experience of the ETPN; the existing research roadmaps, the ETP Nanomedicine Strategic Research Agenda as well as the Nanomedicine Roadmap document (ETPN 2006 Strategic Research Agenda, *Nanomedicine: Nanotechnology for Health*; Joint European Commission/ETPN Expert Report 2009, *Roadmaps in Nanomedicine Towards 2020* – Documents available [on http://www.etp-nanomedicine.eu/public/press-documents/publications/etpn-publications](http://www.etp-nanomedicine.eu/public/press-documents/publications/etpn-publications)).

### 3. Introducing Innovation to the Nanomedicine Research Agenda

The SRAs defined by the Nanomedicine community and in particular the ETP Nanomedicine over the last half decade were mainly based on technology push and clinical demand. The next level of the strategic development of the ETPN is to emphasise the introduction of “Innovation” into the Agenda by improving the translation of nanotechnological R&D into medical applications. This is a Grand Challenge that has been at the core of the ETP since its formation.

Based on the definition given by Wikipedia<sup>i</sup>, innovation applied to Nanomedicine, means for example, to enable personalised medicine through stratification of patients by nano-based diagnostic tests (companion tests for instance) or imaging agents, which is a new and different approach to current medical practice. Another example could be the combination of a diagnostic tests and a therapy within one type of nanoparticle. However, for such an innovation to reach the patient, a close and well informed interaction between public and private partners is mandatory. Therefore special PPP structures are needed, which actively manage communication and collaboration between all stakeholders, including regulatory bodies to effectively translate and commercialise ideas.

### 3.1 Innovation needs effective translation

The ETP Nanomedicine has since its inception defined its role as providing an industrial perspective on the application of nanotechnology to human healthcare. Whilst societal need has been the primary driver for healthcare projects, it is not sufficient without any mechanism to select and fund translatable projects from the inevitably undevelopable majority. The ETPN has already reacted to this translation failure with various papers highlighting the crucial issues (ETPN Opinion paper (June 2010); ETPN White Paper to the Horizon 2020 (2011); ETPN's contribution to the Europe 2020 Flagship Initiative (2010) – Documents available [on http://www.etp-nanomedicine.eu/public/press-documents/publications/etpn-publications](http://www.etp-nanomedicine.eu/public/press-documents/publications/etpn-publications)).

Much has changed in the last decade in healthcare companies, with the result that Pharma companies for example are moving to a global open innovation model, with a reduction in their own research capacities, especially in Europe. They have found their revenues under pressure and their pipeline of new products unable to provide the income to support the headcount without a loss of jobs. Much of large Pharma has now radically changed and embraced in-licencing and Open Innovation (OI) to try to lower costs and to raise innovation standards. One consequence of this move is the cut in R&D staff in Europe's research centres, and an investment in business development with the aim of technology scouting and in-licencing from academia or SMEs. This global strategy aims to recognise novel putative products or concepts, from SMEs and academics, wherever they originate in the world. The advantage for large Pharma as well as for diagnostic and imaging companies is that it does not require early investment of resources, just the use of the knowledge of what makes a good potential marketable product. However, this OI concept will only succeed in Europe, if projects from the emerging healthcare supply chain of SMEs (and even academics) are developable.

The car industry in Europe has seen similar dramatic changes and struggled to compete until a new business model was established, i.e. the setting up of a globally competitive supply chain of SMEs. As a consequence, the car industry has evolved to keep a large part of its manufacturing in Europe. An analogous supply chain is needed in Europe to provide the ideas to feed into the healthcare supply chain. An ideal scenario would consist in innovative SMEs testing the initial clinical proof of concept of new nanomedicines (up to phase I or IIa) and if successful, transferring their proof-of-concept projects to large companies who remain the only financially and technically capable organisations to bring them to the market. Such a system is in operation in the US and has underpinned the development of biologicals, which has been the fastest growing sector for new drugs over the last two decades. The difficulty of such a change in ideas and processes in Europe is the fact that a change in academia is compounded by the lack of exposure to open innovation ideas and the strength of academia's perception of 'freedom of research'. To overcome this situation it will be necessary to

- inform academia and SMEs about the rules and principles of translational research
- introduce course elements on translation/innovation in undergraduate courses in Europe
- increase visibility of selected SMEs with translatable products, to large companies
- involve large companies or industrial experts in the evaluation, selection and tutoring of translational projects under development in SMEs and academia, with perhaps an option to invest resource as an inducement. Only genuinely translational projects should be funded if described as such.

Especially the last point will be crucial for the success of the *Competitive Industries* pillar of the Horizon 2020 Framework Programme. It is important that together with the SRA, horizontal innovation filters are strongly applied to ensure only the best concepts get funded and progressed to the market to help patients. To achieve this, one initial step needs to be the establishment of an ETPN translation advisory committee, with up to ten experts with expertise in intellectual property, market need/market access/reimbursement, manufacturing and CMC, preclinical and clinical development, regulatory, business development, and communication. Based on their experience the experts will apply innovation filters such as:

1. Safety evaluation
2. Technical evaluation
3. Competitive evaluation
4. Regulatory evaluation
5. Reimbursement evaluation
6. Commercial evaluation
7. Clinical trial design
8. Paradigm change

The ETPN will discuss and expand this concept for an overhaul of the proposal evaluation process together with EFPIA, COCIR, and relevant EC units. The main goal is to efficiently link SMEs as main drivers of innovation in nanomedicine with large companies to provide guidance to translatable R&D projects up to proof of concept or clinical phase IIa. At this point projects can be taken over by large companies, which are the only organisations capable of taking products through regulatory approval and reimbursement issues onto the market to help patients.

Together with the infrastructures described below these plans provide a sound structural framework for efficient development of nanomedical innovations within the proposed PPP on Health helping to meet the current and future societal challenges.

#### 4. Infrastructure Measures

In addition to an inefficient selection process of translatable projects there is a lack of technical infrastructures, such as pharmacology and toxicology facilities, which would support innovation in healthcare for both SMEs and academics. Building these infrastructures will keep nanomedicine research in Europe and will contribute to re-industrialisation by making the EU more competitive in nanomedicine development. As a consequence the ETPN proposes as main structural actions to introduce a few new infrastructures such as

- a EU-Nano Characterisation Laboratory (EU-NCL) for physical, chemical and biological characterisation of Nanomaterials for medical use and
- translation facilities with GMP manufacturing capabilities, which both will assist academic groups and especially SMEs to develop their projects faster up to a level ready to be taken over by industry.

Below two concepts are further outlined that are deemed most relevant for ensuring the competitiveness of the European Research and Innovation Area, namely the setup of a nano-characterisation infrastructure, as well as the creation of a translation infrastructure.

### 4.1 Nano-Characterisation Infrastructure

#### Mission

The creation of a European Nano-Characterisation Laboratory (EU-NCL) performing pre-clinical level physical, chemical and biological characterisation of nanoparticles intended for medical applications is required. It will contribute to the competitiveness of Nanomedicine products and tools by increasing the industry readiness of research offerings and thus stimulate private-sector investment in this area. This is also a question of sovereignty to protect EU innovative products from competitors especially in the US. In the US the Nanotechnology Characterisation Laboratory in Frederick, MD, USA (US-NCL) (<http://ncl.cancer.gov>) has offered for several years its characterisation services for free to international projects which have undergone a positive evaluation. As a result, European researchers and also European SMEs work together with the US-NCL and therefore facilitate a know-how drain from Europe to the US. It is therefore an undisputable fact that the best database on nanoparticles for medical use and on the most promising nanoparticles (including those from Europe) is at the US-NCL, so to say handled by an US Agency. To change this the European Nano-Characterisation Infrastructure should serve as a European knowledge base for medical researchers and facilitate the development and translation of nanoparticles for clinical applications. This will ensure that European knowledge is retained in Europe for the benefit of the European economy and healthcare system.

#### Objectives

The European Nano-Characterisation Laboratory will provide a comprehensive set of characterisation parameters (physical, chemical, in vitro and in vivo biological properties) allowing researchers to apply their particles to solving problems that affect patients' health. A direct link with the European Medicines Agency (EMA) is required to facilitate the approval of Nanomedicine products based on the characterisation report delivered by the European Nano-Characterisation Laboratory.

#### Proposed structure

Europe already hosts outstanding centres characterising some of the parameters required for a legal approval. Therefore **no new centre should be created** and the effort should be set on networking and coordinating the existing centres in order to provide a full characterisation set. Because the selection of analytical tests is correlated with the tests required for the approval of clinical trials, this decentralised centre will not only provide service analysis but also will have a strategic and political role in helping newcomers, like SMEs, find their way towards clinical trials. Therefore a distributed network of existing characterisation centres is required. This infrastructure should be managed centrally by an independent unit, whose role would be to coordinate the logistics of the probes between the centres, to guarantee the quality and efficacy of the characterisation process, to manage European funding and to act as a single entry point.

The structure could start with 3 or 4 nodes and integrate further characterisation centres later on, adding additional characterisation procedures and methods, according to the selection criteria set by the management unit. The addition of new centres will be reviewed by the central unit and steering group. European funding is required to build up and run the management unit, as well as to cover the costs linked to the characterisation of nanoparticles by the individual centres.

### Expected Outcome:

- Distributed European Nano-Characterisation Laboratory with central management facility.
- One-stop shop for the European Nanomedicine, clinical and pharmaceutical community facilitating the standardisation of products and the exchange of results for clinical studies.
- Full standardised analytical report ready for IND dossier (Investigational New Drugs) by medicine regulation agencies.

## 4.2 Translation & SME Inclusion Infrastructure

### Mission

Establish a novel translational Nanomedicine infrastructure based on federating existing distributed Nanomedicine research and clinical centres of excellence. The structure to be created will have to interface existing R&D centres and organisations to ensure efficient translational R&D programs, from ideation up to the first in man or proof-of-concept studies according **to industrial and regulatory standards**. The objective of such an endeavour is to increase the attractiveness and success of SMEs by reducing the risks in development and improving progress to clinical practice. The early inclusion of SMEs in this process is essential, as knowledgeable SMEs are the only way to create a productive supply chain in Europe.

### Proposed structure

The nanomedicine translation infrastructures should offer scale up facilities and GMP manufacturing of GMP batches for early clinical trials to SMEs who don't have access to such facilities. This structure needs public funding and political support and should have experience and professional structures in technology transfer and clinical studies, ready for industry to connect to.

### Expected Outcome:

- Distributed Nanomedicine translation infrastructure with central management facility.
- Industrial and clinical Catalysts as advisors.
- GMP manufacturing of nanomedicine batches for early clinical trials (phase I, IIa).

## 5. PPP Governance Structure

The introduction of nanomedicine into the programme and governance structure of a PPP Health needs to be defined together with EC, COCIR and EFPIA, because the latter represent the companies which take nanomedical developments from the Key Enabling Technologies supply chain to the market.

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<sup>i</sup> "Wikipedia defines Innovation as the development of new customer value through solutions that meet new needs, unarticulated needs, or old customer and market needs in new ways. This is accomplished through different or more effective products, processes, services, technologies, or ideas that are readily available to markets, governments, and society."