

Building the European Nanomedicine Research and Innovation Area EuroNanoMed

10 years of funding innovative research projects

Irit Allon¹, Nava Levine¹, and Ignacio Baanante^{2*}

¹Chief Scientist Office, Ministry of Health, Israel

²National Institute of Health Carlos III, Spain

Abstract

It has been 10 years since the establishment of EuroNanoMed (ENM), presently in its third phase. For those 10 years, research and innovation funding organisations in Europe and beyond have been joining forces to fund excellent innovative research projects in three main topics defined by the European Technology Platform on Nanomedicine: targeted drug delivery, diagnostics, and regenerative medicine. Ten joint transnational calls have been launched (the 10th call is ongoing). So far, 90 transnational projects have been funded, including 460 research groups from over 20 countries. In the Joint Transnational Call 2017—co-funded by national and regional funding organizations and the European Commission (EC)—16 projects were funded with a total investment of 14 million euros, including 3.3 million euros from the EC. In addition to ENM's main activity of funding transnational innovative research projects, it collaborates with sister initiatives in nanomedicine and translational research. ENM has organised review seminars as well as safety, ethics, and regulatory affairs training workshops. The purpose of this article is to introduce the ENM initiatives to the scientific community, that together with its collaborators shape the map of nanomedicine in Europe.

Keywords:

Nanomedicine, nanotechnology, transnational research, diagnostics, regenerative medicine, targeted delivery systems, personalized medicine, health, European research and innovation programmes, Horizon 2020, EuroNanoMed.

Rationale and Purpose

The purpose of this article is to introduce the ENM initiatives (I, II, III) to the scientific community including tangential organizations and available infrastructures in Europe that together, shape the map of nanomedicine research in Europe. The article includes an overview of the purpose and structure of ENM, its activities, primarily funded projects, a description of future perspectives, and the environmental crosstalk between ENM and related initiatives for the benefit of the research and innovation community.

Introduction

Over the past few years, Europe has successfully contributed to many of the achievements in basic research dedicated to

nanotechnologies. However, regarding the nanomedicine field in Europe, a critical issue concerns the ability of the research and technology development players to effectively move innovation from basic knowledge to either industrial or clinical applications such as translational research. To bridge this gap between research and clinical/commercial applications in nanomedicine, effort at the European level is essential to reaching a critical mass in terms of research and development (R&D) project portfolios and scientific excellence, and to achieve a sufficient level of competitiveness.

EuroNanoMed (ENM) is a platform for funding agencies and ministries that was established in 2009 with the support of the European Commission (EC). National and

* Corresponding author: ibaanante@isciii.es

regional research-funding programmes joined together with the goal of creating and funding collaborative research and innovative projects and to convert research in nanotechnology into practical gains in medicine. It supports multidisciplinary and translational research and innovation projects that cover **regenerative medicine, diagnostics, and targeted delivery systems**.

Over the years, ENM has invested effort in disseminating the activities related to funded calls to the scientific community, the private sector, programme managers, and owners and policy-makers at the national, regional European, and international levels, and the general public. The various tools used for communication and dissemination include: the ENM webpage, social media (including Facebook, Twitter, LinkedIn, and others), leaflets, posters, and newsletters that are distributed to a continuously updated contact list, and presentations at conferences, especially those linked to innovation and industry. A service for the general public was also produced, consisting of educational video clips that are available to watch on the web.

ENM is not working alone and there are related initiatives in the landscape of nanomedicine. These include: **ETPN**, the European Technology Platform for Nanomedicine (<https://etp-nanomedicine.eu/>), **EU-NCL**, the European Nano-characterisation Laboratory (<http://www.euncl.eu/>), and nanomedicine pilots funded by the EU: **Nanofabrication** (<http://nanofabrication.eu/>) and **Nanopilot project** (<http://www.nanopilot.eu/>), the **EU NanoSafety Cluster** project (<http://www.nanosafetycluster.eu/>), as well as the **NOBEL project** (<https://nobel-project.eu/>) and the **Health Tech TAB** initiative (<https://healthtechtabs.eu/>).

ENM I (2009–2011) and ENM II (2012–2016) were funded under the Seventh Framework Programme (FP7) of the EC. The current ENM III (2016–2021) is the new ERA-Net Co-fund Action on Nanomedicine under Horizon 2020 that builds upon the achievements of its predecessors to support the European nanomedicine research community.

Purpose and structure of EuroNanoMed

ENM is an ERA-Net for nanomedicine. An ERA-Net is a platform for funding agencies and ministries to develop joint activities and programmes with the aim of coordinating high-

quality research in diverse research fields, in this case nanomedicine, across national borders. ENM started officially in January 2009 (2009–2011) and was later referred to as ENM I with the advent of ENM II in 2012.

ENM II was built on the basis of the accomplishments of ENM I. The increasing number of submitted proposals in the successive ENM joint calls, their quality, and the first outcomes of the funded projects reflected a need in the nanomedicine scientific community for such a targeted initiative. The main goal of ENM II was to go further in supporting transnational research and innovation projects through the launch of yearly joint calls for proposals. These calls allowed partner countries to support transnational collaborative and multidisciplinary research and technology development projects that are in line with the strategic priorities of the ETPN. The funded transnational collaborative research consortia had to involve at least two categories of partners among clinical, industrial, and academic research teams carrying out research projects that would boost translational and clinical research in the field.

In addition to the joint calls, which were launched annually, other joint activities were developed. These included fostering the participation of young researchers in ENM II activities, developing a Strategic Research and Innovation Agenda (SRIA)[1], in close cooperation with the ETPN, creating more interactions within the European nanomedicine community, and improving communications pertaining to nanomedicine to the public. Importantly, regulatory, safety, and ethical issues associated with nanomedicine were addressed by launching two workshops on regulatory and safety issues (January 2014 in Dusseldorf and October 2016 in Berlin), and one workshop on ethical issues (December 2nd 2014 in Oslo). Accompanying these activities was continuous monitoring, alongside the development of a long-term sustainable cooperation framework for European nanomedicine research.

The two first ENMs (I and II) were, respectively, 3- and 4-year programmes funded under the FP7 of the EC; however, the current ENM, ENM III, is a 5-year co-fund programme, funded under Horizon 2020.

ENM III (2016–2021) is slated to launch 4 yearly joint transnational calls (JTCs), the first of which was co-funded with the EC, hence a co-fund call.

ENM funded projects

ENM I

The first phase of ENM started with 24 partner organizations from 18

countries/regions, funded within the EC's FP7 from January 2009 to December 2011. During the life of ENM I, 3 JTCs were launched, and 98 research consortia composed of 504 research groups from 25 countries applied. The applications were reviewed by panels of international experts, and 24 consortia composed of 122 research groups from 19 countries requesting a total budget of 24.7 million euros were funded.

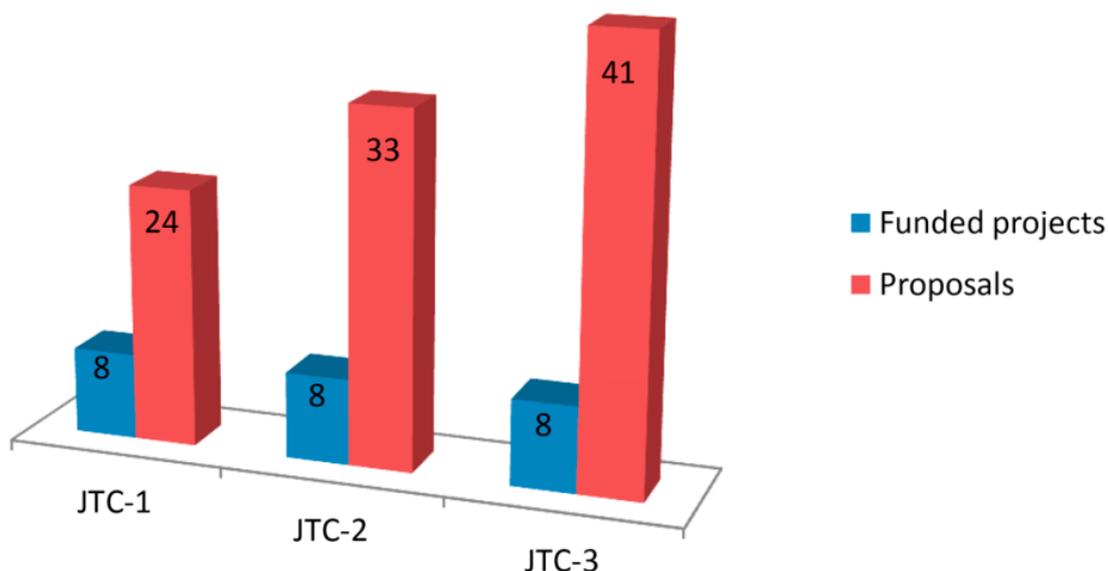


Figure 1. ENM I joint transnational calls (JTC). Under ENM I, 3 JTCs (2009, 2010, and 2011) were launched.

As part of the ENM I activities, an impact assessment was performed for the 24 projects funded during the first phase of ENM. More than **90% of the respondents** declared that the research conducted with this funding resulted in the creation of employment, both through direct influence and by inspiring the future workforce and/or the production of a highly educated and relevant workforce that was in demand by industry and academia. Almost 95% of the respondents confirmed that participation in an ENM-funded project led to increased mobility of researchers compared to nationally funded projects. Also, 35% thought that research conducted through ENM grants had attracted developing businesses through the licensing of technologies/patent applications. Almost 70% of respondents applied to further ENM calls and

to different EU Framework Programmes, and around 60% and 40% of them, respectively, were successful in receiving awards.

ENM II

ENM II was comprised of 20 partner organizations from 17 countries/regions, funded within the EC's FP7 from November 2012 to October 2016. In response to the 4 JTCs launched under ENM II, 228 research consortia composed of 1155 research groups from 25 countries applied. The submitted projects were reviewed by international peer-review panels and 38 consortia composed of 197 research groups from 20 countries requesting a total budget of 28.4 million euros were funded.

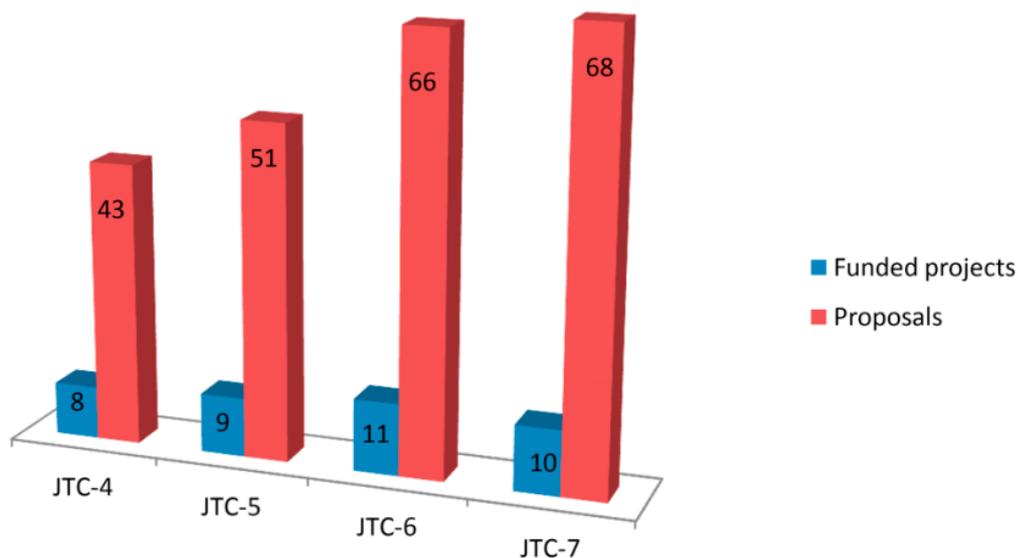


Figure 2. ENM II joint transnational calls. Under ENM II, 4 JTCs (2013, 2014, 2015 and 2016) were launched.

ENMIII

ENM III (2016–2021) is the new ERA-Net Co-fund Action on Nanomedicine under Horizon 2020 that is built upon the achievements of its predecessors to support the European nanomedicine research community. It is comprised of 27 partner organizations from 22 countries/regions. To date, 2 JTCs have been launched under ENM III and a 3rd JTC is ongoing.

Since ENM III significantly extended the number of partner organizations, compared to ENM I and II, the number of applications grew

accordingly. It was therefore decided that the application process, which consisted of a single stage under ENM I and II, would be divided into two stages under ENM III: a first stage for pre-proposals and a second stage for full proposals.

In the 8th and 9th JTCs, 187 pre-proposals were submitted. After review by an international peer-review panel, 68 consortia were asked to submit full proposals. Of these, 28 successful consortia were selected for funding with a total investment of about 23 million euros.

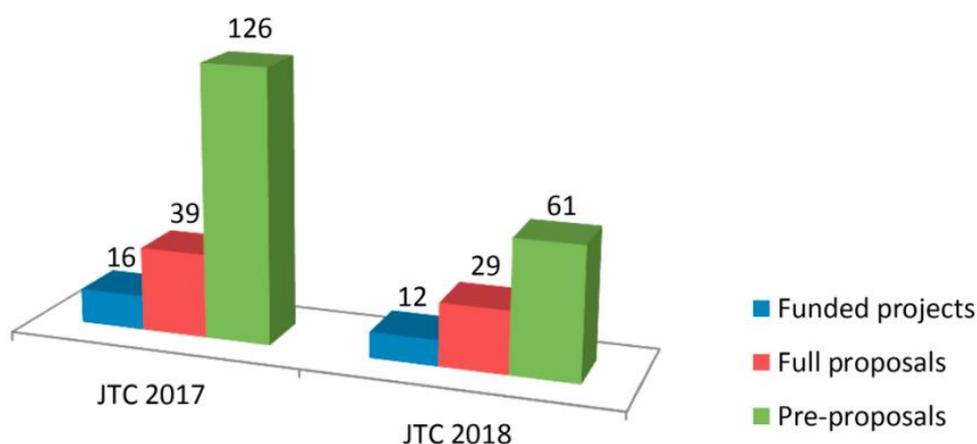


Fig. 3 ENM III joint transnational calls. The application process was divided into two stages under ENM III: a first stage for pre-proposals and a second stage for full proposals.

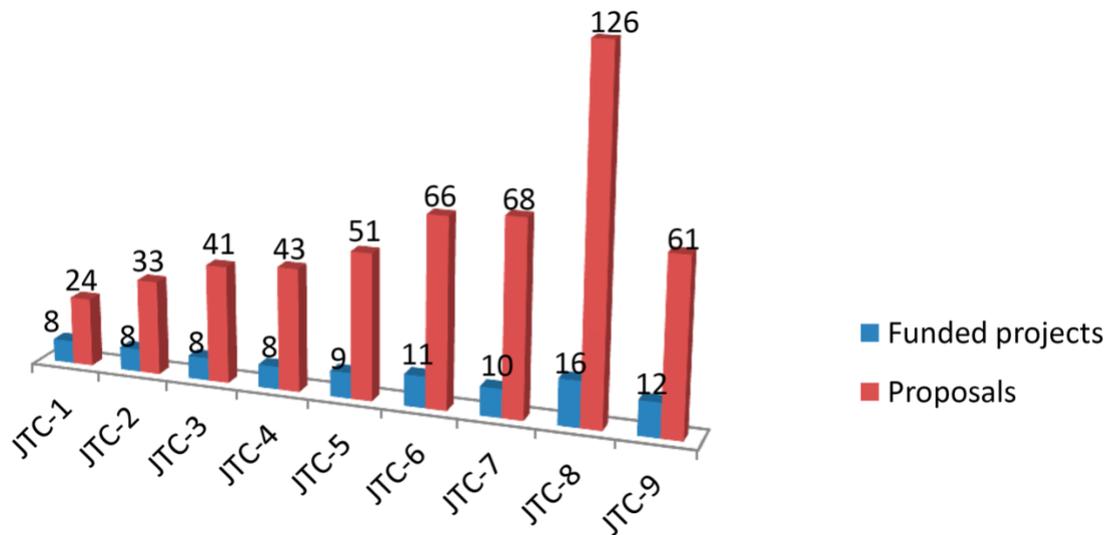


Figure 4. Proposals submitted versus funded projects.

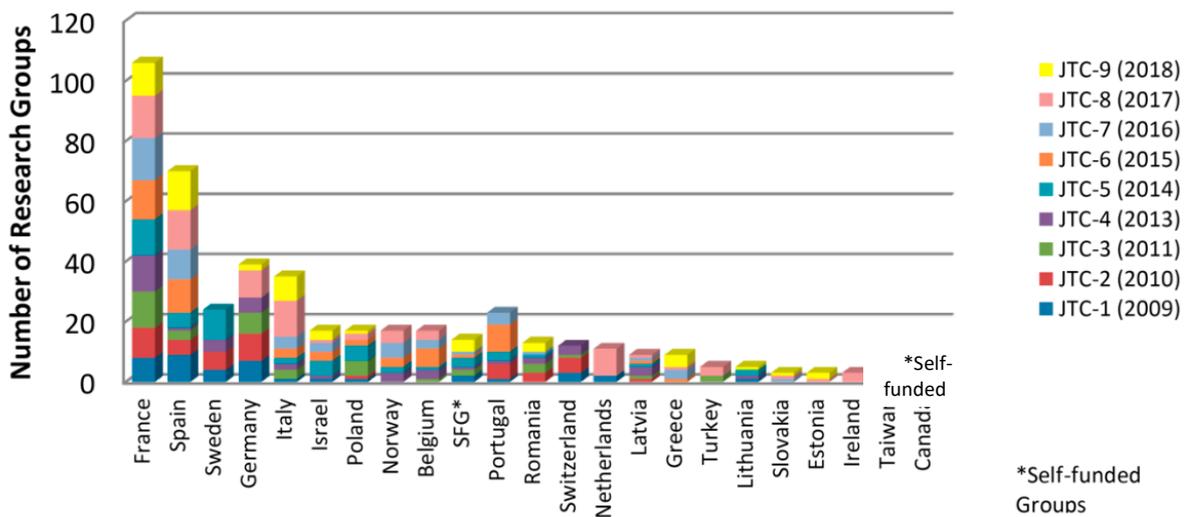


Figure 5. Number of research groups per country.

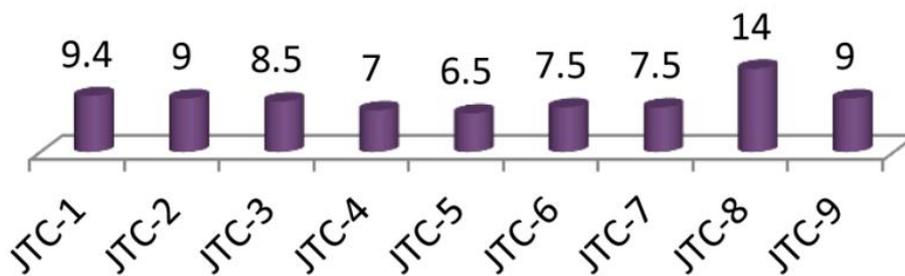


Figure 6. Investments in funded projects (M Euro).

Through 9 successful Joint Transnational Calls launched from 2009 to 2018, ENM has allocated about 75.4 million euros to fund 87

transnational and innovative research projects in nanomedicine

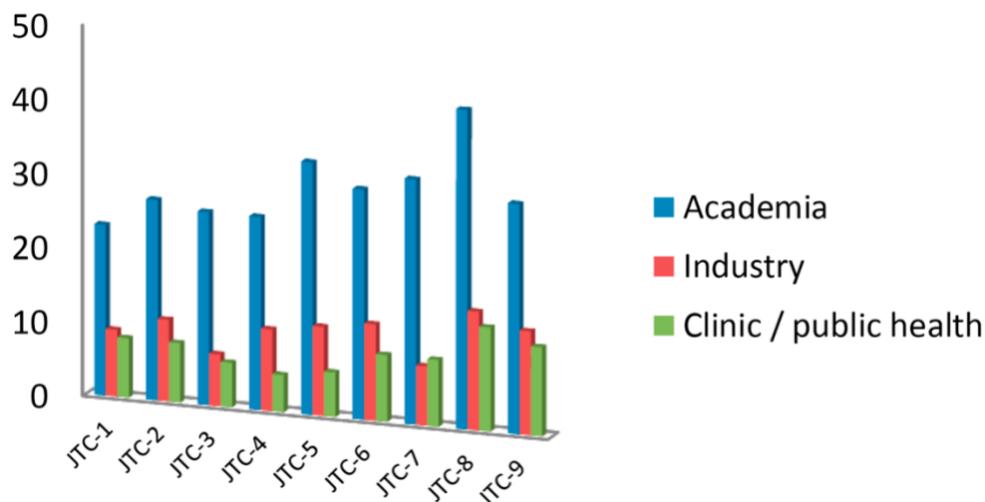


Figure 7. Categories of research groups in funded projects.

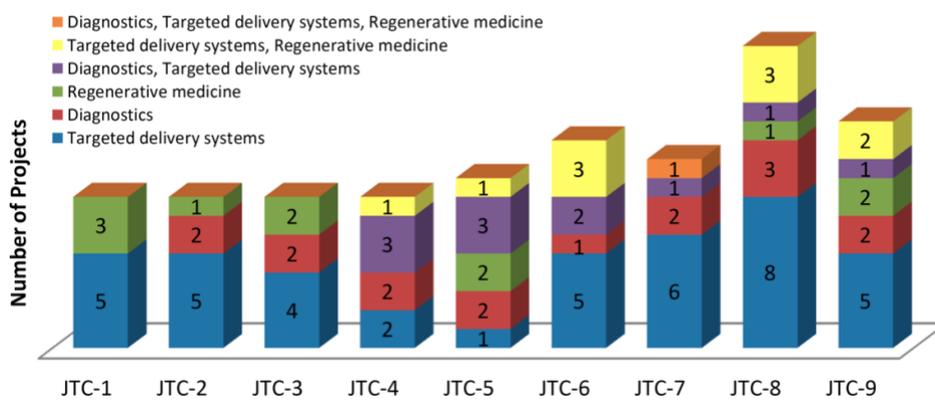


Figure 8. Scientific areas of funded projects

Other ENM Activities

Regulatory, ethics, and safety

Research in nanomedicine is generating new and revolutionary therapeutic and diagnostic solutions that can offer patients more effective therapy and a higher quality of life. Many of these advances cross the classical separation between medical and pharmaceutical products so that classical regulatory frameworks are sometimes inappropriate or even non-applicable to these products. The lack of specific practice protocols and standard criteria for these brand-new nanomedicine products are becoming an important imponderable that may considerably hinder industrial R&D and delay market access for innovative products.

In addition to the technical hurdles that are inherent to scientific research, there are “non-technological barriers” that may hinder market

access to R&D results. One major non-technological barrier in the healthcare sector is the challenging regulatory framework that makes market approval of new drugs time-consuming and costly. This is especially true for nanomedicine, as nanomedical products often lay at, or even cross the border between medical products and pharmaceuticals, and they are therefore subjected to different regulatory frameworks. This is a source of uncertainty for market accreditation. Regulatory frameworks should be discussed at the European level rather than at the national level. In this context, ENM offers a unique platform to deliberate regulatory issues that will facilitate the transfer of nanomedical knowledge from the laboratory to the patient.

Training on regulatory aspects

Aiming to inform and train researchers about regulatory requirements for nanomedical

products, an expert workshop was organised for researchers from ENM (I & II)-funded projects in January 2014. Beyond the training aspect, the workshop also provided a forum for interaction between researchers and experts—especially from funding agencies and European medicine agencies (EMAs)—to call the experts' attention to the researchers' needs and problems. Different topics were addressed, treating the three subfields of nanomedicine with special emphasis on molecular imaging. In addition, a case study of a successful translation of a nanomedical product was presented, and there were presentations on intellectual property rights, ethical, and safety issues in nanomedicine. In addition, representatives of other initiatives relevant to the field of nanomedicine, translational medicine and clinical research were invited, such as ETPN, ECRIN, and EATRIS. A second workshop was organised in Berlin in November 2016, for researchers from ongoing ENM II calls 2013, 2014, and 2015. Topics such as processes and general requirements for the approval of nanomedical products, imaging products, combination products, and cell therapies were addressed, and a case study was presented. Importantly, relevant initiatives in the field of nanomedicine and translational medicine were introduced to the audience, such as ETPN, ENATRANS, EU-NCL, CLINATEC and GMP Pilot Line. The two regulatory workshops also included talks on ethical issues.

Nanomedicine ethical issues

Since the emergence of the field of nanotechnology, ethical issues about nanomaterials have raised concern and have been discussed. As a result, in 2007, the European Group on Ethics published their “Opinion on the Ethical Aspects on Nanomedicine” and in 2008, the EC published the “Code of Conduct for Responsible Nanosciences and Nanotechnologies Research”, as guidance for the responsible development of nanotechnologies. The goal of this task was to explore and frame the ethical issues associated with the field of nanomedicine, with the aim of better taking ethics into account in defining future activities. During ENM II, a report on ethical issues and stakeholders' attitudes towards the code of conduct in nanomedicine was produced. It reviewed ongoing activities in the field of ethics

in nanotechnology and summarised existing studies and articles on the topic.

A workshop on ethical issues in nanomedicine was organised in Oslo, Norway in December 2014. The above-mentioned report was used as input for the discussions during that workshop. As the target audience, researchers from all ongoing ENM projects were invited. The workshop included different lectures on ethical topics given by European ethical experts. In addition, a practical example was given, wherein a researcher presented his project, with a main focus on the ethical aspects. Topics such as occupational peculiarities and hygienic solutions for exposure to engineered nanoparticles, the art of medicine versus technologies of human enhancement: ethical and epistemological considerations, and ethics of nanotechnology were addressed, along with a practical example of the Norwegian project “Multifunctional nanoparticles for drug delivery across the blood–brain barrier,” which was reviewed in terms of ethical issues.

These talks were followed by an ethical matrix exercise, in which the audience was instructed to analyse three chosen ethical questions according to the respective pre-identified stakeholders, of two ENM II-funded projects. In addition, based on this workshop, a scientific article was also published.[2]

Nanomedicine safety issues

Nanomedicine involves engineered nanomaterials, with relevant toxicological issues having a substantial effect on their translation to biomedical products.

Relevant nanotoxicology research and regulation initiatives are being carried out at the European level, along with networking with the EU NanoSafety Cluster, with other more recent projects providing information concerning the safety of nanomaterials, the use of validated methods for nano-risk assessment, roadmaps and priorities for future research, integrated and intelligent testing strategies, and the future regulatory framework for engineered nanomaterials.

During ENM I and ENM II, reviews on the state of the art concerning safety issues in nanomedicine were composed, which took into consideration the general regulations applicable to nanomaterials, and the specific provisions being planned for the future.

Responsible Research and Innovation (RRI)

In ENM III, the network adopted the concept of responsible research and Innovation (RRI). This concept ensures that projects are ethically founded and societally anchored. RRI is based on outreach to, and partnership with potential players in research and innovation, and on wider stakeholder/public engagement, to maximise the relevance of shared knowledge developed and viability of cooperation. As currently defined by Horizon 2020, RRI also includes due consideration of aspects such as education, gender differences and long-term societal, ethical and legal implications.

RRI for ENM includes involving experts in RRI learning, and collaboration with relevant RRI-related projects/pilot lines and with other ERA-Nets by sharing RRI knowledge. Ethics and safety are retained as aspects of RRI, whereas regulatory issues are kept separate. In the running of ENM III, the RRI component crosscuts several work packages. By this, ENM is pioneering the way for the inclusion of RRI in ERA-Net proposals and during the Action.

An RRI Training Workshop for principal investigators of ENM projects funded in 2015–2017, with RRI experts and ENM External Advisory Board is planned for May 2019 in

Future perspectives for ENM

The overall expected impact of ENM III is a thorough, lasting, and forward-looking alignment of current European funding organizations with the goals of creating synergy and coherence in nanomedicine research at national and regional levels.

Nanotechnology applications for healthcare are having a tremendous impact on Europe's industrial sector and international markets. Nevertheless, more effort and partnerships are needed between EU countries to achieve better results, treatments and diagnostic tools. A significant impact on Europe's nanomedical arena is expected by the joint implementation of transnational funding within ENM. Since the main focus of this funding will be on application-oriented research, it is expected that this will tremendously improve coherence and generate stronger synergy in this thematic area. ENM III will go beyond the efforts made in ENM I and II in this respect, by putting in place activities that will create favourable conditions for increased application of project results and their incorporation into industrial medical products. However, these efforts need to show continuity in the mid and long term.

ENM partners are willing to strengthen the alignment and continue their road towards application beyond the current third phase of ENM. Support from the EU is essential, especially for the smaller countries, so first movements have recently begun to ensure the fourth Action, which hopefully will fall into the first year of the next Horizon Europe Framework Programme.

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Bratislava, Slovakia. The aim is to increase RRI competence in both scientist- and research-funding agencies and further develop the RRI guidelines for ENM III.

Young researchers

Encouraging young scientists to pursue a career in nanomedicine is important, as this evolving field is multidisciplinary and consists of diverse areas of expertise. Specific actions regarding young researchers had to be developed to increase the attractiveness of nanomedicine research to the younger generation. These have included networking activities at the review seminars, incentives for outstanding research achievements, and funding measures in the joint calls to encourage the young researchers' participation. During ENM II, mailing lists of young scientists involved in the funded consortia were obtained. Two poster contests with prizes were held for young scientists at the two review seminars.

At the last meeting of ENM II, the young scientist poster award was given to two scientists: **Cyril d'Arros** and **Silvia Pérez**. The award was an invitation to the CLINAM conference held in May 2017, in Basel, Switzerland.