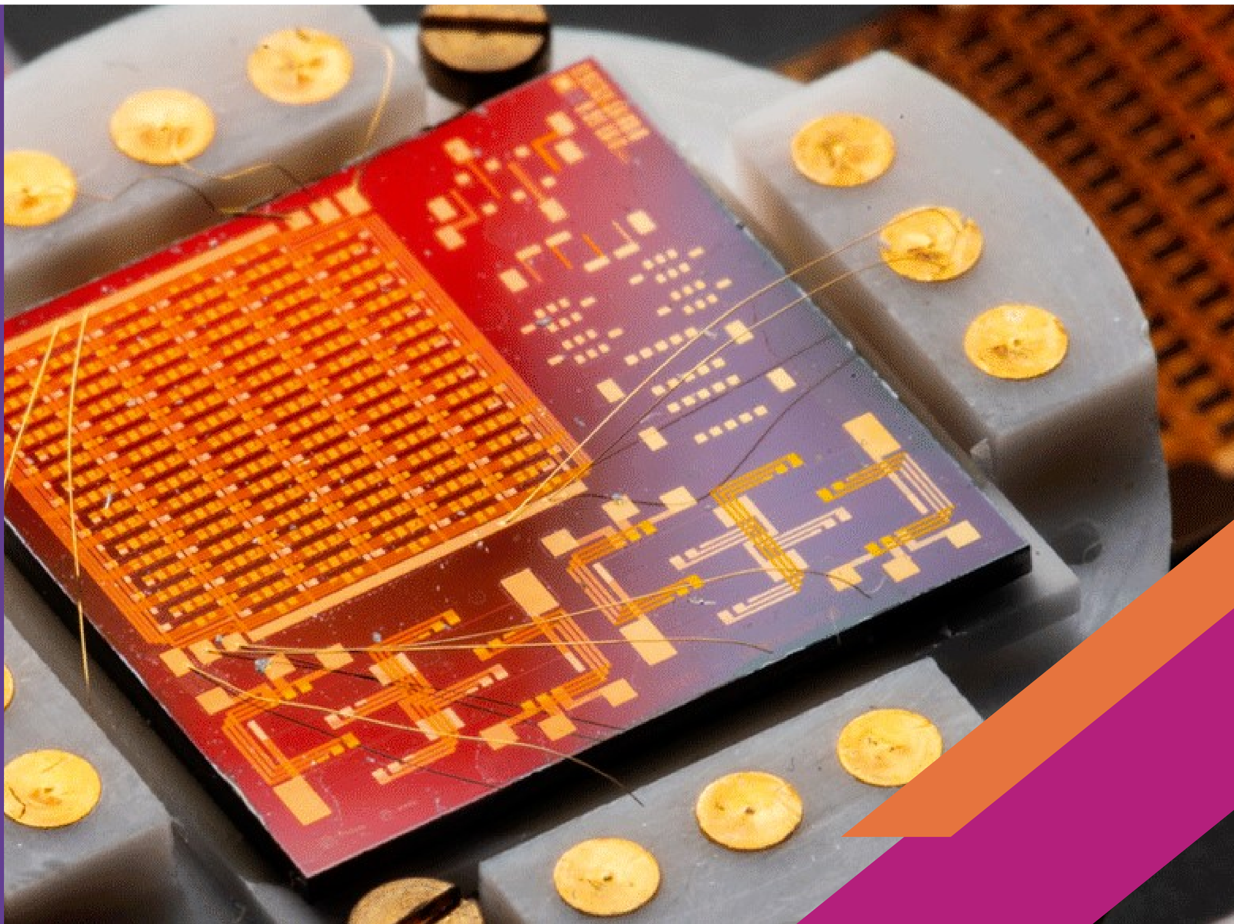
NanoFabNet

international Hub for sustainable industrial-scale Nanofabrication

Challenges & Opportunities of Validating, Harmonising & Standardising industrial-scale Nanofabrication



NanoFabNet Report

NanoFabNet

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Table of Contents

NanoFabNet

Table of Figures

Table of Tables

Table of Boxes

1. Executive Summary

Nanofabrication encompasses many different processes aimed at producing objects and systems with specific properties at this small scale, and academic research laboratories and clean rooms constantly developing new approaches or tools to be taken into account. Beyond the technical difficulties inherent in the production of these advanced technologies, there are also many issues related to their production and integration into complex and interoperable systems in a sustainable framework. The problems to be addressed in order to envisage the implementation of a real sustainable, industrial-scale nanofabrication are therefore very varied, but have several points in common: the conditions for trust must be met between economic actors in the same value chain, between economic actors and public authorities, and finally with civil society.

This requires the development and easy accessibility of the necessary tools to validate different key steps of nanofabrication and the establishment of structuring initiatives on these issues to provide appropriate responses to stakeholders. Harmonisation of the methodologies and tools used, as well as better dissemination of these good practices is another essential prerequisite in order to improve comparability issues and avoid reinventing the wheel; the standardisation framework offers opportunities in this respect, but it is, however, not sufficiently exploited today.

Based on an in-depth desk analysis of scientific literature and the collection of key stakeholders' opinions, a detailed analysis of the challenges & opportunities posed by any validation, harmonisation and standardisation efforts in sustainable nanofabrication has been carried out. This report provides an overview of the main needs identified together with proposals for action to meet these challenges.

The industrial-scale sustainable nanofabrication topic has been segmented in different areas. The first part of the report addresses issues dealing with industrial scale nanofabrication, while the second part is dedicated to issues in the field of sustainability in nanotechnology and nanofabrication. The NanoFabNet concept of sustainability in nanotechnology and nanofabrication, as given in the report of the same name, is retained for this analysis. For each section, the challenges and opportunities regarding technical and scientific topic are examined, as well as those from an organisational/management perspective; standardisation issues are also discussed and presented where relevant.

2. Introduction

Nanomanufacturing is the essential bridge between the discoveries of the nanosciences and real-world nanotechnology products. It encompasses many processes from the design, manipulation and control of matter at the nanoscale to the manufacture of nanoscale materials, nanostructures, components, devices and complex systems that exploit the unique physical and chemical phenomena that occur at these smaller scales, such as quantum and surface effects (Cooper & Wachter, 2013). The dimensional scale for nanofabrication is typically 1 to 100 nm. However, it is usually at the sub-micron scale that unusual or improved material behaviour is observed, which can be exploited for product development.

The international standard ISO/TS 80004-8 *Nanotechnologies -Vocabulary - Part 8: Nanomanufacturing processes* makes an inventory of the different processes, which demonstrates the great diversity of existing approaches, each with their own specificities.[1] The ISO/TS 80004-8 differentiates also between the terms "*nanofabrication*" and "*nanomanufacturing*" by arguing that "*nanomanufacturing*" encompasses a broader range of processes than does nanofabrication, as it takes into account all nanofabrication techniques, as well as techniques associated with materials processing and chemical synthesis. In the following, however, **the terms "*nanofabrication*" and "*nanomanufacturing*" will be used interchangeably**.

In view of all this diversity of processes and nanoscale materials, the implementation of sustainable nanomanufacturing must consider two paths:

- **Novel processes and techniques for scalable and sustainable manufacturing of known beneficial nanoscale materials**, components, or devices, with preference given to energy- and material-efficient processes applicable to broad classes of nanomaterials, components, and devices;
- **Novel beneficial nanomaterial components and devices produced by known scalable and sustainable manufacturing** processes and techniques, such as cellulosic nanomaterials.

For each of these pathways, efforts are needed regarding:

- **Fundamentals** of nanomaterial, component, device, and/or nanomanufacturing process design **specifically focused on scalability and efficient use of materials and energy for sustainability,**
- **Interactions** of nanomaterials, components and devices with nanomanufacturing processes and of finished products with the environment **focused on the environment, health and safety (EHS)**, and
- **Measurement technologies**, which are key to enable industries to produce reliable and safe products through high-quality process development.

2.1 The Key Role of Harmonisation and Validation to support the Implementation of industrial-scale sustainable Nanomanufacturing

As much as nanoscience research can free itself from certain constraints linked to validation and harmonisation issues, the deployment of real scalable sustainable nanomanufacturing cannot do without them. The issues of harmonisation and validation are central to building the conditions of trust between economic actors, but also between economic actors and public authorities/society.

To move beyond the demonstrations of one-off nanofabrication, the following three requirements have to be addressed:

- Production must be scalable up to the required throughput and yield,
- The generation, manipulation, and organisation of nanostructures must be accomplished in a precise, controlled, and sustainable manner as demonstrated by full life cycle assessment, and

[1] ISO/TS 80004-8:2020 Nanotechnologies — Vocabulary — Part 8: Nanomanufacturing processes

- All nanotechnology-based products must perform to specification over their expected lifetimes without the release of harmful nanomaterials or other toxic substances into the environment.

From a technical point of view, the development of increasingly complex nano-enabled systems that integrate various nanoscale components developed by a network of complementary players makes the issues of interoperability between components, but also between nanofabrication equipment and platforms, critical. This complexity can only be addressed **by harmonising and validating several key points,** in order to ultimately provide trust between economic actors in the value chains. These conditions are indeed essential to produce objective and documented information and evidence that nanomanufacturing processes lead to components and products with the expected performances, thus contributing to reduce costs by lowering reject rates. But the implementation of high quality processes is inseparable from the existence of validated measurement technologies that can be used *via* harmonised and reliable protocols to produce comparable and reliable data.

This whole issue can be seen as an iterative process aiming initially at harmonising the ways of doing things, while validating in parallel several key stages, which - in turn - it possible to correct and optimise the performance of the processes implemented and the ones of products as illustrated in Figure 1.

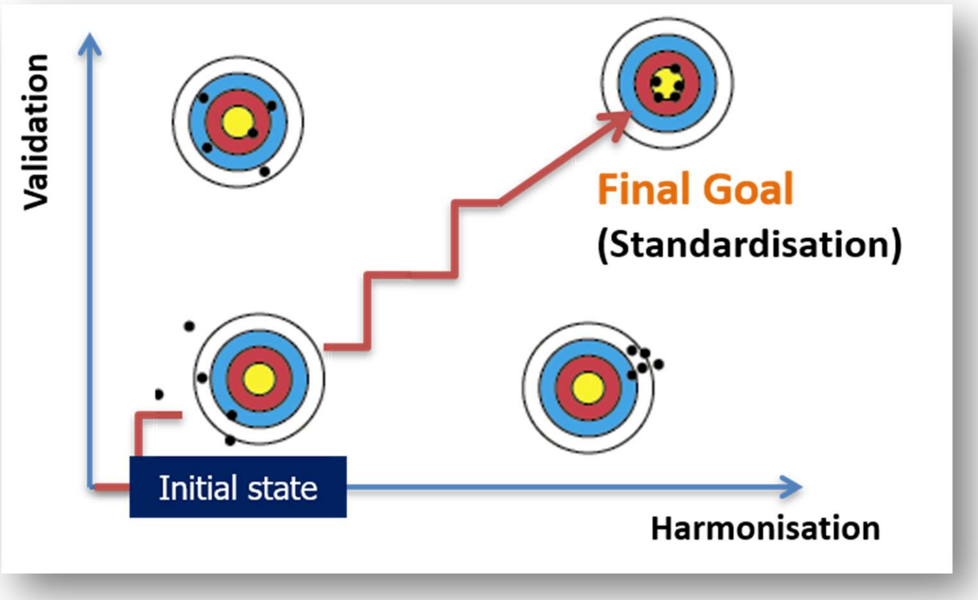

Figure 1: Validation and harmonisation efforts to bring trust within nanomanufacturing processes and products.

From the point of view of sustainability, the same questions arise regarding harmonisation and validation of the necessary tools and methodologies that enable the safe generation and handling of nanostructures; this is also true with regard to the nano-specific regulatory requirements that may exist depending on the applications considered, the life cycle impact of the nano-systems and the ethical concerns that must also be taken into account, in order to allow for the establishment of the confidence necessary for the acceptability of these new technologies and processes.

2.2 Standardisation as the ultimate Goal

2.2.1 Standardisation Landscape

The key role of standardisation in the context of a responsible development of nanotechnologies was stressed in 2010 within the *BASF Dialogueforum Nano* (BASF_Dialogueforum, 2010, pp. 97-98): "*Written standards provide agreed ways of naming, describing, specifying, measuring, testing, managing and reporting things. […] Standardisation thus fulfils a vital function in agreeing on common procedures and making individual achievements available to all stakeholders in a centrally coordinated manner*". More recently standards were considered by stakeholders as highly relevant to the future of nanotechnology to 2025, with over 90% of respondents to the NanoData surveys (European_Commission, 2019) viewing their importance as high (over 60%) or medium (30%). Similar conclusions were drawn from the NanoFabNet survey[2] conducted by Work Package 4 (WP4): 90% of respondents thought that harmonisation/standardisation of nanofabrication processes could help to bring maturity to nanofabrication methods and thus improve product quality, while saving time, a finding confirmed once again during the 2nd NanoFabNet Development Workshop (DW) (Figure 2).

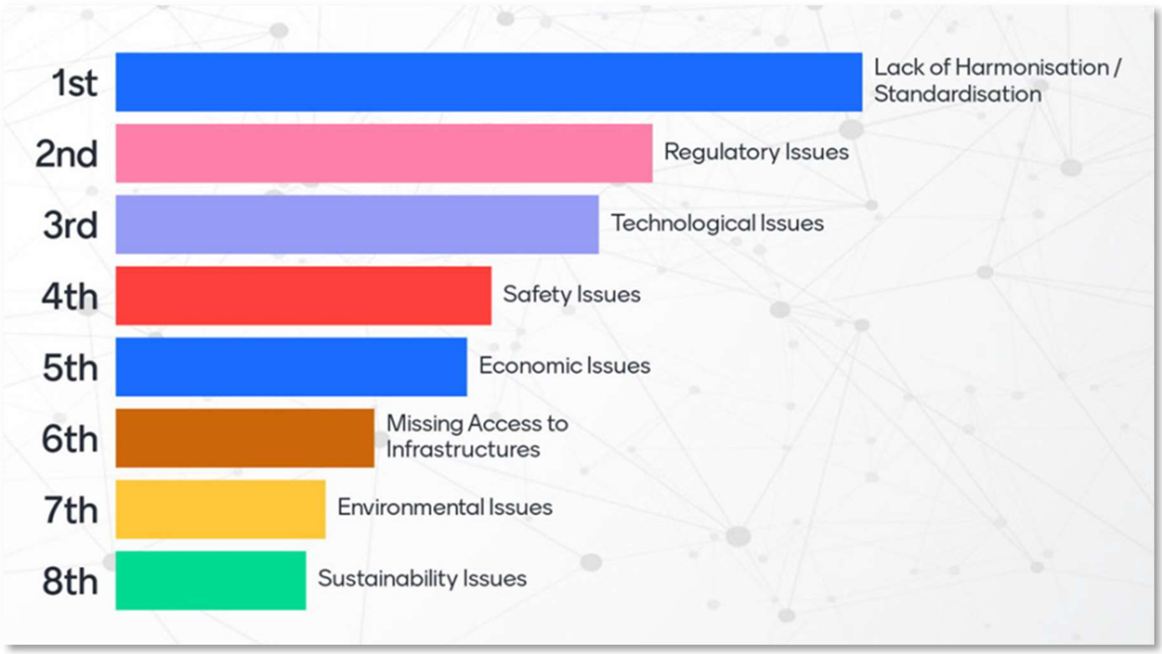

Figure 2: Snapshot of the 2nd NanoFabNet Development Workshop (20th and 21st January 2021) outputs to the question "What are the most relevant barriers to the introduction of nanofabrication in the industrial ecosystem?"

Standardisation in the field of nanotechnology had only emerged a few years earlier with the creation of several technical committees (TCs) dedicated to nanotechnology within the main standardisation bodies. ISO had taken up the challenge of developing standards in the field of nanotechnology and launched TC 229 Nanotechnologies in 2005,[3] while the European Committee for Standardisation (CEN)

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[2] NanoFabNet WP4 Survey on Validation, Harmonisation and Standardisation issues: September 2020 – February 2021.

[3] [ISO Technical Committee on Nanotechnologies (ISO/TC 229)]

and the American Society for Testing and Materials (ASTM) created their own TCs in the wake of this (CEN/TC 352 and ASTM/E56, respectively),[4,5] each of which tackles the subject of nanotechnology in a horizontal, non-sectoral manner. The International Electrotechnical Commission (IEC) created in parallel the TC 113 dedicated to standards on *Nanotechnology for electrotechnical products and systems*,[6] as well as TC119 dedicated to standards on *Printed Electronics*,[7] a field that is highly related to nanotechnology mainly in terms of using nanomaterials as inks but also by creating nanostructures or -layers.

Different liaisons between these different technical committees have been developed over the years to allow for regular exchanges, and thus ultimately avoid duplication of effort or the development of documents that might be in contradiction (Figure 3). Similar liaison exists with the Working Party on Manufactured Nanomaterials of the Organisation for Economic Cooperation and Development (OECD WPMN),[8] while a Memorandum of Understanding has been set up between ISO/TC 229 and the Versailles Project on Advanced Materials and Standards (VAMAS) (see Box 1).[9]

CEN/TC 352 *Nanotechnologies* also has a role in coordinating European standardisation work in the field of nanomaterials within CEN Technical Sector through the Mandate M/461 given by the European Commission. Standards have been developed in this context over the last years within CEN/TC 137 - *Assessment of workplace exposure to chemical and biological agents* and CEN/TC 195 - *Cleaning equipment for air and other gases*.' This mandate was renewed on the 1st November 2020 for 4.5 years and should enable the development within CEN/TC 352 of two high impact documents related to the regulatory aspect of nanomaterials .

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[4] CEN Technical Committee on Nanotechnology (CEN/TC 352)

[5] ASTM Committee on Nanotechnology (ASTM/E56)

[6] IEC Technical Committee for Nanotechnology for electrotechnical products and systems (IEC TC 113)

[7] IEC Technical Committee for Printed Electronics (IEC TC 119)

[8] OECD Working Party on Manufactured Nanomaterials (OECD WPMN)

[9] Versailles Project on Advanced Materials and Standards (VAMAS)

[10] CEN Mandate M/461

[11] CEN/TC 137 - Assessment of workplace exposure to chemical and biological agents

[12] CEN/TC 195 - Cleaning equipment for air and other gases

Box 1: VAMAS - Versailles Project on Advanced Materials and Standards.

VAMAS

The Versailles Project on Advanced Materials and Standards (VAMAS / www.vamas.org/) was established following an economic summit in 1982 held at Versailles by the Heads of State of the G7 group of nations and representatives from the Commission of the European Communities. The membership has expanded over the last few years. The main objective of VAMAS is to promote world trade by innovation and adoption of advanced materials through international collaborations that provide the technical basis for harmonisation of measurement methods, leading to best practices and standards.

The scope of VAMAS research encompasses the processing, characterisation and performance of advanced materials, with the goal of a harmonised technical basis for international standards.

VAMAS has contributed over the last decades to the development of national and international standards through:

- *Pre-standards work in rapidly developing technical areas*
- *Establishing the basis of new standards technical committees*
- *Transfer of results to standards bodies leading directly to international standards*
- *Contribution to the development of reference materials*
- *Development of test methods and procedures*
- *Increased proficiency of laboratories, including industrial laboratories*
- *Agreement of nomenclature*
- *High quality data generation via Interlaboratory comparison exercises*
- *Precision data statements*
- *Provision of reliable material properties*

2.2.2 Harmonisation and Standardisation: what is the Difference?

Harmonisation work can be described as pre-normative activities. It can be carried out by multiple entities, whether they are industrial groups to address a common issue considered as strategic, R&D project consortia, Working Groups within European (*i.e. EuroNanoLab*[13] *GO FAIR Implementation Networks such as AdvancedNano*[14] *or GO NANOFAB*[15]...) or international (*i.e. OECD WPMN, VAMAS...*) initiatives. It lays the foundations for future standards that will be developed by the standardisation bodies. Several bridges exist between these two worlds, for example VAMAS at the international level (see Box 1) or CEN Workshop Agreements (CWA) that can be developed within CEN.

However, although both approaches aim to create the conditions for recognition and trust between stakeholders, they both have their own strengths and drawbacks as presented in Table 1. Harmonisation activities have the advantage that they can be carried out fairly quickly by a small group

[13] EuroNanoLab

[14] GO FAIR Implementation Network AdvancedNano

[15] GO FAIR Implementation Network GO NANOFAB

of actors, whose interests converge, whereas the standardisation process has to respect multiple constraints that lead to projects with timeframes of several years. A consensus between the different national delegations positions must be obtained through numerous exchanges and back and forth meetings, while a timetable is imposed with different enquiries to be conducted at the level of the corresponding National Standardisation Bodies (NSB). Moreover, it is often necessary to pay a membership fee, in order to be able to participate in the discussions, once mandated by its NSB's mirror committee; this *de facto* eliminates a certain number of experts and reduces the stakeholders and expertise involved in the round table.

Table 1: Harmonisation (pre-standardisation) and standardisation activities as complementary approaches to ensure recognition and build trust between stakeholders.

	HARMONISATION	STANDARDISATION
ADVANTAGES	✓ Quick process ✓ Easy to participate ✓ Possibility to represent oneself	✓ Global and wider recognition → CAN BE USED FOR REGULATORY OR ACCREDITATION PURPOSES ✓ Possible cross-fertilisation between sectors
LIMITATIONS	✗ Often specific to a limited group of actors → MOST OF THE TIME NO RECOGNITION BEYOND THAT ✗ No capitalising on what has already been done elsewhere	✗ Action carried out within a standardisation bodies (CEN, ISO, IEC, ASTM) ✗ Long process ✗ Need to be appointed by National Standardisation Body ✗ Mostly paid participation ✗ Representation of National Delegation point of view (*except in the case of ASTM where participation is made on an individual basis*)

In the end, the documents developed in the framework of standardisation usually have greater recognition and thus facilitate better cross-fertilisation between different sectors and/or applications, avoiding having to reinvent the wheel each time.

2.3 Content of the Report and Methodology used

This report provides an overview of the main challenges & opportunities regarding harmonisation and validation issues to support industrial-scale sustainable nanomanufacturing. Standardisation issues are also discussed and presented, where relevant; the report is based on the following information:

- An in-depth desk analysis of scientific literature,
- The collection of opinions of stakeholders who participated to the two NanoFabNet Development Workshop (DW)[16,17],
- A survey carried out between September 2020 and February 2021, which resulted in 57 high-value contributions from 13 countries, and
- Discussions with various experts contributing to major EU or international initiatives, such as the **EuroNanoLab** initiative[13] (*EU nanofabrication / academics clean rooms facilities*), **NNCI** (*US National Nanotechnology Coordinated Infrastructure*)[18], **EU-NCL**[19] **& REFINE**[20] projects (*nanomedicine and nanomedicinal products*), **EC4SafeNano**[21] (*risk assessment services providers*), **Graphene Flagship Validation Service**[22] and **Graphene Flagship Standardisation Committee**[23], **NanoSafety Cluster**[24] (*in particular WG B on Materials and Standards*), **CEN/TC 352 *Nanotechnologies***[4], **ISO/TC 229 *Nanotechnologies***[3], **ASTM/E56 *Nanotechnologies***[5] or **VAMAS**[9]**.**

It should be noted that during the 1st NanoFabNet DW it appeared that characterisation issues came out on top in terms of importance to accompany the development of nanomanufacturing and the associated sustainability issues. A session of the 2nd NanoFabNet DW was thus organised specifically on the harmonisation, validation and standardisation issues associated to the characterisation topic in order to further identify the needs of the stakeholders and the actions to be considered.

In order to facilitate reading, the industrial-scale sustainable nanomanufacturing topic has been segmented into different areas as shown in Figure 3. The first part of the report is therefore dedicated to harmonisation and validation issues concerned with industrial scale nanomanufacturing, while the second part addresses harmonisation and validation issues in the field of sustainability in

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[16] NanoFabNet 1st Development Workshop, held on 12th March 2020.

[17] NanoFabNet 2nd Development Workshop, held on 20th and 21st January 2021.

[18] https://www.nnci.net/

[19] EU-NCL (European Nanomedicine Characterization Laboratory): https://cordis.europa.eu/project/id/654190/fr

[20] REFINE project (Regulatory Science Framework for Nano(bio)material-based Medical Products and Devices) : http://refine-nanomed.eu/

[21] EC4SafeNano (European Centre for Risk Management and Safe Innovation in Nanomaterials Nanotechnologies): https://cordis.europa.eu/project/id/723623/fr

[22] https://graphene-flagship.eu/innovation/industrialisation/validation-service/

[23] https://graphene-flagship.eu/innovation/industrialisation/standardisation/

[24] https://www.nanosafetycluster.eu/

nanotechnology and nanofabrication. Note that the NanoFabNet concept of sustainability in nanotechnology and nanofabrication[25] is considered in the rest of the document.

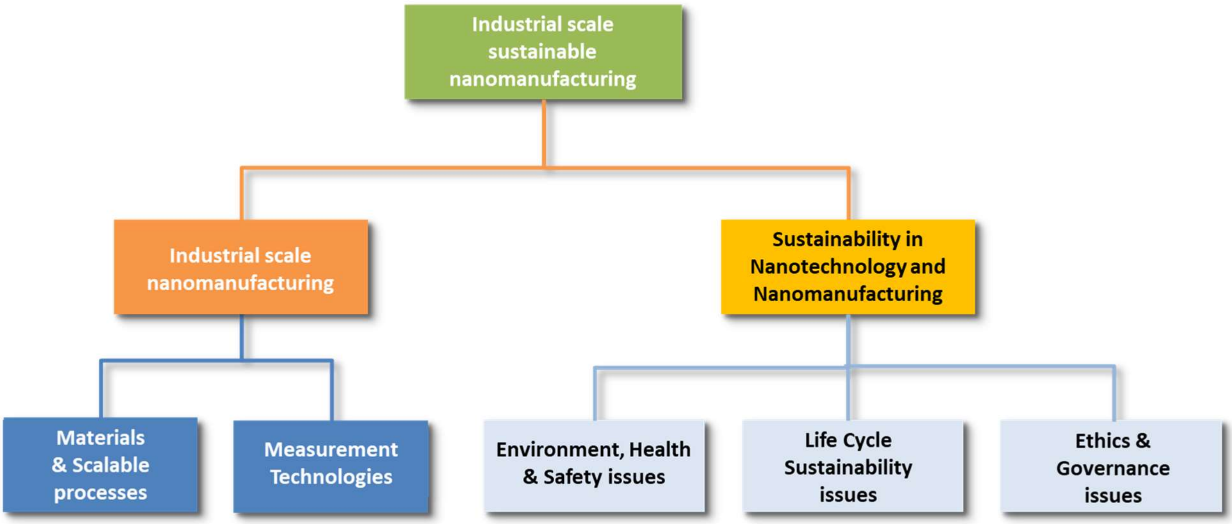

Figure 3: Segmented areas used to examine challenges and opportunities on validation and harmonisation issues in support of sustainable industrial-scale nanomanufacturing.

For each section, the challenges and opportunities regarding the specific technical and scientific topics are examined, as well as those from an organisational/management perspective.

3. Challenges and Opportunities in industrial-scale Nanofabrication

3.1 Materials and scalable Processes

Sustainable nanomanufacturing can be achieved either by **1)** developing novel processes and techniques for scalable and sustainable manufacturing of known beneficial nanoscale materials/devices or by **2)** implementing known scalable and sustainable manufacturing processes and techniques to produce novel beneficial nano-sale materials, components and devices.

The use of simulation tools and the creation of a digital materials representation appear as an essential step to cope with the ever-increasing complexity of materials and systems being developed. This implies a tight interaction between materials data from experiments/on-line sensors and materials models, the latter describing the materials behaviour under the assumption of certain active mechanisms, in contrast to experimental data which mostly provide only a snapshot of one specific material state. The **development of simple and harmonised processes to bring these different elements together** will allow a much more reliable prediction of the product's behaviour, particularly in terms of the durability of these performances under real conditions of use and according to different constraints. Therefore, **creating digital database of materials data and extracting properties to validate and feed simulation is a critical priority** and highly significant for industry. Work on **harmonising the format of materials data and the metadata of materials properties following FAIR**

[25] NanoFabNet D2.1 (2020). Deliverable 2.1: *Report on the Concept & Disciplines of Sustainability in Nanotechnology & Nanofabrication* (NanoFabNet Project).

principles (Findability, Accessibility, Interoperability, and Reuse), with the development of a new smart and consolidated collection of data from reference materials, are the first steps towards this medium to long-term objective

Such complex systems that integrate different nanoscale devices/components as building blocks also requires the successive implementation of several nanomanufacturing processes, sometimes available within different nanofabrication platforms. Each clean room should therefore **use a common language** to enable this needed interaction and interoperability between actors and equipment. The first step is to **harmonise the vocabulary used**, which will also be useful to facilitate interactions between academic cleanrooms and industry and to **deploy a taxonomy of tools and its related processes** with a view to building a database to map the equipment and processes available and make it more visible to users (see Box 2). Nanofabrication cleanrooms are constantly developing new nanofabrication processes to fulfil the requirements of their users. However, many cleanrooms waste time reinventing the wheel by developing nanofabrication workflows already available in other cleanrooms, while expertise and relevant information for process optimisation are often limited to personal or laboratory notebooks, giving the individual operator a significant impact on processes performances. This problem is clearly underlined within the GO NANOFAB Manifesto[15]: "*In the perspective of building a distributed cleanroom infrastructure potentially capable to exchange process building blocks, it is necessary to setup a unified framework for NF process description, storage and accessibility that enables interoperability of these process building blocks and their reusability in other process workflows*". In order to save time (and money), to offer the users more flexibility and reactivity according to the load plans of the cleanrooms, and to ensure an equivalent level of performance of the systems developed in one cleanroom or another, the **development of harmonised process descriptions that are precise enough to be reused by other facilities with minimal development** is therefore key. The **harmonisation of data exchange formats and of associated harmonised metadata with sufficient completeness** is an important action to run in parallel to enable data management methods using FAIR approach and the development of relevant information systems for cleanrooms machines (see Box 2).

Finally, the question of **defining and harmonising the relevant metrics** to validate the performance of these nanofabrication processes (*i.e. Precision of placement, feature size and resolution, overlay registration and nanostructure density, complexity and their rates of forming*) has to be conducted as a direct, subsequent process. These steps are indeed indispensable to be able to evaluate the desired outcomes, such as product quality and durability, process repeatability and reliability, production scalability and affordability, production efficiency and yield, product performance and functionality).

The abovementioned challenges exist for all manufacturing processes, but are exacerbated in nanomanufacturing, because manipulating, measuring and controlling at the nanoscale is not easy and small errors can result in large failures.

ISO/TC 229 *Nanotechnologies*[3] has been developing technical documents on manufacturing at the nanoscale. Nanomanufacturing and nanomanufacturing process are defined in the first part of the joint ISO/IEC 80004 series on nanotechnology vocabulary: the document ISO/TS 80004-8:2020 supports these definitions and gives '*terms and definitions related to nanomanufacturing processes in the field of nanotechnologies*'.

The International Electrotechnical Commission (IEC)[6] is developing several series of technical specifications on nanomanufacturing: the 62565 series covers Material Specifications and the 62607 series covers Key Control Characteristics (KCC). Together with the Institute of Electrical and Electronics Engineers (IEEE)[26], IEC is also writing a document dedicated to nanoelectronics: IEC/IEEE 62659-2015 *Nanomanufacturing - Large scale manufacturing for nanoelectronics* (IEC/IEEE, 2015).

In Europe, CEN/TC 352 *Nanotechnology*[4] has so far not developed any standards relevant to manufacturing. So far, all initiatives mentioned above are focussing on the process part of nanomanufacturing but work is missing on harmonising the equipment and tools, infrastructures (taxonomy of tools).

Box 2: Key initiatives to address nanomanufacturing harmonisation issues.

EuroNanoLab *is a new distributed research infrastructure consisting of over 40 state-of-the-art academic nanofabrication centres across Europe, whose aim is to provide university/industrial users with manufactured nano-objects for research with the highest quality and fastest delivery time. To reach that goal work is underway to develop process descriptions that are precise enough to be reused by other facilities with minimal development. This is why EuroNanoLab is at the origin of the creation of the* ***GO NANOFAB*** *Implementation Network, which aims to achieve this objective by developing the most accurate description of nanomanufacturing processes, standardised data exchange formats and data management methods using the FAIR approach. The methods used are obviously intended to be extended to all actors of nanomanufacturing at the international level, which will enable exchanging know-how in the most effective way during any cooperation between these actors.*

*The National Nanotechnology Coordinated Infrastructure (****NNCI****), established in 2015 and renewed in 2020, is the latest version of the US network of user facilities, initiated in 1977 with the National Nanotechnology Facility at Cornell University. The NNCI sites comprise 16 primary universities with an additional 13 academic, national lab, or other non-profit partners located geographically around the US and represent 69 separate facilities (cleanrooms, characterisation labs, and others). NNCI set up the tool database (https://www.nnci.net/search/tools) with NNCI sites and partners for the development of the currently used taxonomy. This work on terminologies and nanomanufacturing processes classification is a first harmonisation step to help users identify where to find nanofabrication equipment relevant to their needs.*

3.1.1 Harmonisation of Materials and scalable Processes

3.1.1.1 Materials

The main challenges identified regarding harmonisation issues for the production of materials by nanofabrication processes are indicated Table 2; various proposals for action are also mentioned for each of these needs.

[26] Institute of Electrical and Electronics Engineers

Table 2: Challenges and opportunities of harmonisation issues regarding materials produced by nanofabrication processes.

Areas	Specific Challenges	Opportunities
Generating a 'digital twin' of materials	Harmonisation of materials data format and material's properties metadata	• Continue to support projects such as EU OYSTER[27] in order to ensure a follow-up and the dissemination of the corresponding CWA on *Materials characterisation - Terminology, classification and metadata* outputs • EU coordinated contribution to VAMAS in order to lay the foundation for harmonisation process with international partners
Support the materials modelling community in the definition of reference properties	Definition of common ontology and associated metrics / measurands	• Improve the collaboration between nanofabrication centres, materials community (through EMCC and EMMC), characterisation platforms, National Metrology Institutes and standardisation bodies (in particular VAMAS) • Create a new TWA dedicated to this topic within VAMAS • Raise awareness among academic and industrial players of the need (and strategic impact) to develop product standards along the lines of what is being done in IEC/TC 113 for graphene with the BDS (Blank Details Specifications) which gives key materials specifications/metrics
Provide confidence in the performances and properties of nanoscale materials and devices	Develop nanoscale materials specifications and associated metrics	• Raise awareness among academic and industrial players of the need to develop product standards along the lines of what is being done for example in IEC/TC 113 for graphene with the KCC (Key Control Characteristics) or IEC/C 119 for nano material inks which identify relevant characterisation methods for each key material specification/metrics • Identify strategic nanoscale materials/devices for EU and develop corresponding material specifications to be proposed to ISO/TC 229/WG4 *Material specifications*
Workforce development	Raise awareness on FAIR principles (in particular the existing GO FAIR IN[28]) and on standardisation process	• Organise common workshops between the nanofabrication and the materials (including simulation experts) communities • Develop case studies & R&D&I success story due to standardisation activities to be included in academic training course for students and researchers • Set up dedicated training based on the NNCI Innovator's Academy in the US

[27] OYSTER Project (EU H2020)

[28] For example: GO FAIR IN "Novel Materials Discovery" (NOMAD)

3.1.1.2 Scalable Processes

The main challenges identified regarding harmonisation issues associated with scalable nanofabrication processes, as well as the opportunities for each, are indicated in Table 3.

Table 3: Challenges and opportunities of harmonisation issues regarding scalable nanofabrication processes.

Areas	Specific Challenges	Opportunities
Taxonomy	Develop a common vocabulary and a classification of nanofabrication tools/equipment and its related processes	• Capitalise on the work already carried out within NNCI • Orientate EU-US CoRs (Communities of Research) actions on this topic • Initiate a dedicated TWA in VAMAS to provide an international framework for this work • Contribute to the future revision of the ISO/TS 80004-8 *Nanotechnologies -Vocabulary - Part 8: Nanomanufacturing processes on the basis of the EuroNanoLab outputs*
Process steps description	Raise awareness on impact of such harmonisation activities	• Promote the EuroNanoLab initiative • Use EuroNanoLab test cases (dry etching and nanolithography) as demonstrators to convince academia experts of the validity and relevance of the approach • Complete the process by standardising a case at CEN , ISO or IEC level in order to get a success story to be promoted
Process data format and metadata	Raise awareness on impact of such harmonisation activities	• Work with cleanroom equipment makers to make possible to harvest, store and export FAIR cleanroom process data enabling reusability of the cleanroom processes • Promote the GO NANOFAB Implementation Network • Create a new TWA dedicated to this topic within VAMAS to gain an international visibility
Best practices, guidance and standards	Improve the visibility, the sharing and the use of existing harmonised and reference documents	• Create a centralised website containing links to existing lists of international standards and best practice to consolidate the information in a single location • Define relevant criteria to allow the extraction of useful information for the user through a search engine
Workforce development	Accelerate awareness on harmonisation needs and current initiatives outcomes	• Development of course material for universities and life-long learning for the platform • COST Action to support collaboration with experts / high-level facilities and promote the sharing and gain of state-of-the-art practices

NanoFabNet

3.1.2 Validation of Materials and scalable Processes

3.1.2.1 Materials

The main challenges identified regarding validation issues for the production of materials by nanofabrication processes, as well as the opportunities for each, are indicated in Table 4.

Table 4: Challenges and opportunities of validation issues regarding materials produced by nanofabrication processes.

Areas	Specific Challenges	Opportunities
Generating a 'digital twin' of materials	Identification, prioritisation and development of reference materials to validate models	• Involvement of Materials community (through EMCC and EMMC), National Metrology Institutes, Joint Research Centre and standardisation bodies (in particular VAMAS) • Set up an European Metrology Network on Advanced Materials under the EURAMET auspice • Development of test materials that fall under the JRC repository • Create databases of new materials, properties, reference materials, and calibration standards
	Develop and harmonise robust nanoscale material characterisation tools and SOPs (see more details in Section 3.2)	
Validate nanoscale materials properties and/or performances	Identify the most appropriate technique to produce the necessary data	• Raise awareness among academic and industrial players of the need to develop product standards along the lines of what is being done in IEC/TC 113 for graphene with the KCC (Key Control Characteristics) or within IEC/TC 119 for inks which identify relevant characterisation methods for each key material specification • Promote available Material specifications standards (ISO & IEC) to foster cross-fertilisation between sectors / applications • Identify strategic nanoscale materials/devices for EU and develop corresponding material specifications to be proposed to ISO/TC 229/WG4 *Material specifications*

3.1.2.2 Scalable Processes

The main challenges identified regarding validation issues associated with scalable nanofabrication processes, as well as the opportunities for each, are indicated in Table 5.

Table 5: Challenges and opportunities of validation issues regarding scalable nanofabrication processes.

Areas	Specific Challenges	Opportunities
Process steps description	Validation of the nanomanufacturing process description on the basis of a relevant metric	• Creation of a database of characterisation tools and infrastructure to offer the user access to robust characterisation techniques • Set up a consultancy service to help nanofabrication centres to identify fit-for-purpose technique • Creation of a database for materials properties in order to help in the identification of reference samples

3.2 Measurement Technologies for Characterisation

Characterisation is an integral part of materials and devices development, manufacturing processes and applications, as it helps:

- to correlate observed effects with material properties,
- to optimise and validate manufacturing processes,
- to support quality control, and
- to provide evidence of material performance over time.

This is even more critical in the case of nanofabrication complex, multi-step assembly processes in which a large number of variables have to be optimised and controlled, while truly nanoscale, real-time, in-line characterisation techniques are lacking. The metrology tools required to quickly, inexpensively, and accurately characterise products at the relevant scales of one to hundreds of nanometres have yet to be developed. Existing methods are time-consuming, expensive, and require high-tech infrastructures and high skill levels to perform them; for example, a clean-room laboratory infrastructure and advanced expertise are required to perform electron or atomic force microscopy and complex specimen preparation. Often, one must resort to macroscopic, and thus indirect, measurements of functionality that omit crucial information about the causal chain of process, structure, and function. The development and the **validation of metrological performances of new and rapid characterisation techniques and measurement procedures** to reference state-of-the-art off-line approaches are expected to accelerate innovation in European industries (Bosse, Egbert Buhr, Dziomba, Hodoroaba, Klein, & Krumrey, 2018).

The reliable, reproducible characterisation of nanomaterials appears also as the starting point of all nanomaterials risk assessment process and for demonstrating regulatory compliance. Robust and validated characterisation tools and protocols are indeed a key element to support Nano-objects, and their Aggregates and Agglomerates (NOAAs) exposure assessment and emission monitoring, while a comprehensive and reliable nanoscale materials characterisation is a prerequisite to relevant toxicity and ecotoxicity assessment. Finally characterisation methods are crucial for the testing of novel advanced materials that is mandatory prior to approval and introduction to the market.

In the end, **whatever the issue considered, expectations in terms of harmonisation and validation of characterisation tools and protocols are quite similar**. The tool itself is indeed not everything, however effective it may be. It is also necessary to identify and share good practices with all stakeholders, whether this concerns the tool to be used in a relevant way according to a given issue or the field of applicability of each one, and finally to develop and disseminate an appropriate way of using it.

This process requires input from a wide range of stakeholders:

- Industrial end-users of characterisation from processing and manufacturing industry,
- Scientists from academia and industry developing new materials, properties and applications,
- Technology integrators providing materials testing, multiscale analysis, characterisation and consultancy services,
- Scientist from academia, research institutes and instrument manufacturers who develop characterisation methods and methodologies,

- Manufacturers and developers of analytical instruments from both academia and industry,
- Government agencies for risk assessment,
- Member State control laboratories, and
- Metrology Institutes and Standardisation bodies.

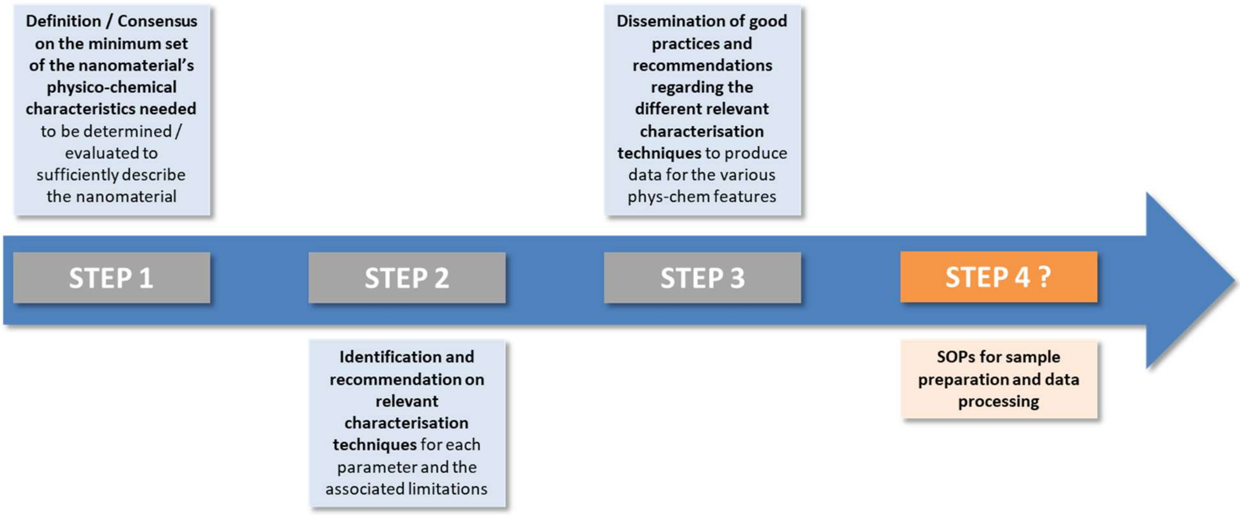

Figure 4: Illustration of the succinct process of developing harmonisation/standardisation documents and their supporting documentation to support reliable and comparable characterisation data.

In terms of harmonisation, a stepwise approach is required from the reliable definition of the relevant material/technique/test to the development of recommendations and good practice guidelines, to the formulation of detailed characterisation standard operating procedures (SOPs) as illustrated in Figure 4. In order to produce meaningful and comparable data, it is therefore necessary for the different stakeholders to agree on:

- STEP 1: the measurands[29] to be characterised,
- STEP 2: the methods/tools to be used for each of them, and
- STEP 3 & STEP 4: the protocols to be implemented.

International standardisation, through ISO/TC 229[3] WG4 "*Material specifications*" or IEC/TC 113[6] and IEC/TC 119[7], is already developing dedicated performances-oriented documents to make progress on the issue of **metrics harmonisation** (STEP 1, Figure 4). Different Blank Detail Specifications (BDS) have been published over the last years with a particular attention to graphene. A similar approach has been applied either to other nanoscale components such as nanoporous material, nano-enabled electrodes and nano-based sensors or to the topic concerning the environment, health and safety (EHS), with Technical Reports (TRs) such as (ISO/TR 13014:2012)[30] providing some highly relevant recommendation.

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[29] Also referred to as 'metrics'.

[30] ISO/TR 13014:2012 Nanotechnologies — *Guidance on physico-chemical characterisation of engineered nanoscale materials for toxicologic assessment*

The next step is to identify and recommend which characterisation techniques will be relevant for each parameter and what limitations may be associated with them (STEP 2, Figure 4). ISO has published such framework documents in recent years that provide this information in matrix form and associated relevant recommendations (i.e. (ISO/TR 18196)[31], (ISO/TR 19733)[32]), while OECD has shared complementary good practice in different reports (i.e. OECD Report n°63 (OECD, 2016), OECD Report n°65 (OECD, 2016)).

Different documentary standards have subsequently been developed at ISO, ASTM or IEC levels to disseminate good practices and recommendations regarding the different relevant techniques to produce data for the various physico-chemical properties previously identified as key (STEP 3, Figure 4)[33]. Some adaptations to the specificities of certain nanomaterials have led to others recent standards[34], while new OECD TGs will provide recommendations in a near future for the determination of several characteristics (*size distribution, specific surface area, surface hydrophobicity, identification and quantification of the surface chemistry and coatings*).

These guidelines, recommendations and good practices are most of the times validated by international comparisons, rendering them widely and generically applicable, and providing them with a long-term applicability. ISO/TC 229[3] has set up a metrology checklist to improve the quality of documents in this area and systematically asks project leaders to use VAMAS framework to organise the necessary inter-laboratory comparisons (see Box 1). ASTM for its part can rely on its Interlaboratory Study Program (see Box 3 for more details). Unfortunately, these actions are not very visible and it can regularly happen that it is difficult to find participants on a European or international scale to help validate the metrological performance of the methods and protocols studied.

[31] ISO/TR 18196:2016 Nanotechnologies — *Measurement technique matrix for the characterisation of nano-objects*

[32] ISO/TR 19733:2019 Nanotechnologies — *Matrix of properties and measurement techniques for graphene and related two-dimensional (2D) materials*

[33] For example: ISO 21363, ISO/DIS 19749, ISO/TS 19590, ISO/CD TS 21357, ASTM E2834 – 12, IEC TR 63258

[34] For example: ISO/AWI TS 23151, ISO/CD TS 21346

Box 3: ASTM 's Interlaboratory Study Program to respond to the need for standards in the marketplace to be of known and documented quality.

ASTM INTERNATIONAL

Developing and standardising test methods requires assessing the metrological performance of the method (i.e. intra-laboratory repeatability, inter-laboratory reproducibility, etc.) in order to document its quality and lead to high quality laboratory data. ASTM launched in 2004 the Interlaboratory Study Program (ILS) as part of its continuing pursuit of excellence in standards development. A commitment was made to fund the development of the ILS Program which allows ASTM to assist those technical committees for which the prospect of implementing an interlaboratory study was either administratively daunting or financially impossible. In order to support the committees in their efforts to produce precision statements for their test methods, so as to incorporate at least a repeatability statement, the ILS Program is available to assist with the following areas:

- *Designing an Interlaboratory Study*
- *Identifying potential samples*
- *Soliciting volunteer laboratories*
- *Finding an available supplier*
- *Contracting with a distributor*
- *Reviewing laboratory instructions*
- *Reimbursing shipping expenses*
- *Collecting data*
- *Analysing data*
- *Producing a draft precision statement*
- *Compiling information for the Research Report*
- *Recognition of participating labs*

Box 4: Graphene Flagship Validation Service (GFVS) & Graphene Flagship Standardisation Committee (GFSC): an organisation to be duplicated?

The Graphene Flagship
Validation Service

*In order to facilitate the development of sustainable and safe graphene-based applications, the Graphene Flagship has set up within its Industrialisation Work Package, the **Graphene Flagship Validation Service** (GFVS) and a dedicated standardisation committee, the **Graphene Flagship Standardisation Committee** (GFSC). The GFVS and the GFSC interact directly with one another. The GFVS brings together 2 NMIs and a national high-level characterisation platform to develop and validate through inter-laboratory comparisons the reference methods needed to support the development of quality graphene and its use in various applications and products and contribute to its appropriation by industry through the delivery of high quality characterisation data. These methods can be then transferred to standardisation through the GFSC. A strong collaboration with VAMAS also makes it possible to include international expert laboratories in some of the inter-laboratory comparisons organised in order to give greater recognition to the work and to facilitate standardisation at ISO/TC 229 or IEC/TC113 level. The GFVS also offers support on the measurement/testing aspect to graphene players (producers and integrators) so that they can benefit from state-of-the-art methodologies to produce data on which to base their decisions.*

These quality criteria with regard to their international harmonisation power, however, are bought at the cost of technical detail and specificity: **they very often still offer too much freedom in the proposed protocols to allow results to be truly comparable between several laboratories**; this is in part due to the variability stemming from different experimental procedures. Additional harmonised documents giving recommendation with reliable guidance and procedural description on sample preparation and data processing are therefore needed to guarantee high reproducibility and robust test results (STEP 4, Figure 4). Such issues have been extensively discussed in a *NanoWorkshop on Reference Nanomaterials* organised by PTB in 2018 (Bosse, Egbert Buhr, Dziomba, Hodoroaba, Klein, & Krumrey, 2018) are beginning to be considered within the standardisation bodies with several projects recently launched or due to start in the coming months to develop SOPs for sample preparation (CEN/TC352/WG4, Under Development) (CEN/TC137/WG3, Sampling of nano-objects and their agglomerates and aggregates in the workplace for electron microscopy, Under Development) (ISO/TC229/JWG2, New Work Item Proposal) or rules for data processing (CEN/TC137/WG3, Under Development). All of these include inter-laboratory comparisons to validate the SOPs. **This type of action should be strengthened rapidly, and priority topics should be identified with all relevant stakeholders, in order to harmonise SOPs and organise the corresponding interlaboratory studies** (Figure 5). The involvement of metrology institutes in these approaches should be systematised (see Box 4 and Box 5). **This need to bring together the nanomanufacturing and nanomaterials communities with European metrology actors through a coordinated structure was requested by 75% of the stakeholders consulted within the NanoFabNet WP4 survey**. It would allow better use to be made of VAMAS or EU calls for proposals regarding R&D projects on metrology / pre-normative aeras, such as the European Metrology Programme for Innovation and Research (EMPIR)[35], the majority of respondents saying they were not aware of the existence of VAMAS (54%) or of these funding opportunities (67%).

The EUROLAB model could be reproduced to the nanotechnologies issues (see Box 6) and representatives of the regulatory bodies involved in the discussions to ensure that the actions launched meet the most urgent needs.

The performance of measurement technologies, methods and protocols can also be validated by using **fully characterised reference materials**. However, these are difficult to access because they are produced in different contexts and by different actors and are referenced in various databases[36]. This information should be centralised in a single database to meet the expectations of the community (93% of respondents in the NanoFabNet WP4 survey); it could be a continuation of the JRC Nanomaterials Repository[36(a)].

[35] European Metrology Programme for Innovation and Research (EMPIR)

[36] To name the main ones: (a) JRC Nanomaterials Repository, (b) COMAR database, (c) Nanoscaled Reference Materials

Box 5: The example of NCI-NCL in US to facilitate the development and translation of nanoscale particles and devices for clinical applications.

NCL
Nanotechnology Characterization Laboratory

Working in concert with the National Institute of Standards and Technology (NIST / Metrology) and the U.S. Food and Drug Administration (FDA / Regulator), the National Cancer Institute (NCI) established in 2004 the Nanotechnology Characterization Laboratory (NCL) to perform preclinical efficacy and toxicity testing of nanoparticles. The NCL serves as a national resource and knowledge base for all cancer researchers to facilitate the regulatory review of nanotechnologies intended for cancer therapies and diagnostics. Physicochemical Characterisation Guides and a standardised analytical cascade protocols that performs physicochemical characterisation as well as preclinical testing of the immunology, pharmacology and toxicology properties of nanoparticles and devices have been developed with the support of NIST experts to help the sponsor meet regulatory requirements on the basis of comparable and reliable measurement data.

The NCI-NCL helped to establish a European counterpart (EU-NCL) some years ago, ***but the lack of an EU National Metrology Institute bringing together complementary state-of-the-art resources, organising inter-laboratory comparisons to validate methods identified as priorities and interacting with standardisation was one of the obstacles to the success of this initiative****, which ended in 2019.*

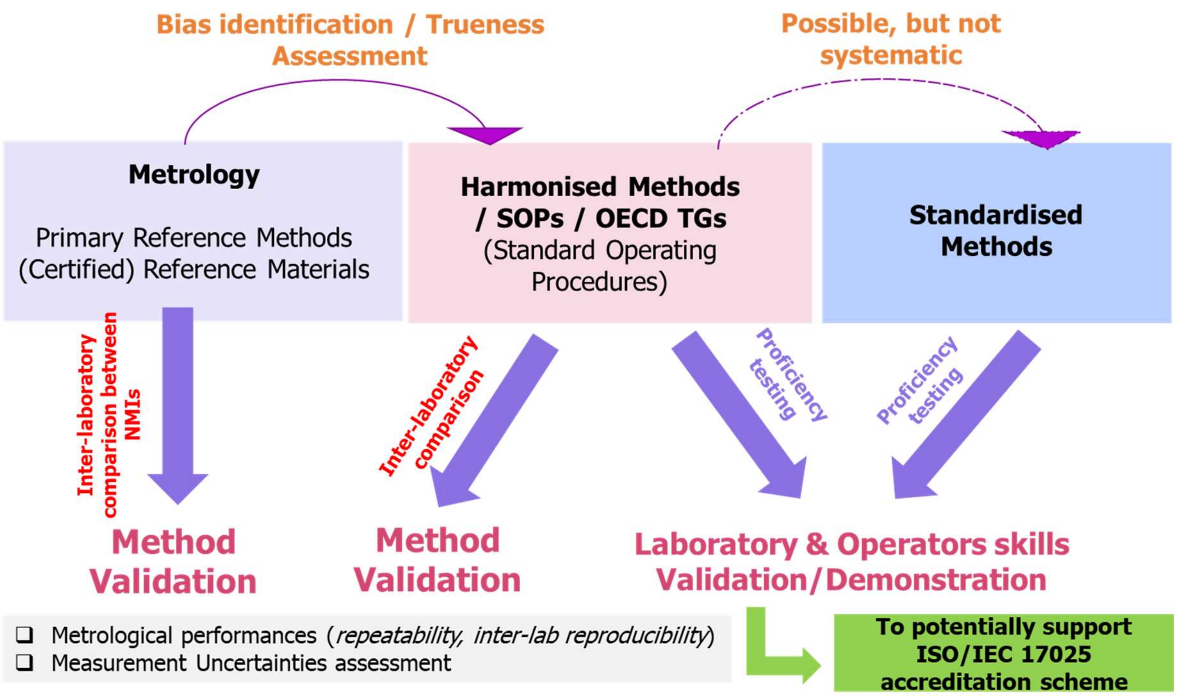

Figure 5: Validation, Harmonisation and Standardisation of measurement methods: Which process to improve quality/comparability of data?

Beyond the **validation of characterisation tools** (measurement technologies, SOPs, etc.), it appears that the **validation of the mastery of methods and protocols by the various stakeholders** is just as, if not more, critical for the production of reliable and comparable data. This usually involves laboratories participating in proficiency testing to demonstrate their competence against reference values issued by expert laboratories. 67% of the people questioned in the framework of the NanoFabNet WP4 survey thus consider that, in terms of characterisation, their choice of partner would rather be actors who have participated in inter-laboratory comparisons or in a proficiency testing.

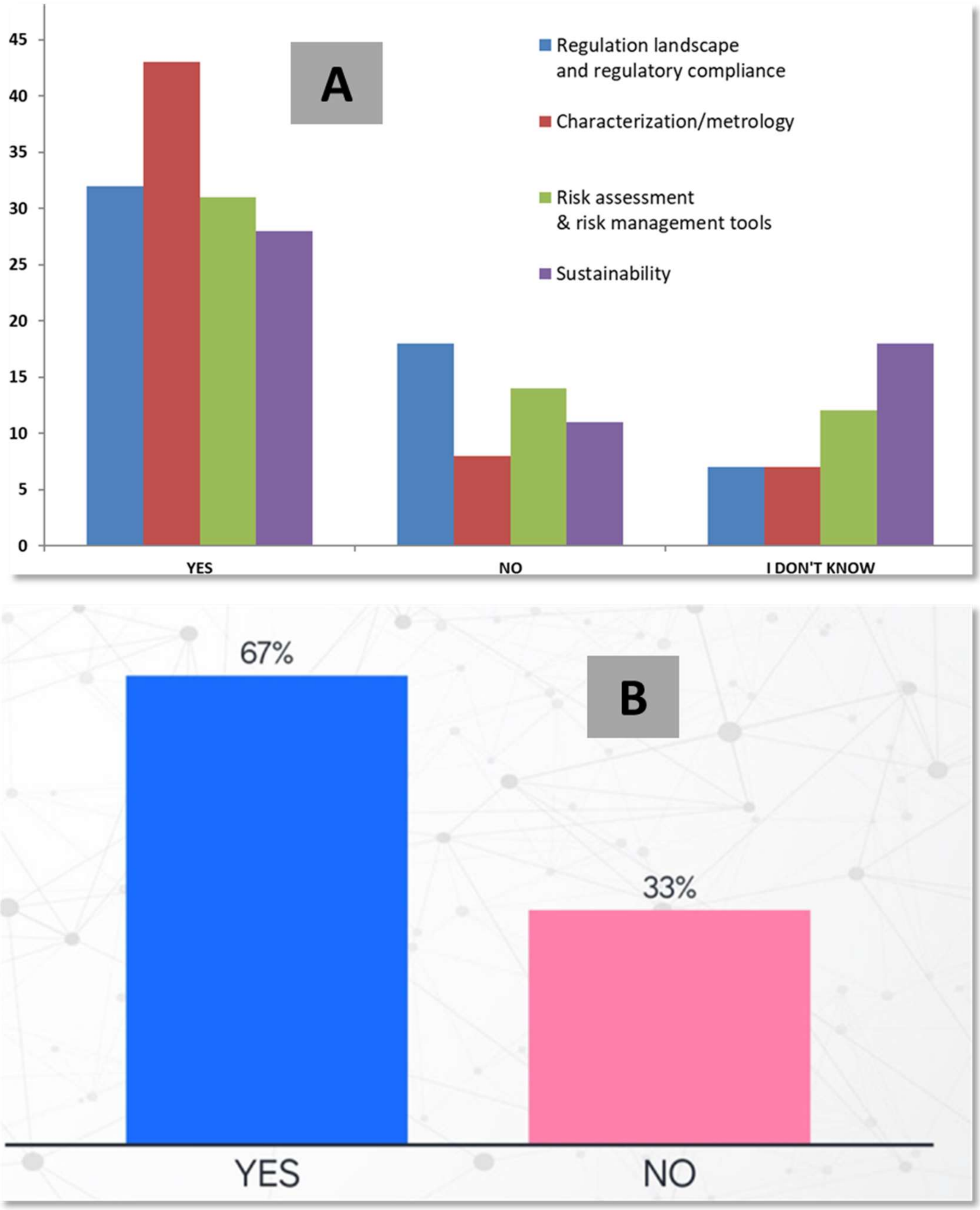

*Figure 6: Snapshot of the outputs from **A/** the NanoFabNet WP4 survey (Question: Would you be interested in setting up a mechanism to demonstrate your knowledge and expertise regarding specific issues specific to nanotechnologies/nanomaterials?) and **B/** the 2nd NanoFabNet DW (Question: Do you think that ISO/IEC 17025 accreditation scheme is needed to improve quality of measurement data and support sustainable innovation in nanotechnologies?)*

However, few proficiency tests are currently offered in the field of nanoscale materials characterisation, which leads to a very uneven quality of service and to measurement data of very heterogeneous quality that are difficult to compare. The coordination of an action on this subject seems to be critical and to meet a strong expectation of the stakeholders questioned (81% of the participants in the survey conducted in the framework of NanoFabNet WP4). It is indeed an essential prerequisite for the implementation of laboratory accreditations according to the ISO/IEC 17025 standard[37], a process called for by the vast majority of stakeholders interviewed in the framework of the NanoFabNet Project (Figure 6).

Box 6: EUROLAB, a place where harmonise and validate testing methods at EU scale.

eurolab

EUROLAB was created in 1990 on the basis of a Memorandum of Understanding, signed by delegations representing the private and public laboratories of 17 out of the 19 countries of the EEC and EFTA. It is the European Federation of National Associations of Measurement, Testing and Analytical Laboratories, whose objectives are:

- *Representation by formulating and voicing the opinion of European laboratories regarding political and technical issues having a direct impact on their activity, both on the European scene and worldwide;*
- *Coordination by interfacing with all European organisations having activities of interest to the laboratory community, and striving to avoid duplication of efforts and activities;*
- *Action by providing adequate means for exchange of information and experience, such as the publication of our Position Papers, Technical Reports, Newsletter, Seminars, and Working Groups etc;*
- *Promoting cost-effective testing, calibration and measurement services, for which the accuracy and quality assurance requirements should be adjusted to actual needs.*

Different thematic Working Groups have been created to bring together ISO/IEC 17025 accredited testing laboratories. They are offering a place where harmonisation and inter-lab validation of testing methods can be initiated where standard methods are not available to meet regulatory requirements.

[37] ISO/IEC 17025:2017 *General requirements for the competence of testing and calibration laboratories*

3.2.1 *Harmonisation of Characterisation*

The main challenges identified regarding harmonisation issues associated with measurement technologies and characterisation methods are indicated in Table 6; various proposals for action are also given.

Table 6: Challenges and opportunities of harmonisation issues regarding the topic of characterisation.

Areas	Specific Challenges	Opportunities
Measurands/Metrics	Develop dedicated Materials Characterisation Specifications	• Identify EU strategic nanoscale materials and corresponding applications • Foster CEN Workshop Agreements • Fund EU R&D projects aiming at producing Materials Specifications standards/BDS
New rapid characterisation tools	On- and off-line characterisation connection *via* standardised data interfaces	• Continue to support projects such as EU OYSTER27 in order to ensure a follow-up and the dissemination of the corresponding CWA on *Materials characterisation - Terminology, classification and metadata outputs* • Create an European Metrology Network on Advanced Materials under the EURAMET auspice
Use of relevant measurement technologies and SOPs	Share best practices and raise awareness on available guidance and standards	• Organise dedicated training and/or webinar • Create a database/documents repository with search functionality for best practice and standard sharing
Sample preparation and data processing	Develop and validate SOPs	• Support better coordination and synergy in Test Guidelines for regulatory systems through enhancement of international collaboration • Create an European Metrology Network on Advanced Materials under the EURAMET auspice with strong interactions with standardisation bodies (i.e. Graphene Flagship or NCI-NCL examples) • Creation official bridges between OECD WPMN and regional metrology organisations (RMOs such as EURAMET for EU, APMP for Asia, SIM for America, etc.) • Further enhancement of research and development collaboration in favour of supporting harmonisation and development of new standards by promoting some of the mechanisms already in place (i.e. EU funding opportunities for pre-standardisation metrology activities through the new European Partnership on Metrology (EPM) Programme)

3.2.2 *Validation of Characterisation*

The main challenges identified regarding harmonisation issues associated with measurement technologies and characterisation methods are indicated in Table 7; various proposals for action are also provides.

Table 7: Challenges and opportunities of validation issues regarding the topic of characterisation.

Areas	Specific Challenges	Opportunities
Measurement technologies *(sensors, new instruments…)*	Validate metrological performances	• Create a Validation Service to benchmark new measurement technologies and assess their metrological performances on the basis of reference methods
Reference materials	Facilitate access to reference and fully characterised materials	• Create a single database as a continuation of the JRC Nanomaterials Repository
Methods/Procedure	Develop and validate SOPs	• Inform about running inter-laboratory comparisons in order to raise the participation of expert laboratories • Promote VAMAS activities • Identify and prioritise inter-laboratory comparisons to be organised as regards EU specific needs • Create an European Metrology Network on Advanced Materials under the EURAMET auspice with the participation of regulation bodies • Set up a dedicated and funded ILC program to be backed by the CEN/TC 352
Laboratory expertise	Validation of laboratory proficiency	• Organise proficiency tests in a coordinated manner on topic (material, property, technique) identified as a priority to support accreditation of laboratory according to ISO/IEC 17025 standard

4. Challenges and Opportunities for Sustainability of industrial-scale Nanofabrication

4.1 Environment, Health and Safety Issues

The awareness on the need of having shared practices about development, manufacturing, handling of nanomaterials has grown significantly in the last years. However, how to approach this challenge has not been completely addressed yet. Several European initiatives aimed to contribute to fill ambitiously this lack, have been recently implemented. They concern the **development of harmonised and validated tools and methodologies to assess and manage the risks of nanomaterials** to human health and the environment, but also issues of potential exposure to nano-objects, their agglomerates and aggregates (NOAAs) throughout the life cycle of products, with a focus on occupational exposure issues.

One first big step in terms of setting dedicated **Test Guidelines** (TG) and **Guidance Documents** (GD) for some specific endpoints in the testing of engineered nanomaterials (ENMs) was the so called

"**Malta Initiative**" (MI). The main purpose of this European initiative is the reviewing of TGs and GDs to ensure that nano-specific issues for fulfilling regulatory requirements are addressed[38]. The activities of the MI are supported through national, international and EU resources by means of direct funding, in-kind contributions, or providing expertise.

The **NanoSafety Cluster** (NSC) was born over 10 years ago under the initiative of the European Commission Directorate-General for Research and Innovation (DG RTD) with the aim to target safe and sustainable nanomaterials and nanotechnology innovations. The platform allows both the dialogue and the exchange among different projects focused on specific topics (e.g. toxicology, ecotoxicology, exposure assessment, mechanisms of interaction, risk assessment and standardisation) and the interaction among researchers, regulators, administrators, industry, civil society representatives[39]. In terms of outputs, in addition to expert guidance/opinions and publications a "compendium" was periodically released. In particular, the "2017 Edition" contains a complete list of the projects running under the umbrella of the Cluster and tackling the emerging safety and health challenges of novel engineered nanomaterials and nanotechnologies. The Compendium provides descriptions of the EU funded nanosafety projects in sufficient detail to allow readers/end-users/stakeholders to assess which projects might provide relevant information for them, or which might be relevant to collaborate with, as well as to provide a first channel for dissemination of the good practices developed (NSC, 2017).

Two relevant projects hosted by the NSC and already ended were **NANoREG** and **NANOREG2**. The first was focused on the development of harmonised protocols for ENM toxicology testing and the second on prioritisation and grouping. The open platform **eNanoMapper**[40] was a continuation of these projects; it represents a rich database offerings, such as ontology, modelling and nanosafety data (Jeliazkova & al, 2021).

Part of the Cluster are three European interconnected projects **Gov4Nano**[41], **NANORIGO**[42] and **RiskGONE**[43], which are collaborating together to achieve the ambitious goal of being promoters of the creation of a Nanotechnology Risk Governance Council (NRGC). This new institution would support the translation of research advances into regulation and industrial practice, and integrate research, development and innovation (R&D&I) (Isigonis & al., 2020). This approach would increase the opportunity of large acceptance of new recommendations, perceived as regulation, by the stakeholder community. All projects mentioned above revolve around aspects of risk governance:

- promoting the incorporation of the Safe by Design (SbD) concept, alongside the sustainability by design and quality by design concepts,

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[38] Malta Initiative [Online] (accessed: May 2020)

[39] EU NanoSafety Cluster

[40] eNanoMapper Project (EU FP7)

[41] Gov4Nano Project (EU H2020)

[42] NanoRIGO Project (EU H2020)

[43] RiskGONE Project (EU H2020)

- fostering the creation of guidance and standardisation documents, for enhancing the regulatory compliance and acceptance of the developed framework and the incorporated tools, and
- promoting the FAIRification processes (Jeliazkova & al, 2021).

This last point concerning raising public awareness of the need to produce FAIR data to support more reliable and relevant risk studies associated with nanomaterials seems critical; indeed 70% of the stakeholders questioned in the NanoFabNet WP4 survey stated that they were not aware of initiatives on these issues, and in particular the **AdvancedNano GO FAIR Implementation Network**[14], whose objective is to work towards the **harmonisation of data sets format and corresponding metadata**.

NanoCommons[44], **NanoInformaTIX**[45] and **NanoSolveIT**[46] are three other H2020-funded research projects running under the NSC platform and strictly linked to the previous mentioned consortia. They represent the "informatic core", which is developing models that can make predictions based on prior experimental inputs. In this specific case, the projects are mainly compliant with the SbD concept. They are using previously acquired knowledge about ENM physico-chemical characteristics, enabling ENMs developers to screen the potential effects induced by the compounds *in silico* (Isigonis & al., 2020), even before producing them and eventually make proper changes to reduce their impact.

The involvement of stakeholders in the decisional processes and in the development of frameworks mainly targeted to the evaluation of the exposure and safety of ENMs is becoming more and more obvious; the already completed project **NanoFASE**[47] aimed to deliver an integrated exposure assessment framework (*protocols, models, parameter values, guidance* …) to help stakeholders during the environmental fate assessment of nano-enabled products. These tools would increase the chances of direct acceptance in regulatory registrations (e.g. REACH[48]) reducing the costs of a multiple steps procedure.

Together with the direct involvement of stakeholders, the other key aspect that has to be taken into consideration, in order to provide impacting tools, is the compliance with the existing regulation or the chances that the outputs of the project/initiative in question could be translated in regulation. The **NanoHarmony** project supports the development of a set of scientifically reliable test methods and good practice documents, based on the translation of existing scientific knowledge and data into a form that has regulatory relevance[49]. Within the project, a few ENMs have been selected as representative test cases to develop OECD TGs and GDs and the different endpoints have been identified considering the OECD WPMN priority recommendations.

In the previous paragraph the active role of stakeholders was often underlined. The point is "*how stakeholders could contribute to the different initiatives?*" and "*how the outputs of the different initiatives could be implemented by stakeholders?*" Thinking about industry and commercial

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[44] NanoCommons Project (EU H2020)

[45] NanoInformaTIX (EU H2020)

[46] NanoSolveIT (EU H2020)

[47] NanoFASE (EU H2020)

[48] REACH: Registration, Evaluation, Authorisation and Restriction of Chemicals

[49] NanoHarmony Project (EU H2020)

enterprises there are a few soft law instruments that is worth to mention. They have been developed to **provide confidence in risk assessment and management issues**.

The French National Institute for Industrial Environment and Risks[50] has developed its own certification (**Nano-CERT**) targeting people potentially exposed to nanomaterials on the workplace[51]. The certification process is based on ENM Risk Assessment, training about specific risks associated to ENMs and use of personal protective equipment against ENMs. All the categories of workers (from producers to researchers or e.g. technicians with maintenance duties) are involved. **However, such kinds of certification mechanisms, despite their central role in improving confidence in nanofabrication processes and nanotechnologies, are not sufficiently visible to the industrial actors involved.** Moreover, most are not endorsed by the regulators, and thus bring little or no advantage to those using them before submitting their processes or materials for official risk assessment procedures.

Other complementary measures should be developed to meet the expectations of stakeholders, as identified through the NanoFabNet WP4 survey: 54% of the stakeholders interviewed appear indeed interested in setting up a mechanism (e.g. *Certification Training programme, Certification*) to validate their knowledge and expertise regarding nano-specific risk assessment and risk management tools *via* an independent third party. The majority of stakeholders questioned during the survey (58%) are also interested in taking part in the implementation of this system (Figure 7).

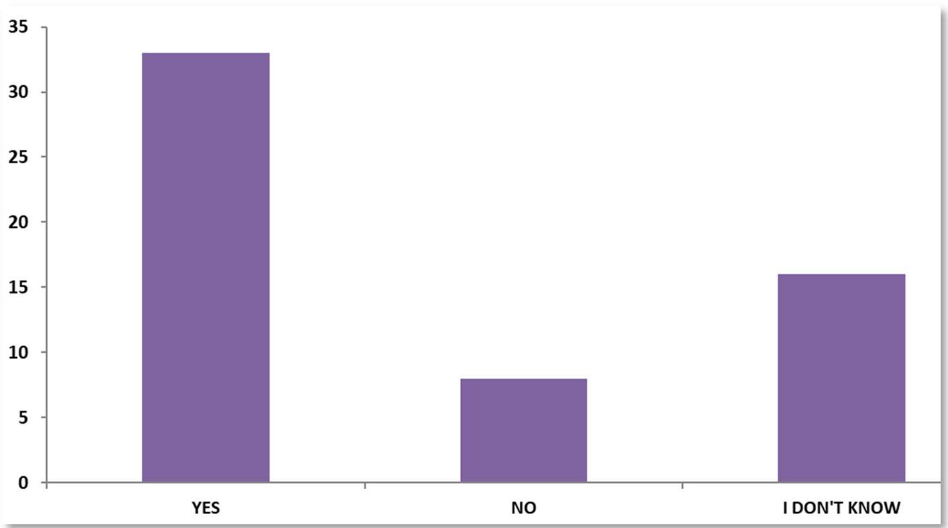

Figure 7: Would you be interested in being involved in the development of such a mechanism (scope, criteria, audit system…)?

[50] French National Institute for Industrial Environment and Risks

[51] Nano-CERT

From a standardisation point of view, most of the work on these issues is carried out at the level of ISO/TC 229[3] (WG3 – Health, Safety and Environment), although CEN/TC 352 - *Nanotechnologies*[4], CEN/TC 137 - *Workplace exposure*[11] and ASTM/E56 - *Nanotechnologies*[5] have produced in recent years (or are producing) some relevant documents[52]. A roadmap has been established for the period 2015-2023 and allows ISO/TC229/WG3 to set its work programme according to the following issues:

- Standard methods for controlling occupational exposure to nanomaterials,
- Standard methods for determining relative toxicity/hazard potential of nanomaterials and for toxicological screening of nanomaterials,
- Standards for environmental sound use of nanomaterials,
- Standards methods for ensuring product safety of nanomaterials products, and
- General health, safety and environmental standards.

It is interesting to note, however, that few documents on environmental issues have been published, with the majority of efforts focused on toxicity issues (Figure 8).

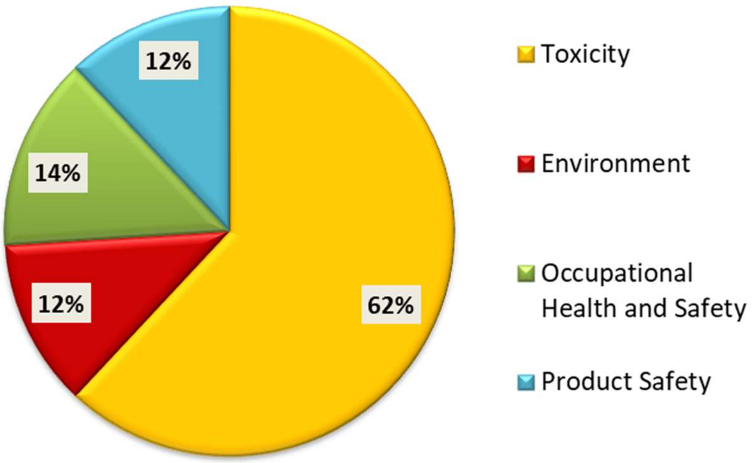

Figure 8: ISO/TC 229 WG3 – Health, Safety and Environment projects by application area (total 33 / April 2020).

[52] For example : EN 16966:2018, EN 17058:2018, EN 17199-1:2019, ASTM E2535 – 07, ASTM E2864 – 18

4.1.1 *Harmonisation & Standardisation of EHS Practices*

The main challenges identified regarding harmonisation and standardisation issues associated with the area of EHS and corresponding opportunities are indicated in Table 8.

Table 8: Challenges and opportunities of harmonisation and standardisation issues regarding the area of EHS.

Areas	Specific Challenges	Opportunities
Harmonisation	Availability of globally accepted and detailed protocols for human and environmental hasard and risk assessment of ENMs (data quality)	• Promote international collaboration • Foster the organisation of joint meetings among projects focused on the same topics, belonging to the same call or to interconnected calls • Set the boundaries for a "controlled circulation" of safety data
	Guidance for assessing the comparability of methods	
	Guidance for assessing the comparability of data already acquired/pre-existing data	
	Lack of transmission of NanoSafety information through the Safety Data sheets*	• Implementation of ENM-Safety Data Sheets
	Comprehensive, harmonised exposure inventories*	• Build a library with harmonised data
	Harmonisation of existing databases	• Promote the AdvancedNano GO FAIR IN[14]
	Lack of Occupational Exposure Limits (OELs) and safety parameters for reactive NMs (explosion/fire, runaway reactions)*	• Implementation of valid globally harmonised Occupational Exposure Limits (OELs), as well as reactivity parameters (explosion & flammability limits) e.g.; *via* transcription from scientific knowledge and OSH expertise to Occupational Exposure Limits and reaction safety Limits
	Lack of regulation specifying requirements to ensure the safety and health of workers exposed to nano-risks (the game board)*	• Creation of "hubs" or "platforms" to help networking between different stakeholders. These virtual places should ensure the meeting among actors belonging to all the stages of the value chain, as well as global active bodies in standardisation and regulation
	Which answer to provide when no standards/TG exist	• To offer the possibility of a harmonised response from a collaborative working group
	Data accessibility	• Disseminate FAIR principles and outcomes of AdvancedNano GO FAIR IN
Standardisation	Documents to address environmental issues	• Promote international collaboration • Identify the needs at EU level in the field and build the CEN/TC 352 roadmap

* From the NanoSafety Cluster 2015-2025 Roadmap.

4.1.3 Validation of EHS Practices

The main challenges identified regarding validation issues associated with the area of EHS and corresponding opportunities are indicated in Table 9.

Table 9: Challenges and opportunities of validation issues regarding the area of EHS.

Areas	Specific Challenges	Opportunities
Technical aspects	Validate appropriate *in vitro* models for ENMs*	• Submit application to ECVAM for starting the procedure of validation of new *in vitro* models • Business opportunities
	Validate appropriate *in vivo* and *ex vivo* models for different diseases* (AOPs)	• Submit application to ECVAM for starting the procedure of validation of new appropriate *in vivo* and *ex vivo* models • Business opportunities
	Identify relevant QIVIVE models	• Reducing animal use → compliance with 3R principle
	Build reliable and robust QNAR models	• Reducing animal use → compliance with 3R principle
	Define Methods and Benchmarks for Toxicity Assessment	• Increasing chances to uniform the procedures adopted in different laboratories
	Validation of High Throughput Toxicity Screening * approaches and High Content Analisys methods	• Saving resources (time, consumables, money) • Increasing number of samples tested → increasing statistical weight of the study → opportunity to compare much more data → increasing robustness of the model
	Correlation between physico-chemical properties and uptake	• Increasing possibilities of predicting the NM fate in *in vitro* models
	Exposure assessment : Protocols (sampling and real-time tools performances for different NM)	• Development of new devices → prototypes/patents
	Data curation	• Build a library with harmonised data
Management aspects	Lack of validated reference control banding tools*	• Validated, harmonised and standardised Control banding tools based on state-of-the-art safety management should be available for OSH consultants and managers
	Check competence of laboratories in performing measurements and proficiency in delivering accurate testing results	• Implementation of Good Laboratory Practices (GLP) rules in some specific laboratory
	Demonstrate knowledge and expertise regarding nano-specific risk assessment & risk management tools	• Promote some already existing nano-specific certification • Set up a mechanism (Certification Training programme, new certification...) supported by an independent third party actor

* From the NanoSafety Cluster 2015-2025 Roadmap.

4.2 Life Cycle Sustainability Issues

Life cycle assessment (LCA) methodology is standardised by the ISO 14040 (Environmental management — Life cycle assessment — Principles and framework, 2006) and ISO 14044 (Environmental management — Life cycle assessment — Requirements and guidelines, 2006) defining its principles and requirements. These standards are fully applicable for nanomaterials, nanotechnologies and nano-enabled products. However, the nano-specificities raise additional challenges; these were addressed in the CEN/TS 17276 (Nanotechnologies - Guidelines for Life Cycle Assessment - Application of EN ISO 14044:2006 to Manufactured Nanomaterials, 2018). They mainly concern the determination of physico-chemical properties to identify and group nanomaterials, to model their release along the life cycle and the related (eco)toxicity impact (i.e. fate, exposure and effect modelling).

The life cycle costing (LCC), social life cycle assessment (S-LCA) and life cycle sustainability assessment (LCSA) methodologies are not standardised, but some guidance documents exist (e.g. UNEP, 2011; 2020). The latter also refer to the ISO 14040/14044 as framing standards.

At European level, several research projects were carried out to integrate life cycle sustainability aspects for the development of nano-enabled products or processes. Initial works focused on LCA application, as for the **LICARA** project[53]. This FP7 project, whose full name is "*Life Cycle Assessment and Risk Assessment of Nanoproducts*", provided **guidelines and an associated tool called LICARA nanoSCAN**, to assess the benefits and risks of engineered nanoparticles, nanomaterials and nanoproducts. Particularly addressed to small and medium-sized enterprises, the LICARA nanoSCAN can perform a semi-quantitative evaluation. The tool was further integrated into the **SUNDS** platform[54], developed within the FP7 project **SUN** "*Sustainable Nanotechnologies*"[55]. This decision support system allows for a more quantitative assessment. LCA results obtained from LCA software tools can be uploaded on the platform to be considered for the multi-criteria decision analysis. The assessment of economic impacts focuses on market price, while the one of social impacts on employment and value added for companies. These two evaluations do not follow the principles of LCC and S-LCA. Although the SUNDS tool can be useful, **it does not provide guidance to perform the LCA calculation**. The SUN project nevertheless produced a report (UniHB, 2016) to describe criteria and guiding principles for green nanomanufacturing. This led to the **definition of 12 design principles for "Green Nano"** (similarly to the ones for Green Chemistry or Green Engineering).

Numerous public deliverables related to the sustainability assessment of nanomaterials were published within the RiskGONE project[43]: D3.2 for the environmental impacts (Elorri Igos, Evert Bouman, & Elena Semenzin, 2020), D3.3 for the economic impacts (Murphy & Bouman, 2020) and D3.5 for the social impacts (Antunes, Rodrigues, Trump, & Dias, 2020). The deliverables D3.2 and D3.5 specifically provide some guidance related to the application of LCA and S-LCA, which can support stakeholders to evaluate the impacts of nanomaterials and support them in decision-making process.

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[53] LICARA Project (EU FP7)

[54] SUNDS Platform

[55] SUN Project (EU FP7)

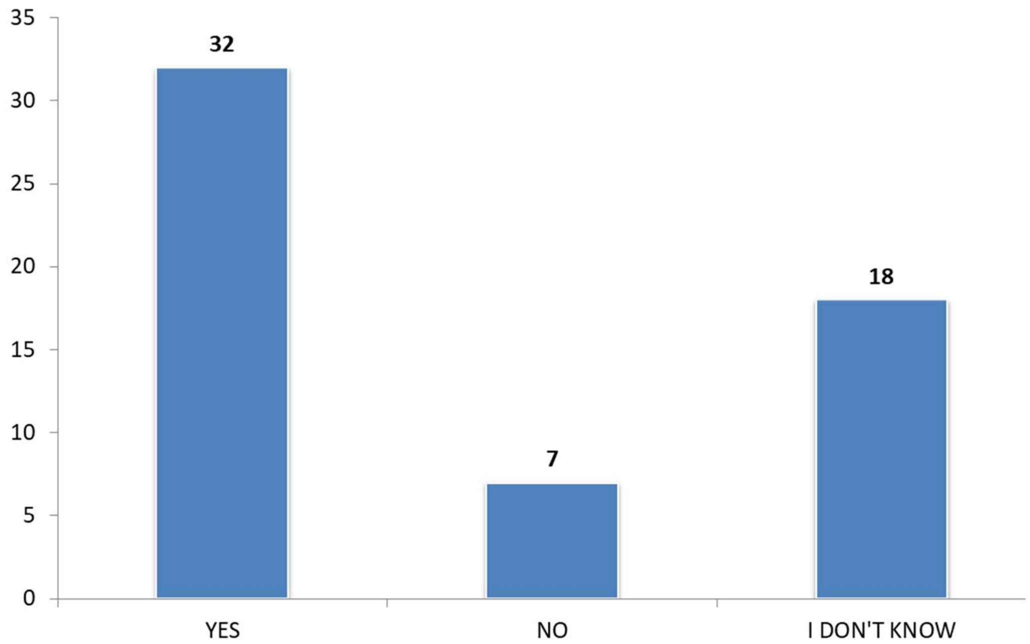

Figure 9: Do you think that a label based on standard(s) would be necessary to spread these sustainability concepts in the field of nanotechnologies? (Question from the survey carried out within the NanoFabNet project)

Besides guidelines that need to be further developed and consolidated for the assessment of the sustainability of nano-enabled products and processes, the concept of Sustainable-by-Design rose recently to **identify the key design criteria/indicators and development choices that should be adopted to ensure their sustainability once deployed on the market**. The European Commission is developing efforts towards this direction and already published a mapping study[56] for the **development of Sustainable-by-Design criteria** with some information related to nanomaterials. To support this initiative, the two projects **DIAGONAL**[57] and **SUNSHINE**[58], recently funded under the NMBP-16-2020 call, should developed Safe-and-Sustainable-by-Design (SSbD) strategies for products enabled by multi-component nanomaterials (MCNMs) and high aspect-ratio nanomaterials (HARNs).

All these initiatives should contribute to fill research and data gaps for the life cycle sustainability assessment of nanomaterials, nano-enabled products and nanomanufacturing processes identified in the CEN/TS 17276 mentioned above (Nanotechnologies - Guidelines for Life Cycle Assessment - Application of EN ISO 14044:2006 to Manufactured Nanomaterials, 2018). Further work would still be required for the harmonisation and standardisation of the related methods and tools (see sections 4.2.1 and 4.2.2 below and also NanoFabNet Deliverable D1.4 (Belloncle, 2021)).

These approaches could potentially also contribute to the establishment of a label based on standard(s) to spread these sustainability concepts in the field of nanotechnologies, as expected by the majority (56%) of stakeholders questioned during the survey set up in the framework of NanoFabNet WP4 (Figure 9). 50% of them are also interested in contributing to its development.

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56 Mapping study for the development of sustainable-by-design criteria

57 DIAGONAL Project (EU H2020)

58 SUNSHINE Project (EU H2020)

4.2.1 *Harmonisation of Life Cycle Sustainability*

The main challenges identified regarding harmonisation issues associated with the Life Cycle Sustainability topic and corresponding opportunities are indicated in Table 10.

Table 10: Challenges and opportunities of harmonisation issues regarding the topic of Life Cycle Sustainability.

Areas	Specific Challenges	Opportunities
Research needs	Definition of the necessary physico-chemical properties to model the release mechanism, environmental fate and exposure (e.g. surface properties, coating, size, shape, dissolution and dispersion properties)	• Use of harmonised/standardised characterisation methods to measure nanomaterials emissions • Use of harmonised/standardised test guidelines to derive toxicity • Guidelines for defining and integrating nano-specificities for nanomaterials release and related impact
	Modelling of nanomaterials release along the lifecycle	
	Modelling of the fate and exposure of nanomaterials	
	Modelling of ecotoxicity and human toxicity effects (e.g. correlation between in-vitro and in-vivo endpoints)	
Data needs	Lack of characterisation factors for nanomaterials in LCIA methods	• Include nano-specific properties in LCA database formatting (e.g. ecospold2) • Harmonise (eco)toxicity characterisation factors of nanomaterials (including their key properties) to integrate them in LCIA methods (e.g. USEtox) • Harmonise data collection protocols, top-down control and maintenance procedures to develop LCI datasets for nanomaterial and integrate them in LCA database • Develop product category rules (PCR) for nanomaterials to generate environmental product declaration (EPD) • Develop product environmental footprint category rules (PEFCR) for nanomaterials to publish product environmental footprint (PEF)
	Lack of inventory data regarding nanomaterials production, and value chain processes	
Decision support needs	Definition of eco-design and sustainable-by-design criteria for nanomaterials/nanotechnologies	• Case studies to identify key parameters and leverage actions, and define eco-design and sustainable-by-design criteria
	Development of decision support tools including harmonised inventory data and characterisation factors for nanomaterials	

4.2.2 *Validation of Life Cycle Sustainability*

The main challenges identified regarding validation issues associated with the Life Cycle Sustainability topic and corresponding opportunities are indicated in Table 11.

Table 11: Challenges and opportunities on validation issues regarding the topic of Life Cycle Sustainability.

Areas	Specific Challenges	Opportunities
	Comparison of impacts for nanomaterials with different properties	• Validation of physico-chemical properties and rules to identify and group nanomaterials
	Critical review of published LCA (LCC, S-LCA and LCSA) studies to ensure their transparency, consistency and reliability	• Publication of LCA case studies on nanomaterials in a transparent manner following standards and guidelines, and including critical review from experts with knowledge of nanomaterials

4.3 Ethics and Governance Issues

In very general terms, ethics and governance approaches related to nanotechnology and nanofabrication face two recurrent challenges:

- **The first one is linked to the “nano-specificity” of the issues discussed**. The relevance of a “nano-specific” approach in ethics is still an open question widely discussed by ethicists. Some very general approaches in terms of ethics and governance apply also for nanotechnology and nanofabrication. Nevertheless, there is a need for tools and documents specifically designed for nanotechnology and nanofabrication proper issues;
- **The second one is linked to the generic and enabling nature of nanotechnology and nanofabrication**. Their different sectors of application and their different disciplines give raise *de facto* to a diversity of ethical issues: as an example, the issues associated to nanomedicine are not the same as those associated to nano-enabled ICT applications (even if the technological convergences of the disciplines gives sometimes rise to a convergence of the ethical issues and the corresponding emergence of new ones). Besides the need mentioned above, there is thus a true **need of operational tools and approaches specifically designed for the different sectors of application**, taking into account the fact that it is not possible to cover all the possible issues[59].

Validation in ethics and governance is something difficult, since ethics and governance are more matters of discussion and interpretation than matters of objectivity. It can be said that there is currently no corpus allowing an authentic *validation* of the approaches relating to ethics and governance in the framework of the development of nanotechnology and nanofabrication for the different categories of concerned stakeholders. Nevertheless, some frameworks rather attached to CSR (Corporate Social Responsibility), although not at all "nano-specific", define some indicators and

[59] The ethical questions associated to nanomedicine, which benefit already from important ethical and regulatory frameworks, will not be considered here.

metrics sometimes relevant in terms of ethics, allowing a form of *validation* if applied to the particular fields of nanotechnology and nanofabrication. One can mention in particular:

- **The United Nations (UN) Sustainable Development Goals framework**[60], for which the validation is defined by the contribution to some relevant indicators (231 indicators split into 17 goals, some of them relevant in terms of ethics and governance);
- **The Global Reporting Initiative (GRI) framework**[61] where the validation is defined by the reporting according to some relevant indicators (91 indicators split into 3 categories – economic, environmental and social). Among them are 48 "social" indicators sometimes relevant for ethics and governance, split into 4 areas (16 in Labor Practices and Decent Work, 12 in Human Rights, 11 in Society, and 9 in Product Responsibility).

It would be useful to adapt the above mentioned frameworks to the case of Nanotechnology and Nanofabrication and to complete or amend them accordingly.

Harmonisation of ethics and governance related to the development of nanotechnology and nanofabrication is *de facto* addressed by different kinds of tools and frameworks, not all formalised. These can be distinguished into 2 categories:

- **Codification** (*codes of conducts, ethics charters, etc.*);
  - ✓ The International ethical Compendium which are not nano-specific but of course must be considered in the development of nanotechnology and nanofabrication (The International Bill of Human Rights[62], the ten United Nations Global Compact (UNGC) principles[63], the International Labor Organization's Declaration on Fundamental Principles and Rights at work (ILO, 1998), the Rio Declaration on Environment and Development (UN, RIO DECLARATION ON ENVIRONMENT AND DEVELOPMENT, 1992), the United Nations Convention Against Corruption (UN, 2003)). **They need probably to be complemented with more specific guidelines**,
  - ✓ Some codes related to the Responsible Research and Innovation in Europe, among them the 2008 European Commission Code of Conduct for Responsible Nanosciences and Nanotechnologies Research (EC, 2008) and the European Code of Conduct for Research Integrity (ALLEA, 2017), and
  - ✓ Other governmental or industry codes (more or less nano-specific), for which some examples are listed below : the 2008 German NanoKomission report on the Responsible Use of Nanotechnologies (NanoKommission, 2009), the CEFIC Responsible Care Management Framework (CEFIC, 2021), the BASF code of conduct on nanotechnology (BASF), the Applied Nanoparticles SL Code of Conduct (Busquets-Fité, Casals, Gispert, Puntes, & Saldaña, 2019).

[60] UN Sustainable development Goals

[61] Global Reporting Initiative

[62] International Bill of Human Rights

[63] United Nations Global Compact

- **Other non-formalised frameworks**, which contribute to the harmonisation of ethics and governance in nanotechnology and nanofabrication:
    - ✓ Ethical reports and recommendations, many of which were written in the 2000s (The_Royal_Society, 2004), (UNESCO, 2007), (European Group on Ethics in Science and New Tech, 2007), (Commission de l'éthique de la science technologie, 2006), EGE (2007);
    - ✓ Some OECD reports are also of interest, among them the OECD Planning Guide for Public Engagement and outreach in nanotechnology (OECD, 2012) which provides some guidelines for consideration when planning and evaluating public engagement activities in nanotechnology, the *'Nanotechnology for Green Innovation'* Report (OECD, 2013) and the *'Nanotechnology in the Context of Technology Convergence'* Report (OECD, 2014), which address partly the issues of the finality and of the responsible development of nanotechnology. More recently, as examples, the *'Recommendation of the Council on Responsible Innovation in Neurotechnology'* Report (OECD, 2019) and the *'Recommendation of the Council on Artificial Intelligence'* Report (OECD, 2019) **provide guidelines and references for dealing with ethical issues in different fields in which nanotechnology can be involved**;
    - o Ethical assessment methodologies, which are mostly not nano-specific (Reijers, Brey, Jansen, Rodrigues, Koivisto, & Tuominen, 2016) (Rowena Rodrigues, Brey, Warso, Hanson, Tambornino, & Lanzerath, 2018) and some first attempts to develop "ethics-by-design" methodologies (Brey, Lundgren, Macnish, & Ryan, 2019);
    - o Toolkits (CEA, 2010) and Guidance (McGinn, 2010)

There are very few standards directly related to the ethics and governance of nanotechnology and nanofabrication. CEN published in 2016 an important TS dedicated to the responsible development of nanotechnologies (CEN/TS 16937, 2016), while some other more general existing standards (ISO 26000, 2010) or sectorial ethics standards (i.e. IEEE Responsible Innovation of AI and the life science initiative[64]) can have interesting applications for ethics and governance of Nanotechnology and Nanofabrication. It should be noted that two important CWA dealing with ethics assessment for research and innovation in general have been developed over the last years (CEN, CWA 17145-1) (CEN, CWA 17145-2). **They would require some additional effort and funding to turn them into real standards and fit into a more-encompassing decision support system for risk governance of nanomaterials by following recommendations given in** (Malsch, 2020).

[64] Responsible Innovation of AI and the Life Sciences (IEEE, 2021)

4.3.1 *Harmonisation & Standardisation of Ethics and Governance Practices*

The main challenges identified regarding harmonisation and standardisation issues associated with ethics and governance area are indicated in Table 12. Proposals for action are also provided.

Table 12: Challenges and opportunities of harmonisation and standardisation issues regarding the area of ethics.

<table>
<tr><th>Areas</th><th>Specific Challenges</th><th>Opportunities</th></tr>
<tr><td rowspan="6">Harmonisation</td><td>Identify the best approaches, elements and documents that can support the research and innovation communities in Nanotechnology and Nanofabrication in integrating the ethics dimension into their research and innovation protocols</td><td rowspan="6">Collaborate with some ongoing European projects on the aforementioned topics (in particular TECHETHOS, PANELFIT, SHERPA, EnTIRE, I-CONSENT, ENERI, PRINTEGER, TRUST projects)
Raise awareness about ethical approaches and tools available
Motivate actors around the ethics and governance issues of Nanotechnology and Nanofabrication</td></tr>
<tr><td>Develop research ethics guidelines and protocols for research and innovation in Nanotechnology and Nanofabrication (both general guidelines applying to a broad range of actors and practices, and operational, detailed and practical guidelines developed for specific practices by specific actors).</td></tr>
<tr><td>Develop more operational codes of professional ethics and of responsible conduct for researchers and developers in Nanotechnology and Nanofabrication</td></tr>
<tr><td>Complete the existing general and professional codes in Nanotechnology and Nanofabrication and to make them more applied and more operational</td></tr>
<tr><td>Develop end-user guidelines for ethical usage of nano-enabled products and services</td></tr>
<tr><td>Develop ethics-by-design methodologies and guidelines for emerging Nanotechnology and Nanofabrication</td></tr>
<tr><td rowspan="3">Standardisation</td><td>Enhance the existing ethical standardisation framework at EU and at an international level, to enable the effective ethical governance of these technologies</td><td rowspan="3">Collaborate with some ongoing European projects (in particular RiskGone project) on the aforementioned topics
Develop collaborations with IEEE in the building of both generic and sectorial nano-specific ethical standards</td></tr>
<tr><td>Develop both generic and sectorial ethical standards for research and innovation in Nanotechnology and Nanofabrication</td></tr>
<tr><td>Adapt the existing standards to the case of Nanotechnology and Nanofabrication</td></tr>
</table>

4.3.2 *Validation of Ethics and Governance Practices*

The main challenges identified regarding validation issues associated with ethics area are indicated in Table 13; proposals for action are also provided.

Table 13: Challenges and opportunities of validation issues regarding the area of ethics.

Areas	Specific Challenges	Opportunities
Frameworks attached to CSR (Corporate Social Responsibility)	Define some indicators and metrics relevant for nanotechnology and nanofabrication	• Adapt the existing frameworks (UN Sustainable Development Goals, GRI…) to the case of Nanotechnology and Nanofabrication

5. Conclusions – Consideration of Standardisation Issues

In general, it appears that the standards available or under development are very often ignored by many stakeholders (50% of the respondents to the NanoFabNet WP4 survey). This of course concerns – but is not limited to - scientists in the academic sector (see example given in Box 7), although the consideration of standards could provide a useful frame of reference, capable of giving some confidence to nanofabrication actors in many situations. There are several reasons for this, including not knowing what standards exist, where to find them or how to sort through the large number of existing documents (55% of respondents who said they did not use these documents). Around 10% also state that existing documents do not provide them with the answers they may need. This justifies the need to work on better identifying the documents to be developed in the years to come and to contribute to bringing up to the TCs of the standardisation bodies the documents to be developed, even if it means producing preliminary drafts for proposal.

Box 7: Key role of standardised documents, but limited visibility.

EU academic nanofabrication centres are brought together in EuroNanoLab. This distributed research infrastructures aims to accelerate research in the micro- and nanotechnology sector by enabling the transformation of a fragmented landscape of nanofabrication facilities into an integrated knowledge base supporting scientific excellence and providing researchers a fast-track to results. EuroNanoLab seeks to reach an agreement on the standardisation of cleanroom process steps description and data sharing to enable interoperability between tools and clean rooms. The first step in this ambitious objective is to develop a shared taxonomy of nanofabrication processes to enable a common understanding. Work is therefore needed to harmonise the vocabulary associated with these processes.

ISO/TC 229 Nanotechnologies developed over the last years the ISO/TS 80004-8 Nanotechnologies - Vocabulary - Part 8: Nanomanufacturing processes for exactly that purpose, but EU academic nanofabrication centres weren't involved in the process and even aware of the existence of this document, although it was crucial for them.

An effort to promote the available standards and reference documents is therefore essential (Jillavenkatesa, 2017). This can be envisaged by organising workshop and conference symposia to accelerate awareness on harmonisation needs and standardisation process or by including sessions dedicated to standardisation topic in scientific conferences on nanomanufacturing. The objective would be to provide an overview of existing documents and work in progress, while highlighting success stories that show the key role of standardisation in innovations based on nanomaterials and nanodevices. The production and the dissemination of regular summary reports of CEN/TC 352[4], ISO/TC 229[3] or IEC/TC 113[6] meetings should be also envisaged.

Finally, the creation of a centralised website containing links to existing lists of international standards and best practice would allow consolidating the information in a single location, as already pointed out as an outcome of the GSRS16[65]. This would also meet a need clearly expressed by the stakeholders interviewed in the framework of NanoFabNet (86% of positive answer). The implementation of a search functionality with relevant criteria would also help to promote cross-fertilisation between sectors and avoid stakeholders reinventing the wheel when inspiring approaches have already been developed in a given sector or for a given application as the nanomedicine community has recently pointed out (Halamoda-Kenzaoui & al., 2019).

The general challenges associated with standardisation issues and opportunities to support sustainable nanofabrication are listed in Table 14.

It was also identified during the 2nd NanoFabNet Development Workshop that for many stakeholders **standardisation is a particular world with its own codes and particularities that are foreign to them**. This partly explains the reluctance of a certain number of stakeholders not to invest in these processes, with the direct consequence that the expertise developed in the framework of R&D&I projects is poorly valued at the normative level. The development of documentation standards also requires resources to participate in meetings at different levels (national, European, international), to draft the initial document and then to take into account the different comments that may be expressed by experts from national delegations. **Many stakeholders don't have the human resources available** to do this work. For these two reasons, it could be useful to entrust the steering of standards work to nanotechnology experts who are already familiar with the world of standardisation.

[65] GSRS16 = Global Summit on Regulatory Science – Nanotechnology Standards and Applications, September 7-9, 2016, Maryland, USA.

Table 14: General challenges associated with standardisation issues and opportunities to support sustainable nanofabrication.

Specific Challenges	Opportunities
Identify topics to be supported by standardisation	• Promote the creation of links between CEN/TC 352 and different groups working on harmonisation of practices in order to facilitate the transfer of these documents to standardisation. If necessary, create an antechamber to standardisation, as EUROLAB can be in the case of testing (the participation of regulatory bodies is a key element)
Facilitate the transfer of work to standardisation	• Support capacity building in the scientific community to take a bolder role in the development of harmonisation to support sustainable nanofabrication to improve the efficiency of knowledge transfer for the creation of standards • Foster CEN Workshop Agreements • Offer to coordinate and lead the development of standardisation documents for stakeholders who do not have the human resources or for whom the world of standardisation is not sufficiently familiar
Recruit new experts	• Develop and communicate on internationally recognised Standardisation Certificates to acknowledge standardisation work on the basis of the mechanism, already implemented by the EU Graphene Flagship Standardisation Committee • Make existing document and work in progress better known to the various stakeholders, including industrialist
Promote documents developed by standardisation bodies	• Organise workshop and conference symposia to accelerate awareness on harmonisation needs and standardisation • Highlighting success stories that show the key role of standardisation in innovations based on nanomaterials and nanodevices • Produce and disseminate regular summary reports of CEN/TC 352, ISO/TC 229 or IEC/TC 113 meetings • Create a centralised website containing links to existing lists of international standards and best practice. The implementation of a search functionality with relevant criteria should be considered to promote cross-fertilisation between sectors
Provide the possibility to validate SOPs by inter-laboratory comparison	• Support inter-laboratory assessments initiatives • Promote VAMAS activities • Create a counterpart to VAMAS at EU level • Promote funding mechanism already in place (i.e. EU funding opportunities for pre-standardisation metrology activities through the new European Partnership on Metrology (EPM)) • Set up a dedicated and funded ILC program to be backed by the CEN/TC 352 (based on the ASTM programme model)

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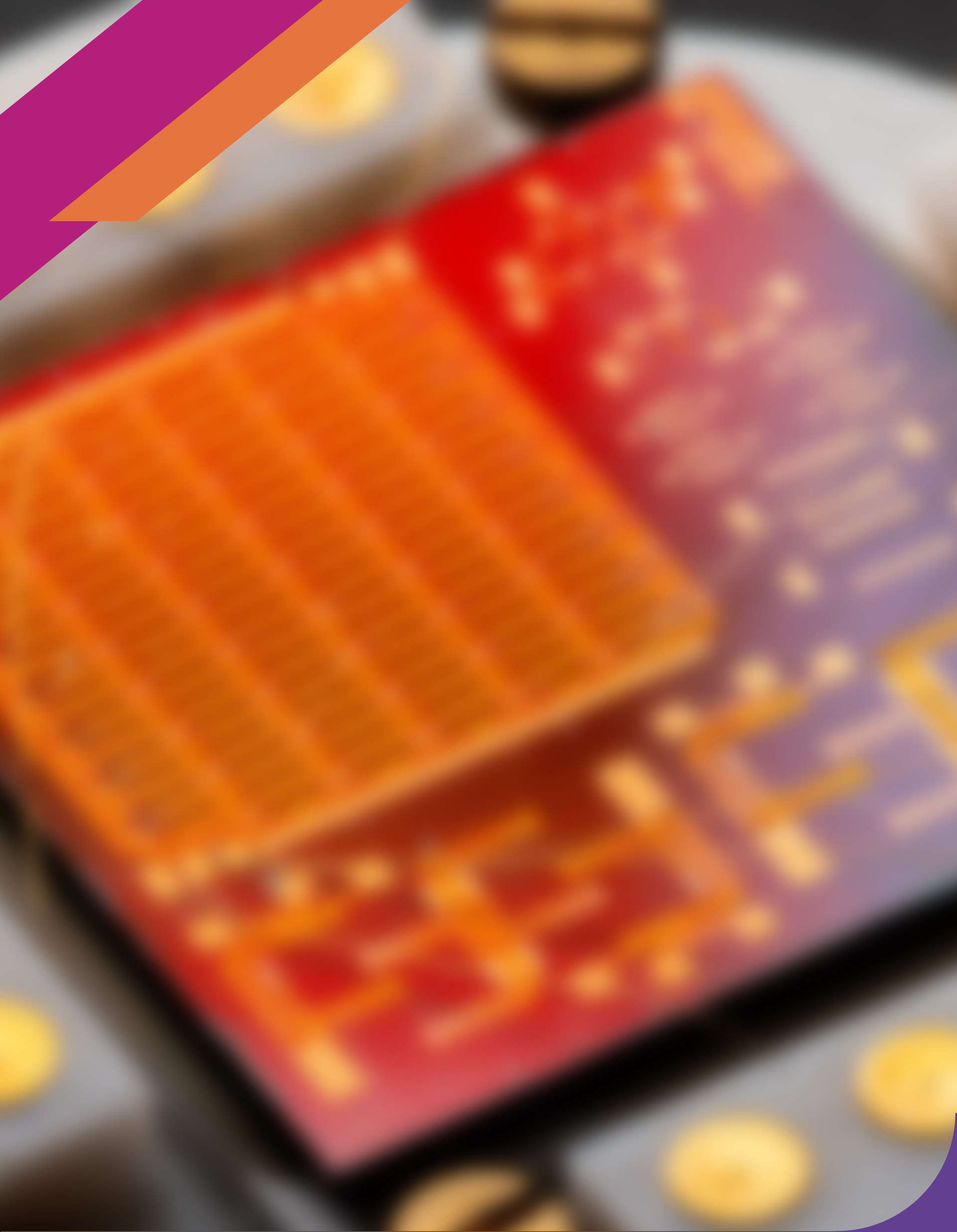

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