1. Colorobbia Consulting

"We consider pivotal to our R&D efforts an open and continuous dialogue with stakeholders, patients, in the first place, and regulators, health-care professionals, policy makers, media, the society at large. It is vital to improve functionalities, quality and reliability, acceptability, of the NanoMed technologies and products.

With PRISMA we learned the importance of focusing on the ethical and social impacts of NanoMed since the early phases of the development, to become responsive and trustworthy toward needs and requests from users and society. This experience has convinced us of the strategic value of RRI for NanoMed and our organization."

Giovanni Baldi
Director, Ce.Ri.Col - Colorobbia Consulting Research Centre

The company and the technology

Gruppo Colorobbia is specialised in the production and distribution of raw materials, semi-finished products and chemicals for the ceramics and glass industry.

Colorobbia Consulting S.r.l. is the technology service company of Gruppo Colorobbia, with activities on research, chemical and chemical-physical analysis, compliance with environmental and safety regulations, IT and process plant engineering.

The company is active in research and development, prototyping and production of nano-based products to be used in the industrial fields of pharmaceuticals, nanomedicine, coatings and environmental protection, as well as to provide services in term of research, chemical and chemical-physical analysis, compliance with environmental and safety regulations in force, IT and process plant engineering.

The core values of the company include: quality and excellence in R&I; attention to environmental health and safety (EHS) issues in R&D and production processes; respect of ethical standards in R&I; development of innovative solutions to tackle societal challenges. These values guide the overall business model of the company.

The NANOMED project, a large research project based on in-house resources from the company and funding by different cooperative projects, aims to create a technology platform providing an integrated and modular system, for the diagnosis and treatment (theranostic) of cancer and nervous system diseases. It is a nanotechnology based system using a combination of targeted and controlled drug delivery, hyperthermia and radiofrequency and laser imaging methods.

The time to market of these products is expected in a medium to long term time frame.

The technology platform will lead to different products, including a contrast agent, a formulation (drug), a cell therapy system and a portable and integrated medical device to produce the cell therapy system.

For all products, the key research challenge is to realize a personalized and point of care therapy, for a highly effective, accessible and affordable treatment for severe diseases.

Key ethical and social issues of NanoMed include: safety and use/biodistribution of nanomaterials (NM) into the human body, regulatory challenges for NM, including specific issues for NM in ATMP (Advanced Therapy Medicinal Product), open access/information along the value chain for NM, users and stakeholders perspectives/acceptability/ethical aspects, related to nanomaterial and to personalized, point of care therapies and nanomedicine, socio-economic impacts of the new treatments.

Working with Colorobbia Consulting

Activity included a series of meetings in person and by telephone with staff of the company, organization of a multi-stakeholder dialogue designed to address the specific ethical and social issues identified by PRISMA,[3] a public workshop to discuss on the application of RRI in NanoMed,[4] and engagement of the pilots in activities organized by the PRISMA project. The main contact person has been the R&D Manager and a business manager of Colorobbia Consulting and the NanoMed project. Meetings and interaction has been conducted also with people working in R&D and quality, as well as external partners of the NanoMed project.

The company has actively cooperated in all PRISMA pilot activities: has allowed PRISMA partners to get access to extensive information and to get in contact and engage relevant stakeholders of the NanoMed project; has cooperated in the participatory events organized within PRISMA; has provided information to select and measure RRI-Key Performance Indicators for the NanoMed project; has taken part in the the PRISMA pilot kick-off workshop in Brussels (April 2017), and the stakeholder dialogues in Berlin (Nov. 2017) and Milan (Oct 2018); has co-operated in filming a video interview, has discussed, reviewed and agreed on actions to continue pursuing RRI during the next product development phases (roadmap for RRI implementation in NanoMed).

[3] The agenda of the PRISMA and NanoMed multi-stakeholder workshop is available here: https://www.airi.it/wp-content/uploads/2018/11/Programma_workshop_Prisma_Nanomed.pdf

[4] The workshop "Responsible Innovation in Nanotech applications for healthcare and wellbeing" was held on September 13th, 2018 in Rome, within the NanoInnovation 2018 Conference, with the aim to promote the RRI activities of the two PRISMA pilots dealing with nanotechnologies.

Advice

There are some particular social and ethical issues that have received focus in the course of the pilot and for which specific advice has been developed through discussion with the company and interaction with stakeholders. These include:

Product key (social) values

Reflection with the company and dialogue with stakeholders helped to identify the most relevant values to pursue for NanoMed products. It turned out that Colorobbia should work to address these values in product design, in order to provide scientific evidence of them and as well identify suitable ways to communicate these values to all actors along the supply chain, including end-users. These values include (vision):

- Product efficacy
- Safety of the product, in particular regarding safe use of nanomaterials along the value chain
- Excellence in R&D
- Ethics (respect of patients' rights) and patient-centric procedures for both clinical trials and cure (principles of precaution, beneficence, dignity, informed consent, data protection and data ownership)
- Transparency about the ways of production and use of nanomaterials, toward all actors along the R&I value chain and the product supply chain
- Affordability, accessibility of the treatment: ensuring the final system, delivering the personalized therapy at the point of care, will be affordable for health-care professionals (e.g. local hospital structures) and patients

Addressing quality, reliability, safety and efficacy of the R&I process and NanoMed products by state-of the art practices and standards

How quality and safety aspects related to the use of nanomaterials in advanced therapies should be addressed during the development process and all along the life cycle, considering the novelty of the application (and related uncertainties).

Quality procedures are in place all along the R&D and production process of NanoMed, including characterization, synthesis, testing , safety, and reliability phases. In particular, NanoMed ensured

early certification of the R&D labs, based on Good Manufacturing Practice for Medicinal products. A safe by design approach is implemented within NanoMed since the beginning of the project. Since the early stages of R&D, nanomaterials are selected (adapted and in case re-designed) to ensure they have a very low risk profile.

Fundamental and applied research is on-going to compare and validate results with state of the art scientific knowledge, and as well as with benchmark products, in order to carefully understand the mechanisms of action of the treatment, understand long term effects and improve reliability.

Cooperation and co-creation of the R&I products with regulatory bodies, authorities (cell therapy) and with patients (e.g. for clinical trials)

Cellular therapies, in particular in combination with the use of nanomaterials and the development of point of care devices (as in the case of NanoMed), are at the forefront of the existing regulatory frameworks. Problems of definitions and classifications, overlaps, lack of consistent guidance are some of the challenges in the application of regulation. How could these aspects be faced within the NanoMed Project?

- Regular monitoring of normative developments and early cooperation with EU and national authorities active on medicinal products, ATMP and nanomaterials is already part of the NanoMed activities
- A dialogue on ethical and social impacts with actors along the value chain of the R&I project, including researchers, suppliers, hospitals, authorities, patients' associations, ethical committees, has been started (also thanks to the PRISMA project), and will need to continue in the future
- Dialogue with stakeholders, will help in particular to plan and design protocols to ensure respect of patients' rights, including appropriate procedure for data management and informed consent with regard to data collected during clinical trials and therapy.

Assessment and dialogue on business models/costs/benefits with investors and the healthcare system

The assessment of socio-economic impacts of medicinal products is a step usually performed once the product is close to the market phase, considering the final application, and the actual market. In

the case of personalized and point of care therapies, this is complicated by the novelty of the approach, including issues related to the potential impact on the existing healthcare system and the type of business models suitable for these new therapies. Developing (responsible) business models, ensuring affordable and equitable access to the treatment (also taking into account the potential life-saving character of these new therapies) is an open and challenging issue.

- NanoMed should plan specific activities for early analysis of cost-benefit impacts of the new therapies, and screening of potential novel (responsible) business models
- This could be informed by dialogue and cooperation with risk managers and potential public and private investors, including the health-care system (e.g. local authorities and hospitals)

Create a communication and dialogue strategy toward professional, patients and society

How could a patient centric approach be implemented in NanoMed, taking into account patients' rights and needs?

- Design an informed consent protocol together with health-care professionals, patients' associations, and ethical committees, considering the peculiar aspects of personalised medicine and nanomaterials. Include information on uncertainties related to the new therapies
- Create informative events targeted to health-care professionals and patients to raise awareness on opportunities and challenges of personalized therapies, in particular the use of nanomaterials and ATMPs
- Identify appropriate communication means and channels to inform the wider public on NanoMed technologies and products. Ensure an easily accessible and understandable communication of benefits and risks of the product. Consider engagement of scientific journalists and media experts to realize the communication strategy
- Engage a multi-disciplinary panel of independent experts and end-users in order to assist the project regarding strategic choices on ethical, legal and social aspects (e.g. risk-benefit evaluation) taking into account also technical developments (e.g. safety of nanomaterials) and socio-economical aspects

The aspects underlined above will be structured and elaborated in a roadmap to integrate RRI into the

NanoMed products, covering all the period until the commercialization and use of the product. The agreement with the company on the final roadmap will the conclusive step of the pilot.

Final remarks

The cooperation with Colorobbia on RRI implementation has been quite fruitful, also thanks to the experience and attitude on social responsibility of the company.

The NanoMed project is complex and ambitious and there is little chance of success without a broader alignment with the needs and perspectives of the final users, in particular the healthcare system, health professionals and the patients.

A set of detailed actions that could promote RRI uptake within the NanoMed project emerged during the pilot, some already planned in the R&I strategy of the company, others that will be considered in future developments of NanoMed.

The experience with PRISMA supported the company in better understanding (anticipating) potential ethical, legal and social risks (and benefits), and finding ways to address uncertainties in existing and

future developments in norms and standards, and exploring ways to ensure societal acceptability of the final products of NanoMed.

RRI is expected to create value for R&D and innovation activities, improve corporate image and reputation, and help to gain a competitive advantage.
Defining practical RRI actions for NanoMed has been a long process, requiring an in-depth self-reflection process involving the management and researchers participating in the project, and interaction with stakeholders. RRI integration requires the company to open up (part of) their processes, and foster cooperation with different stakeholders, at different levels in the company and as well in different phases of R&D development.

A formal (or informal) strategy for RRI should be developed to put RRI in practice, and the challenge is to align it with the company practices and business strategy.

Resources (human and financial) are needed to implement RRI actions, and the PRISMA analysis of the NanoMed project clearly shows that the more RRI is embedded in existing process, the more this could be resource demanding.