International Network Initiative on Safe & Sustainable Nanotechnology

INISS-Nano: revised concept and action plan (International Network Initiative on Safe and Sustainable Nanotechnologies)

"This concept paper shall prepare the ecosystem for global collaboration in selected fields of action (see pillars), enabling "collaboration without borders" within joint projects, joint funding initiatives, and any further way of cooperation."

Comments:

Interested colleagues are invited to connect with the coordinators of the initiative. Furthermore, any comments, contributions and remarks that are meant to support INISS-Nano are highly welcome and shall be sent to the corresponding author.

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Content

Abbreviations

AECEN – Asian Environmental Compliance and Enforcement Network
ANF – Asia Nano Forum
AOPs – Adverse Outcome Pathways
API – Active Pharmaceutical Ingredients
APMP – Asia Pacific Metrology Programme
ASTM – American Society for Testing and Materials
ATP – Adenosine Tri Phosphate
BCG – Bio-, Circular and Green economy
BIAC – Business at OECD
BIPM – International Bureau of Weights and Measures
CEFIC – European Chemical Industry Council
CEN – European Committee for Standardization
COMEST – World Commission on the Ethics of Scientific Knowledge and Technology
CWA – CEN Workshop Agreement
DCS – Distributed Control Systems
DNA – Desoxyribo Nucleic Acid
EC – European Commission
ECHA – European Chemicals Agency
EFSA – European Food Safety Authority
EHS – Environment, Health & Safety
ELISA – Encyme-Linked Immuno Sorbent Assay
EMA – European Medicines Agency
ENMs – engineered, manufactured or manmade nanomaterials
ETPN – European Technology Plattform Nanomedicine
EU – European Union
EU FP7 – 7th Framework Program of the EU
EU-US-CoR's – EU-US-Communities of Research
EUON – European Union Observatory for Nanomaterials
EURAMET – EURAMET e.V., European Association of National Metrology Institutes
FAIR(-principles) – findable, accessible, interoperable and reusable
FTIR – Fourier Transmission InfraRed
GDPR – General Data Protection Regulation
GMO – Genetically Modified Organisms
GMP – Good Manufacturing Practice
ILCs – Inter Laboratory Comparisons
ILO – International Labour Organization

INFRAMES – International Network for Researching, Advancing, and Assessing Materials for Environmental Sustainability

INIC – Iran Nanotechnology Innovation Council

INISS-Nano – international network initiative on safe and sustainable nanotechnology

INLN – Iran Nanotechnology Laboratory Network is a network affiliated to INIC

IRISS – The International ecosystem for accelerating the transition to Safe-and-Sustainable-by-design materials, products and processes

ISO – International Organization for Standardization

IUCLID – International Uniform Chemical Information Database

JRC – Joint Research Centre (of the European Commission)

MAD – Mutual Acceptance of Data

MoAs – Modes of Action

MNMs – Manufactured Nanomaterials

mRNA – micro Ribo Nucleic Acid

nano-QSARs – nano- Quantitative structure-activity relationship

NANOTEC – National Nanotechnology Center, Thailand

NGO – non-governmental Organization

NMI – National Metrology Institute

NRGC – Nanotechnology Risk Governance Council

NSC – European NanoSafety Cluster

OECD – Organization for Economic Co-operation and Development

OECD TG – OECD Test Guideline

OEL – Occupational Exposure Level

OITBs – Open Innovation Test Bed projects

OSHA – European Agency for Safety and Health at Work

PAT – Process Analytical Technologies

PARC – Partnership for the Assessment of Risks from Chemicals

PBMNC – Peripheral Blood Mono Nuclear Cells

QA – Quality Assurance

REACH – (EU legislation for) Registration, Evaluation, Authorisation and Restriction of Chemicals

RMOs – Regional Metrology Organizations

RRI – Responsible Research and Innovation

SAICM – Strategic Approach to International Chemicals Management

SbD – Safe by Design

SbPD – Safety by Process Design

SDS – Safety Data Sheet

SDGs – United Nations Sustainable Development Goals

SIM – Inter-American Metrology System

SSbD – Safe and Sustainable by Design

TC – Technical Committee

TR – Technical Report

UNEP – United Nations Environment Programme

UNESCO – United Nations Educational, Scientific and Cultural Organization

UNITAR – United Nations Institute for Training and Research

US-EPA – United States Environmental Protection Agency

US-FDA – United States Food and Drug Administration

VAMAS – Versailles Project on Advanced Materials and Standards

WHO – World Health Organization

WPMN – OECD Working Party on Manufactured Nanomaterials

1.1 Introduction

The numerous application possibilities of engineered nanomaterials (ENMs) have created immense interest in various industry sectors to invest in this emerging technology. This has resulted in a rapid entry of nanotechnology-based products into the market and has obviated the need of scientific research to provide solid and consistent basis for regulation policies to ensure their safe and responsible/sustainable manufacturing, quality control, efficacy and use. In order to be successful in nanotechnology research, commercialisation and regulation, international collaboration is crucial. This works quite well in Europe and between and within North America; however, international collaboration especially between Europe and Asia is still in its infancy. Since the creation of the EU NanoSafety Cluster (NSC) in 2010[1], the international collaboration is an important activity. The EU-US-CoR's[2] (established 2011) as well as NSC-initiated international exchange-meetings (e.g., with South Korea, Mexico, Iran, Brazil) are successful examples towards international cooperation; however, a single, independent global **scientific collaboration** platform is still missing.

The "**EU-Asia dialogue on NanoSafety**", organised by members of the EU NanoSafety Cluster and the Asia Nano Forum (ANF)[3], started in 2017 as a series of annual conferences, to focus on synergies between Asian and European countries in science and research, with respect to (safer) nanomaterials, including standardization and test guideline development pertaining to them. Based on the proposal of a "network of networks", first presented during the 2nd EU-Asia dialogue on NanoSafety (2018), at the 4th Meeting (2020) a further developed idea of that was shown. Thus, it was decided to move one next step forward: make this collaboration more formal and open it to the world. Apart from this the European Commission has always encouraged to include partners from outside the EU into consortia that responded to calls for proposals.

A group of experts (see section 4) in different aspects of NanoSafety research - already including world-wide partners - started to discuss the goals and content of the initiative entitled "**International Network Initiative on Safe and Sustainable Nanotechnologies" (INISS-Nano)**, and how this network could be put into practice.

1.2 Focus and value-added by INISS-Nano

Based on the idea of a "network of networks" and supported by activities within the NSC, a core group of some volunteers (i.e. the authors of the 1st version of the concept paper, published in June 2021) have formed **INISS-Nano**, initially focussing on safety and

1 https://www.nanosafetycluster.eu
2 https://us-eu.org/
3 https://www.asia-anf.org/

sustainability of nanotechnologies, with the potential to expand the scope towards the general SSbD landscape.

The **aim** of the initiative is to bring together science, industry and government from all over the world, **not duplicating structures but connecting** with them (e.g., NSC, ANF, EU-US-CoR's). Such contacts can assist the work of standardization bodies (such as CEN, ISO, ASTM, etc.), of international organizations (e.g., OECD, CEFIC) and of agencies (e.g., ECHA, EFSA, US-EPA, US-FDA, AECEN).

The **focus** shall be on the **collaboration in different fields pertaining to nanotechnology research in general and nanosafety research in particular**. This shall include collaboration in terms of, e.g., training, knowledge and data sharing, standardization efforts, test-guidelines development, metrology, commercialisation, ethical aspects, sustainability, and joint research supporting governance and regulatory guidance. The scope can be extended to further joint working items.

The **added value of INISS-Nano** shall be the collection and analysis of available information worldwide, always in collaboration with existing organizations or working groups (e.g., for definitions and ontologies of nanotechnology; analysing differences between markets; common strategies on transfer of scientific results into policy; regulation; standardization; harmonization of methods, such as risk assessment methodologies). INISS-Nano will aim at making this knowledge accessible for the stakeholders worldwide and, based on identified gaps and/or bottlenecks, initiate common activities to achieve this goal. Joint activities could be (but shall not be limited to) development of:

- joint funding programs,
- joint research projects and develop common publications,
- reduce/avoid duplication in research and innovation,
- exchange programs for students,
- data sharing,
- sharing laboratory infrastructure,
- expert exchange,
- consultancy services,
- support of the development of harmonised and validated protocols, e.g., for characterization methods, and
- gaining an overview on available certification protocols, to understand the process but also to contribute to this towards harmonization and validation of methods.

Additionally, INISS-Nano has the ambition to support with its scientific know-how the work of global organizations active in the nano field, e.g., the OECD, to contribute to international harmonization and to the development of standardization documents, such as OECD test guidelines and guidance documents or ISO/CEN standards, technical specifications and technical reports[4]. The creation of official bridges with regional metrology organizations (such as EURAMET, APMP, SIM, etc.)[5] will be key, not only to bring metrology expertise on board, but also to help guide the activities of this community. This shall enable INISS-Nano to make a real contribution to advancing pre-standardization and validation in the field of metrology for the benefit of nanosafety issues.

The **following four pillars** have been identified by the INISS-Nano core group as **important action fields** that shall be in the focus and actions to be implemented at the start of INISS-Nano:

- Harmonization
- Support industrial understanding
- Sharing / facilitate sharing of resources / infrastructures
- International collaboration on ethical and societal aspects of nanotechnology

The “NanoSafety Dialogue” events [5th EU-Asia Dialogue on NanoSafety, July 18th, 2022, Malaysia; 6th EU-Asia Dialogue on NanoSafety, June 21st, 2023, Germany] shall be continued and be the place to discuss the output generated so far, to evaluate the progress, and to define further actions to be put into the **international nano-community roadmap for the mid- and long-term**.

[4] Standardization documents are developed at 3 levels of decreasing order of authority: full standards, technical specifications and technical reports.
[5] https://www.bipm.org/en/liaison/regional/

2 Implementation strategy of INISS-Nano

The implementation strategy of INISS-Nano is structured as follows:

a) Overview of the organizational form incl. governance bodies; description of the organizational form including the secretariat, which is the central point the organization is meant to offer at the beginning; description of the role of the secretariat of INISS-Nano.
b) Management of INISS-Nano and financial aspects
c) Key strategies of INISS-Nano
d) Activities and Action Plans

2.1 Organizational form of INISS-Nano

Regarding the organization of the network, a steering committee shall be installed that shall make strategic decisions for INISS-Nano, supported by the secretariat in the operative day-2-day business and by collaboration partners in terms of the implementation of the actions.
The **Steering committee** shall be the functional decision body. For the starting phase of INISS-Nano, the Committee shall not have more than 13 members, lasting for a period of 3 years (July 2022 – June 2025) and consist of the volunteers that have initiated and shaped INISS-Nano (see 4.1), complemented by the pillar leaders.
The **secretariat** shall run the collaboration activities, specifically organise the continuous dialogue (i.e., NanoSafety dialogue), support the pillar leaders with their action plans (i.e., implementation, monitoring, updating, workshops, etc.), and serve for smooth communication within the community (i.e., INISS-Nano as a vehicle for several, collaborating communities). Furthermore, the conceptualisation of the **terms and conditions** for the collaboration and the organizational establishment shall be done by the INISS-Nano secretariat.
The **collaboration partners** shall be a community of contributors from several international networks/communities, who will help/collaborate in the implementation of the actions.

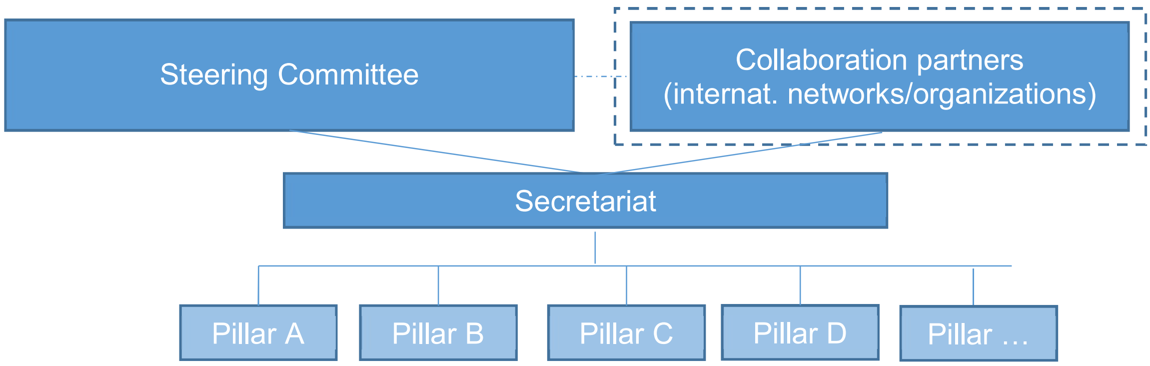

Figure 1: Proposed structure for INISS-Nano.

A matrix structure (see figure 1) is envisaged to shape the proper work division in the INISS-Nano; there are already a few functional pillars, dedicated to harmonization, support industrial understanding, sharing/facilitate sharing of resources/infrastructures, and international collaboration on ethical and societal aspects of nanotechnology (other pillars might appear at a later stage) along with several key expertise areas such as nanomedicine, medical devices and materials, agriculture, etc.
If needed, working groups within the functional pillars could be established, including focused experts for the specific area. They could support the implementation of the actions of the pillars' action plans, and might become connections of INISS-Nano with the relevant working groups of other networks as well as engage with them to collaborate.

The organizational form of the network shall be an independent international NGO, however, the specific terms and conditions need to be developed by the secretariat. Depending on its organizational form, INISS-Nano might be able to also act as an external liaison body to international and regional standardization organizations

Other roles that will be interacting with INISS-Nano:

- governmental organizations with responsibility or interest in the area of nano-safety are expected to contribute in two ways, by coordinating their national bodies to contribute, and by financial and/or in-kind contribution to activities of INISS-Nano.
- regional, national or international public and private sector institutions shall support the activities of INISS-Nano. It is expected that at least in the first years, INISS-Nano will need to benefit from support of these institutions.

However, all the organizational structure is object to be discussed, (i) if a new organization is needed, or (ii) if an existing one can take over the secretariat, running INISS-Nano as an initiative.

2.2 Management of INISS-Nano and financial aspects

The success of INISS-Nano will depend on the intensity of the international collaboration. The efforts in the coordination of this collaboration and continuous further development of the initiative need to be structured, at least, with a **secretariat** and thus will require resources. These resources might come from the following sources (but are not limited to those):

- existing **networks** manage/coordinate INISS-Nano as in-kind contribution;
- ongoing **projects** (national/international) dedicate in-kind contribution to INISS-Nano (similar approach as the NSC);
- **governmental funding** of a secretariat (e.g., rotating funds to one common secretariat);

- the secretariat might be **(co-)financed** within a/several future project/s (e.g., Horizon Europe);

Thus, INISS-Nano requires **resources** to

(i) conduct the coordination/management of the initiative itself (secretariat), as well to

(ii) implement and finance the activities (i.e. action plans).

This includes human resources, infrastructure, and financial resources for other direct costs. Part of these resources are and hopefully will in future be provided through in-kind contributions of the founding members (mainly in-kind contributions in terms of human resources e.g., co-creation of action plans; and infrastructure e.g., hosting of workshops) and shall be complemented via above mentioned sources. This shall support the initial establishment of INISS-Nano. It is expected that the initial establishment of the network and the first 3-5 years of its operation rely mainly on these resources.

For the implementation of the activities (see action plans at each pillar) a potential model could be a financed **partnership**, in which the main budget would be dedicated to financing international scientific collaboration, and a certain amount is used to run the secretariat. Thus, the management of the partnership would be done by the INISS-Nano secretariat i.e., be organised in a way that most of the budget (everything other than what is needed for the secretariat) would be assigned to specific actions that are agreed on within the pillars. The participation in these actions would be open for everyone, including but not limited to the INISS-Nano core group.

Furthermore, the following sources could help to make the INISS-Nano network a long-term sustainable driver for global scientific collaboration:

- direct support from international sources: e.g., EC, relevant institutions; and/or projects (ongoing and/or new projects).
- membership system: resources needed for continuous operation of INISS-Nano might be collected via membership fees e.g., of INISS-Nano-members (states, institutes, organizations, etc.)
- fee-for-service incomes: in case, INISS-Nano shall create an own competence profile with specific services, this might become an option.

However, a dedicated financial planning needs to be conducted and the best option for the implementation to be discussed and decided within the INISS-Nano Steering Committee.

2.3 Key strategies of INISS-Nano

Some key strategies of the network are listed here:

- Nurturing **international scientific collaboration** will be the main target of all activities and programs.
- Implementation of INISS-Nano would happen in two parallel paths:
    - a **top-down** track which pursues formal registration and establishment of the network, determine the position of the INISS-Nano in the nano-safety ecosystem, and tries to allocate specific initial resources for establishment of the network. It is expected that formal shaping of the network will be ready by the end of the year 2023.
    - The second track would follow a **bottom-up** path in which the founding members and contributors initiate a range of relevant activities and programs through existing platforms and ongoing projects (supported by e.g., EU HorizonEurope projects, Asian and/or international initiatives) where the required resources are already available. The second track shall start by the end of 2022 and shall continue based on each activities' progress.

  The proposed double track implementation strategy makes sure that while a sound and long-term vision is outlined, feasible useful activities within the network start as soon as possible.
- The implementation will benefit at the beginning from a decentralised operation with emphasis on **voluntary membership and contribution** of enthusiastic individuals and organizations.
- Along the implementation, there is a **need for adequate incentive mechanisms** to motivate individuals and institutions to continue their efforts, to engage newcomers to become members and contribute; for example, in infrastructure sharing platforms, incentives and gains, both for those who share their facilities and those who benefit from the shared facilities need to be identified and proper incentive mechanisms need to be devised.

The INISS-Nano secretariat will be responsible to prepare and implement the strategy.

2.4 Activities and Action Plans

The INISS-Nano concept paper presents below already a first set of actions for each of the defined pillars (see at the end of each Pillar). Each pillar has a dedicated action plan for the short-, medium- and long-term actions of INISS-Nano. The implementation of the action plan(s) will strongly depend on the developments in terms of organizational structure, support and resources for the initiative. This shall be seen as starting points for any further development of the initiative, and as an entry point for further partners. Pursuing the goal of international scientific collaboration, the activities and future programs shall be continuously monitored, extended and/or adapted, to fully support the common goal.

In addition to the list of relevant activities and programs, all contributors will compile further actions in the different fields and/or new pillars through brainstorming sessions e.g., during dialogue events. This shall increase the impact of INISS-Nano actions and shall contribute to the establishment of future programs (e.g., via feeding into roadmaps, strategy documents, work programs, etc.).

Importantly, and to avoid redundancy of efforts, overlapping or similar programs elsewhere in the world will be recognised and the possibility of partnership or merge evaluated. A number of programs (e.g., PARC, IRISS, INFRAMES) with higher feasibility/importance will be candidates to go through a prioritisation process to build any type of interaction with INISS-Nano. After the selection, the details of those programs will be worked out by the secretariat to identify common objectives, potential business models, and/or work division, and shall enable joint programs.

3.1 Pillar "Harmonization"

Pillar-leaders: Steffi Friedrichs, Ali Beitollahi.

Supporters: Miguel Banares; Sophie Briffa; Flemming Cassee; Fernand Doridot; Andreas Falk; Patricia Farias; Georges Favre; Giancarlo Franzese; Danail Hristozov; Ramjitti Indaraprasirt; Ineke Malsch; Cris Rocca; Pushplata Singh

The harmonization pillar consists of two elements: 3.1.1 Standardization efforts, and 3.1.2 Transfer of Scientific information into harmonised Guidance and Standards.

3.1.1 Standardization efforts

Standardization in general and more specifically in the field of nanosafety, the **materials' characterization/metrology standards** play a **key role** in further responsible development of safe and sustainable nanotechnologies. There is a critical need to harmonise nanomaterials characterization methodologies (e.g., instrumentation, instrumentation use, protocols, data analysis) so that those will deliver quantitative interoperable characterization data. Standardized nano-characterization is a critical need to seamlessly connect characterization with safety assessment.

Despite considerable international investments on nanosafety and nanomaterials characterization research and the establishment of relevant technical committees in standardization bodies (e.g., ISO/TC 229, ASTM/E56, CEN/TC 352) in the past 15 years, there seems still to be a need for additional nanosafety-related published standards. Furthermore, harmonized (or even standardization) documents are needed to be used to develop as well as implement OECD Test Guidelines, to support the ever increasing demands of the relevant industries and regulatory bodies. EU-funded projects are underway to support the development of testing guidelines and guidance documents (e.g., Gov4Nano[6], NanoMET[7], NanoHarmony[8]). Other EU-projects (e.g., ACEnano[9]) have shown efforts towards harmonization of characterization protocols and methodologies, performing inter laboratory comparisons (ILCs) as well as publishing the results, together with global partners. Furthermore, this is also the case for example of EU-H2020 project CHARISMA[10] for Raman

[6] https://www.gov4nano.eu/ ; https://cordis.europa.eu/project/id/814401
[7] https://cordis.europa.eu/project/id/887268
[8] https://cordis.europa.eu/project/id/885931
[9] https://cordis.europa.eu/project/id/720952
[10] https://www.h2020charisma.eu/ ; https://cordis.europa.eu/project/id/952921

spectroscopy or e.g., projects EMPIR nPSize[11], and ISO-G-SCoPe[12] for improved traceability chain of nanoparticle size measurements and graphene characterization, respectively. Harmonised measurements will facilitate accurate quantitative characterization of given materials with, e.g., multiple Raman instruments (CHARISMA), thus enabling the development of standards. Harmonised characterizations are a key pillar to enable a one-characterization/one-assessment paradigm. These mentioned projects may be seen as cases that already include relevant action items for the international scientific collaboration, envisaging to contribute to international standardization activities (e.g., via ISO).
Furthermore, the EU-funded Open Innovation Test Bed projects (OITBs) (e.g., FlexFunction2Sustain[13], INNOMEM[14], NewSkin[15], NextGenMicrofluidics[16], PHOENIX[17]) have huge potential to contribute to characterization and measurements according to standards. Finally, the process analytical technologies fitting to nanotechnologies are another characterization competence that is funded by the EU in specific projects (e.g., CHALLENGES[18], NanoBat[19], NanoPAT[20], NanoQI[21], PAT4Nano[22], RealNano[23]) that might become relevant for INISS-Nano actions.

Addressing these issues demands reinforced international scientific collaboration, which supports the need of the overarching platform INISS-Nano for facilitating enhanced communication and sharing knowledge among the related stakeholders, and sharing the burden in terms of resource allocation. Furthermore, INISS-Nano could embrace a large number of international collaborating experts/responsible bodies (notably from academia and regulatory agencies) by initiating smart and persuading strategies, paving the way towards more harmonized approaches regarding international regulations and laws to be developed in the future. This globally organised platform, could also act as an international consulting body or as external liaison partner to international standardization bodies such as ISO/TC229, supporting e.g. with its overview about science and research results around the globe, or CEN/TC 352, supporting standardization in the field of nanotechnologies in Europe.

INISS-Nano will be aiming at facilitating and boosting cooperation in the field of nanosafety and nanomaterial characterization standardization. An important element of its work will be to

[11] https://www.bam.de/Content/EN/Projects/nPSize/npsize.html
[12] https://www.euramet.org/research-innovation/search-research-projects/details/project/standardization-of-structural-and-chemical-properties-of-graphene/
[13] https://flexfunction2sustain.eu/ ; https://cordis.europa.eu/project/id/862156/en
[14] https://www.innomem.eu/ ; https://cordis.europa.eu/project/id/862330/en
[15] https://www.newskin-oitb.eu/ ; https://cordis.europa.eu/project/id/862100/en
[16] https://www.nextgenmicrofluidics.eu/ ; https://cordis.europa.eu/project/id/862092/en
[17] https://www.phoenix-oitb.eu/ ; https://cordis.europa.eu/project/id/953110/en
[18] https://cordis.europa.eu/project/id/861857
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[21] https://cordis.europa.eu/project/id/862055
[22] https://cordis.europa.eu/project/id/862413
[23] https://cordis.europa.eu/project/id/862442

facilitate that the national and international scientific projects (including EU funded projects) are working in the same direction and are sharing their results, e.g., contributing to OECD work.

The following added values in collaboration with existing platforms/networks/organizations are foreseen:

- Facilitate and accelerate the development of joint nanosafety and harmonised/pre-standardised nano-characterization to enable its standardization, which will eventually benefit the consumer and governmental risks agencies as well as relevant industrial sectors, as this will lead to reliable nanosafety-relevant data. This will be done through sharing the information related to human resources, infrastructure, knowledge, etc. to feed into consistent agreed harmonised methods. This shall be done via existing infrastructures (e.g., metrology infrastructure).
- Support capacity building in the scientific community to take a bolder role in the development of nanosafety and nano-characterization harmonization to improve the efficiency of knowledge transfer for the creation of standards. A possible solution for this could be, for example, to develop and communicate on internationally recognised standardization certificates to acknowledge standardization work on the basis of the mechanism, already implemented by the EU Graphene Flagship Standardization Committee[24], and foster CEN Workshop Agreements.
- Enable capacity clustering in a way that a mechanism is installed for scientific collaboration to sign onto harmonization efforts of e.g., a project, and that this specific harmonization related work then could be claimed on some other (funded) project even if it is not 100% related to the project that is leading the harmonization efforts.
- Make existing documents and work in progress better known to the various stakeholders, including industrialists, with a view to wider use of the documents, to recruit new experts and to promote cross-fertilisation between different sectors or geographical areas.
- Further enhancement of research and development collaboration in favour of supporting harmonization and development of new standards by promoting some of the mechanisms already in place (i.e. EU funding opportunities for pre-standardization metrology activities through the new European Partnership on Metrology (EPM)[25] Programme or Graphene Flagship Validation Service and Standardization Committee)[26].
- Support inter-lab assessments initiatives (in particular through the implementation of a dedicated funding programme similar to the ASTM Interlaboratory Study Program)[27],

[24] https://graphene-flagship.eu/innovation/industrialisation/standardization/
[25] https://metpart.eu/
[26] https://graphene-flagship.eu/innovation/industrialisation/validation-service/
[27] https://www.astm.org/products-services/training-courses/member-training/interlaboratory-studies-program.html

help in the prioritisation of inter-lab comparisons and promote, among others, VAMAS[28] and ASTM/E56 activities in the field.

- Involve the National Metrology Institutes (NMIs) in the process so that the actions of the actors in this community can be aligned with the needs in the field, taking into account the opportunity in EU to build a European Metrology Network to address metrology issues associated to advanced materials/nanomaterials.[29]
- Support better coordination and synergy in test guidelines for regulatory systems through enhancement of international collaboration, i.e., MALTA initiative[30], and successor programs, and/or supporting the Mutual acceptance of data approach (see section 3.4.2).
- Enhance the existing collaboration between international standardization bodies like ISO/TC 229, CEN/TC 352, etc. as well as national standardization bodies in the area of nanosafety and nano-characterization standards with the nanosafety community.

3.1.2 Transfer of Scientific information into harmonised Guidance and Standards

From the Creation via Safe and Sustainable by Design (SSbD) and Regulatory Preparedness towards Implementation

In over a decade of research, the European projects in the NSC have collaborated with partners from around the world to generate fundamental knowledge and data on the intrinsic and extrinsic physicochemical properties of engineered nanomaterials, as well as their key release/exposure pathways, nano-bio/eco interactions, biodistribution, environmental fate, (eco)toxicity and related Modes of Action (MoAs) such as Adverse Outcome Pathways (AOPs). This coordinated effort, that needs expansion and further enhancement, has formed a starting point for advancing the research from the consideration of the (regulated) safety of current nanomaterials to the future-oriented sustainability of advanced materials and processes under the concepts of Safe and Sustainable by Design (SSbD)[31]. The relevant EU initiated and funded projects in that field (ASINA[32], Sabyna[33], SbD4Nano[34], SABYDOMA[35], SUNSHINE[36], DIAGONAL[37], HARMLESS[38]) aim to address new and future generations of materials. This is done in collaboration with a wide range of international partners and collaborators including e.g., USA, Canada, China, South Korea, South Africa, Israel, Brazil and Japan. These projects study the environmental, health and safety (EHS) implications of advanced multi-component

[28] www.vamas.org
[29] https://www.euramet.org/european-metrology-networks/?L=0
[30] https://www.bmu.de/en/topics/health-chemical-safety-nanotechnology/nanotechnology/the-malta-initiative/
[31] http://doi.org/10.5281/zenodo.4652587
[32] https://cordis.europa.eu/project/id/862444
[33] https://cordis.europa.eu/project/id/862419
[34] https://cordis.europa.eu/project/id/862195
[35] https://cordis.europa.eu/project/id/862296
[36] https://cordis.europa.eu/project/id/952924
[37] https://cordis.europa.eu/project/id/953152
[38] https://cordis.europa.eu/project/id/953183

and smart nanomaterials, while the projects NanoFabNet[39] and SusNanoFab[40] aim to form a (digitally established) collaborative space for sustainable nanofabrication as a large-scale high-tech industrial manufacturing process.

The projects' underlying bottom-up generation of scientific knowledge, methods and data(bases), supported by the coordinated effort to foster and establish international, interdisciplinary activities between both academia, public laboratories and industrial players of all sizes, should be complemented by a top-down process of ensuring that their results both relevant for regulation and policy making, and implementable by the sustainable nanotechnology community. Finally, some EU-funded projects (CHARISMA**Fehler! Textmarke nicht definiert.**, nanoMECommns[41], EASI-STRESS[42]) are instrumental to harmonize nanomaterials characterization, thus enabling their standardization.

The process of transferring the state-of-the-art science of safe and sustainable nanotechnology into internationally harmonised and accepted guidelines, standards, regulations, and policies was pioneered by the NANoREG project[43] and further explored or elaborated via several follow-up projects (e.g., PROSAFE[44], NanoReg2[45]). These aim(ed) to provide policy makers with scientific opinions on how certain challenges could be addressed through policies and guidance documents. The projects thus play a pivotal role in increasing regulatory preparedness; they enable collaborative outreach to academia, industries and regulators, thus providing a real-world grounding of both the scientific and industrial state-of-the-art. By this, capacity to anticipate any regulatory concerns to take timely and appropriate action is increased.

The Need for a globally harmonised approach

The process of knowledge transfer from state-of-the-art R&I into relevant, appropriate and implementable policies has been developed and perfected throughout the past Framework Programmes of the European Commission (i.e. FP7 (2007-2013) and FP8=Horizon 2020 (2014-2020)) and is now firmly established and enforced within the European community. International collaborations are both required by the complexity of any advanced technology, and commanded by the need for approaches to sustainability that are neither limited to borders, nor defined by hard regulations. However, this relies on the ad-hoc responsibility and outreach capacity of the individual project partners.

[39] https://cordis.europa.eu/project/id/886171
[40] https://cordis.europa.eu/project/id/882506
[41] https://cordis.europa.eu/project/id/952869
[42] https://cordis.europa.eu/project/id/953219
[43] https://cordis.europa.eu/project/id/310584
[44] https://cordis.europa.eu/project/id/646325
[45] https://cordis.europa.eu/project/id/646221

The establishment of INISS-Nano will relieve the burden and limitation of *ad-hoc* call-specific international collaborations that are newly established on a case-by-case basis, and that may not be able to allow productive, cross-border collaborations to take place. The proposed INISS-Nano could become a permanent collaborative space for the exchange of knowledge and ideas across borders and beyond the immediate regulatory requirements of a single jurisdiction, thus supporting the development of a community for sustainable nanotechnology, based on principles and values that are jointly agreed on a global level. The vision would be harmonization, the way to achieve this shall be the collaboration. Furthermore, within the concept of INISS-Nano all collaboration partners will comply with the FAIR-principles of data[46,47,48], more specifically with the goal to be achieved, that metadata standards shall be community-agreed.

[46] FAIR-principles: Wilkinson, M., Dumontier, M., Aalbersberg, I. et al. The FAIR Guiding Principles for scientific data management and stewardship. Sci Data 3, 160018 (2016). https://doi.org/10.1038/sdata.2016.18

[47] https://doi.org/10.1038/s41565-021-00911-6

[48] https://pubs.rsc.org/en/content/articlehtml/2020/nr/c9nr08323e

3.1.3 Action Plan – Pillar 1

Action	Short-term (till Dec 2023)	Medium-term (till 2025 and beyond)
Pre-standardization / Harmonization efforts (including interaction with the metrology community)	Documents to support Regulatory Preparedness in Nanotechnology [lead: tbd] Prioritizing and listing the needs of standards by crowd sourcing approaches [lead: Hasan Pouypouy] Promote already available funding mechanisms (i.e., dedicated annual calls for proposals regarding pre-standardization activities within the new European Partnership on Metrology programme) [lead: Georges Favre]	Initiate a collaboration with VAMAS [lead: Georges Favre] Contribute to identify and prioritize the needs regarding OECD TG implementation documents [lead: Miguel Banares, Georges Favre, Steffi Friedrichs] Work to establish a funded programme to support the organization of inter-laboratory comparisons to validate methods/protocols prior to their standardization (on a similar model to the ASTM programme) [lead: Georges Favre]
Standardization	Communicate on standardization programme (available and under development documents upon availability) [lead: Hasan Pouypouy] Produce and disseminate summary reports of CEN/TC 352 and ISO/TC 229 meetings, if permitted [lead: Hasan Pouypouy] Outreaching international experts [lead: tbd]	Contribute to the development of an internationally recognised Standardization Certificates to acknowledge standardization work (in particular for academic experts) [lead: tbd] Contribute to identify and prioritize the needs regarding standardization work in order to optimize resource allocation [lead: tbd] Becoming liaison of regional and international standardization organization [lead: Hasan Pouypouy] Joint development of standard in the field of: [lead: tbd] -Characterization and measurement methods -Guidelines -Protocols
Nanometrology	Promotion and facilitating inter-laboratories comparisons [lead: Georges Favre] Implementation of an European Metrology Network to coordinate effort on metrology to support the Advanced Materials/Nanomaterials topic [lead: Georges Favre]	Collaboration with Regional Metrology Organizations (RMOs like EURAMET, APMP, SIM...) and BIPM [lead: Georges Favre] To develop collaborative roadmap jointly with regional /international metrology institutes (eg. BIPM, EURAMET, ...) [lead: Georges Favre, Steffi Friedrichs]

		To develop collaborative roadmap jointly with regional /international metrology institutes (e.g., BIPM, EURAMET, ...) [lead: Georges Favre-Steffi Friedrichs]
Regulations	Sharing and exchange of experiences and policies regarding nanosafety regulations and laws [lead: tbd] Policy data sharing [lead: tbd]	Organizing joint meeting in the field of regulation and laws [lead: tbd] Promoting harmonizing approaches among regional/international regulatory bodies [lead: tbd]
Capacity building	Training workshops (virtual and face to face) bilateral and multi-lateral [lead: tbd] Summer and winter school [lead: tbd]	Knowledge /data sharing and transfer [lead: tbd] Tutorial packages [lead: tbd]

3.2 Pillar "Support industrial understanding"

Pillar-leaders: Patricia Farias, Vinicius Bim.

Supporters: Miguel Banares; Nils Bohmer; Thomas Exner; Andreas Falk; Georges Favre; Steffi Friedrichs; Effie Marcoulaki; Ali Marjovi; Cris Rocca; Pushplata Singh

INISS-Nano is meant to establish a collaboration between the NSC and all interested countries globally, including those already organized in their own network such as the ANF or the EU-US CoR's, to expand the common knowledge base for nanomaterials of regulatory significance and to support the needs of various stakeholders including industry. The first meeting of INISS-Nano, attended by various stakeholders, identified that "supporting industrial understanding" should be one of the four pillars that the initiative should address. INISS-Nano can support industry by first understanding some of the barriers faced and then investigating the viability of some mechanisms to overcome these barriers. The renewed focus of governments in both EU Member States and Asia on sustainability and management of climate change (e.g., EU Chemicals Strategy for Sustainability[49]; Thailand's drive towards a bio-, circular and green (BCG) economy[50]) can assist engagement with programs developed by INISS-Nano.
Industry can face several barriers to progress a product from research through development to commercialisation. Some of these are acceptable, such as regulatory obligations that ensure the safety of products to humans and the environment; in fact, these can even trigger new areas of innovation. However, other barriers, such as poor knowledge transfer, are barriers that can and should be reduced. Although the European Agency for Safety and Health at Work (OSHA)[51] has provided some information on safety of workers[52] (last update in 2017), there are still lots of gaps in practical safety (e.g., (nano) particles during manufacturing, etc.). This is of particular importance in a growing sector such as nanotechnology. During the process of conceptualization of INISS-Nano a number of barriers were identified. It is felt the initiative could help to reduce these barriers.

Inefficient Knowledge Transfer

Poor dissemination from and among research projects can lead to duplication of work and delay the widespread uptake of the best cutting-edge methods and tools by industry. This barrier results the too narrow dissemination of data and results by projects which often only happens after very long embargo periods, and due to the unwillingness or inability of industry to adopt new research. It is felt by some (industrial) parties that the disseminated results from

[49] https://ec.europa.eu/environment/pdf/chemicals/2020/10/Strategy.pdf
[50] https://www.nstda.or.th/thaibioeconomy/138-bio-circular-green-economy-to-be-declared-a-national-agenda.html
[51] https://osha.europa.eu/en
[52] https://osha.europa.eu/en/legislation/guidelines/guidance-protection-health-and-safety-workers-potential-risks-related

these projects are technically too complex to be easily used and implemented at factory floor level. There is a critical need to devise strategies to foster communication of knowledge among these communities. The implementation of FAIR-principles for data sharing across the globe and further use of already installed data repositories and platforms (e.g., European Union Observatory for Nanomaterials – EUON[53], IUCLID[54]) will be considered. More specifically, the OECD and ECHA both use IUCLID as a data platform, and while the content of nano-relevant data may not be large, the database is internationally recognised, and the data exchange format agreed with OECD harmonised templates.

Inconsistent measures and mechanisms between regions

The aim is to encourage the alignment of measures and mechanisms in regulation implementation and market access to reduce complexity for multinational companies. The issue of complexity of different regulatory regimes is addressed in the chapter of "legal aspects" in chapter 3.4.2. Beyond that, if there is excessive disparity of the protocols and tools required to meet regulatory obligations, the industry might not recognise where they can use a single set of data across many jurisdictions and see a barrier to expansion where none exists.

Variable confidence in products using nanotechnology (both from industry and the consumer)

Nanotechnology has been *de facto* present in industry for decades (e.g., catalysis, sensors), but the industry has only recently become aware of it due to an exponential growth of its applications.

- Perceived uncertainty over hazards and risk from nanomaterials and nano-enabled products, leading to the implementation of high regulatory barriers due to regulators needing to take a precautionary approach until enough data is available to clearly prove its safety. A number of governments have found difficulties around the introduction of Genetically Modified Organisms (GMO) into their markets and do not want to face the same issues around nanotechnology. Thus, the support for companies to facilitate the implementation of updated REACH annexes[55] is needed[56].
- In some regions, "*nano*" is regarded positively to such an extent that its use can be associated with premium products. This can lead to this term being used as a marketing tool even where neither nanomaterials nor nano-enabled products are present potentially causing confusion and distrust to the consumer.
- Missing communication of the risks and appropriate risk management measures of nanomaterials to the factory floor, which will benefit from making use of EUON.

[53] https://euon.echa.europa.eu/

[54] https://www.oecd.org/chemicalsafety/risk-assessment/electronictoolsfordatasubmissionevaluationandexchangeintheoecdcooperativechemicalsassessmentprogramme.htm

[55] Commission Regulation (EU) 2018/1881 of 3 December 2018 amending Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards Annexes I, III,VI, VII, VIII, IX, X, XI, and XII to address nanoforms of substances. OJ L 308, 4.12.2018, p. 1–20

[56] https://echa.europa.eu/-/updated-guidance-for-registering-substances-in-nanoform

INISS-Nano can assist in braking down these barriers and shall identify some approaches that will be investigated in the next few years in form of case studies.

A Thai Case-Study - The introduction of a labelling standard for products containing nanomaterials

Governments and regulators across both Asia and the EU are recognising the importance of nanotechnologies and the barriers to its exploitation. To increase market share both domestically and overseas, some Asian countries have introduced unique and innovative measures. In the case of Thailand, for example, awareness of nano-safety is an integral part of nanotechnology development. The same can also be said when it comes to safe use of nanomaterials in industry. Safety of workers is a priority and for this reason, the Thai government approved the NanoSafety and Ethics Strategic Plan in 2012. The national plan is designed to be used as a guideline for creating action plans by relevant agencies. To achieve the goal, the Plan identified three strategies:

1) the creation and management of knowledge,
2) the development and strengthening of measures and mechanisms for supervision and enforcement, and
3) the strengthening and promotion of public participation.

Thai companies have been adopting practices that are internationally accepted. Companies have been requesting to use the **NanoQ** label which is issued by the Nanotechnology Association of Thailand and approved after verification. The label only confirms that the production process utilizes nanoscale materials and has specific properties such as anti-bacterial and water repellent. The label serves to assure consumers' confidence and helps to eliminate fake nano products from the market. For example, Iran (NanoTrust), Malaysia (NANOVerify), and Taiwan (nanoMark) have also implemented similar nano labels and it is under consideration in other countries such as Vietnam. These schemes are focused, *inter alia*, on ensuring public confidence and fair trade by guaranteeing the authenticity of a product marketed as one containing nanomaterials and are intended to be a label for safety.

In Europe, legislation requires the labelling of nanomaterial ingredients in cosmetics, food and biocidal products and there are labelling schemes focused on the environmental sustainability of a product such as the EuroEco Label (see more labels identified in: Mapping study for the development of sustainable-by-design criteria[57]). A Study Group on *Labelling* has been recently formed within CEN/TC 352 *Nanotechnologies* to collect stakeholders' views on this topic before considering the possible production of a document. B2C-labelling and B2B-

[57] https://ec.europa.eu/info/publications/mapping-study-development-sustainable-design-criteria_en ; page 12ff

labelling are currently discussed by the group, which stressed that in order to possibly support B2C labelling the issue of measurements is key to produce reliable information and that more transparency in the supply chain in B2B is needed. The aim of the Study Group could be to develop in the near future a document providing guidance on how to improve the traceability of nanomaterials all along the different value chains by paying attention to the key role of measurements.

We believe INISS-Nano is well suited to investigate and assess various existing labelling schemes and to suggest common practices that could be applied with the view to a cross regional label, in particular as a number of the experts involved here are also contributing to the ongoing discussions on the subject of labelling (including the CEN/TC 352 Study Group).

INISS-Nano could also support to develop basic concepts and compile identified common sense approaches in the involved countries, and to disseminate this information (Concept of Nanotechnology), rather than creating legislation or standards. In a second step, based on the results from the compilation of the knowledge, training for industry should be provided by each country's representative; coordinated and supported by INISS-Nano. Within this framework industry from distinct countries can receive oriented understanding and support.

Repository of new research tools from across both regions

Projects from the EU FP7, Horizon2020 and other funding programmes have produced a wide range of tools that can help industry with their development goals, from estimating hazard and risk of new nanomaterials to identifying regulatory obligations. Currently running NMBP-13-2020 risk governance projects (RiskGONE,[58] Gov4Nano[59] and NanoRiGo[60]) and NMBP-14-2020 nanoinformatics projects (NanoInformaTIX[61] and NanoSolveIT[62]) complement each other on the assessing the safety of nanomaterials and how to serve regulatory decisions. Similar initiatives towards the expanding the development of nanotechnology have been actively pursued within the ANF.

- Applications of nano hybrid resin (GreenEpoxy Technology, Taiwan)
- Water Treatment for Self-Sustaining Toilets (Nanopac, Malaysia)
- Silica-based Solar Coat for Solar Thermal and Solar Photovoltaic application, (NANOTEC, Thailand)
- Commercialization of Nanofibers produced by Hybrid Electrospinning (Amogreentech Co., Ltd., Korea)

[58] https://riskgone.eu/2020/ ; https://cordis.europa.eu/project/id/814425
[59] https://www.gov4nano.eu/ ; https://cordis.europa.eu/project/id/814401
[60] https://nanorigo.eu/ ; https://cordis.europa.eu/project/id/814530
[61] https://www.nanoinformatix.eu/ ; https://cordis.europa.eu/project/id/814426
[62] https://nanosolveit.eu/ ; https://cordis.europa.eu/project/id/814572

Within each region, the dissemination of research is actively pursued. The NSC is doing an annual review of active EU projects. In Thailand the National Nanotechnology Center (NANOTEC) have initiated the NanoSafety Network for Industry with an aim of utilizing the partnership of 9 state agencies to drive the **NanoSafety and Ethics Strategic Plan 2017-2024**[63] to enhance industrial understanding and awareness of how new nano-enabled products can pose concerns regarding to human health and environmental risks. In addition to using existing industrial standards related to nanotechnology the network is also exploring implementation of other activities such as production of industrial databases, easy to read safety publications, manuals, and applications including organization of seminars and exhibitions. Within the EU, the REACH Annex II on information content for Safety Data Sheets (SDS) has been revised[64] to include obligations for nanomaterials. ISO has developed a technical report (TR)[65] on how to prepare a material safety data sheet for nanomaterials.

It is felt that, whilst the OECD, including its Working Party on Manufactured Nanomaterials (WPMN)[66] play a vital role in disseminating information at a high level, knowledge about the underlying research and tools (i.e., testing guidelines[67,68]) is not reaching all relevant levels of the factory floor effectively between regions. However, mutual acceptance of data (MAD) is at least in place for many countries. These MAD adherents[69] include OECD member countries[70] as well as non-OECD member countries, namely Argentina, Brazil, India, Malaysia, Singapore, South Africa and Thailand, which are full adherents to MAD. As nanomaterials do not change their fundamental nature between regions there is no reason why these tools cannot be homogenously utilised by industry across the globe, but lack of awareness. INISS-Nano is an ideal position to both identify testing providers from member's own regions but also to disseminate information about tools developed across the globe **in a manner that can be easily accessed and understood at all relevant technical units of a factory**. It has strong links to the industrial, research and regulatory communities, meaning that it is ideally placed to support the development of protocols and schemes that promote the safe and sustainable expansion of nanotechnology across regions without the perception of vested interests. INISS-Nano feels that facilitating the transfer of information from SDS to the factory floor in a clear and understandable way is instrumental for the safe implementation of nanotechnology across

63 https://www.nanotec.or.th/en/wp-content/uploads/2018/09/Nanosafety-Soft-file.pdf ; https://www.nanotec.or.th/en/?page_id=9279 (extension of the plan to 2024)

64 Commission Regulation (EU) 2015/830 of 28 May 2015 amending Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) OJ L 132, 29.5.2015, p. 8-31
Available at https://eur-lex.europa.eu/legal-content/GA/ALL/?uri=CELEX%3A32015R0830

65 ISO/TR 13329:2012. Nanomaterials — Preparation of material safety data sheet (MSDS)

66 https://www.oecd.org/env/ehs/nanosafety/publications-series-safety-manufactured-nanomaterials.htm

67 The OECD Test Guidelines Programme (TGP) is responsible for developing all test guidelines, including those aimed at nanomaterials, and the TGP is recognised worldwide through the mutual acceptance of data (MAD) by countries adhering to MAD.

68 https://www.oecd.org/chemicalsafety/nanosafety/testing-programme-manufactured-nanomaterials.htm

69 https://www.oecd.org/chemicalsafety/testing/non-member-adherens-to-oecd-system-for-mutual-acceptance-of-chemical-safety-data.htm

70 https://www.oecd.org/about/document/ratification-oecd-convention.htm

the globe and is intrinsically linked with effective dissemination of research and tools discussed previously.

3.2.2 Case study "Nanomedicine"

Safety by Design of Nanotechnology Enabled Medical Products for *In Vivo* Applications

3.2.2.1 Introduction

Nanotechnology products for *in vivo* applications fall into two categories differentiated by: a) their manufacturing processes, b) their clinical applications and c) residence times *in vivo*. All three of features can affect the exposure and toxicology profiles of the nanomaterials used[71]. These categories are as follows:

1. Nano-enabled pharmaceutical products manufactured by continuous materials processing (e.g. drugs, vaccines and *in vivo* imaging agents).

2. Nano-enabled devices by discrete product fabrication (e.g. implanted replacement joints or medical devices).

The recent covid-19 (SARS COV 2) pandemic has accelerated the use of PEGylated liposomes as 70nm nano-delivery agents for mRNA vaccines. Whilst the risks of adverse effects are extremely low, there are reports of pseudoanaphylaxis associated with this class of vaccines.[72]

3.2.2.2 Safety-by-design of Processed Nanotechnology Products for Pharmaceuticals

The fundamental principles of safety by process design (SbPD) lie in the evolution of engineering principles initially developed in the mid-1990s by the chemical industry for manufacturing nanotitanium dioxide[73] and subsequently integrated into pharmaceutical industry manufacturing[74]. A holistic approach is adopted which starts with standard medical product Good Manufacturing Practice (GMP) and Quality Assurance (QA) procedures. Safety with respect to nanomaterials is built-in throughout the manufacturing chain from raw materials, product design to finished products. SbPD guarantees the safety features optimized at the R&D stage, are maintained throughout process development, scale up and full scale manufacturing, as described in Figure 2.

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[71] Giubilato E., et al.. Materials 2020, 13(20), 4532; https://doi.org/10.3390/ma13204532

[72] Mohamed M., et al. Sci Technol Adv Mater. 2019 Jun 26;20(1):710–24.

[73] Joint EASAC-JRC Report. Impact of Engineered Nanomaterials on Health: Considerations for Benefit-Risk Assessment; 2011. https://doi.org/10.2788/29424

[74] Besson, J. P., et al. Calcination of Titanium Dioxide. 1996.

SbPD of medical products made by materials processing is built on the principles of the United States Food and Drug Administration (US-FDA) regulatory guidelines of 2003 and adopted by EMA in 2003 as described by Brenderlberger (2003).[75]

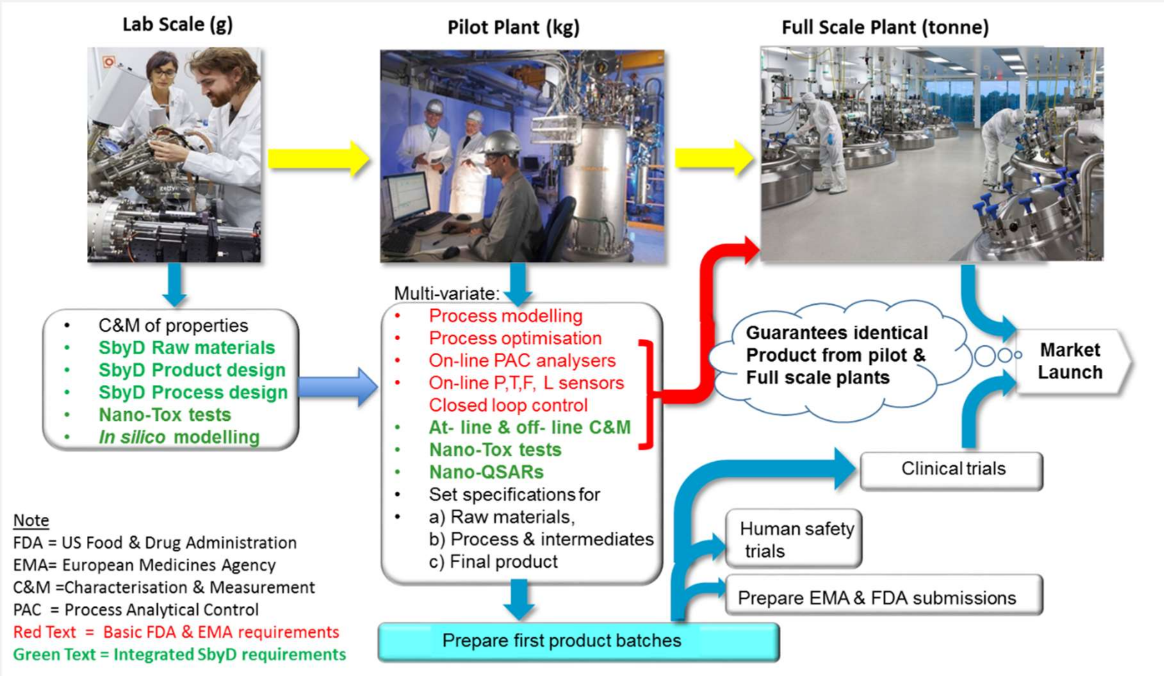

Figure 2: Integration of nanotechnology Safety-by-design principles into FDA/EMA Process Analytical Control Risk Management Regulations (2003) for Pharmaceutical Products

Since 2003, pharmaceutical companies have adopted the FDA scheme for Process Analytical Technologies (PAT) of active pharmaceutical ingredients (API). To control complex batch or continuous processes to manufacture API, a large number of inputs from low-functionality process sensors (e.g., pressure, temperature, flow, level and mass - P, T, F, L & M) are collected. These sensors are linked with electrical controllers in nested hierarchical systems of distributed control systems (DCS) together with coordinator control systems and in the case of very large manufacturing plants, super coordinator control systems.

In PAT strategies it is essential to have specific high-information content analysers on-line at critical stages in the process. They are coupled to closed-loop control systems. Such analysers might be Raman and IR spectrometers, or Mass Spectrometers. They could also involve process tomography or automated sample and flow injection analysis through "lab-on-a chip" biosensor devices or particle sizers. During the pilot plant development stage, the process parameters together with reagent quantities and additives, are varied to enable the process to be optimised simultaneously for product yield, quality and process profitability. Importantly, *in silico* methods (e.g., nano-QSARs) are included in these calculations to minimise risks. Once

[75] U.S. Food and Drug Administration (FDA). Guidance for Industry, PAT-A Framework for Innovative Pharmaceutical Development, Manufacturing and Quality Assurance. 2004, No. September.

optimised and tested by multivariate process modelling for the full-scale plant, all manufacturing specifications and control set points are then fixed. This guarantees that both "pilot" and "full scale" process plants will produce products of identical quality. These approaches collectively form the core part of safe by process design. It allows batches of products to be prepared for: i) safety ("*first in man*" trials); ii) clinical trials and iii) the EMA/FDA regulatory claims support file. This work can continue whilst the full-scale plant is being built and commissioned, thus shortening the time to market but guaranteeing the best possible products within a process intensification perspective[76],[77].

To achieve "safe-by-design" of products, additional characterization and measurements tests and *in vitro* toxicology tests are added into the raw materials and pilot plant development stages (shown in green in Figure 2). These can be performed off-line or at-line using high-throughput parallel processing analysers including electron microscopy. On-line analysers are chosen for the pilot scale to enable full process analytical and product quality control. The results are analysed by nano-QSARs data analytics[78],[79],[80] using critical characterization and measurement parameters together with data from the high information content on-line analysers, e.g. Raman, FTIR, mass spectrometers[81] to build multivariate statistical process control models. Together these devices are used to maintain the optimised SbyD performance throughout full-scale manufacturing during the life of the product.

3.2.2.3 Safety-by-design of Fabricated Nanotechnology Devices

Safe by Design for discrete object fabricated products begins with the same paradigm illustrated above for products made by materials processing**Fehler! Verweisquelle konnte nicht gefunden werden.**. A significant range of materials must be tested at the raw materials stage to minimise product toxicology downstream. The approach differs at the pilot plant stage where initially material "test coupons" are produced on prototype fabrication unit operations. The latter are small but mimic the automated device used in the full manufacturing plant. Critical in this early stage is to test the biocompatibility of the materials to be used for 'implantability' of such devices. Once suitable materials have been chosen, the implantable device geometry and performance characteristic are mathematically modelled, and the first manufacturing devices are engineered. Full scale manufacturing for fabricated products is achieved by "scale out" rather than "scale up". The imperative is to ensure the unit operations are optimised. These are replicated to create a manufacturing line with banks of identical unit operations accurately producing the product in parallel to a full set of specifications, including

[76] U.S. Food and Drug Administration (FDA). Guidance for Industry, PAT-A Framework for Innovative Pharmaceutical Development, Manufacturing and Quality Assurance. 2004, No. September.
[77] Brenderlberger, G., New PAT (Process Analytical Technology) Draft Guidance from FDA; 2003.
[78] Strube, J.; et al., Process Intensification in Biologics Manufacturing. Chem. Eng. Process. - Process Intensif. 2018, 133 (October), 278–293. https://doi.org/10.1016/j.cep.2018.09.022
[79] Babi, D. K.; et al., Fundaments of Process Intensification: A Process Systems Engineering View. In Process Intensification in Chemical Engineering: Design Optimization and Control; 2016.
[80] Tantra, R.; et al., Nano(Q)SAR: Challenges, Pitfalls and Perspectives. Nanotoxicology 2015, 9 (5), 636–642. https://doi.org/10.3109/17435390.2014.952698
[81] Oksel, C. NanoSAR : In Silico Modelling of Nanomaterial Toxicity. 2016, No. April.

nanobiomaterials hazard reduction. Using nano-enbabled SbD replacement hip joints as an exemplar, this generic SbD process development has been described by Wilkins et al[82] [14]. In this model, the design objects were:

a. Substantial reduction in ball and cup friction
b. Substantial reduction in joint wear debris, especially nanoparticles
c. Substantial reduction in toxicity of wear nanoparticles
d. Reduction of stress induced toxic metal ions from the metal shaft.
e. Whole life use in vivo (to eliminate revision surgery)
f. Reduce morbidity and mortality arising from inflammatory process stimulated by metal and cup wear micro- and nano- particles

All the above design objectives were achieved by coating the joint's shaft, ball and cup with nanostructured silicon nitride using plasma enhanced chemical vapour deposition**.** As part of the manufacturing fabrication development, product performance is assessed by simulation and accelerated mechanical testing for *in vivo* use. In addition, the authors noted that international standards (ISO, CEN, etc.) addressed only the risks of bulk materials of devices and not the risk of micro- and nano- wear particles created during lifetime wear. These wear particles accelerate the degradation of the joints and cause inflammatory effects within subject affecting morbidity and mortality causing joints to replaced surgically. They have set a benchmark for standards (CWA: 17253-1 and CWA: 17253-2) respectively for nanoparticle wear characterization and toxicology testing, to be applied to all nano-enabled replacement joint devices to ensure artificial joints are Safe-by-Design.

A structured set of methods were developed as a workflow for evaluating test joints under load using parallel robot testing units with the test joints encased in plastic jackets containing simulated synovial fluid containing serum albumin and lubricin. The wear debris was fractionated to collect micro and nano-scale fractions. These were treated with peripheral blood mono nuclear cells PNMNC) to evaluate the nanoparticles using 4x toxicological assays: Cytokine release (ELISA), ATP cytotoxicity (TNF-α), Oxidative Stress and DNA Strand break (Comet Assay) described in Figure 3.

[82] Gajewicz, A.; et al., Decision Tree Models to Classify Nanomaterials According to the DF4nanoGrouping Scheme. Nanotoxicology 2018, 12 (1), 1–17. https://doi.org/10.1080/17435390.2017.1415388

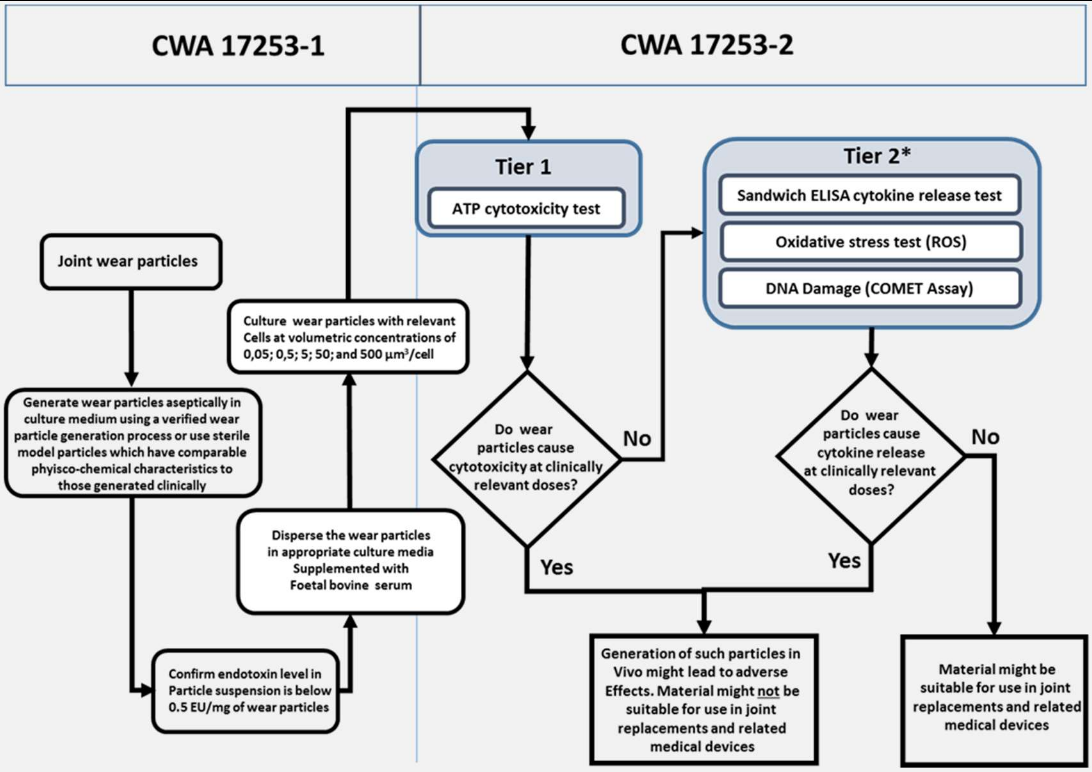

Figure 3: Workflow diagram for: a) Isolation of wear particles under accelerated robotic testing of replacement hip joints under simulated in vivo conditions and subjecting peripheral blood mononuclear cells (PBMNCs) to the wear particles produced; and b) flow diagram of 4 toxicology tests. A CEN Workshop Agreement standard (CWA 17253-1) has been secured for a) and a second CEN Workshop agreement (CWA 17253-2) has also been secured for b). Note: *Tier-2 tests can be performed in any order.

The above same principles can also be applied to other personalised medicine devices such as patient-specific 3D printed implants, containing nanohydroxyapatite to replace bone loss, following maxillary facial surgery to remove of cancerous bone[83].

[83] Vazquez-Vazquez, F. C.;et al., Biocompatibility of Developing 3D-Printed Tubular Scaffold Coated with Nanofibers for Bone Applications. J. Nanomater. 2019, 2019. https://doi.org/10.1155/2019/6105818

3.2.3 Action Plan – Pillar 2

Action	Short-term (till Dec 2023)	Medium-term (till 2025 and beyond)
Facilitate knowledge transfer	Collection of (reliable) sources for data of different complexity by INISS partners, gap analysis [lead: Patricia Farias, Vinicius Bim]	Common global (web) portal with clearly laid out guidance for industry (where to find what and how to use it) for different sectors [lead: Patricia Farias] Closing of gaps for industry, Global database/portal [Vinicius Bim]
Harmonized characterization	Collection of techniques/fields, projects, existing working groups [lead: Miguel Bañares]	Network of stakeholders for particular areas (techniques, sectors), knowledge exchange, round robins to close gaps [lead: Miguel Bañares] Global expert groups identifying future areas of interest, harmonized approaches [lead: Patricia Farias]
Targeted communication and outreach	Definition of target audiences and available channels [lead: Patricia Farias, Miguel Bañares]	Series of workshops / conference sessions (e.g., in conjunction with current projects in this field and existing networks like ETPN) [lead: Patricia Farias, Miguel Banãres] Communications toolbox [lead: tbd]

3.3 Pillar “Sharing / facilitate sharing of resources/ infrastructures”

Pillar-leader: Ali Marjovi

Supporters: Miguel Banares; Ali Beitollahi; Nils Bohmer; Andreas Falk; Patricia Farias; Georges Favre; Steffi Friedrichs; Ramjitti Indaraprasirt; Effie Marcoulaki; Cris Rocca; Pushplata Singh

Despite significant advances in nano safety-related knowledge and practice, the high cost of sophisticated laboratory instruments, lack of expertise in some regions, different experimental procedures, and lack of communication and experience exchange among different regions have created a patchwork of activities and output that show little harmonization across political borders. Through the establishment of a worldwide network of nano safety-related laboratories and facilities and a community-based sharing platform, this pillar of the proposal advances the theme of a sustainable solution to overcome some of the challenges concerning nano-safety research. While there are several local and regional projects aiming at advancing the safety and sustainability of nanotechnology and its products through networking and sharing mechanisms, there is no single network/platform that could sponsor, promote, and govern a sharing tool for laboratory resources at a global scale.

Under the mentioned circumstances, INISS-Nano's mission to facilitate access for researchers and experts, relevant industries, academic institutions, and research centers to the existing infrastructures, including laboratories, instruments (e.g., QNano[84]), and information system platforms (e.g., NanoCommons[85]) seems justifiable. The European Commission has started an open access initiative[86] to its research infrastructure, including laboratories specializing in nanomaterials.

We suggest a broader view of the term infrastructure to include relevant information and experts' tacit knowledge. As a result, such a platform not only can facilitate access to laboratory services but can also make existing data and knowledge of nano safety accessible to a broader community across the world.

Beyond the provision of easier access for academic researchers, technologists, and industries with nanosafety-related activities with sophisticated instruments and testing facilities, the proposed network can also expose partners to a vast field of cutting-edge technologies, protocols, novel ideas, opportunities, recent projects, and talents outside their organization, hence resulting in a win-win situation with an incentive for all players to join the network. The

[84] https://cordis.europa.eu/project/id/262163
[85] https://cordis.europa.eu/project/id/731032
[86] https://ec.europa.eu/jrc/en/research-facility/open-access

identification of specific barriers shall be one of the action items. Interactions in this network can also inspire the development of novel instruments, infrastructure, and know-how which will be much needed in the future. As part of the network, a matchmaking mechanism can help connect partners with relevant experts/organizations resulting in more efficient use of knowledge and skills and more versatile mobility of experts, researchers, and perhaps students.

The proposed INISS-Nano can help provide better visibility of nanosafety-related infrastructures on a global scale and thus support the exchange and training of both staff and users. The network can facilitate upgrading the technical knowledge of experts through various targeted short-term virtual or otherwise training programs/workshops; this would culminate in an added value of an improvement of laboratory services for the partner organizations in the field of nanosafety and sustainability research. Another function of the proposed network would be to promote harmonization between laboratories and testing facilities, for example by arranging laboratory comparison schemes (e.g., round-robin tests, technology validation exercises, infrastructure sharing) and harmonization of test guidelines, protocols and procedures (link with pillar 1). In addition, the platform can highly facilitate the engagement of its stakeholders in joint standardization activities. INISS-Nano will support the knowledge exchange related to digitalisation, automation, FAIRification and many other aspect of good data management and sharing practices.

Similar experiences such as the EC-funded NanoFabNet[39] project and other relevant initiatives (e.g., EuroNanoLab[87]) worldwide can inspire the organizational structure underlying the sharing of facilities that would immensely benefit the community of safe and sustainable nanotechnologies.

Future work

INISS-Nano will facilitate sharing and better use of the existing infrastructure through a step-by-step scenario. The first step starts with a thorough study of the current situation going beyond previous studies (e.g., EC4SafeNano[88]), that helps structure the problem. It involves listening to the field experts about their needs to understand better current gaps in this regard. Based on the gained information and insight, the conceptual design of a platform (which facilitates the formation of the network and the exchange of information and services across it) will proceed and be discussed with stakeholders. If setting up such a platform is deemed feasible and helpful in the study phase, then the implementation will be pursued in the subsequent phase, given that the needed resources be acquired from the stakeholder community. The action plan below explains more details about each step.

[87] http://euronanolab.eu/

[88] Marcoulaki, E., et al. 2021. Blueprint for a self-sustained European Centre for service provision in safe and sustainable innovation for nanotechnology. NanoImpact, 23, p.100337. https://doi.org/10.1016/j.impact.2021.100337

3.3.1 Action Plan – Pillar 3

Action	**Short-term (till Dec 2023)** **(STUDY and DESIGN stage)**	**Medium-term (till 2025 & beyond)** **Implementation**
implementation of a **community-based platform** for sharing facilities used in nanosafety area	1- Conducting a **study** on the current situation of nanosafety-related facility networks including: - Compiling a list of facilities and services used in nanosafety area - Identifying the existing **networks, platforms, networking/knowledge/data bases, and facilities (not yet covered in these),** existing and upcoming platforms from existing networks; seeking synergies with knowledge (data and tools) platforms, and research infrastructures worldwide - Identifying **stakeholders** and conducting a **stakeholder analysis** - Performing a **survey** on the current gaps and shortcomings - Performing a **foresight** of the future needs [lead: Ali Marjovi/INLN Team, Steffi Friedrichs/NanoFabNet] 2- **Prioritisation** of approaches - Identification of existing infrastructure components to be integrated - Identification of gaps and ranking of importance and addressability - Interface definition [lead: Thomas Exner] 3- **Conceptual design** of the platform - Motivation strategy for collaborating in the platform - Communication channels to relevant stakeholders - IT requirements - Business model for running the platform - Governance	**Implementation** of the platform to provide the following activities and services: - IT platform implementation - Promotion and marketing - Expanding the platform by adding new members [lead: tbd] Provision of the following services: - Information sharing - Exchange of experience - Mobility of human resources - Training and capacity building - Facilitation of standardization related activities among members - Community-based evaluation and feedback - proficiency testing [lead: tbd] **2025+** **Implementation** of the **second phase** of the platform including: - On-line system for exchange of various services related to laboratory tests, services, certifications etc. [lead: tbd] On-line system for facilitation of joint research activities [lead: tbd]

	- Functions, activities and processes - Architectural design of domain subnetworks (e.g. Eco-toxicity, Genotoxicity, inhalation toxicity …) [lead: Steffi Friedrichs/NanoFabNet, tbd] 4- Sharing the conceptual design with stakeholders and **refining** it based on the stakeholders opinions [lead: tbd] 5.Finalization of detailed design [lead: tbd]	

3.4 Pillar "International collaboration on ethical and societal aspects of nanotechnology"

Pillar-leader: Ineke Malsch.

Supporters: Miguel Banares; Ali Beitollahi; Sophie Briffa; Flemming Cassee; Fernand Doridot; Thomas Exner; Andreas Falk; Patricia Farias; Georges Favre; Giancarlo Franzese; Steffi Friedrichs; Ramjiti Indaraprasirt; Kirsten Rasmussen; Cris Rocca; Pushplata Singh; Waluree Thongkam

Introduction

International collaboration in nanosafety involves addressing some specific ethical issues e.g.:

- Addressing global health and safety inequalities: protection of the safety of workers, consumers and environment in developing countries,
- Closing the gap between developed and developing countries to guarantee that developing countries will not be used as testing grounds of nano-enabled products,
- Implications for nanotechnology exporters in a situation when there are differences in legal regimes in different world regions and countries,
- Quality in public communication about nanotechnologies,
- The related legal framework and international collaboration in responsible nanotechnology research, including its transferability,
- Understanding what general framework could be used and where specific modifications to local settings have to be allowed.

In the following pages, INISS-Nano briefly addresses these issues and makes some suggestions how INISS-Nano may help to overcome or achieve these.

3.4.1 Nanosafety in developing countries

The issue is ensuring that consumers, workers and the environment exposed to nanomaterials in developing countries are as safe as in developed countries. UNITAR has published guidelines, containing some suggested ideas, for developing-countries´ governments about how to formulate their policy for nanotechnology governance[89]. In addition, UNITAR has organised regional workshops and national projects to address nanosafety all over the world[90].

89 https://cwm.unitar.org/publications/publications/Nano.aspx
90 https://unitar.org/sustainable-development-goals/planet/our-portfolio/nanotechnology-

See also Aungkavattana et al. (2022)[91]. Furthermore, the World Health Organization (WHO) has developed guidelines for occupational health and safety of workers handling nanomaterials[92]. In 2021, the International Labour Organization (ILO) recommended that "National regulations based on evidence from risk assessments should be developed for MNMs [manufactured nanomaterials]. Different OELs have been implemented, but evidence of the effectiveness of these OELs is still limited and harmonised OELs are missing."[93]
For reference, in 2016, these and some other initiatives related to international collaboration in safe and responsible governance of nanomaterials and nanotechnologies taken by UN bodies have been listed in the Nanotechnology and International Law Research Guide[94].

Future work

INISS-Nano will target the protection of workers and consumers exposed to nanomaterials in developing countries and thus support international organizations (e.g. the International Labour Organization) in terms of addressing inequalities in health and safety protection by the following measures:

- Invite policy makers and nanosafety experts from developing countries to all events organised by the NanoSafety Cluster.
- Engage with the coordinators of the nanotechnology activities of UNITAR and other international organizations to identify their needs and interests in continuing support and training in nanosafety.
- Advertise research jobs in nanosafety to students and researchers from developing countries, through the network established by UNITAR and INISS-Nano partners.
- Promote the UNITAR and WHO guidelines through the NanoSafety cluster newsletter and other media.

3.4.2 Legal aspects

In this section, we propose a strategy for reviewing and analysing philosophical concepts and values underlying differences in legal systems governing nanomaterials in different parts of the world, to generate better understanding of each other's views among international negotiators on international nanoregulation. This strategy builds upon earlier work exploring philosophical foundations for international governance of nanotechnology including Malsch et al. (2015)[95]

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91 Pavadee Aungkavattana, et al. (2021) The nanosafety and ethics strategic plan of Thailand in the context of the strategic approach to international chemicals management, Toxicological & Environmental Chemistry, 103:4, 438-465, DOI: 10.1080/02772248.2022.2045990

92 https://apps.who.int/iris/bitstream/handle/10665/259671/9789241550048-eng.pdf?sequence=1

93 ILO (2021) Exposure to hazardous chemicals at work and resulting health impacts: a global review. P 10, p41-44. International Labour Office. Geneva. www.ilo.org/publns

94 https://www.nyulawglobal.org/globalex/Nanotechnology_International_Law1.html#UnitedNations

95 I. Malsch, V. Subramanian, E. Semenzin, D. Hristozov, A. Marcomini, M. Mullins, K. Hester, E. McAlea, F. Murphy, and S. A. M. Tofail, "Empowering citizens in international governance of nanotechnologies," J. Nanoparticle Res., vol. 17, no. 5, pp. 1–19, 2015, doi: 10.1007/s11051-015-3019-0.

and studies analysing differences in international legal regimes (e.g., Karim et al, 2013)[96] as well as research on nanotechnology and international law. This section complements activities proposed in sections 3.1 and 3.2.

As mentioned in section 3.2, there is currently no specific and direct international legal instrument dealing with nanotechnologies, ENMs or nanosafety. The reason for this may be that ENMs are nanoscale chemicals and the chemicals related international legal provisions are generally encapsulated within the international environmental law related legal instruments. Moreover, even until 1960s, environmental matters were considered as national issues, and therefore, did not receive concerted international attention. Legal regimes in the fields of environmental protection, occupational health and safety, and consumer protection, etc. are often fragmented between States, international and regional levels such as the European Union. In the EU some of its Member States have over the last 20 years been proactively adopting additional (to EU legal instruments) legally binding instruments dealing with nanotechnology-based products, while also respecting the EU legislation. Some inter-governmental organizations have adopted policy documents which are not legally binding and enforceable including the abovementioned UNITAR and WHO guidelines. At the level of a world region, the legislative experience of the European Union and its Member States could serve as a good practice example for broader harmonization of legislation governing nanomaterials and nanotechnologies.

One of the drivers of regulatory action is the precautionary principle, which is recognised and incorporated in many international instruments e.g. the Rio Declaration on Environment and Development, and adopted by a vast majority of states across the world, as it incentivises regulators to adopt measures in the absence of scientific certainty[97]. In the European Union, the precautionary principle is enshrined in article 191 of the Treaty of the Functioning of the European Union[98] and has been further interpreted in a 2000 communication from the European Commission[99]. COMEST (2005)[100] analysed international differences in interpretations of the precautionary principle. Since then, precaution has been the topic of continued discussion, including proposals at EU-level to consider the need for innovation. INISS-Nano could review the current discussion and suggest policy recommendations building upon the COMEST recommendations.

[96] http://eprints.um.edu.my/13185/1/Nanotechnology_through_the_Lens_of_Law_Defence_University_Md._Ershadul_Karim.pdf
[97] https://www.un.org/en/development/desa/population/migration/generalassembly/docs/globalcompact/A_CONF.151_26_Vol.I_Declaration.pdf
[98] https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:12008E191:EN:HTML
[99] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A52000DC000
[100] https://unesdoc.unesco.org/ark:/48223/pf0000139578

3.4.3 Quality in communication

The propagation of nanotechnology-related misinformation and disinformation (rumours[101] and "fake news"[102]) increases with severe risks for society (e.g. discouraging people from COVID 19 vaccination[103]). The information problems propagate for different reasons: Technological factors (e.g., digital platforms making a profit from 'any' kind of sharing); Psycho-sociological factors (e.g., confirmation bias, echo chambers, and filter bubbles); Political factors (e.g., populism and polarization); and Media factors (e.g. news avoidance, lack of media literacy[104]). The effects and consequences of disinformation include social destabilization, media distrust, and suspicion against real science, which may ultimately create barriers to utilizing science for the betterment of humankind. Hence, debunking false information about nanotechnology is a global need of industry[105] and society[106]. However, among the worldwide organizations in the Fact-Checking Network[107] for information evaluation following a strict code of principles[108], only one specializes in science (Science Feedback[109], mainly focusing on climate and health), while others (AFP Fact Check[110] and Reuters Fact Check[111]) are large international news agencies also covering science. Furthermore, very few agencies fact-check in various languages (e.g., the French-language Détecteur de Rumeurs[112], in the Reporters' Lab-database[113], or those with a base in Southeast Asia[114]).

Future work

The INISS-nano can contribute to cleaning the "information pollution" by:

- Organising training courses for young researchers and tabling discussions during international nanosafety events on good practices in communicating nanoscience. Such events should help educate the INISS-nano scientists on communicating better-sound science to all (e.g., following the European Science Media Hub[115] initiative or good practice initiatives from other countries). Furthermore, after evaluating national good practice experiences in nanoscience communication in Europe and other INISS partners' countries, INISS-nano could recommend partners adopt identified good practices if these fit the

[101] https://www.timharper.net/the-science-behind-fake-news-and-fake-products/
[102] https://firstdraftnews.org/latest/fake-news-complicated/
[103] https://www.reuters.com/article/idUSKBN28F0I9
[104] Source: https://www.unav.edu/en/web/grupo-investigadores/digital-news-media
[105] E.g.: https://blog.agchemigroup.eu/top-5-myths-on-nanotechnology-exposed/
[106] E.g.: https://sciencemediahub.eu/
[107] https://ifcncodeofprinciples.poynter.org/know-more/the-commitments-of-the-code-of-principles
[108] https://ifcncodeofprinciples.poynter.org/
[109] https://sciencefeedback.co/
[110] https://factcheck.afp.com/
[111] https://www.reuters.com/fact-check
[112] https://www.sciencepresse.qc.ca/detecteur-rumeurs
[113] https://en.wikipedia.org/wiki/List_of_fact-checking_websites#cite_note-36
[114] https://theconversation.com/three-fact-checking-challenges-in-southeast-asia-148738
[115] https://sciencemediahub.eu/

context of their regions/countries. The recommendation should consider cultural factors variables and other socio-economic/legal differences.

- Organizing world-wide events during the European Media Literacy Week[116] to educate society to media literacy (i.e., the capacity to access, have a critical understanding of, and interact with the media). This event has the specific purpose of promoting good quality science communication. This can contribute to the debate of the EU Expert Group on Media Literacy[117] which meets annually and implementing their suggestions to the nanoscience area.
- In addition we could organise worldwide events promoting good quality nanoscience communication during appropriate initiatives such as EuroScience Open Forum[118] or European Researchers Night[119],
- Initiate international dialogue on quality standards for nanoscience communication in collaboration with science communication specialists with experience in communicating nanoscience. INISS-nano could promote actions that are specific to the nanoscience in forums such as the European Union Action Plan against Disinformation[120]. This might be enabled with the emphasis of targeting specific science communication in nanotechnology, by engaging communication specialists[121].

3.4.4 Responsible Research and Innovation

Much is expected from nanotechnology in terms of sustainable development, and for the achievement of the UN Sustainable Development Goals, particularly in developing countries. Nevertheless, related to the discussion in section 3.4.1, the development of nanotechnology globally raises a set of social and economic issues, including the risk of “nano-divide” (e.g., will nanotechnology increase or decrease the gap between industrialized and developing countries?), the impacts on the workforce of developing countries, on the primary materials markets, and on the economy of countries dependent upon them. There are also concerns that, taking advantage of less stringent regulations, the developing countries might be used as testing grounds of nano-enabled products developed by the manufacturers from industrialised countries. More generally, this development questions strongly the respective roles of technology and of politics in addressing the different challenges of developing countries.[122]

In addition, the development of nanotechnology applications (in nanomedicine, robotics, information and communication technologies, etc.) raises a set of social and ethical questions,

[116] https://digital-strategy.ec.europa.eu/en/events/european-media-literacy-week
[117] https://ec.europa.eu/transparency/expert-groups-register/screen/index.cfm?do=groupDetail.groupDetail&groupID=2541
[118] https://www.esof.eu/
[119] https://ec.europa.eu/research/mariecurieactions/actions/msca-citizens
[120] https://digital-strategy.ec.europa.eu/en/library/action-plan-against-disinformation
[121] Factor Social (partner in RiskGONE): https://factorsocial.pt/index.php?lng=en&page=homepage
[122] J.Schummer, “Impact of nanotechnologies on developing countries”, in F.Alhoff and alii, Nanoethics: The Ethical and Social Implications of Nanotechnology, Wiley, 2007, pp.291-307

which require the development of ethical impact assessment procedures and tools. The international ethical compendium (including the Universal Declaration of Human Rights) is frequently mentioned accordingly. Nevertheless, there remain cultural differences all over the world in the promoted ethical principles and values, and in the interpretation of them, which make such an ethical impact assessment difficult and limited.[123]

The European Commission strategy for the development of nanotechnology comes within the general framework of Responsible Research and Innovation (RRI), with e.g., anticipatory and participatory processes, upstream public and stakeholder engagement. There exists currently an ambition to export this model all over the world.[124] The possibility and legitimacy of such an ambition deserves nevertheless to be questioned, regarding the specificities of nanotechnology.

The INISS-Nano initiative can help to address these issues in organizing works and meetings on these topics with relevant experts and stakeholders, in the general framework of the OECD, UNITAR and UNESCO initiatives. INISS-Nano activities could consider the conclusions of the recent OECD event Technology in and for Society[125] and engage in testing of the CEN CWA 17796[126] on Responsibility-by-design on a comparison of international case studies.
INISS nano can also build upon relevant work exploring ethical impacts[127], social aspects and risk governance issues performed in projects e.g., in the NanoSafety Cluster. An example could be to test the ethical impact assessment guidelines and online tools on international case studies of ethically sensitive applications of nanomaterials and nanotechnologies.[128]

[123] S.Dalton-Brown, Nanotechnology and Ethical Governance in the European Union and China, Springer, 2015

[124] R.Von Schomberg and J.Hankins (eds.), International handbook on responsible innovation: A global resource, Edward Elgar Publishing, 2019

[125] https://oecd-events.org/technology-in-and-for-society/

[126] C.f., https://www.nen.nl/cwa-17796-2021-en-288066

[127] The CEN CWA on ethical impact assessment offers a procedure to identify and evaluate which ethical issues a specific product or project raises, and how severe the expected impacts on these issues are. Then, the procedure guides the user through a process of formulating recommendations for remediation and for a stakeholder and expert consultation. See: https://riskgone.eu/wp-content/uploads/sites/11/2021/01/RiskGONE-D3.6.pdf

[128] C.f. https://ethicschool.nl/demonstration-ethical-impact-assessment-of-nanomaterials-in-dentistry and https://riskgone.eu/wp-content/uploads/sites/11/2021/01/RiskGONE-D3.6.pdf

3.4.5 Action Plan – Pillar 4

Action	Short-term (till Dec 2023)	Medium-term (till 2025 & beyond)
Action 1 – capacity building for nanosafety in developing countries TBC	Establish working relations with nanosafety specialists at UNITAR, SAICM, WHO, ILO and in developing countries. Draft common long term training agenda for policy makers and stakeholders. [lead: tbc]	Agree on long term international capacity building programme with EU and national funding commitments? [lead: tbc] Engage in long term capacity building for nanosafety, e.g., by: • Inviting policy makers and nanosafety experts from developing countries to all events organised by the NanoSafety Cluster. • Advertising research jobs in nanosafety to students and researchers from developing countries, through the network established by UNITAR and INISS Nano partners. • Promoting the UNITAR and WHO guidelines through the NanoSafety cluster newsletter and other media. [lead: tbc]
Action 2 – towards international nanoregulation – possibly incorporated in pillar 1: Harmonization?	Review article on political philosophical and legal value differences influencing dialogues on international regulation of nanomaterials [lead: Ineke Malsch]	[If possible, in the scope of INISS: help organise global summit on nano-regulation? Politicians should agree on minimum standards for nanosafety including mutual acceptance of data on nanomaterials.] [lead: XY] to be coordinated with pillar 1: Harmonization
Action 3 – setting standards for quality in nano-communication – lead Giancarlo Franzese, contributors: Fernand Doridot, Ineke Malsch, others?	Organise science communication training and dialogue sessions during Nanosafety Cluster events and other international nanotechnology conferences [lead: Giancarlo Franzese]	establish an Erasmus-mundus master course on nanoscience communication? [lead: Giancarlo Franzese] NSC, ANF and other platforms: Integrate science communication training in curricula for (nano) scientists Initiate international dialogue on quality standards for nanoscience communication in collaboration with science communication specialists with experience in communicating nanoscience [lead: tbc]

Action 4 – international dialogue on responsible nano research and innovation – lead Fernand Doridot, contributors Waluree Thongkam, Giancarlo Franzese, Ineke Malsch, others ?	Test selected tools stimulating ethical and responsible nanotechnology on cases highlighting international value conflicts (e.g., the RiskGONE ethical impact assessment tools, the CEN CWA 17796 on Responsibility-by-design, the anticipatory ethics framework) [lead: Ineke Malsch] Make a review of the existing tools/indicators/standards useful for addressing and assessing ethical impacts of nanotechnology and nanomaterials (including social life cycle assessment tools) [lead: Fernand Doridot]	Integrate ethics and international dialogue on values in stakeholder dialogue on risk governance of nanotechnology (building on work of NMBP13 projects and others) [lead: tbc] Develop more links between nanotechnology community and "ethics of technology" communities in Europe and worldwide [lead: tbc] Politicians should agree on ethical quality standards in international nano & chemicals management [lead: tbc] Develop and promote "ethical-by-design" concept and tools [lead: tbc]

4 Acknowledgement

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4.3 Involved Projects, Initiatives and Partnerships

4.3.1 Projects

BIORIMA

[129] In June 2021, the first version of the concept was published and opened for comments and contributors. These colleagues started to comment/contribute/support INISS-Nano afterwards.

caLIBRAte
CHARISMA
DIAGONAL
EASI-STRESS
Gov4Nano
HARMLESS
ISO-G-SCoPe
LifeLongJoints
NanoCommons
NanoFabNet
NanoHarmony
NanoInformaTIX
nanoMECommns
NanoMET
NanoRiGo
NanoSolveIT
NanoSyn
NanoSyn2
NanoSyn3
nPSize
RiskGONE
SABYDOMA
SbD4Nano
Sinfonia
SUNSHINE
(open to further contributions)

4.3.2 Initiatives/Partnerships

Asia Nano Forum
DBT -TDNBC - DEAKIN – Research Network Across continents for learning and innovation (DTD-RNA)
EU NanoSafety Cluster
EURAMET
(open to further contributions)

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