REGULATING NANOTECNOLOGY IN BRAZIL AND THE EUROPEAN UNION

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REGULAÇÃO DA NANOTECNOLOGIA NO BRASIL E NA UNIÃO EUROPEIA

Versão em português (traduzido)

REGULATING NANOTECHNOLOGY IN BRAZIL AND THE EUROPEAN UNION

Versão em inglês (original)

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CONTEXTUALIZAÇÃO

A Nanotecnologia consolidou uma dinâmica de rápido desenvolvimento e aplicação diversificada em virtualmente todos os setores econômicos e não configura uma promessa ou uma ficção futurista: ela já é uma realidade observada em inúmeros produtos comercializados por diferentes setores. Dados recentes da Organização para a Cooperação e Desenvolvimento Econômico (OCDE) indicam que o mercado de produtos nanotecnológicos movimenta cerca de US$ 350 bilhões e, em 2015, estima-se que esse valor será superior a US$ 1 trilhão. Já existem no mercado mundial diversos produtos que incorporam nanotecnologias, inclusive produtos de uso diário e amplo, como os cosméticos e produtos de higiene pessoal.

Entretanto, ao mesmo tempo em que a nanotecnologia revoluciona a sociedade introduzindo novos produtos e processos, ela também traz uma preocupação crescente sobre os riscos associados aos seus usos disseminados. Dessa forma, para se tornar um ator nesta área, é essencial compor o corpo internacional de discussões sobre regulação da nanotecnologia. Acompanhar e contribuir com os diálogos em torno da regulação em nanotecnologia possibilitarão ao Brasil colocar em pauta as particularidades nacionais, de forma que os benefícios do intercâmbio comercial sejam equitativamente compartilhados por todos os envolvidos, com vistas ao desenvolvimento sustentável.

A regulação e a regulamentação da nanotecnologia se assentam sob três pilares principais: a percepção social sobre os benefícios e riscos da nanotecnologia, a geração e o compartilhamento de dados científicos sobre as nanopartículas, manufaturadas ou naturais, e o interesse público.

A regulação e a regulamentação do uso, da pesquisa, do desenvolvimento e da inovação (P,D&I) em nanotecnologia passaram para o topo da agenda tanto dos governos como da comunidade científica e tecnológica, uma vez que a insegurança jurídica é um dos principais fatores de represamento dos investimentos em novas tecnologias. Várias organizações internacionais vêm mantendo discussões, fóruns e reuniões para o estabelecimento de definições de nanomateriais e de métodos de caracterização e de avaliação da sua segurança. Entretanto, até o momento, não existe um Marco Regulatório específico para o tema, sendo os produtos registrados em diferentes países, incluindo o Brasil, pelas suas respectivas Agências Reguladoras, em análises caso-a-caso.

A necessidade de regulação e de regulamentação é urgente e se reflete em projetos de lei no parlamento brasileiro e como assunto prioritário no âmbito da Iniciativa Brasileira de Nanotecnologia (IBN). Os dois assuntos são frequentemente debatidos nas reuniões do Comitê Consultivo de Nanotecnologia (CCNANO) e do Comitê Interministerial de Nanotecnologia (CIN), tendo sido criado um Grupo de Trabalho em Regulação (GT-Reg). Foram criadas, também, seis Redes Cooperativas de Pesquisa e Desenvolvimento em Nanotoxicologia com o objetivo de avaliar a segurança de nanomateriais e para dar suporte nos assuntos relativos à regulação.

Em junho de 2013, uma comitiva brasileira participou do *Nanoeuroforum*, realizado em Dublin, Irlanda, e promoveu reuniões de trabalho com representantes da Direção Geral para Investigação e Inovação e do *Joint Research Centre* (JRC, sigla em inglês), especificamente sobre os aspectos científicos, tecnológicos, metodológicos e metrológicos da regulação em nanotecnologia. A regulação da nanotecnologia é um dos temas prioritários no novo programa europeu Horizonte 2020 (H2020). Pelo lado brasileiro no *Nanoeuroforum*, e a partir das reuniões realizadas, ficou acertado o interesse mútuo de atuar no sentido de dar suporte a ações visando colaborações e pesquisas que gerem conhecimentos técnico-científicos, metodologias e protocolos para caracterização, determinação e modelamento dos mecanismos físicos, químicos e biológicos associados aos impactos ambientais, em sistemas biológicos e na saúde humana e animal, de nanomateriais e de produtos e processos nanotecnológicos. Essa é a base de suporte para o processo que levará ao marco regulatório da nanotecnologia.

Com a participação brasileira no *Nanoeuroforum* e em outras ações correlatas, surgiu a oportunidade do país ingressar no maior projeto mundial voltado a dar respostas científicas às questões regulatórias associadas à nanotecnologia - o projeto NANoREG. Conduzido pela Comissão Europeia (CE) dentro do programa FP7, o NANoREG é um esforço de 16 países europeus e de outros países, como Japão, Coréia do Sul, Austrália e Canadá. A entrada do Brasil no NANoREG foi aprovada pelo CIN, em reunião realizada em agosto de 2014.

O Brasil conta hoje com um sistema maduro de P,D&I em nanotecnologia. O Sistema Nacional de Laboratórios em Nanotecnologia (SisNANO), criado pela Portaria nº 245, de 5 de abril de 2012, é um dos elementos do Programa Nacional de Nanotecnologia, contemplado no âmbito da Estratégia Nacional de Ciência Tecnologia e Inovação (ENCTI) 2012-2015 e associado ao Plano Brasil Maior (PBM), juntamente com as Redes Cooperativas de Pesquisa e Desenvolvimento em Nanotoxicologia e as Redes de Nanoinstrumentação contribuirão para responder perguntas e fornecer dados importantes voltados para a questão regulatória da nanotecnologia.

A União Europeia vem realizando diversos estudos para estabelecer normas e recomendações voltadas para a regulação e regulamentação dos nanomateriais. A Segunda Revisão Regulamentar Relativa à Nanomateriais, da Comissão Europeia - COM(2012) 572 Final – tem o objetivo de fornecer dados para a adequação e aplicação da legislação da União Europeia aos nanomateriais. O documento trata de assuntos essenciais para o início da discussão em torno da regulação e regulamentação para a área da nanotecnologia, que são a definição de nanomateriais, os

mercados de nanomateriais, as utilizações, os benefícios, os aspectos de saúde e de segurança, a avaliação de riscos, bem como as informações e bases de dados sobre nanomateriais. Além disso, de acordo com o Regulamento CRE (Certificação, Rotulagem e Embalagem), é obrigatório que substâncias introduzidas no mercado europeu, entre elas os nanomateriais, sejam notificadas à Agência Europeia das Substâncias Químicas (ECHA) de acordo com classificação referente ao perigo, independentemente de sua tonelagem.

Considerando as diversas ações e protocolos estabelecidos pela União Europeia, o projeto "Diálogos Setoriais União Europeia-Brasil" voltado para a regulação de produtos baseados em nanotecnologia teve como objetivo geral ajudar a estabelecer um conjunto de metodologias, técnicas e protocolos necessários para o estabelecimento da regulação cientificamente referenciada, reconhecida e compatibilizada internacionalmente. A padronização dos métodos de certificação e da regulamentação da nanotecnologia, em consonância ao que vem sendo desenvolvido com outros países, é essencial para promover a cooperação internacional e para facilitar a importação e exportação de produtos baseados em nanotecnologia. A colaboração, no escopo desta proposta, entre Brasil e União Europeia permitirá um diálogo rumo à contribuição para o estabelecimento de normas seguras para a nanotecnologia, na tentativa de balancear equitativamente a profusão de interesses econômicos, sociais, sanitários e ambientais.

O relatório dos peritos contratados no âmbito do projeto "Diálogos Setoriais União Europeia-Brasil" apresenta uma visão geral das iniciativas e ações voltadas para a regulação da nanotecnologia, tanto no Brasil quanto na União Europeia, e apresenta recomendações baseadas em conhecimentos científicos e na infraestrutura laboratorial brasileira, objetivando o desenvolvimento e a implementação de medidas regulatórias cientificamente referenciadas e compatíveis internacionalmente. O estudo apresenta também o relato das missões realizadas no Brasil e na Europa, com a participação de membros do governo brasileiro e de especialistas europeus e brasileiros na área de nanotecnologia.

REPORT ON THE INITIATIVES AND ACTIONS AIMED AT REGULATING NANOTECHNOLOGY IN BRAZIL AND THE EUROPEAN UNION

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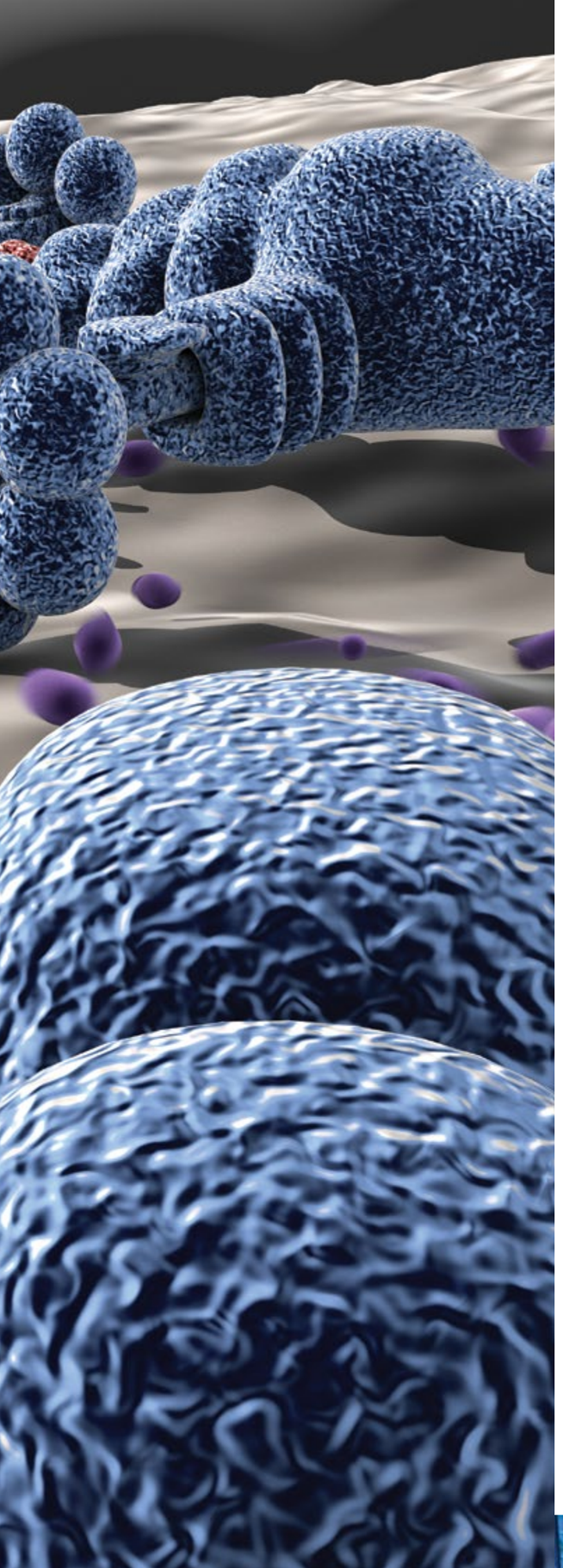
1 INTRODUCTION

For nanotechnology to reach its full potential, a balance is required between regulating the risks and developing the technology for societal benefit, and at the same time taking responsible and reasonable protective measures where there is uncertainty. The established and holistic process of risk assessment has been employed for many years to underpin the safe management of chemicals, and this is widely considered to be the appropriate thing to do for nanomaterials. Risk assessment provides the basis for the characterization, management and communication of potential harm from substances, processes or technologies, and provides a rationalized scientific structure to taking a precautionary approach when needed. Contributing to risk assessment are a range of emerging and evolving recommendations, codes of practice, standards, and accreditation schemes for organizations in research, manufacturing and applications sectors wishing to demonstrate publicly a responsible approach to nanomaterials safety. The benefits to industry in adopting a proactive and comprehensive approach to nanotechnology risk management are that it provides i) a basis for responsible stewardship of nanoproducts and nanotechnologies, providing evidence of compliance with existing (and future) legislation; ii) foresight of emerging issues along



the supply chain which can influence how risk is identified and controlled; and iii) help to support strategic decision-making, investment, market access and product/process developments.

Research into nanomaterials safety, the consideration of regulatory approaches, and the development of Standards, are taking place around the world and through international collaborative efforts. It is therefore prudent for Brazil to identify, cooperate and integrate with relevant initiatives and programmes to maximize the opportunity to contribute to, and gain from, these activities for the benefit of Brazil.

The Brazilian Parliament is currently examining two bills dealing with the labeling of products that make use of nanotechnology (Bill No. 5,133/2013) and the creation of a National Nanotechnology Policy (Bill No. 6,741/2013). This is placing a requirement on the Ministry of Science and Technology (MCTI) to demonstrate that Brazil's scientific and technical expertise and infrastructure is cognizant of the issues about nanotechnology safety and is taking a coordinated and valued approach to addressing the issues, thereby mitigating risks from the development of nanotechnology in Brazil. This specifically includes Brazil seeking cooperation and collaboration with international research and the development of regulation for nanomaterials, to inform the approach that should be taken domestically.

In Brazil, several actions are being conducted relating to nanotechnology regulation. This subject is often discussed at meetings of the Nanotechnology Advisory Committee (CCNano) and the Interministerial Committee for Nanotechnology (ICN), and a Working Group on Regulation (GT-Reg) has even been created. Six Nanotoxicology Networks have also been set up with the aim of assessing the safety of nanomaterials, as well as providing support in matters relating to their regulation. Appendix 1 provides an overview of the Brazilian Networks.

The development of regulation for nanomaterials is well advanced in the jurisdiction of the European Union, at a Community-wide level and by individual Member States. As a result, a Sector Dialogue with the European Union on the Regulation of Nanotechnology-based Products was established and is intended to underpin the process leading to the development of a nanotechnology regulatory framework or frameworks in Brazil.

In the European Union, substantial work to consider and address the issues concerning the regulation of nanomaterials has been undertaken including, for example, the REACH Implementation Projects on Nanomaterials (RIP-oNs) and several reviews and consultations carried out by individual Member States. The European Commission's Second Regulatory Review on Nanomaterials[1] outlines the position with regard to adjusting and implementing measures under REACH for nanomaterials regulation, on the basis of namely the definition of nanomaterials, nanomaterial markets, their uses, benefits, health and safety aspects, risk assessment, as well as nanomaterials information and databases. Under the EU's CLP Regulation (which addresses Certification, Labeling and Packaging), it is mandatory that substances introduced into the European market, including nanomaterials, be notified to the European Chemicals Agency (ECHA) according to their hazard classification, regardless of their tonnage.

Complementing the legal and technical considerations of nanomaterials regulation is a significant programme of multidisciplinary research, under the European Commission's Framework Programmes, that is contributing to the knowledge on nanomaterials risk assessment. The NanoSafety Cluster's compendium[2] provides information on the status of these important EU-funded projects on nanomaterial toxicity and exposure monitoring, integrated risk management, research infrastructure and coordination and support activities as well as regulatory-focused research on nanosafety. The summary table showing the research themes of the current NanoSafety Cluster projects is shown overleaf.

1. http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX-:52012DC0572

2. http://www.nanosafetycluster.eu/home/european-nanosafety-cluster-compendium.html

Temas de pesquisa dos projetos do *Nanosafety Cluster*

Project Acronym	eNanoMapper	FutureNanoNeeds	GuideNano	INSTANT	MARINA	MembraneNanoPart	ModNanoTox	NanoDefine	NanoDetector	NanoFATE	NanoHeter	NanoMICex	NanoMILE	NanoPolyTox	NanoPuzzles	NanoREG	NanoRisk	NanoSolutions	nanoSTAIR	NanoSustain	NanoTransKinetics	NanoValid	NanoXtMet	PreNanoTox	QualityNano	SanoWork	Scaffold	SIINN	SIRENA	SUN
Start year	2014	2014	2013	2012	2011	2013	2011	2013	2012	2010	2013	2012	2013	2010	2013	2013	2013	2013	2012	2010	2011	2011	2013	2013	2011	2012	2012	2013	2013	2013
End year	2017	2017	2016	2015	2015	2015	2013	2017	2015	2014	2016	2014	2017	2013	2015	2016	2016	2017	2014	2013	2014	2014	2016	2016	2015	2015	2015	2016	2015	2016
Measurement		X			X			X	X	X				X				X		X		X								
Physico-chemical properties		X	X	X	X	X		X	X	X	X	X	X	X		X	X	X		X		X	X	X	X	X		X		X
Analysis of "next generation" nanomaterials (2nd, 3rd or 4th generation)		X	X					X									X											X		X
Exposure assessment for humans and the environment		X	X		X					X	X	X		X			X			X		X								X
Develop & validate exposure measurement and modelling methods		X	X		X		X			X	X	X		X	X	X	X				X	X					X	X	X	X
Human Exposure: Applica-tion of measuremente and		X	X		X					X		X		X		X				X		X		X	X	X	X			X
Environmental Exposure Assessment		X	X		X		X			X	X	X		X		X	X			X		X						X	X	X
Interaction of NM with biological systems		X			X					X				X				X		X		X								
Interaction with physiological mechanisms		X			X	X				X				X	X	X				X	X	X	X	X	X	X				
Toxicokinetics					X	X				X		X		X	X	X				X		X				X				
Variability										X				X	X	X									X					
Predictive models					X	X	X			X		X		X	X	X		X		X	X	X	X				X			
Long term monitoring and assessment										X				X		X														
Human Health					X												X	X		X		X								
Develop & validate testing & assessment strategy					X									X	X	X	X	X		X	X	X			X					
Apply testing and assess-ment strategy					X							X		X	X	X	X	X		X		X				X				
Coexposures / Misture		X																				X								
Ecotoxicology		X	X		X					X			X		X			X		X		X								
Develop testing and assessment strategy		X	X		X					X		X	X		X	X		X		X		X			X					X
Apply testing and assessment strategy			X		X		X			X			X		X	X		X		X		X								X
Control measures at workplace					X												X			X		X								
Develop & validate methods to evaluate control measu-res at workplaces					X				X							X	X	X		X		X					X			X
Apply methods to evaluate control measures at workplaces					X				X			X				X	X			X		X				X	X			
Control banding approach					X							X					X									X	X			
Preliminary handling guidelines					X										X		X	X		X		X								X
Collect available and ongoing approaches					X										X	X	X	X		X		X					X		X	X
Evaluation and further development		X			X										X	X	X	X		X		X				X	X		X	X
Information transfer		X	X							X				X				X				X								
Database generation	X	X	X		X		X			X	X		X	X	X	X		X		X	X	X	X	X	X	X	X		X	X
Public dialogue			X		X					X	X				X		X					X				X	X			
Information to and training of workers, business and		X	X							X		X	X	X			X			X		X	X			X	X		X	X
National and international collaboration					X					X	X			X	X			X	X	X		X								
Development	X	X	X		X				X	X	X			X	X	X	X	X		X		X	X	X	X	X	X	X	X	
Testing	X	X	X		X	X			X	X	X	X		X	X	X	X	X		X		X	X	X	X	X	X	X	X	
Validation	X		X		X	X		X		X	X			X	X	X		X		X	X	X		X	X		X	X	X	
Standardisation	X				X			X		X	X			X	X	X			X		X	X	X	X	X		X		X	
Assessment activities			X		X					X	X	X		X	X	X		X		X	X	X		X	X	X	X			

Source: 2014 Compendium of Projects in European NanoSafety Cluster

DIt should be noted that the compendium is not intended to be a guidance document for human health and environmental safety management of nanotechnologies, as such guidance documents already exist and are widely available. Neither is the compendium intended to be a medium for the publication of scientific data and research results, as this task is covered by scientific conferences and the peer reviewed press. The compendium aims to showcase the exciting and important European-wide collaborative research being undertaken to ensure the safe implementation of nanotechnologies, and to act as a one-stop-shop for all stakeholders interested in acquiring an overview of current research activities. The 2014 edition of the compendium contains information on 30 running (or very recently finished) projects, including new entries describing the projects resulting from the last call of FP7, including eNanoMapper, NanoDefine and FutureNanoNeeds. In addition, updates from several of the Nanosafety Cluster Working Groups (WGs) are included, outlining their short, medium and long term goals, and progress to date. The compendium also aims to bring the research community closer together and show them the potential for synergy in their work. It is a means to establish links and communication between them during the actual research phase and well before the publication of their results. It thus focuses on the communication of projects' strategic aims, extensively covers specific work objectives and the methods used in research, and documents human capacities and partnerships. As such, the compendium supports collaboration on common goals and the joint elaboration of future plans, whilst compromising neither the potential for scientific publication, nor intellectual property rights.

These research themes will continue as a priority issue in the new Horizon 2020 (H2020) programme which is furthermore underpinned by a published strategy[3] on nanosafety research for 2015-2025, identifying the knowledge gaps and goals for research on cross-cutting issues. Those considered particularly pertinent for Brazil include:

- the regulatory framework for engineered nanomaterials and nanotechnologies, coupled to the important issue of standardization to promote good practice and to facilitate communication;
- the development of infrastructures for nanosafety to promote research, education, and innovation;
- international collaboration and global dialogue, with a view towards a global research area in nanosafety;
- communication and dissemination of research to key stakeholders beyond the research community, including industry, regulatory bodies, and others.

As a result, the objectives developed for the Sector Dialogue between the EU and Brazil on the Regulation of Nanotechnology-based Products are to:

- investigate the processes of characterization, certification, safety assessment and regulation of nanotechnology products, both in Brazil and in the European Union;
- identify measures that can be implemented to promote the certification and regulation of nanotechnology, as well as to facilitate the international trade of nano products;
- create a roadmap of actions related to nanotechnology regulation in Brazil with a focus on its scientific, technological and metrological

3. http://www.nanosafetycluster.eu/news/83/66/Nanosafety-in-Europe-2015---2025.html

aspects so that these actions will be performed in a manner that is referenced and made compatible internationally;

- propose interaction and integration mechanisms between the activities and projects associated with the regulation of nanotechnology in Brazil and Europe;
- create research clusters around the topic of nanotechnology regulation.

By way of the initial liaison activities carried out towards achieving these objectives, a Brazilian delegation attended the EuroNanoForum 2013 conference held in Dublin, Ireland and held meetings with representatives of the EC Directorate General for Research and Innovation and representatives of the Joint Research Centre (JRC), specifically to address the scientific, technological, methodological and metrological aspects of nanotechnology regulation. This is also a priority issue in the new Horizon 2020 (H2020) programme. As a result, a mutual interest developed in supporting actions aimed at cooperation and research to generate scientific know-how, methodologies and protocols for the characterization, determination and modeling of the physical, chemical and biological mechanisms associated with impacts on the environment, on biological systems and on human and animal health related to nanomaterials and nanotechnology products and processes. This has led to an agreed involvement of Brazilian laboratories in the flagship NANoREG project (www.nanoreg.eu). Building on the Brazilian mission to Europe, the activities of several of the European research projects (e.g. NANoREG, MARINA, SUN) that are contributing to addressing the scientific, technological, methodological and metrological aspects of nanotechnology regulation, feature in the EU Mission to Brazil and accompanying workshop (September 2014). The stated aim of the mission is to intensify and coordinate the cooperation between Brazil and the European Union on the field of environmental, health and safety aspects of nanomaterials, including the development of instruments for "safe by design" aimed at a more upfront incorporation of EHS aspects in the design, production and application of these materials. Collaboration in addressing these topics is seen as beneficial for both Brazil and the European Union.

Specific objectives of the mission are:

- To elaborate the agreement made in May 2014 in Paris between the EU, Brazil and the NANoREG coordinator on the involvement of Brazilian parties in the NANoREG project; more specifically to:
  - √ define and elaborate potential Brazilian contributions to the NANoREG project;
  - √ establish what Brazilian laboratories will take the main responsibility over the Brazilian participation in NANoREG;
  - √ establish contacts with the representatives of potential collaborating parties;
  - √ elaborate the formal aspects of the collaboration.
- To explore and select possible collaborations between Brazilian parties and other NanoSafety Cluster projects.

A more detailed account of the abovementioned liaison which has already taken place is given in Appendix 2.

On the basis of the objectives developed for the Sector Dialogue between the EU and Brazil on the Regulation of Nanotechnology-based Products, the expected results from the Sector Dialogue are:

1. a technical and scientific report on the initiatives and actions aimed at regulating nanotechnology in Brazil and the European Union, especially but not exclusively, in their scientific, technological and metrological aspects, including the question of how the scientific, technological and metrological parties interact and collaborate with other sectors involved in regulation;
2. establishment of the activities and research methods needed for the investigation, characterization, metrology, modeling, certification and assessment of nanomaterials and nanotechnology products and processes in their physical, chemical and biological aspects, so that they will be recognized internationally;
3. increased interaction between researchers and companies from Brazil and the European Union, so that nanotechnology products are developed following internationally recognized standards;
4. establishment of measures which will support the creation of a Regulatory Framework for nanotechnology that will facilitate the international trade of nanotechnology products;
5. creation of an action plan and detailed outline of Brazil-European Union cooperation in aspects related to nanotechnology regulation.

This report provides principally provides an overview of initiatives and actions aimed at regulating nanotechnology in Brazil and the European Union, and recommendations on the scientific knowledge, engagements and technology for consideration as part of the ongoing development and establishment of scientifically-referenced regulation, that is recognized and compatible internationally.

2 NANOTECHNOLOGY REGULATION & THE CHALLENGES

The discussion and development of risk assessment and regulation appropriate to nanomaterials has been ongoing for a number of years and has largely involved consideration of definitions, identifying the information requirements for regulatory assessments, and the evaluation of characterization and toxicological testing methods. These considerations can be seen to manifest in the emerging notification/reporting schemes and in the regulations (often derived from existing chemicals regulation) being applied or developed for nanomaterials. Current regulatory efforts are primarily focused at the national and regional level (e.g. REACH in Europe and TSCA in the US), with international-level discussions and developments taking place largely through the OECD and ISO, with a number of reviews, Standards and guidance documents being published[4]. However, to date, there is no specific global or unified regulatory framework for nanomaterials, with products being registered in different countries, often according to the type of product, by their respective regulatory Agencies on an ad hoc basis.

The development and commercialization of nanotechnologies and nano-enabled products

4. A bibliography of relevant published documents from OECD, ISO and other organisations is provided in Appendix 4.

is occurring at an increasingly rapid pace and product innovation and manufacturing processes are likely to change frequently. The diverse nature of nanomaterials and nano-enabled applications means they cut across a number of sectors and regulatory jurisdictions and can pose significant, but not insurmountable, challenges for regulation. Risk assessments for engineered nanomaterials need to be able to counter significant scientific uncertainty and lack of data, but also take into account a wide range of different materials and their diverse properties and applications. Risk assessment of more complex generations of nanotechnologies will undoubtedly present even more challenges.

A number of published regulatory and policy reviews[5],[6] have highlighted the need for greater international cooperation and harmonization in addressing the aforementioned uncertainties and developing effective regulatory and governance approaches for nanomaterials. Given the rapid globalization and expansion of international trade in nanomaterials, demand for cooperation and harmonization looks set to increase. A wide range of proposals for filling the global governance gap have been made, from the use of soft law approaches (e.g. codes of conduct) to the creation of an international framework convention.[7]

However, current regulatory efforts are primarily focused at the national and regional level; the international dimensions of nanotechnology regulation are still poorly understood and rarely feature on the international agenda. A number of challenges to coordination at national and international levels exist, as highlighted by Widmer et al.[8]:

- Traditionally, regulatory organizations and measures are fragmented by the area of jurisdiction (subject), type of regulation (product, process, etc.), and intervention levels. This makes it difficult to implement life-cycle considerations and a consistent regulatory framework, particularly for nanotechnologies which are used in a variety of sectors, applications and industries;
- Although there is the potential for risks to cross international borders, there is no international framework at this time yet which would allow addressing the risk governance of nanotechnology on a global level and which would provide means of enhancing consistency in such issues among the nations;
- Although several international institutions and programmes have been established with the intention to foster standardization, co-operative development of health and safety data and harmonization among involved nations (e.g. through OECD or ISO), such approaches usually do not have a focus on coordination of regulatory issues, and many current national and international systems may be inadequate for coping with the unique properties of nanomaterials.

The International Risk Governance Council (IRGC), whilst emphasizing the importance of international collaboration and harmonization of risk governance approaches for nanotechnology, recognizes that the risk governance process cannot itself be standardized, which relates to the view that is no "one-size-fits-all" prescription[9]. IRGC considers that governance approaches required for nanotechnologies will change as the technology develops, proposing that first generation nanotechnologies at minimum require a precautionary approach (e.g. no data – no market, labeling etc.) while later generations may require a shift to wholly new ways of sustainable, precaution-based technology assessment and management.

Another important challenge facing the regulation of nanotechnologies, is the limited exchange of information amongst stakeholders along the value chain. IRGC highlighted a number of risk communication issues for nanotechnology, specifically:

- Lack of communication and understanding about the science, application and regulation of nanotechnology among all stakeholders may have negative effects on societal impressions and political/regulatory decision making;
- Gaps in communication between different scientific disciplines – from the natural, technical and ecological sciences to the economic, social and psychological disciplines – limit the ability to fully consider and act on potential innovations and risks;
- Gaps in communication between various regions of the world, which may lead to their developing different expectations and adopting different and contradictory regulatory measures;
- Lack of engagement with stakeholders with different perspectives and value systems in a continuous dialogue about the best procedures to exploit the benefits and avoid most of the risks has caused an increased polarization between nanotechnology's optimists and those who are more pessimistic.

Widmer et al. also highlighted a number of difficulties concerning the transfer of knowledge among stakeholders in the supply chain, most notably:

- *Material safety data sheet (MSDS):* Nano-specific information on the properties and potential risks needs to be available along their life cycle in order to correctly handle nanomaterials. MSDS are a key tool for ensuring the safe use of chemical substances, allowing the communication of information on hazards and instructions for safe handling throughout the supply chain. The current MSDS needs to be adapted for nanomaterials to enable effective risk communication;
- *Confidentiality of data:* Transfer of safety information between manufacturers, regulators and the public is often hampered by claims of confidentiality of data, retaining the development or disclosure of data due to (legitimate) confidentiality reasons. In the current situation of a lack of reliable and validated data on the safety of manufactured nanomaterials, this is expected to hamper progress in the validation and development of additional health and safety data on nanomaterials;
- *Communication in a situation of uncertainty*: The traditional role of regulators and authorities in defining rules and penalties based on scientific evidence is complicated in the case of nanomaterials as such evidence is only fragmentary at best or inconsistent. Such uncer-

5. IRGC. Nanotechnology Policy Brief. Recommendations for a global, coordinated approach to the governance of potential risks. (International Risk Governance Council (IRGC), Geneva, 2007).
6. Breggin, L., Falkner, R., Jaspers, N., Pendergrass, J. & Porter, R. Securing the promise of nanotechnologies. Towards transatlantic regulatory cooperation., (Chatham House (Royal Institute of International Affairs), London, 2009).
7. Abbott, K. W., Marchant, G.E., Sylvester, D.J. A framework convention for nanotechnology? Environmental Law Reporter 36, 10931-10942. (2006).
8. Widmer, M., Meili, C., Mantovani, E. & Porcari, A. The FramingNano Governance Platform: A new integrated approach to the responsible development of nanotechnologies. (FramingNano Project, 2010).
9. Linkov, I., Satterstrom, F. K., Monica Jr, J.C., Hansen, S. F. & Davis, T. A. Nano risk governance: Current developments and future perspectives. Nanotechnology Law & Business 6, 203-220 (2009).

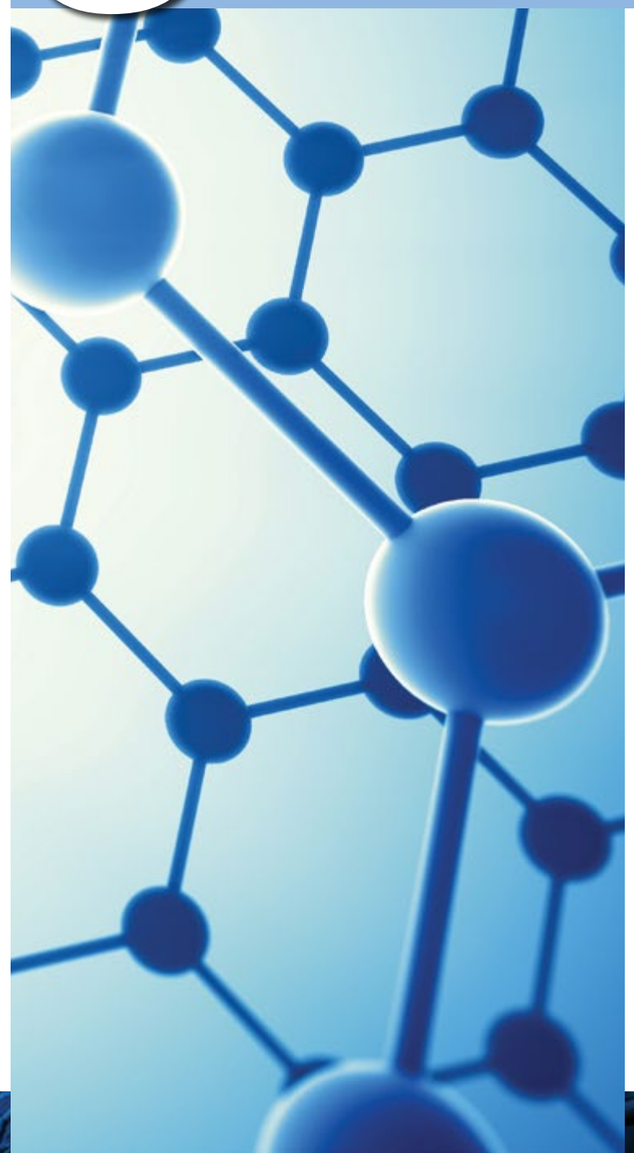
tainties prevent authorities from implementing clear rules and regulations and pose significant challenges in communicating clear messages regarding whether certain applications of nanotechnology are to be considered “risky” or “safe”.

The Organization for Economic Co-operation and Development Working Party on Manufactured Nanomaterials (OECD WPMN), amongst others, make attempts to coordinate information exchange and data development with a view to easing this situation.

A further challenge relates to the public’s awareness and perception (actual and perceived) of nanotechnologies, which has the potential to impact on governance, future investment and development of the nanotechnology industry. A number of recent research initiatives and consumer polls have indicated that public awareness of nanotechnologies remains low but generally positive (on the back of general pro-science and technology perception) and there is, therefore, a risk of public rejection as has been seen in the past with the case of GMO, for example. The prospect of unfounded public rejection suggests that there is a need for improved knowledge and good risk management and communication, such that governance tools must be identified and implemented explicitly to consolidate and increase public confidence in the industry.

Hence, the prevalence and variety of uncertainties suggests that an effective regulatory approach should include an appropriate precautionary element and a foundation of good governance, and be capable of anticipating (even if it cannot reliably predict) future technological developments within a framework that offers flexibility and adaptability to ensure long-term effectiveness.

3 COMMENTARY ON THE REGULATION OF NANOMATERIALS IN EUROPE



In Europe, the Registration, Evaluation, Authorization and Restriction of Chemicals Regulation (REACH) provides the over-arching legislation applicable to the manufacture, placing on the market and use of substances on their own, in preparations or in articles, and nanomaterials fall within the scope of REACH. They are covered by the definition of a “substance” in REACH, even though there is no explicit reference to nanomaterials. The general obligations in REACH, such as registration of substances manufactured at 1 tonne or more and providing information in the supply chain apply as for any other substance. The first registration deadline under REACH (30 November 2010) applied to substances manufactured or imported at 1000 tonnes or more per year and the second one (1 June 2013) to volumes higher than 100 tonnes and lower than 1000 tonnes per year. The European Chemicals Agency (ECHA) receives the registrations and the Agency plays a central role in the collection, evaluation and dissemination of information on substances and preparations, including nanomaterials. Nanomaterials that fulfill the criteria for classification as hazardous under Regulation 1272/2008 on classification, labeling and packaging (CLP) of substances and mixtures must be classified and labeled. Many of the related provisions, including safety data sheets and classification and labeling apply already today, independently of the tonnage in which

the substances are manufactured or imported. Substances, including nanomaterials, meeting the classification criteria as hazardous and put on the market must be notified to ECHA.

In parallel to the Community-wide Regulation, a number of Member States are giving consideration to the regulation of nanomaterials and have developed or are considering Notification/Reporting schemes. An overview of the main considerations is presented below.

The German Federal Environment Agency (UBA) has posted on February 2014, an English translation of a 2012 document entitled 'Concept for a European Register of Products Containing Nanomaterials'. The document states that, due to the particular uncertainties concerning evaluation of the possible risks of nanomaterials for human health and the environment, UBA supports the establishment of a European register of products containing nanomaterials as a precautionary measure. The objective of the product register would be to provide an overview of products containing nanomaterials that have applications in the consumer area and in an open environment. According to UBA, this would enable public authorities to set priorities in enforcement and monitoring, to estimate exposure for humans and the environment, and, in the case of adverse effects, to ensure traceability. For actors in the supply chain, a product register would create transparency. UBA states that the establishment of the product register should take place at the European Union (EU) level and be managed centrally. UBA acknowledges that a national product register would overlap with EU legislation and obligations and regulations in individual EU Member States, which would mean increased costs for authorities and stakeholders subject to notification. Substances and mixtures (manufactured or imported) that comprise or contain nanomaterials would be subject to notification, as well as articles that intentionally or unintentionally release nanomaterials.

In March 2014, the German Federal Environment Agency (UBA) issued a report entitled Assessment of Impacts of a European Register of Products Containing Nanomaterials, which was intended to analyze the impacts of a European register of products containing nanomaterials (ENPR). The study identified the sectors and companies that would be affected by an ENPR, and estimated the number of notifiers and notifications, categories of substances, concerned mixtures, and articles. Based on that result, the study quantified the administrative costs for notifiers and the competent authority, and described the benefits of an ENPR for public authorities, consumers, and notifiers.

In March 2014, ECHA published a report entitled 'Human health and environmental exposure assessment and risk characterization of nanomaterials: Best practice for REACH registrants'. The report summarized the outcomes of the third meeting of the Group Assessing Already Registered Nanomaterials (GAARN). The September 30, 2013, meeting focused on discussing the approach and challenges faced by participant registrants when documenting the human health and environmental exposure assessment and risk characterization of their substances while registering them under the REACH regulation. In summary, the report states that the provisions that apply to the registration of nanomaterials are the same as those for any other chemical substance. According to the report, the registration dossier should contain a comprehensive physicochemical characterization of the registered nanoform(s). Only when well-characterized nano-forms are reported in the dossier, can a read-across approach or use of existing data be considered for the purpose of hazard assessment. In general, it is important to conclude with the reminder of the legal obligation that registration dossiers need to be updated with new nano-specific studies as scientific developments are progressing. Safe use claims under REACH should be based on explicit and transparent documentation supporting the hazard, exposure and risk assessment of NMs.

According to the report, a register could bring additional value for public authorities, consumers and companies involved in nanotechnology. However, the introduction of a register is the mildest legal instrument to control the production and use of nano-products compared to a restriction, a ban or a moratorium on one or more of these products.

The French Agency for Food, Environmental and Occupational Health and Safety (ANSES) published in May 2014, a review of the available literature on health and environmental issues relating to manufactured nanomaterials. According to ANSES, the review will help clarify scientific understanding and demonstrate the toxic effects of some nanomaterials on living organisms and the environment. ANSES states that it is difficult to assess the specific risks associated with nanomaterials.

In May 2014, the European Commission (EC) Joint Research Center (JRC) announced the availability of a report discussing labeling and reporting schemes for nanomaterials in consumer products in the European Union (EU). The JRC notes that current EU legislation requires nanomaterials to be reported in the list of ingredients, with "nano" added in brackets after the substance name, for food, cosmetics, and biocides. According to the JRC, manufacturers sometimes add voluntary "nanoclaims" indicating the presence or absence of nanomaterials. The JRC states that a product register may give a better overview of the overall application of nanomaterials and potential exposure of humans and the environment. The EC already requires mandatory reporting for cosmetic products containing nanomaterials. Some EU Member States (France, Belgium, and Denmark) have or are introducing mandatory reporting schemes for a wider range of consumer products.

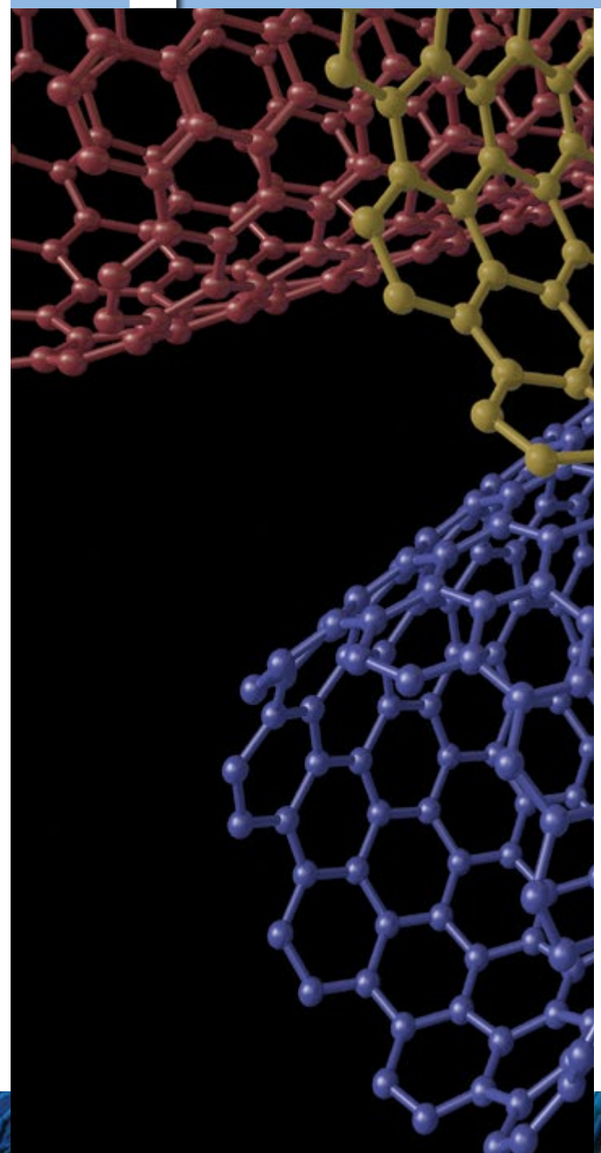
The European Commission's Second Regulatory Review discusses the nanomaterial definition, nanomaterial markets, uses, benefits, health and safety aspects, risk evaluation, information and databases related to nanomaterials. The EC announced the launch of an impact assessment intended to identify and develop the most adequate means to increase transparency and ensure regulatory oversight on nanomaterials. The EC has provided a working document, which contains a draft problem definition, policy objectives, and a description of the preliminary policy options that are under consideration. The EC will update the working document over the course of the impact assessment. In support of the impact assessment, the EC is conducting a public consultation to obtain stakeholder views on the currently available information on nanomaterials on the market, the problem definition that forms the basis of the impact assessment, as well as the potential positive and/or negative impacts of the aforementioned policy options.

On May 2014, the Centre for International Environmental Law (CIEL) and its European partners published a position paper on the regulation of nanomaterials at a meeting of the EU Competent Authorities. According to the position paper, current EU legislation "does not guarantee that all nanomaterials on the market are safe by being assessed separately from the bulk form of the substance." The position paper asks the European Commission to produce "concrete proposals for a comprehensive revision of the existing legal framework addressing the potential risks of nanomaterials."

ECHA will hold a topical scientific workshop on October 23-24, 2014, on regulatory challenges in the risk assessment of nanomaterials. The workshop will bring together experts in the field of risk assessment of nanomaterials to discuss and update scientific principles and guidelines for assessing human health and environmental risks of chemicals substances in nano-form. According to ECHA, the workshop will also provide a platform for academia and regulators to address how the main long-term challenges from the regulatory perspective can be reflected and employed in the current and future research topics on nanomaterials.

Belgium announced that the Council of Ministers agreed on the royal decree concerning the marketing of substances containing nanomaterials. The royal decree creates a national register of nanomaterials, requiring manufacturers to register nanomaterial substances and mixtures containing such substances. It is claimed that the register will ensure the traceability of these nanoparticles. The register will open on January 1, 2016, for nanomaterial substances, and on January 1, 2017, for mixtures containing nanomaterial substances. Belgium states that it will evaluate the registration of products containing nanomaterials and that they will be recorded later.

4 METROLOGY TO SUPPORT NANOTECHNOLOGY RISK ASSESSMENT AND REGULATION



The ability to characterize nanoparticle hazard and exposure appropriately is essential for understanding the both the efficacy and potential risk associated with engineered nanomaterials interacting with human and environmental systems. A number of high profile reviews have acknowledged the importance nanometrology plays as an enabling technology, but have also identified significant gaps in the knowledge base relating to the characterization of hazardous properties of nanoparticles and the risks arising from them.

Whilst several of the reviews have explicitly pointed to the limitations in the characterization and measurement of nanoparticles for exposure and toxicological assessment, effort is being made towards establishing the prerequisites for toxicological studies such as identifying the key physical characteristics of nanoparticles, how to measure them, and the development of suitable reference materials. The REFNANO project[10], amongst others, has significantly advanced the debate in this area and research is underway both on the characterization of nanoparticles and the development of reference materials.

10. http://www.iom-support.co.uk/Portals/3/SN_Content/Documents/REF-NANOReport.pdf

Often it is the case that the quantity of interest cannot be measured directly (or completely) because of limitations in existing analytical methods. Moreover, no single technique provides adequate information to completely characterize and support the toxicity and risk assessment for any given material. Fibre-like aerosols present distinct challenges when characterized using many of today's routine measurement techniques that focus on spherical particles. Fibrous nanoparticles such as CNTs, nanorods and nanowires have an extreme shape (high aspect ratios), potentially distinct physical behavior in the lungs that differs substantially from many more compact particles, and may persist for long periods in the lungs following deposition. Although the toxic mechanisms associated with exposure remain unclear, it is known from asbestos that ill-health following exposure is associated with physicochemical properties such as fibre length and surface chemistry, and that the significance of these properties is exacerbated by persistence of the fibres in the lungs. As a result, exposure is not characterized in terms of averaged mass and composition, but rather by the number (concentration) of fibres in the air with a specific shape and composition.

To compound matters further, not all particles with the same 'apparent' composition have the same potential to cause harm and an understanding and control of the variability in the composition of batches is very important. The contribution that size, surface phenomena including reactivity and structure, and other key attributes make to the relative toxicity of particles remains to be fully elucidated. The limited but increasing number of published quantitative data on nanomaterials including fullerenes and metal oxides support the need to consider carefully how nanomaterials are characterized when evaluating biological activity. The range of approaches and methods used to study the effects of engineered nanomaterials has led to different results. This inconsistency indicates the need for standardized approaches to comparable studies that facilitate the collection of information to allow retrospective interpretation of toxicity data in the light of new findings.

In order to develop appropriate strategies for characterization, it is important to consider the purpose(s) for which the data collected are to be used, the context(s) within which (and possibly across which) a material is being evaluated, the importance of measuring a specific parameter within that context, and the feasibility of measuring the parameter within a specific context. Nanoparticle characterization plays an essential role in a variety of overlapping contexts ranging from fundamental and applied research, through process and product commercialization, to health and environmental protection. The debate on the characterization requirements for nanotoxicology and risk assessment is frequently expressed in the contexts of i) as-supplied nanoparticles, ii) administered nanoparticles, and iii) human exposure. The attributes potentially associated with mechanisms leading to nanoparticle toxicity likely to be of significance across a range of particle and material types, adapted from the ILSI Nanomaterial Toxicity Screening Working Group[11], are compiled below:

ATTRIBUTE	CHARACTERISATION CONTEXT			
	AS SUPPLIED	ADMINISTERED	IN VITRO / IN VIVO (AFTER-ADMINISTRATION)	HUMAN EXPOSURE
Size distribution	Essential	Valuable, but complex or costly	Essential	Essential
Surface area	Essential	Valuable, but complex or costly	Valuable	Valuable, but complex or costly
Shape	Essential	Valuable	Valuable	Valuable, but complex or costly
Chemical composition / purity	Essential	Valuable	Valuable	Essential
Surface contamination	No significant value	Valuable, but complex or costly	No significant value	Valuable, but complex or costly
Heterogeneity	Essential	Essential	Valuable, but complex or costly	Valuable, but complex or costly
Surface chemistry	Essential	Valuable, but complex or costly	Valuable, but may be complex or costly	Valuable, but complex or costly
Charge (in suspension / solution)	Essential	Essential	Valuable	Valuable
Agglomeration state	Not significant	Essential	Valuable, but complex or costly	Essential
Crystal structure	Essential	Valuable	Valuable	Valuable
Porosity	Valuable, but complex or costly	No significant value	No significant value	Valuable, but complex or costly

There is consensus across the scientific community that attributes associated with particle size, surface phenomena, composition and shape play some role in the particle interactions and nanometrology developments to appropriately characterize these attributes are needed.

The implementation of reliable findings from experimental studies into regulatory frameworks with the desired objective of protecting human and environmental health is also subject to the limitations of inadequately characterized materials and the complexity of mixtures of particles in 'real world' exposures. The current paucity of information on the potential effects of nanomaterials on human health and the environment may be leading to inappropriate control procedures being implemented. The absence of a reliable evidence-base that considers the relative contributions from engineered, combustion, and natural nanoparticles, hinders progress in the consideration of whether specific regulation of nanomaterials is required, whilst the lack of sufficient information and knowledge available on toxicological hazards and appropriate exposure limits makes it difficult to provide relevant data in safety advice and undertake necessary risk assessments to protect workers, consumers and the environment at all stages in the life cycle of the material.

11. Oberdörster G, Maynard A, Donaldson K, Castranova V, Fitzpatrick J, Ausman K, Carter J, Karn B, Kreyling W, Lai D, Olin S, Monteiro-Riviere N, Warheit D, and Yang H. Principles for characterising the potential human health effects from exposure to nanomaterials: elements of a screening strategy. Part. Fiber Toxicol. 2005, 2(8): doi:10.1186/1743-8977-2-8.

Set against these contexts, a number of metrology challenges have been identified and stated in various publications and reports, including:

- development of the metrics of surface properties; area, reactivity, topography, charge, and chemical composition;
- capability to characterize and detect nanoparticles across a variety of biological and environmental media;
- characterization of agglomeration and aggregation in terms of size and stability as a function of time and local environmental and biological conditions;
- capability to differentiate routinely the shape and aspect-ratio of particles in mixtures, particularly the discrimination between fibre-like and non-fibre-like nanoparticles;
- discrimination between target (e.g. engineered) and background nanoparticles;
- simultaneous measurement of multiple metrics of the same target in a variety of biological and environmental media;
- development of 'indices' that combine key multiple metrics to give an online rapid characterization of the nanomaterial.

There is significant international research effort underway to address these issues and it is therefore prudent for Brazilian researchers to integrate with relevant networks and ongoing activities to be able to contribute and exploit the outcomes of the effort.

Moreover, as the capability in nanometrology and its application in supporting the responsible commercialization and use of nanotechnologies develops, it is evident that there will be a degree of overlap in the benefits this brings to the manufacturing, scientific and regulatory communities in Brazil.

5 STANDARDIZATION ACTIVITY

Standardization activities in the field are taking place both at the international level and in many countries, involving a broad range of interests and organizations. At the forefront of these activities is the International Organization for Standardization (ISO). The area of measurement and characterization has a fundamental supporting role in nanotechnology development. In particular, there is a pressing need for the development, validation and approval of standardized methods for physico-chemical characterization of manufactured nanomaterials to support (eco) toxicology testing.

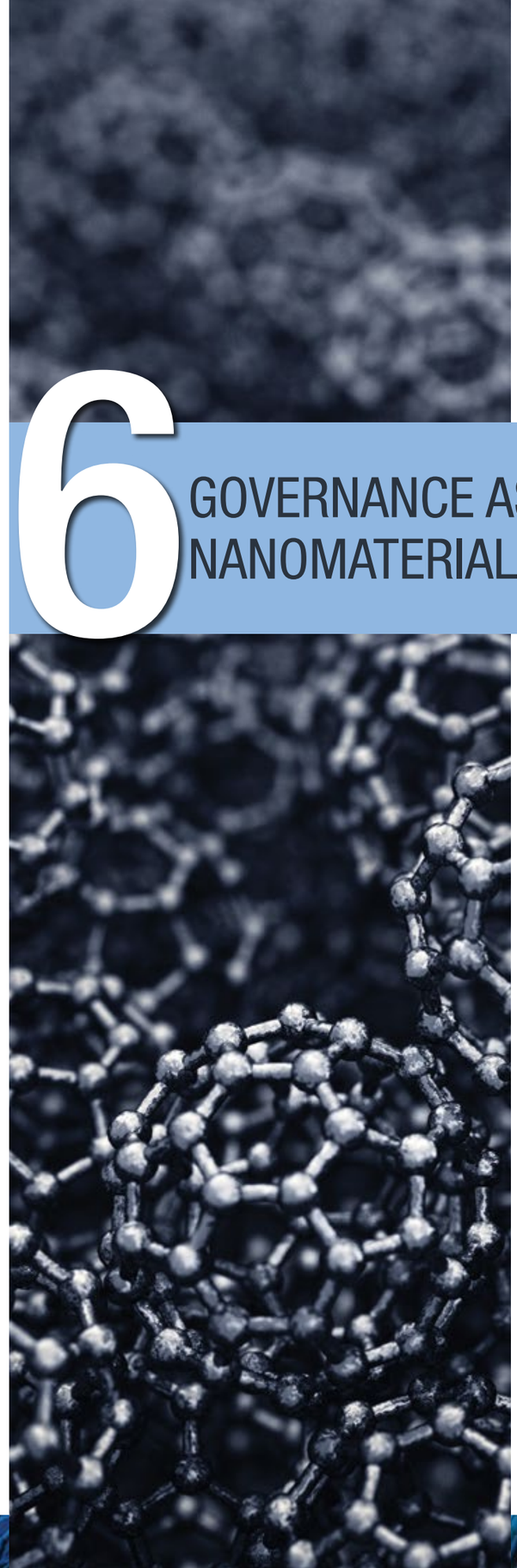
Within ISO, current standardization activities specifically related to nanotechnologies are led by TC229[12], with Working Group 2 (WG2) focusing on measurement, characterization and test methods. TC229/WG2 began its activity by giving higher priority to characterization relating to industrial application (i.e. focusing on purity and quality assurance standards), and developing standards for carbon nanomaterials (especially carbon nanotubes) in particular. However, recent activity is evident on toxicology-related characterization

12. http://www.iso.org/iso/iso_technical_committee?commid=381983

and standardization for potential risk assessment of nanomaterials, in order to address growing concerns in this area.

As an example, ISO has published two standards relevant to toxicity testing: ISO/TR 16197:2014 – Nanotechnologies – Compilation and description of toxicological screening methods for manufactured nanomaterials; and ISO/TS 16550:2014 – Nanotechnologies – Determination of silver nanoparticles potency by release of muramic acid from Staphylococcus aureus. ISO/TR 16197 is a Technical Report that provides a compilation and description of in vitro and in vivo methods that can be useful for the toxicological, including ecotoxicological, screening of engineered and manufactured nanomaterials. Rather than replace or compete with existing regulatory requirements, it is intended to complement other international efforts that address nanomaterial toxicology by focusing on screening methods used for preliminary assessment. ISO/TS 27687:2008 and ISO/TS 80004-1 are said to be indispensable for application of this new standard. ISO/TS 16550 is a Technical Specification that provides a test method for evaluating potency of silver nanoparticles to cell wall degradation of Staphylococcus aureus. This standard was seen as necessary as 'the antimicrobial properties of silver nanoparticles are being increasingly utilized in consumer products and industries are producing wide varieties of silver nanoparticles with little concern to their side effects.

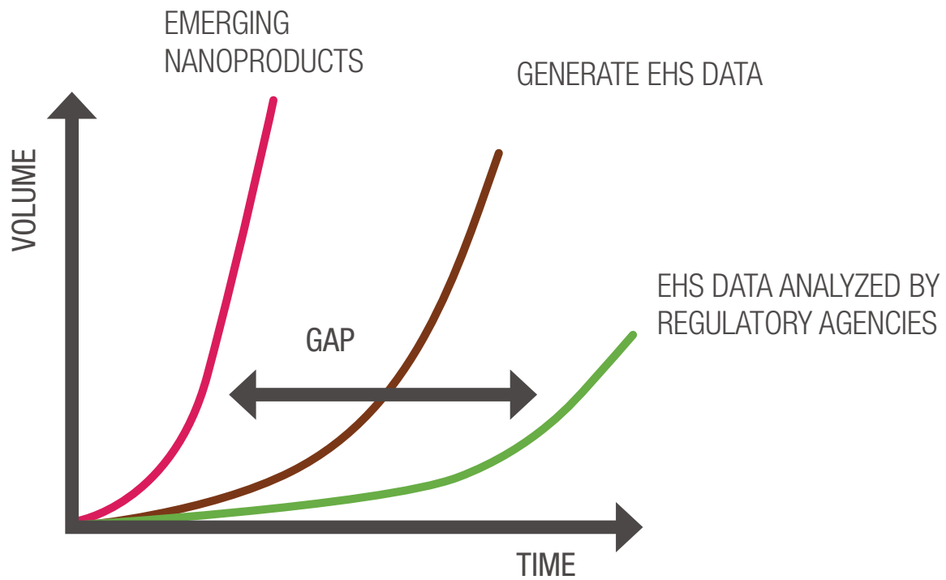
All published standards and standards under development from ISO in the areas of nanomaterials characterization and testing can be seen on the ISO website.



6 GOVERNANCE AS PRELUDE TO NANOMATERIALS REGULATION

Over the last five years or so, the development and commercialization of nano-enabled products has occurred at an increasingly rapid pace. However, knowledge about "nanotechnology-induced change" with respect to potential safety, ethical, legal and societal issues, and the development of governance approaches for nanotechnologies, lags behind. Studies by the Project on Emerging Nanotechnologies[13] and Hansen et al.[14] have found that the emergence of nano-enabled products has occurred much faster than the generation of corresponding EHS data, depicted qualitatively in the figure below (reproduced from Linkov et al.9).

13. http://www.nanotechproject.org/
14. Hansen, S. F. et al. Categorization framework to aid exposure assessment of nanomaterials in consumer products. Ecotoxicology 17, 438-447, (2008).



Linkov et al.9 suggested that this is partly related to the inherent challenges in the research underpinning EHS data generation for nanomaterials (e.g. need for new analytical approaches, the requirement of standards for testing, and the adaptation of existing test methods for nanomaterials), but also that there is currently a lag between the time EHS data is available and the time when regulatory agencies use this data due: i) to limited resources and; ii) the time required to potentially adapt risk assessment procedures for application to nanomaterials.

Uncertainty regarding whether the established regulatory systems are actually capable of adequately handling nanotechnologies and nano-enabled products within their frameworks has been highlighted, and the policies and regulatory approaches across various countries largely remain fragmented. It is feared that nanotechnologies may cause EHS impacts before appropriate strategies based on quantitative risk assessment can be implemented. This may explain calls for implementation of a precautionary approach to the regulation of nanotechnologies, with the view to avoid such a situation and also prevent public backlash. In any case, numerous stakeholders have emphasised the need for regulatory approaches for nanotechnologies to be flexible, adaptable and dynamic in light of the anticipated emergence of new knowledge and understanding regarding the potential impacts of nanotechnologies.

Apenas há pouco tempo que os especialistas It is only relatively recently that experts have started to consider how the regulatory and promotion aspects of innovation might be better integrated. Risk governance is traditionally concerned with minimising the risks of harmful effects and is thus a back-end response to innovation. Conversely, innovation governance is aimed at purposefully influencing technological choices, such that innovation is directed to socially agreed purposes, benefits and priorities. Building trust and confidence among all stakeholders, including the public, is considered to be essential to gain acceptance and ensure continued development of a new technology. Trust and confidence cannot be created at will, however, and are the result of stakeholder perceptions deriving from an effective governance system and recognised trustworthiness bestowed by stakeholders. There have been calls for an inclusive governance approach, which facilitates stakeholder dialogue and stakeholder involvement. An effective and integrated governance approach must facilitate the realisation of benefits (focussed around meeting societal goals, not just economic competitiveness), whilst at the same time limiting the potential risks posed and remaining sensitive to public concerns and changes nanotechnologies may induce. Whilst open and transparent discussion and stakeholder involvement is acknowledged as a vital part of the governance process, it is important to note, however, that stakeholder engagement will not necessarily deliver consensus, as has been demonstrated with the genetically modified foods case. Indeed, consensus around value-laden issues among diverse populations is a most unlikely outcome. Ensuring the safe and sustainable development of nanotechnologies is widely agreed to be essential, and an effective governance approach would ideally enable a safe, sustainable and society-focused technology to be developed, without stifling innovation – indeed, safety, sustainability and meeting societal goals could be the source of innovation; providing stimulus to innovation for specific purposes. This presents a challenge, however, given the potential lag time between the generation of knowledge on the potential environment, health and safety risks of nanomaterials and the pace of commercialization of nano-enabled products. The resulting uncertainties are considered by some to be a major barrier to the sustainable and responsible development of nanotechnologies in the long term. A crucial pre-requisite for governance of emerging technologies, is reliable information about the network of agents that are involved. In addition, to support governance there is a clear need to develop and nurture relationships between members of the actor network to ensure strong risk communication along the value chain. Effective governance will require a high level of cooperation, coordination and communication between various institutions and stakeholders, including those who develop, manufacture, market and regulate nano-enabled products, as well as representatives of civil society, in order to promote a proactive and adaptive process. Orientating research and development towards Grand Challenges is therefore a critical strategy in ensuring sustainable development as a key outcome of scientific advances and technological development.

Given the anticipated increase in complexity and significant technical and social uncertainties of future generations of nanotechnologies, many stakeholders have highlighted the need for a more anticipatory approach to nanotechnology governance. Such an approach would act to anticipate and realize future developments, whilst also identifying and reacting to potential risks. However, an anticipatory approach to governance faces significant challenges, notably in terms of the necessary scale and support, organization and engagement of stakeholders from the serendipity of innovation processes and outcomes and a limited ability to anticipate. Nevertheless, such an approach could have the benefit of 'futureproofing' the consideration of risks and uncertainties in the diverse range of themes in nanoscience and nanotechnologies and as future generations of nanomaterials and applications emerge.

ACCREDITATION SCHEMES FOR NANOTECHNOLOGY SAFETY PRACTICES

Currently, three risk management frameworks/ systems (Nano Risk Framework, CENARIOS® and AssuredNano™) have been identified that are considered to facilitate the use of best available knowledge and technology, flexibility and versatility, and provide sufficient means/ detail for implementing and demonstrating safe practices as part of the responsible development of nanotechnology.

NANO RISK FRAMEWORK[15]

The Nano Risk Framework was published in June 2007 and outlines a proposal for a comprehensive, practical, and flexible framework to evaluate and address the potential risks of nanomaterials. It is intended to help users organize and evaluate what they already know; assess, prioritize and address data needs; and communicate clearly how they are mitigating risks related to nanotechnology.

The Framework is intended as a practical guide for use both on its own and as a supplement to existing product stewardship processes for the responsible development of nanomaterials. The Framework establishes a systematic and disciplined process for product developers to identify and reduce potential risks. It is intended that companies could adopt the Framework and its guiding principles as part of their product stewardship programmes.

The Framework is based upon traditional risk management elements, with the incorporation of several additional new or atypical elements. For example, it recommends developing informational profiles (or "base sets") — regarding the properties, hazards, and exposures associated with a given nanomaterial and its application — for evaluating risks and guiding decisions. In particular, the Framework recommends developing lifecycle profiles that provide more information on physical-chemical properties, ecotoxicity, and environmental fate than has typically been the case in traditional risk management profiles.

The Framework is designed to be flexible, but that flexibility comes with an obligation for users to be transparent and accountable in its implementation. Toward that end, the Framework serves as a tool to organize, document, and communicate what information the user has about the material; to acknowledge where information is incomplete; to explain how information gaps were addressed; and to justify the rationale behind the user's risk management decisions and actions.

The framework consists of six distinct steps:

Step 1. Describe Material and Application.
Develop a general description of the nanomaterial and its intended uses, based on information in the possession of the developer or in the literature.

Step 2. Profile Lifecycle(s):
Defines a process to develop three sets of profiles. Identify and characterize: 1) the nanomaterial's physicochemical properties, 2) potential safety, health, and environmental hazards, and 3) associated human or environmental exposures throughout the material's lifecycle (intended use or accidental release). The user must take into account the nanomaterial's full lifecycle and consider how the material's properties, hazards, and exposures may change.

Step 3. Evaluate Risks.
Review all the information generated in the profiles in order to identify and characterise the nature, magnitude, and probability of risks presented by this particular nanomaterial and its anticipated application.

Step 4. Assess Risk Management.
Evaluate the available options for managing the risks identified in Step 3 and recommend a course of action.

Step 5. Decide, Document, and Act.
Consult with the appropriate review team and decide whether or in what capacity to continue development and production. Consistent with a transparent decision-making process, document those decisions and their rationale and share appropriate information with the relevant stakeholders. The user may also decide that further information is needed and initiate action to gather it.

Step 6. Review and Adapt
Through regularly scheduled reviews as well as triggered reviews, update and re-execute the risk evaluation, ensure that risk management systems are working as expected, and adapt those systems in the face of new information (e.g., regarding hazard data) or new conditions (such as new or altered exposure patterns).

The framework is designed for iterative use as development advances and new information becomes available. It includes an output worksheet which is intended to facilitate evaluation, management, and communication. The worksheet provides a template for organizing all the information requested by the framework, capturing overall evaluations of that information, and recording consequent decisions.

DuPont has also conducted and published three case studies in order to evaluate the Nano Risk Framework for three different materials, available on the Nano Risk Framework website.

CENARIOS®[16]

The Innovation Society, in cooperation with TÜV SÜD Industry Service (Munich), developed in 2008 CENARIOS®: a certifiable risk management and monitoring system to cater to the specific needs of nanotechnology risk assessment.70

The CENARIOS® risk management system was especially developed to enable objective risk assessment in the nanotechnology sector which is a rapidly developing market characterized by a high level of uncertainty. It covers the risks associated with the design and development, production and use of nanotechnology products and focuses on the following risk categories:

- HSE Risks: Risks for staff producing and handling nanotechnology products (occupational health and safety), both at the producers of basic nanomaterials and at the companies which use and further process these nanomaterials;
- Production-related risks for the surroundings of the company and the environment;
- Consumer risks resulting from the use of nanotechnology products which may affect company staff, users and third parties.

15. http://www.nanoriskframework.com/

16. http://www.tuev-sued.de/uploads/images/1219824286015340810363/CENARIOS_Zertifiziergrundlage_e.pdf

Certification according to this standard is restricted to the above risks and does not cover any other risks which must also be considered by companies, such as investment risks, liability risks and risks resulting from changes in legal or social framework conditions and/or corporate mismanagement. Periodic certification ensures adaptation of the system to state-of-the-art science and technology.

The CENARIOS® risk management and monitoring system comprises four modules that can be combined individually:

- Risk Assessment / Risk Evaluation: This module identifies the current product and process-related risk inventory;
- 360°-Risk Monitoring System: As foresight instrument, focusing the relevant trends in science, regulation and technology;
- Issues Management & Communication: Including tools for rapid and safe crisis management;
- Certification: By opting for certification, you ensure optimization of your internal coordination processes and continuous improvement of risk management.

The certification standard defines the general requirements applicable to such a product-specific risk management system and is a generally applicable document for the assessment and certification of all risk management processes based on the CENARIOS® standard. It describes the requirements, in particular staff and organizational requirements that companies must satisfy when they implement a risk management system. Further key elements of the CENARIOS® standard are the criteria related to the assessment and treatment of risks.

The CENARIOS® standard consists of the following parts:

A. General Requirements, Scope, Procedure, Documentation;

B. Staff-Related Requirements;

C. Organizational Requirements;

D. Risk Assessment and Monitoring Requirements;

E. Requirements Related to Risk Treatment and Risk Communication.

The organization has published several risk and innovation management strategies. Specifically related to nanomaterials are the NanoRisk Check [17] and 360° Risk - Monitoring.[18]

ASSUREDNANO™

AssuredNano™ is a comprehensive nanomaterial safety accreditation scheme featuring annual compliance auditing. It was developed in 2008 to overcome the obstacles to nanomaterial commercialization resulting from safety, health and environmental (SHE) concerns. AssuredNano™ offers a way for responsible manufacturers to address nanomaterial SHE concerns based upon the use of good current practice. In so doing, it provides a demonstration to all stakeholders in nanomaterials and nanotechnology that SHE issues are being taken seriously and tackled responsibly and that the health and safety of people exposed to nanomaterials or nano-enabled products will be ensured. Most importantly, AssuredNano™ is designed by industry experienced SHE experts to deliver a common sense and realistic approach to nanomaterial SHE.

It is expected that successfully accredited organizations will wish to demonstrate their status to their stakeholders and in particular their supply chain partners. It is probable that successfully accredited organizations will wish to encourage their suppliers and customers to also accredit in order to assure their in-bound and out-bound processes and reinforce the commitment to nanomaterial SHE throughout a supply chain.

The AssuredNano™ Accreditation Scheme is all-embracing, covering all facets of a nanomaterial or nano-enabled product's life including:

- Management of manufacturing risk and exposure;
- Loss of containment;
- Packaging and transportation;
- Life cycle analysis;
- Disposal or recycle.

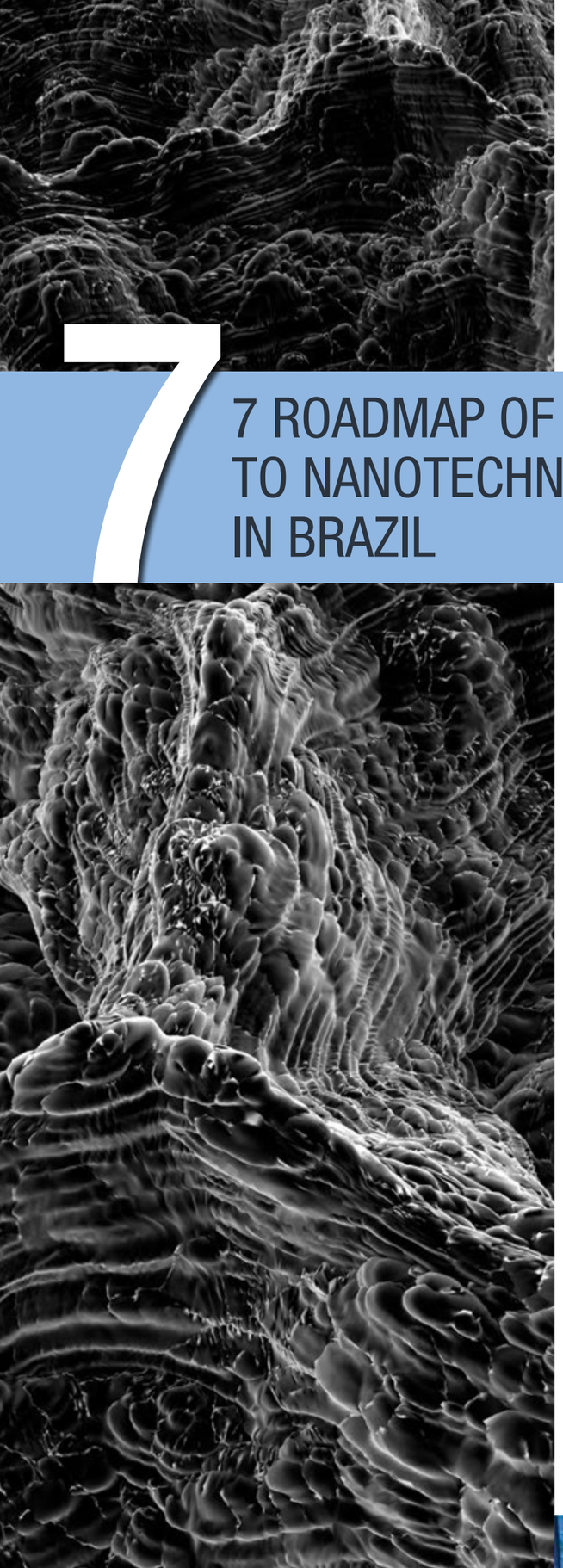
The AssuredNano™ Accreditation Scheme is annually audited for compliance demonstrating not only adherence to SHE good current practice, but also a commitment to continuous SHE improvement, reflecting progressively evolving nanomaterial SHE knowledge. Success in the rigorous annual audit is not however a given, the credibility of the AssuredNano™ scheme will be maintained by the power to de-register organizations which cease to demonstrate adequate compliance with the audit protocol.

INTEGRATED NANO-SCIENCE AND COMMODITY EXCHANGE (INSCX)[19]

A new and evolving initiative that is pertinent to the international regulation of nanomaterials is the commercial trading of nanomaterials via a commodity exchange platform, which provides a centralized market allowing for full transparent listing and certification of quality and compliance requirements is being developed. The Exchange is designed to provide tools for insurers and regulatory agencies to work with and a low-cost entry for producer/downstream user participation. The Exchange system establishes conformity to specification as a condition of each individual trade, providing proof of trade unique to the nanomaterial specification in real-time and the ability to sequence and/or reverse audit.

Where regulatory structures continue to evolve, the Exchange operates self-regulatory rules governing supply of nanomaterials and/or variants. The rulebook is designed to support ongoing legislative regulatory structures safeguarding commercial, but also societal interest. The Exchange Trade reporting system, Downstream Audit Sequencing (DAS) for example, delivers a comprehensive Track/Trace capability in the sale/use of nanomaterials in a manner which safeguards commercial confidences while delivering the capability to target Lifecycle analysis. Producers can also task the Exchange to act as their Substance Information Exchange Forum (SIEF) only representative where compliance with the REACH Regulation in Europe is required.

17. http://innovationsgesellschaft.ch/en/kompetenzen/risikomanagement/nanorisk-check/
18. http://innovationsgesellschaft.ch/en/kompetenzen/risikomanagement/360-risiko-monitoring/
19. http://inscx.com/



7 ROADMAP OF ACTIONS RELATED TO NANOTECHNOLOGY REGULATION IN BRAZIL

In view of the analyses of the National Strategic Laboratory, Associated Laboratory and Networks in nanotechnology related to the NanoDialogues Programme, the following recommendations are made:

1. Establish a sustainable means of engagement with the European NanoSafety Cluster, to facilitate dialogue with the coordinators of current and future projects contributing to goals and specific objectives relevant to Brazil. This may be achieved by establishing a designated liaison with the NanoSafety Cluster and/or specific project coordinators.

2. Continue and enhance Brazil's engagement with relevant OECD and ISO activities.

3. For industry and research organizations, consideration should be given to engaging with relevant accreditation / certification schemes or to developing a governance programme, both in the intervening period whilst a regulatory system is developed and subsequently.

4. It is suggested that consideration be given to developing a regulatory databank, via consideration of a specification to identify the information relevant to reference scientifically the processes of characterization, safety evaluation, certification and regulation of nanotechnology and products being created from this technology from Brazil. This can consider similar databanks and information systems developed in other jurisdictions, including the European Union.

5. Regarding the Brazilian contribution into the EU NANoREG project, after considerations of the capabilities presented at the national meeting in Brasilia it is suggested that principal responsibilities be placed mainly with the National Strategic Laboratories that are independent of the Universities. Involvement of Brazil's established government / private institutions are considered critical to supporting the development of possible regulation, for example Brazil's nanometrology institute (INMETRO, RJ), LNNano (CNPEM-SP) and LNNA (EMBRAPA). The Associated Laboratories from SisNANO should support the actions of these centers (e.g. NanoBioss-IQ-UNICAMP), together with the Nanotoxicological Networks (e.g. Nanotox-INMETRO, Nanotox-USP).

Recommendations for the engagement of Brazilian institutions in the NANoREG project:

a) Contribute to tasks already defined in the DoW for WP2 (Synthesis, supplying and characterization):

i. establish a suite of both commercial and tailored high-quality NM test materials;

ii. develop and adopt Standard Operating Procedures (SOPs) for analyzing the size-distribution and Volume-Specific Surface Area (VSSA) of NM in powders and complex viscous matrices;

iii. validate "generic" or "test specific" dispersion protocols (for characterization and toxicological testing);

iv. validate methods for quantitative characterization of the exposure and dose rate for NMs in air and liquids dispersions;

v. develop recommendations for NMs analysis and categorization considering the wide range of NMs and chemical derivatives.

Involvement in these activities is considered possible at INMETRO (DIMAT and LABIO) and at LNNano (CNPEM) and should include:

- characterising 'old' and 'new' batches of NMs (including BET, microscopy, x-ray diffraction, endotoxin test, bulk chemicals, VSSA round robin, TEM protocol);
- OECD Guidelines appraisal;
- strengthening test methods for number size distribution and VSSA.

b) Contribute to tasks already defined in the DoW for WP4 (Biokinetics and toxicity testing in vivo):

i. acute and repeated nose-only inhalation toxicity study;

ii. escalation dose pharmacokinetic study;

iii. in vivo genotoxicity of NM;

iv. prenatal toxicity study;

v. repeated-dose 90-day oral toxicity study;

vi. biological effects of inhalation of HARN in rats;

vii. chronic & carcinogenicity testing of GBP nanomaterials;

viii. biokinetics and toxicity in aquatic organisms:

√ eco toxicity;

√ fate and transformation of NMs along the lifecycle.

Involvement in these activities is considered important for Brazil. INMETRO and NanoBioss (associated to LNNano and the Microbiology Department at UFMG - Prof. Ary Correa Jr.) are considered able to do contribute to these activities through:

- in vivo genotoxicity of NM;
- repeated-dose 90-day oral toxicity studies;
- biokinetics and toxicity studies in aquatic organisms.

c) Contribute to tasks already defined in the DoW for WP5 (Advancement of Regulatory Risk Assessment and Testing):

i. similarities and extrapolation (grouping in categories with similar biological, ecological and/or toxicological effects);

ii. stability and elimination: developing solubility testing procedures;

iii. studying the relevance of barriers;

iv. inhalation toxicity modelling in vitro (identification of suitable in vitro models to assess inhalation toxicity);

v. in vitro toxicity assays (evaluate suitability of standard in vitro assays as compare to in vivo experimentation);

vi. rapid high throughput screening methodology;

vii. decision tree for risk assessment (based on results from other tasks):
- estabelecimento dos "nós" de uma árvore de decisão para análise de risco;

i. establishing the 'nodes' of a risk assessment decision tree;

ii. high throughput screening (HTS), validation of alternative tests, creation of SOPs.

It is considered likely that the only activities that can be contributed to in Brazil are i) the development of solubility testing procedures and ii) in vitro toxicity assays, by validation of alternative tests and creation of SOPs. INMETRO (LABIO) and NanoBioss (associated to LNNano) are considered able to engage in these activities.

d) Utilize results from WP6 (Keeping pace with innovation (safe by design)):

i. linking risk analysis with innovation;

ii. safe by design: lessons learned from drugs;

iii. practical approaches and examples.

Given the recent announcement of ANVISA regarding the creation of an Internal Committee of Nanotechnology (CIN) to coordinate institutional efforts to strengthen the control of nanotechnology products used in human health, these NANoREG activities may be anticipated to provide Brazilian regulatory agencies (ANVISA, etc.) and industry (NanoBusiness Informação e Inovação Ltda., ABIHPEC (+ ITEHPEC), etc.) with valuable results, with special emphasis on SOPs and Standards.

e) Utilize results from WP3 (Exposure through life cycle analysis):

i. identification and elaboration of exposure scenarios (workplace, consumer, environment)

ii. release of NM

iii. measurement of exposure

iv. exposure modelling

v. effectiveness of risk management measures including Personal Protection Equipment

√ exposure measurement: environment as well as workplace, including background exposure

It is considered that engagement with this workpackage will, at the present time, be difficult for any center in Brazil. It is suggested that EMBRAPA may consider the topic in the context of exposure through agricultural processes.

In order to implement the abovementioned engagement (for an anticipated start of 1 January 2015), the following actions by MCTI are necessary:

1) Preparation of a draft Collaboration Agreement (for subsequent approval and acceptance by NANoREG), defining:

- roles and responsibilities of the Brazilian coordinator;
- expected activity contributions from Brazil (as per the Brazilian Workplan suggested below);
- provisions for access to data;
- Confidentiality / non-disclosure requirements.

2) Preparation of a Brazilian NANoREG Workplan, detailing the expected contributions of Brazilian partners. Critically, it is recommended that this is developed giving cognizance to i) Brazilian priorities, ii) progress made in the NANoREG project and refinement of the research questions being addressed, to inform the prioritization of Brazilian activities.

3) Adoption of an agreed and approved Guidance Document (i.e. protocols defining the minimum requirements for measurement and characterization), and engagement with relevant NANoREG Workpackage Leaders.

APPENDIX 1: BRAZIL'S NANOTECHNOLOGY LABORATORY & NETWORK INFRASTRUCTURE

Brazil has sixteen National Institutes for Science and Technology (INCTs) created by the Ministry of Science and Technology in 2008:

1. NanoBiostructures and NanoBioMolecular Simulation (NanoBioestruturas e Simulação NanoBioMolecular) (UFC).

2. Pharmaceutical Innovation (Inovação Farmacêutica) (UFPE).

3. Photonic (Fotônica) (UFPE).

4. Nanotechnology for Integrated Labels (Nanotecnologia para Marcadores Integrados) (UFPE).

5. Nanobiotechnology at West and North Center (Nanobiotecnologia do Centro Oeste e Norte) (UnB).

6. Carbon Nanomaterials (Nanomateriais de Carbono) (UFMG).

7. Nano Biopharmaceuticals (Nano Biofarmacêutico) (UFMG).

8. Material Sciences in Nanotechnology (Ciência dos Materiais em Nanotecnologia) (UNESP).

9. Semiconductors Nanodevices (Nanodispositivos Semicondutores) (PUC/RJ).

10. Organic Electronics (Eletrônica Orgânica) (USP).

11. Optics and Photonics (Óptica e Fotônica) (USP).

12. Photonics for Optical Communication (Fotônica para Comunicação Óptica) (UNICAMP).

13. Functional Complex Materials (Materiais Complexos Funcionais) (UNICAMP).

14. Micro and Nanoelectronics Systems (Sistemas Micro e Nanoeletrônicos) (UNICAMP).

15. Nanostructures (Nanoestruturados) (UFSC).

16. Surface Engineering (Engenharia de Superfície) (UFRGS).

At the same time, the following six Nanotoxicology Networks were created in order to evaluate nanomaterials safety, and provide support for regulation items:

1. Aquatic Nanotechnology Network (Rede de Nanotoxicologia Aquática do Centro-Oeste (UnB).

2. Nanotoxicology of Nanostructured Compounds: Cytotoxicity, Genotoxicity of Industrial Potential Products (Rede de Nanotoxicologia de Compostos Nanoestruturados: Citotoxicidade e Genotoxicidade de Produtos com Potencial Industrial (CIGENANOTOX) (UNICAMP).

3. Cooperative Research on Nanotoxicology Applied to Nanoparticles in Petroleum and Inks Industries Network (Rede Cooperativa de Pesquisas em Nanotoxicologia Aplicada a Nanopartículas de Interesse da Indústria Petrolífera e de Tintas) (UFSC).

4. Occupational and Environmental Nanotoxicology: Scientific Support for Regulatory Framework and Risk Evaluations (Nanotoxicologia Ocupacional e Ambiental: Subsídios Científicos para Estabelecer Marcos Regulatórios e Avaliação de Riscos) (FURG).

5. Toxicity Evaluation of Nanomaterials Applied to Medicine and Agriculture: development of in vitro, in vivo and membrane model studies (Avaliação da Toxicidade de Nanomateriais Aplicados em Medicina e Agricultura: Desenvolvimento de Estudos in vivo, in vitro e em Modelos de Membrana) (USP).

6. Nanoparticles Toxicity in Biological Systems: Production of Reference Materials, Development of Normalized Methods for Physico-Chemical Characteristics and Interactions of Nanoparticles with Cells and Tissues (Toxicidade de Nanopartículas em Sistemas Biológicos: Produção de Material de Referência, Desenvolvimento de Métodos Normalizados para Caracterização Físico-química e Estudo das Interações de Nanopartículas com Células e Tecidos) (REDE NANOTOX) (INMETRO).

Complementing the six Nanotoxicology Networks two Instrumental Networks were created:

1. Brazilian Research Network on Optical Nanospectroscopy Instrumentation (Rede Brasileira de Pesquisa e Instrumentação em NanoEspectroscopia Óptica) (UFMG)

2. Integrated Cooperative Research in Instrumentation: Technological Scaffold for New components manufacture, Systems and Instruments based on new nanostrctured materials (Rede Cooperativa Integrada de Pesquisa em Nanoinstrumentação: Plataforma Tecnológica para Fabricação de Novos Componentes, Sistemas e Instrumentos Baseados em Materiais Nanoestruturados) (UNICAMP).

After this development, an initiative from the Brazilian Government created the National Associated Laboratories in Nanotechnology (SisNano Programme) in 2012.

A further eight Strategic Laboratories were created under the SisNano Programme:

1. Multiuser Laboratory of Nanosciences and Nanotechnologies (Laboratorio Multiusuario de Nanociencias e Nanotecnologia) (LABNANO) (CBPF).
Nanomanufacture, materials and devices, MEMS and NEMS and nanostructure characterization.

2. Chemical laboratory in Carbon Nanostructures (LQN) (CDTN).
Production of graphene and post-synthesis manipulation of carbon nanotubes.

3. Multiuser Nanotechnology Laboratory (Laboratorio Multiusuario de Nanotecnologia) (LMNano) (CETENE).
Nanomagnetismo, espectroscopia aplicada a produtos farmacêuticos e nanomateriais, ligas metáli-
Nanomagnetism, spectroscopy applied to pharmaceuticals and nanomaterials, metallic alloys, nanos-tructured carriers applied to cosmetics and pharmaceuticals, sensors, nanostructured materials and nanobiotechnology.

4. National Nanotechnology Laboratory (Laboratorio Nacional de Nanotecnologia) (LNNano) (CNPEM).
Advanced processing of nanometals, semiconductors membrane, nanoneedles and nanoparticles, nanosensors, and devices, nanobiotechnology, characterization of materials.

5. Nanotechnology Laboratory for Agribusiness (Laborátorio de Nanotecnologia para o Agronegócio) (LNNA) (EMBRAPA).
Characterization and production of materials of interest in agribusiness.

6. Characterization Center in Nanotechnology for Materials and Catalysis (Centro de Caracterização em Nanotecnologia para Materiais e Catalise) (CENANO) (INT).
Synthesis, processing and characterization of nanoparticles and nanostructures.

7. Nanometrology Strategic Laboratory (Laboratório Estratégico de Nanometrologia) (INMETRO).
Nanometrology and characterization of material properties.

8. Integrated Nanotechnology Laboratory (Laboratório Integrado de Nanotecnologia (LIN) – IPEN.
Nano-structuring of materials and characterization of nanostructures and their raw materials.

AND EIGHTEEN ASSOCIATED LABORATORIES WERE CREATED UNDER THE SISNANO PROGRAMME:

1. Regional Nanotechnology Laboratory (Laboratório Regional de Nanotecnologia) (LRNANO) (UFRGS).
Nanomaterials: Fabrication, characterization and applications of materials in the nanometric scale (Chemistry, Physics, Engineering, Geosciences and Biosciences). Nanobiotecnology: Applications of nanomaterials to fabricate and characterize systems with potential application in therapeutics (human and animal health) and diagnostics (analysis and imaging). Nanoelectronics: Projects, characterization, simulation and use of nanometric-sized circuits for electronic systems.

2. Characterization Center and Development of Protocols for Nanotechnology (Centro de Caracterização e Desenvolvimento de Protocolos para Nanotecnologia) (CCDPN) (UNESP).
The Center aims to promote integration between the university and business, as well as encourage the formation of spin-off companies, providing advanced tools for characterization of nanomaterials. Its main focus is on characterization by SEM, TEM and AFM, as well as providing services to other techniques and the development of nanomaterials (synthesis and characterization).

3. Analytical and Microscopy Center (Electronic and Optics) of Ceara University (Central Analítica em Técnicas de Microscopia (Eletrônica e óptica) da Universidade Federal do Ceará) (UFC).
Provide infrastructure and analytical and microscopy techniques (electronic and optical), with the aim of enabling, enhancing, and promoting scientific and technological research in UFC and other research institutions, integrating with teaching at an undergraduate and post-graduate level, and to provide support to the productive sector.

4. Nanostructures Synthesis and Interaction with Biosystems (Laboratório de Síntese de Nanoestrutura e Interação com Biossistemas (NANOBIOSS) (UNICAMP).
Contribute to the development of basic science connected to a prospective purposeful action and the generation of knowledge related to applied research and its transfer to the national productive sector. Synthesis of various nanomaterials and studying their impact on man and the environment, from the perspective of risk assessment of nanotechnologies.

5. Structural Characterization Laboratory (Laboratório de Caracterização Estrutural (LCE) (UFSCar).
Provide facilities for high-level structural characterization and scientific support for the academic and industrial communities interested in the use of transmission electron microscopy, scanning probe, and confocal optical microscopy and x-ray diffraction.

6. Associated Laboratory of Development and Characterization of Nanodevices and Nanomaterials (Laboratório Associado de Desenvolvimento e Caracterização de Nanodispositivos e Nanomateriais) (LANano) (UFMG).
UFMG Center for Microscopy offers adequate infrastructure to execute research projects using high resolution microscopy and microanalysis. The Processing Laboratory Devices DF / UFMG (LPD) is a clean room with infrastructure for photolithography, electron beam lithography, lithography direct writing laser film deposition, wet and dry corrosion, optical metrology of films and surfaces.

7. Nanobiotechnology Laboratory for Development, Prototyping and Validation of Products for Single Health System (SUS) (Laboratório de Nanobiotecnologia para Desenvolvimento, Prototipagem e Validação de Produtos para o Sistema Único de Saúde (SUS) (IBMP).
Industrial production: Inputs for molecular testing and molecular tests. Technological development: Molecular tests, immunoassays, diagnostic devices and diagnostic and therapeutic proteins.

8. Associated Nanotechnology Laboratory (Laboratório Associado para Nanotecnologia) (LARnano) (UFPE).
Nanostructured products applied to health: RD&I for nanostructured diagnostic and therapy products (production and physicochemical and biological characterization); RD&I for nanostructured products for cosmetics; toxicological studies in vitro and in vivo; in vitro and in vivo preclinical efficacy trials; biodistribution and bioavailability; clinical trials.

9. Associated SisNano Laboratory (Laboratório Associado SisNANO) (UFV-MG).
Nanocomposites for applications in active packaging and guided tissue regeneration. Nanotechnology applied to the pulp and paper industry. Nanoparticles applied to animal and plant production. Ultra-thin films and nanostructures for applications in devices and sensors. Nanocomposites for catalysis and removal of pollutants. Nanostructures for transport and controlled release of drugs and study of DNA-ligand interactions.

10. Amazonia Nanoscience and Nanotechnology Laboratory (Laboratório de Nanociência e Nanotecnologia da Amazônia) (LABNANO-AMAZON) (UFPA).

Scientific and technical support services for the characterization of nanoparticles, nanotubes, graphene, nanofluids and related materials (composites of nanostructured materials and carbonaceous materials). Nanobiotecnologia: Development of new drugs, cosmetics and environmental monitoring and remediation. Catalysis and Bioenergia. Available equipment for thin films manufacturing.

11. Electrochemical and Nanostructurated Materials Laboratory (Laboratório de Eletroquímica e Materiais Nanoestruturados) (LEMN) (UFABC).
Providing infrastructure, methodologies and consolidated processes to the National Productive Sector on lines of research in Nanoscience and Nanotechnology; mainly polymers, functional materials and computational modeling & simulation from UFABC, in order to training of highly qualified personnel, innovation and technology transfer to the productive sector.

12. Surface Engineering and Nanostructured Material Laboratory from Institute of Graduated and Engineering Research (Laboratórios de Engenharia de Superfícies e Materiais Nanoestruturados do Instituto de Pós-Graduação e Pesquisa de Engenharia (COPPE) (LabEngNano) (UFRJ).
Development of nano- and micro-fluidic systems.

13. Interdisciplinary Laboratory for Nanostructures Development (Laboratório Interdisciplinar para o Desenvolvimento de Nanoestruturas (LINDEN) (USP).
Nanotechnology solutions for the productive sector. Polymeric composites and nanoparticles, synthesis and catalysis of metallic nanoparticles and their biological activities. Control release of nano-pharmaceuticals and nano-cosmetics.

14. Bionanomanufacturing Center (Núcleo de Bionanomanufatura) (IPT).
Synthesis, deposition, dispersion and characterization of metal nanoparticles, ceramics, semiconductors, magnetic materials and polymers. Production of nanocomposites. Preparation of synthetic emulsions and dispersions by high pressure homogenizers. Laboratory-scale production of nanostructured particulate systems (polymer matrix) containing encapsulated active agents through various encapsulation routes.

15. Semiconductor Components Center (Centro de Componentes Semicondutores) (CCS) (UNICAMP).
To develop quantitative, basic and applied microelectronics, microsystems, micro and nanofabrication research, including semiconductor devices, integrated circuits, inputs and production equipment; expand training in research and development in microelectronics, microsystems, micro and nanofabrication; advising institutions and professionals in the field of microelectronics, microsystems, micro and nanofabrication in the acquisition, installation, maintenance and deactivation processes and microelectronics and photonics equipment; provide services in the area of microelectronics, microsystems, micro and nanofabrication. Focus: technology integration (macro / micro / nano) device fabrication (proof of concept, prototype).

16. Support Center for Research in Nanotechnology and Nanoscience (Núcleo de Apoio a Pesquisa em Nanotecnologia e Nanociências) (NAP-NN) (USP).
To support research and development in nanomaterials and nanosystems through infrastructure, equipment and expertise of researchers from SisNANO-USP, with strong inter- and multi-disciplinary approaches involving physics, chemistry and engineering. Execution of projects focused on the study and resolution of problems, especially nanotechnology by nature, using expertise and infrastructure, particularly through the establishment of cooperation and partnerships: developing products and processes, technology transfer, development of method for characterizing nanomaterials, compatibility/ functionalization of nanoparticles, development of hybrid and mesoporous nanomaterials, and polymer nanocomposites, development of sensors and devices.

17. Central Laboratory in Nanotechnology (Laboratório Central em Nanotecnologia) (LCNano) (UFPR).
Morphological, chemical and structural characterization. Application of nanosciences in developing materials: synthesis and fabrication of various materials. Nanotechnology applied to health. Nanotechnology applied to the development of renewable energies. Applied nanobiotechnology. Characterization of physical properties and biological activities.

18. Laboratory for Manufacturing and Characterization of Nanodevices (Laboratório de Fabricação e Caracterização de Nanodispositivos) (LABDIS) (PUC).
Production and characterization of devices based on inorganic semiconductors covering all life cycle stages, including physical, chemical and structural properties, through to the final evaluation of the devices in real-world applications..

APPENDIX 2: OVERVIEW OF THE EU-BRAZIL MISSIONS, WORKSHOPS AND BRAZIL'S LABORATORY & NETWORK INFRASTRUCTURE FOR ENGAGEMENT IN DEVELOPING REGULATORY POLICY AND SCIENCE FOR NANOTECHNOLOGY

Preceding the EU-Brazil dialogue, discussions at the Advisory Committee on Nanotechnology (Comitê Consultivo de Nanotecnologia-CCNano) and the Inter-ministerial Nanotechnology Committee (Comitê Interministerial de Nanotecnologia (CIN) led to the creation of a Working Group on Regulation (GT-Reg). Alongside these discussions, two Bills (Law Projects) are progressing through the Brazilian Parliament, that are related to i) Product Labeling that use Nanotechnology (PL.5 133/2013) and ii) the creation of a National Policy on Nanotechnology (PL 6.741/2013).

On basis of these discussions and the development of Brazilian infrastructure in nanotechnology, the Brazilian Government initiated a more detailed interaction with the European Union.

VISIT OF THE BRAZILIAN MISSION TO EUROPE

A dialogue between the Brazilian Government and the European Union was initiated in June 2013 with a visit by the Brazilian Ministry of Science and Technology and Innovation (MCTI) to the EuroNanoForum conference (Dublin, Ireland), where specific contact was established with the EC's Directorate Generals for Research and Innovation and the Joint Research Center (JRC). The aspects that were discussed included scientific, technological, methodological, and metrology aspects associated with nanotechnology regulation, which feature in the new Horizon 2020 European research programme. From this meeting MTCI expressed interest in supporting the actions that generate technical and scientific knowledge, methodologies, and protocols for the characterization, determination and modeling of physical, chemical and biological effects associated with the environmental impact of nanomaterials. This support is intended to act as a base for a process that can lead to a regulatory framework for nanotechnology in Brazil. The aims of the MCTI-sponsored involvement providing the aforementioned support are to establish a set of methodologies, techniques and protocols for the establishment of science-based regulation that is recognized and compatible internationally. The standardization of certification methods and the nanotechnology regulation in accordance with what has been developed in other countries, is essential to promote international collaboration and for facilitating the import and export of nanotechnology based products.

VISIT TO THE CENTRE FOR BIO-NANO INTERACTIONS - UNIVERSITY COLLEGE DUBLIN (CBNI-UCD), IRELAND

A visit to the Centre for BioNano Interactions (CBNI) and Schools of Chemistry and Chemical Biology University College Dublin, provided the opportunity to learn about the operation of the center which is dedicated to aspects of the interaction of nanomaterials with biological systems. Members of the Brazilian Mission included Drs. Flavio Orlando Plentz Filho (General Coordinator of Micro and Nanotechnologies, Ministry of Science and technology and Innovation STEC-MCTI), Anna G. Tempesta (Analyst in Science and technology, general Coordination of Micro and nanotechnologies-SETEC - MCTI), Ary Corrêa Junior (Professor UFMG), and Nelson Duran (Professor UNICAMP).

The lead for the Center, Prof. Kenneth Dawson, has considerable experience in the management of EU projects, including multi-sectoral cross-disciplinary research projects (e.g. NanoInteract and NeuroNano). The most important aspects discussed were the formation and characterization of the nanoparticle-protein corona. CBNI has funds of approximately € 4.8 million from European sources. Most of the work conducted at the Center involves collaborative interaction with partners from other institutions, industry and government on issues of bionano. In addition, the CBNI interacts with both national, European and international industrial partners ranging from small and medium-sized to large multinationals. The Center expressed interest in collaboration with Brazilian institutions involved with regulatory issues, safety and toxicology, with students and researchers through the Brazilian Science Without Borders programme.

DISCUSSIONS TO CONSIDER PARTICIPATION IN THE NANOREG PROJECT (PARIS).

A meeting with the NANoREG project was organized with Dr. Tom van Teunenbroek who is currently the coordinator of NANoREG and has worked with the Ministry of Infrastructure and Environment in various positions as a consultant, including Coordinator of Policy and Research, Head of Delegation to the OECD-WPNM Netherlands. The meeting involved Drs. Flavio O. Plentz (Brazil), Anna Tempesta (Brazil), Nelson Duran (Brazil), Ary Corrêa (Brazil), Georgios Katagarianakis (Belgium), Tom van Teunenbroek (Netherlands), Aart Dijkzeul (Netherlands), Hugues Crutzen (Italy) and Joke Vroom (Netherlands).

The NANoREG project was created to provide the necessary answers to regulators and legislators on environmental health and safety bodies, linking them to the scientific evaluation of the data and methods of test.

Based on questions and requirements provided by regulators and legislators, the project aspires to:

- provide answers and solutions from existing data, supplemented with new knowledge;
- provide a set of relevant tools for risk assessment, characterization, toxicity testing and exposure measurements of manufactured nanomaterials (MNMs);
- develop long-term test new strategies tailored to the needs of innovation;
- establish close cooperation between authorities, industry and science leading to an efficient and practically applicable approaches in management of risks to MNMs and products containing MNMs.

The project involves 40 countries with resources of around €50 million.

The main points discussed and decided were:

- Brazil is willing to collaborate with the NANoREG project in addressing the regulatory issues relating to aspects of the design, production and implementation of Environmental, Health and Safety approaches for nanomaterials;
- both parties intend to reach a binding agreement to discuss the formal aspects of this collaboration;
- after implementation of a collaboration agreement, the National Coordinator (Brazil) may participate in discussions involving the coordinators from the different countries linked to the NANoREG project group.

It was pointed out that the new partners becoming involved in the NANoREG project should preferentially focus on topics that are not yet, or not sufficiently, covered by the tasks already defined in the Description of Work (DoW). The topics were:

1. Metrology (WP2);
2. Exposure measurement: Environment as well as workman place (WP3);
3. Ecotoxicity;
4. End of fate and transformation of MNs along the lifecycle;
5. Standardization (WP5).

At the time, MCTI considered that Brazil could be able to participate in the characterization of nanomaterials with respect to hydrodynamic size and zeta-potential, and also through use of range of different techniques for physic-chemical characterization including XRD, TEM, SEM/SEM-EDX, AFM, TGA, FT-IR, TOC, DLS and BET. In addition, it was considered that Brazilian researchers are probably able to participate in the econanotoxicology topic area.

It was indicated that Brazil's participation/contribution with the NANoREG project and activities requires a total value of at least EUR 2 million support in Brazil for this participation and that the maximum number of participant organizations/industries will be three. In this meeting, itwas also suggested by the coordinators of NANoREG that the signing of the participation agreement by Brazil should happen in the next three months.

VISIT TO VENETO NANOTECH - ROVIGO, ITALY

The European Center for the Sustainable Impact of Nanotechnology (ECSIN) -Rovigo, opened in 2010 is the new Veneto Nanotech lab dedicated to the study of the impact of nanotechnology on the health, environmental and ethical and social aspects. Dr. Federico Benetti (Senior Research) at Veneto Nanotech and his collaborators received the Brazilian Mission.

The main interest of the Centre is to monitor industrial nanomaterials and to obtain knowledge of the impact on human health and the environment of these materials with a view to sustainable development of the environment. ECSIN aims to conduct research and studies to assess what would be the possible effects on human health and the environment following exposure of nanoparticles and/or nanomaterials. The Centre is also involved in the perception of nanotechnology by companies to facilitate understanding and social acceptance.

Another important aspect is its affirmation as an international Centre of Excellence for the application of nanotechnology leading to the development of business start-ups in nanotechnology. ECSIN works directly with the Laboratory of Nanofabrication (Nanofab) that has operated in Marghera, Venice, since 2005 with the Universities of Padua, Venice and Verona. The research team is involved in a collaborative European research project "Development of sustainable solutions for nanotechnology-based products based on hazard characterization and evaluation of life cycle", funded under the 7th Framework Programme (FP7) started in March 2010, along with several other projects and other national initiatives. The team is involved in collaborations with the Universities of Veneto Region, University of Rochester and is also involved in national and trans-national initiatives for discussion of development issues and the safety of nanotechnology in sustainable systems.

ECSIN is involved in the FP7 SUN Project (Sustainable Nanotechnologies) with funds of about €14 million, and participated in ITS-Nano (Intelligent Testing Strategy for engineered nanomaterials) and NanoValid (where two Brazilian institutions also participate: INMETRO and UFMG).

Researchers at the Center, together with Dr. Bregoli Lisa (Senior Researcher), briefly presented their research and highlighted some key issues related to NANoREG. The important role of the Center encouraging enterprising in nanotechnology through competitions (Nanochallenge Award) was also discussed. The Director of the Nanofabrication Laboratory presented the main activities of the laboratory, showing the existence of several partnerships with companies. The Center showed interest in the Science Without Borders programme with Brazil.

VISIT TO THE EUROPEAN COMMISSION JOINT RESEARCH CENTER (JRC) - ISPRA, ITALY

This visit was coordinated by Dr. Juan M. Riego Sintes of the Nanobiosciences Unit, in the JRC's Institute for Health and Consumer Protection (IHCP). Those attending the meeting (and giving presentations) included the Director of IHCP Dr. K. Maruszenwski (Introduction to JRC); Dr. H. Stamm (JRC activities in Nanotechnology); Dr. Flavio Plentz (Nanotechnology in Brazil); Drs. J.Riego-Sintes and H. Crutzen (NANoREG). Also participating were Drs. Anna Tempesta (Brazil), Ary Corrêa (Brazil) and Nelson Duran (Brazil).

The mission of JRC is to provide scientific support to the development and implementation of EU policies related to health and consumer. Competence areas include:

- Biotechnology and GMOs;
- Biomedical Materials and Systems;
- European Centre for the Validation of Alternative Methods;
- Physical and Chemical Exposure;

- Toxicology and Chemical Substances (former ECB – European Chemicals Bureau).

JRC has 250 researchers from 26 nationalities and has expertise and facilities in analytical chemistry of foods, molecular biology, nanobiosciences, toxicology, computational toxicology, risk assessment and validation methods. Other Institutes at the Ispra Campus include the Institute for Environment and Sustainability (IES), Institute for Protection and Security of the Citizen (IPSC), part of the Institute for Energy and Transport and part of the Institute of Transuranium Elements. JRC participates in the direction of the NANoREG project, and they suggested that Brazil could initiate studies together with the EU in the NANoREG project. Among the topics discussed were cooperation with the regulatory issues in nanotechnology; devices; in vitro studies; risk assessment (ecotoxicity); and radioactive markers. An important aspect discussed at this meeting was the difficulties of having standards nanomaterials, particularly carbon nanotubes and others. JRC has a reference materials repository and a data platform that handles information (www.nanohub.eu). It was indicated that a programme of cooperation with JRC should start with a specific call under the Science Without Borders programme in the area of regulating nanotechnology.

SIBRATEC-SISNANO (BRAZILIAN SYSTEM OF TECHNOLOGY-NATIONAL SYSTEM LABORATORIES IN NANOTECHNOLOGIES) WORKSHOP: NANOTECHNOLOGY AS A PLATFORM FOR INNOVATION (JULY 2014-BRASILIA, DF, BRAZIL).

In order to evaluate the Brazilian competence in nanotechnology and the possibility of interaction with the NANoREG project, a National Workshop on Nanotechnology was organized by Ministry of Sciences and Technology and Innovation (MCTI) in Brasilia, DF, in July 2014.

An overview and results were presented by each of the laboratories from the SisNANO programme, with scientific, technological, methodological and metrological aspects discussed in order to see the applicability of expertise from the SisNano programme for supporting the development of a regulatory framework for nanotechnology in Brazil. The workshop promoted the integration between institutions and research groups in Brazil with the intention of cooperating with the European Union.

Comments on activities of the Strategic Laboratories, in the context of the possible participation in NANoREG, are provided below:

1. Multiuser Laboratory of Nanosciences and Nanotechnologies (Laboratorio Multiusuario de Nanociencias e Nanotecnologia) (LABNANO) – CBPF.
Comment: The expertise is related to nanofabrication and characterization of nanostructures. The laboratory has a clean room. This center is specialized in nanofabrication rather than different nanostructures' characterization as needed for the NANoREG project.

2. Chemical laboratory in Carbon Nanostructures (LQN) – CDTN.
Comment: This Laboratory has a good competence for chemical processing of carbon nanotubes and graphene, but limited expertise in fundamental studies and biomedical applications as needed for the NANoREG project.

3. Multiuser Nanotechnology Laboratory (Laboratorio Multiusuario de Nanotecnologia) (LMNano) – CETENE.
Comment: This Laboratory supports multiple technological applications, with excellent infrastructure for applications of nanotechnology, mainly in the energy area and some biological applications. . The LMNano is considered to be well placed to support nanomaterial characterization in NANoREG, although it has no expertise at the moment in nanotoxicological aspects as required for the project.

4. National Nanotechnology Laboratory (Laboratorio Nacional de Nanotecnologia) (LNNano) – CNPEM.
Comment: This Laboratory is extremely well equipped for microfrabrication, characterization and processing of materials, preparation of nanostructured materials, microscopy, with staff having a deep knowledge of surface science. An important activity of this Laboratory is the support to innovation in companies and the provision of high-tech services. LNNano is in the process of applying for ISO 17025 accreditation for all of its facilities. The Laboratory is also implementing, as part of a CNPEM effort, a Laboratory Information Management System (LIMS) and an Electronic Laboratory Notebook (ELN). This system will integrate facilities and research groups from three different National Laboratories at CNPEM. This Laboratory is considered able to participate in any stage of characterization of nanomaterials in the NANoREG project.

5. Nanotechnology Laboratory for Agribusiness (Laborátorio de Nanotecnologia para o Agronegócio) (LNNA) – EMBRAPA.
Comment: This Laboratory's activities in nanotechnology related to agriculture are of great importance and its infrastructure is complete. The central focus of this Laboratory in nanotoxicology will be the toxicological assessment on plant cells, animal cells, embryos and laboratory animals, in order to compose an overview of interference of nanoparticles and nanostructured systems in living organisms, in technologies related to agricultural and related activities. Thus, these studies will support future activities on the recommendation of using nanosized systems in agriculture, or refocus ongoing research to better tailor the development of nanostructures and formulations containing them, to minimize or eliminate the negative impact without significant loss on their performance in the final application. It is considered that this Laboratory can assist in future studies related to econanotoxicology in agriculture. At the present time, it is considered that this Laboratory would be able to assume responsibility for some specified aspects in the NANoREG project.

6. Characterization Center in Nanotechnology for Materials and Catalysis (Centro de Caracterização em Nanotecnologia para Materiais e Catalise) (CENANO) – INT.
This Center is involved in corrosion and degradation; processing and characterization of materials; testing of materials and products; catalysis and chemical processes, which are not needed by the NANoREG project.

7. Nanometrology Strategic Laboratory (Laboratório Estratégico de Nanometrologia) – INMETRO.
This center is developing standardized procedures and methods of analysis, reference materials, measurement systems and procedures for the nanotoxicity testing validated through inter-laboratory comparisons. It is considered that the expertise and capability in characterization and toxicological expertise at INMETRO places them in a key position to act as the principal institution leading the Brazilian involvement in NANoREG (together with LNNano at CNPM (SP) and LNNA-EMBRAPA (SP)).

8. Integrated Nanotechnology Laboratory (Laboratório Integrado de Nanotecnologia (LIN) – IPEN.
Comment: This Center is a nuclear facility with activities and applications complementing areas of nanotechnology, with some initial studies in econanotoxicology (Daphnia and Zebrafish), but considered not able to participate at the level required in the NANoREG project.

COMMENTS ON ASSOCIATED LABORATORIES:

1. Regional Nanotechnology Laboratory (Laboratório Regional de Nanotecnologia) (LRNANO) (UFRGS).
Comments: This Associated Laboratory is dedicated to the fabrication, characterization and applications of materials at the nanometric scale and to nanobiotechnology, including applications of nanomaterials to fabricate and characterize systems with potential application in therapeutics (human and animal health) and diagnostics (analysis and imaging), but not in the context of nanotoxicology. Hence, this Associated Laboratory is not considered relevant to participate in the NANoREG project.

2. Characterization Center and Development of Protocol for Nanotechnology (Centro de Caracterização e Desenvolvimento de Protocolos para Nanotecnologia) (CCDPN) (UNESP).
O Laboratório Associado foca a síntese e caracterização de nanomateriais, mas não tem conhecimento
The Associated Laboratory focusses on the synthesis and characterization of nanomaterials, but has not nanotoxicological expertise and is therefore not relevant to the NANoREG project.

3. Analytical and Microscopy Center (Electronic and Optics) of Ceara University (Central Analítica em Técnicas de Microscopia (Eletrônica e óptica) da Universidade Federal do Ceará) (UFC).
Comments: This Associated Laboratory provides infrastructure and analytical and microscopy techniques for characterization but not in nanotoxicology, and is therefore not relevant to the NANoREG project.

4. Nanostructures Synthesis and Its Interaction with Biosystems (Laboratório de Síntese de Nanoestrutura e Interação com Biossistemas (NANOBIOSS) (UNICAMP).
Comments: This Associated Laboratory contributes to the development of basic science connected with the national productive sector, through expertise in syntheses and characterization of various nanomaterials and studying their impact against the man and the environment, from the perspective of risk assessment of nanotechnologies. It is considered that this Associated Laboratory could strongly support and supplement their activities, jointly with a National Center such as INMETRO, by participation in the NANoREG project.

5. Structural Characterization Laboratory (Laboratório de Caracterização Estrutural (LCE) (UFSCar).
Comments: This Associated Laboratory provides facilities for high-level structural characterization and scientific support for the academic and industrial communities interested in the use of transmission electron microscopy, scanning probe, and confocal optical microscopy and X-ray diffraction.
However, there is no expertise in nanotoxicology and therefore the Laboratory is considered relevant to involvement in the NANoREG project.

6. Associated Laboratory of Development and Characterization of Nanodevices and Nanomaterials (Laboratório Associado de Desenvolvimento e Caracterização de Nanodispositivos e Nanomateriais) (LANano) (UFMG).
Comments: This Associated Laboratory focusses on microscopy studies and offers infrastructure to execute research projects using high resolution microscopy and microanalysis. The Laboratory has no activities pertinent to nanotoxicology, and is therefore not relevant to the NANoREG project.

7. Nanobiotechnology Laboratory for Development, Prototyping and Validation of Products for Single Health System (SUS) (Laboratório de Nanobiotecnologia para Desenvolvimento, Prototipagem e Validação de Produtos para o Sistema Único de Saúde (SUS) (IBMP).
Comments: This Associated Laboratory is dedicated to industrial And technological development of molecular tests, immunoassays, diagnostic devices and diagnostic and therapeutic proteins. However, the Laboratory is not involved in nanotoxicological studies, and is therefore not relevant to the NANoREG project.

8. Associated Nanotechnology Laboratory (Laboratório Associado para Nanotecnologia) (LARnano) (UFPE).
Comments: Toxicological studies on nanostructured products applied to health and to cosmetics (in vivo; in vitro assays and in vivo preclinical efficacy trials; biodistribution and bioavailability. Although the Laboratory has no experience with inter-laboratories assays, it is considered that LARnano may eventually be able to provide support to studies related to the NANoREG project.

9. Associated SisNano Laboratory (Laboratório Associado SisNANO) (UFV-MG).
Comments: This Associated Laboratory is dedicated to the development of nanocomposites (nanoparticles-polymers) for applications in active packaging, guided tissue regeneration and to the pulp and paper industry. However, the Laboratory is not involved in nanotoxicological studies, and is therefore not considered relevant to involvement with the NANoREG project.

10. Nanoscience and Nanotechnology Laboratory from Amazon (Laboratório de Nanociência e Nanotecnologia da Amazônia) (LABNANO-AMAZON) (UFPA).
Comments: This Associated Laboratory has established infrastructure to support nanomaterials analyses. The main focus is the development of new drugs and cosmetics and environmental remediation. No nanotoxicology studies are in progress, and current activities are not considered relevant to involvement with the NANoREG project.

11. Electrochemical and Nanostructurated Materials Laboratory (Laboratório de Eletroquímica e Materiais Nanoestruturados) (LEMN) (UFABC).
Comments: This Associated Laboratory has good infrastructure for the analyses of nanomaterials but not in the area toxicology studies and the Laboratory is therefore not considered relevant to involvement with the NANoREG project.

12. Surface Engineering and Nanostructured Material Laboratory from Institute of Graduated and Engineering Research (Laboratórios de Engenharia de Superfícies e Materiais Nanoestruturados do Instituto de Pós-Graduação e Pesquisa de Engenharia (COPPE) (LabEngNano) (UFRJ).
Comment: This Associated Laboratory's activities concern the development of nano- and microfluidic systems and have no relation with nanotoxicology, and hence are not considered relevant to involvement with the NANoREG project.

13. Interdisciplinary Laboratory for Nanostructures Development (Laboratório Interdisciplinar para o Desenvolvimento de Nanoestruturas (LINDEN) (USP).
Comments: This Associated Laboratory has extensive expertise with a focus on providing the nanotechnology productive sector with solutions to problems. Some aspects related to biological activities are currently being developed, but there is currently no expertise in nanotoxicological assays and the Laboratory is therefore not considered relevant to involvement with the NANoREG project.

14. Bionanomanufactory Center (Núcleo de Bionanomanufatura) (IPT).
Comments: This Associated Laboratory is dedicated to the synthesis, deposition, dispersion and characterization of metal nanoparticles, nanocomposites, ceramics, semiconductor, magnetic and polymer. These activities are not considered relevant to involvement with the NANoREG project.

15. Semiconductors Components Center (Centro de Componentes Semicondutores) (CCS) (UNICAMP).
Comments: The focus of Associated Laboratory is technology integration (macro / micro / nano) and device fabrication (proof of concept, prototyping). These activities are not considered relevant to involvement with the NANoREG project.

16. Support Center for Research in Nanotechnology and Nanoscience (Núcleo de Apoio a Pesquisa em Nanotecnologia e Nanociências) (NAP-NN) (USP).
Comments: This Associated Laboratory has highly developed capability in synthesis, characterization and applications of nanomaterials. Execution of projects is focused on the study and resolution of problems. ,. Early-stage development of toxicological expertise suggests that NAP-NN may eventually be able to provide support to studies related to the NANoREG project.

17. Central Laboratory in Nanotechnology (Laboratório Central em Nanotecnologia) (LCNano) (UFPR).
Comments: This Associated Laboratory focusses on morphological, chemical and structural characterization, which may provide some value through specific nanomaterial characterization in support of activities connected to the NANoREG project.

18. Laboratory for Manufacturing and Characterization of Nanodevices (Laboratório de Fabricação e Caracterização de Nanodispositivos) (LABDIS) (PUC).
Comments: This Associated Laboratory is dedicated to producing and characterizing devices based on inorganic semiconductors. The infrastructure for characterization of nanomaterial interacting with biological systems is limited and hence this Laboratory is not considered relevant for involvement with the NANoREG project.

COMMENTS ON BRAZILIAN NETWORK IN NANOTOXICOLOGY

1. Aquatic Nanotechnology Network (Rede de Nanotoxicologia Aquática do Centro-Oeste (UnB).
Comments: This network has expertise in ecotoxicology and cellular behavior using mainly fish (Zebrafish) and mollusks. However, it was considered that the current depth of knowledge in nanotoxicology in aquatic media is still to be clarified and developed prior to this network having an effective role in NANoREG.

2. Nanotoxicology of Nanostructured Compounds: Cytotoxicity, Genotoxicity of Industrial Potencial Products (Rede de Nanotoxicologia de Compostos Nanoestruturados: Citotoxicidade e Genotoxicidade de Produtos com Potencial Industrial (CIGENANOTOX) (UNICAMP).
Comments: This network has significant experience in nanotoxicological inter-laboratory assays for cytotoxicity (MTT, NR, DNA, Rezorufin, lynphocytes); genotoxicity in vitro (Allium cepa, Comet, Cytogenic assay), in vivo (Fisher 344 rats; micronucleus assay; hepatotoxic assay: alanine aminotransferase-ALT; hepatic and cardiac damages assays: aspartate aminotransferase-AST; nephrotoxic assay: urea and creatinine; histopathology: toxicity evaluation by degree of inflammation). Mutagenecity: Ames assay: Salmonella strains. Toxicity assay on Caenorhabditis elegans, (aquatic organism evaluations (crustaceous: Daphnia, Fish: Zebrafish, Mosquito: Chironomus, Fish: Nile tilapia, Coelenterates animal: Hydra, Aquatic bacteria: Vibrio)._ It is considered that this network could collaborate with the NONOTOX network (INMETRO) in the NANoREG project.

3. Cooperative Research on Nanotoxicology Applied to Nanoparticles in Petroleum and Inks Industries Network (Rede Cooperativa de Pesquisas em Nanotoxicologia Aplicada a Nanopartículas de Interesse da Indústria Petrolífera e de Tintas) (UFSC).
Comments: This network is well equipped and has an excellent infrastructure for econanotoxicology experiments. Assays are available for acute toxicity (Daphnia magna, Aliivibrio fischeri , Chlamydomonas reinhardtii, Landoltia punctata, Mysidopsis juniae), chronic toxicity (Daphnia magna); genotoxicity (micronuclei, Comet, DNA fragmentation,aApoptose); epigenetics (DNA methylation by m5dC dosage), oxidative stress assays (lipoperoxidation by MDA dosage and oxidative enzymes) and cytotoxicity. This network could possibly contribute tothe NANoREG project.

4. Occupational and Environmental Nanotoxicology: Scientific Support for Regulatory Framework and Risk Evaluations (Nanotoxicologia Ocupacional e Ambiental: Subsídios Científicos para Estabelecer Marcos Regulatórios e Avaliação de Riscos) (FURG).
Comments: This network has a connection with others centers involved with the production and characterization of nanomaterials, for toxicological assays and chemical analysis. Assays are available for aquatic toxicology (Zebrafish and Litopenaeus vannamei (shrimp) and for soil toxicology (C. elegans). This network could potentially provide support for the aquatic toxicology in NANoREG.

5. Toxicity Evaluation of Nanomaterials Applied to Medicine and Agriculture: Studies development for in vitro, in vivo and membrane models (Avaliação da Toxicidade de Nanomateriais Aplicados em Medicina e Agricultura: Desenvolvimento de Estudos in vivo, in vitro e em Modelos de Membrana) (USP).
Comments: This network is mainly dedicated to nanomedicine associated with projects unrelated to those addressing regulatory issues. However, they have several assays related to characterization of materials (DLS, Zeta Potential, Spectroscopy, AFM Morphology) and nanotoxicological asays (in vivo, cyto- and genotoxicity, and ecotoxicity in algae). This network may have some potential use with the NANoREG project.

6. Nanoparticles Toxicity in Biological Systems: Production of Reference Materials, Development of Normalized Methods for Physico-Chemical Characteristics and Interactions of Nanoparticles with Cells and Tissues (Toxicidade de Nanopartículas em Sistemas Biológicos: Produção de Material de Referência, Desenvolvimento de Métodos Normalizados para Caracterização Físico-química e Estudo das Interações de Nanopartículas com Células e Tecidos) (REDE NANOTOX) (INMETRO).
Comments: This network is establishing standardized procedures and methods of analysis, reference materials, measurement systems and procedures of relevance to nanotoxicity and is engaged with their validation through inter-laboratory comparisons.The activities of this network include the selection and production of nanoparticles and nanostructured materials for toxicological evaluations; preparation of Standard Operating Procedures (SOP) for analytical characterization of nanoparticles; production of Reference Materials for toxicity evaluation; studies of the interaction between cells and NPs; biocompatibility testing of NPs (preclinical), clinical trials of nanostructured materials (carbonanoapatite). This Network is considered ideally suited to contribute to the NANoREG project

COMMENTS ON THE TWO NANO-INSTRUMENTATION NETWORKS:

1. Brazilian Research Network on Optical NanoSpectroscopy Instrumentation (Rede Brasileira de Pesquisa e Instrumentação em NanoEspectroscopia Óptica) (UFMG).
Comments: This network develops innovative instrumentation for the generation of products, supporting technology transfer to established companies or the generation of spin offs from the university. It has initiated some biomedical applications and it is expected that this network in near future could support some techniques for toxicological studies together with INMETRO.

2. Integrated Cooperative Research in Instrumentation: Technological Scaffold for New Components Manufacture, Systems and Instruments based on New Nanostrctured Materials (Rede Cooperativa Integrada de Pesquisa em Nanoinstrumentação: Plataforma Tecnológica para Fabricação de Novos Componentes, Sistemas e Instrumentos Baseados em Materiais Nanoestruturados) (UNICAMP)
Comments: This network deals with instrumentation related to the nanomanufacture of new materials, which is considered not relevant to the NANoREG project.

VISIT OF THE EU MISSION (NANOREG AND SELECTED NANOSAFETY CLUSTER PROJECT REPRESENTATIVES) TO BRAZIL (SEPTEMBER 21-26, 2014)

A reciprocal visit to Brazil by representatives of NANoREG and related EU projects in the nanosafety area took place in September 2014. This was attended by the following European delegates: Drs. Georgios Katalagarianakis (European Commission, DG Research, Belgium), Aart Dijkzeul (representing NANoREG, Netherland), Lang Tran (representing MARINA, Institute of Occupational Medicine, Edinburgh, United Kingdom), Marco Monopoli (Centre for BioNano Interactions, University College of Dublin, Ireland), Sergio E. Moya (Centre for Cooperative Research in Biomaterials-CIC biomaGUNE, San Sebastián, Spain), Steffi Friedrichs- (NIA,Belgium), Danail Hristozov (representing SUN, University Ca' Foscari Venice, Italy), Hermann Stamm (DG-JRC, Italy), Wim de Jong (representing SUN, Nanomile, FNNs, National Institute for Public Health and the Environment (RIVM), The Netherlands). Brazilian interests were represented by Drs. Flavio O. Plentz (MCTI), Anna G. Tempesta (MCTI) and Nelson Durán (UNICAMP).

MISSION VISIT TO INMETRO, RIO DE JANEIRO, 21-22 SEPTEMBER 2014.

AThe European Mission was received by Dr. Oscar Acserald, President of the National Institute of Metrology Quality and Technology (INMETRO), Dr. João Alziro Herz de Jornada and Dr. José Mauro Granjeiro.

By way of introduction, Dr. Granjeiro highlighted the main activities of INMETRO and nanotoxicology, the interactions with the FP7 NanoValid project involving INMETRO and UFMG, and the importance of the Brazilian Nanotoxicology Network (Nanotox 2012 at INMETRO) (CNPq/MCTI), in which 9 institutions from 4 Brazilian States (MG, RJ, RS and SP) participate. A further important aspect of INMETRO is its participation in SisNano – the National System of Laboratories on Nanotechnology.

The concerns and activities of INMETRO regarding nanotoxicology include addressing sample preparation (dispersion), mycoplasma contaminations, and some of the strategies being followed for nanomaterials such as TiO2 (requested by ABIHPEC (Industrial Association of Cosmetics), CNT, Au, Ag and Hydroxyapatite (implantable medical devices). INMETRO is interested in the effects of nanoparticles and nanomaterials on cell and tissues. For this strategy, they are validating toxicological tests (ISO and OECD), European Pharmacopoea and classic assays (interferences) and have interests in new tools such as Tox-21c (evidence based toxicology and OMICs, high content, HTS, bio-informatics and engineering).

Dr. Georgios Katalagarianakis made an introduction to the European Union and NANoREG. Dr. Steffi Friedrichs made a presentation on "Opportunities for transatlantic collaboration", in which she emphasized

the NANoREG triangle structure which portrays accelerating regulatory processes with a center point on scientific answers to regulatory issues, supported by two lateral concepts of credibility in the regulatory context and keeping pace with innovation. This strategy is intended to provide legislators with a set of tools for risk assessment and decision making instruments, new characterization and testing strategies and establishes a close collaboration among authorities and industry with regard to the knowledge required for appropriate risk management. The project is structured to deliver answers to questions relevant to regulators, generation of reliable, comparable and exchangeable data using a top-down approach (mandatory framework for partners regarding materials, methods, characterisation). Dr. Friedrichs described in detail all of the Workpackages in NANoREG:

- WP1: Scientific answers to regulatory issues;
- WP2: Synthesis, supplying and characterization;
- WP3: Exposure through life cycle analysis;
- WP4: Biokinetics and toxicity testing in vivo;
- WP5: Advancement of Regulatory Risk Assessment and Testing;
- WP6: Keeping pace with innovation (safe by design);
- WP7: Liaisons, Dissemination, Exploitation and Communication.

Discussions suggested that a Guidance Document is one of the minimum requirements for measurement and characterisation during testing. Also it was suggested that WP6 could provide Brazilian regulatory agencies (ANVISA, etc.) and industry (NanoBusiness Informação e Inovação Ltda., ABIHPEC (+ ITEHPEC), etc.) with results with special emphasis on SOPs and Standards. After the presentations, a visit to the INMETRO facilities took place.

NANOREG INTEGRATION WORKSHOP, CURITIBA, PARANÁ, 22-24 SEPTEMBER 2014

The European Commission and Brazilian representatives participated in a Workshop on Integration with NANoREG. The first day's session focused on Nanotechnology, Society and Industry. Several industries presented their expertise in nanotechnology applied to different products (Federação das Indústrias do Estado de São Paulo (FIESP) System). Important aspects were presented by Dr. Noela Invernizzi (UFPR) and Dr. Victor M.P. Alvarez (UFPR) in a keynote lecture entitled "Nanotechnology and Society". Presentations were given by selected SisNano Laboratories (NanoSus, NanoTox) and all represented SisNano Laboratories presented their activities in a Poster session. The second day of the Workshop was dedicated to the regulation of nanotechnology. Prof. Flavio Plentz gave an introduction entitled "Brazilian Nanotechnology Initiative".

Dr. Georgios Katalagarianakis presented on "HORIZON 2020: Key Enabling Technologies for European Growth. Nanosafety Research Policy in the EU". He pointed out that the new aspects of Horizon 2020 included major simplification, an integrated programme coupling research to innovation, challenge-based less prescriptive topics and new forms of funding aimed at innovation. The three important priorities highlighted are Excellence science, Industrial leadership and Society challenges:

The programme has a principle of general openness: the programme will be the most open funding programme in the world. It is open to the association of acceding countries, candidate countries and potential candidates and selected international partner countries. Targeted actions will be implemented taking a strategic approach to international cooperation. The highlighted benefits of participation in transnational collaborative research and development projects include sharing complementary knowledge and experience, economies of scale and expanded scope, increased research quality, efficiency, speed and impact gains, joining existing/ creating new networks and contacts along with many unintended indirect benefits. An important Call in the topic area of Nanotechnology, Advanced Materials and Production (NMP) is related to Safety of nanotechnology-based applications and support for the development of regulation, where it is desired that risk management becomes an integral part of supply chain. Discussions focussed on aspects including all projects needing to align with the EU Nanosafety Cluster and other international activities. International cooperation is encouraged, in particular with leading nanotechnology developing Nations (US, Canada, Australia, Korea, Japan, China, Brazil). Responsible governance determining the future impact of nanotechnologies on society and economy (KET-support)

Dr. Wim de Jong presented on the topic of "FP7 & H2020 ProjectsHow do the results fit into a Grand Strategy for NanoSafety. Examples of projects on risk characterization". He pointed out that the current EU nanosafety landscape can be broadly described as contributing to 4 Themes: Risk Characterisation, Risk Mitigation, Risk Transfer and Risk Communication. Examples of EU projects on the evaluation of risks include NanoMILE (Engineered nanomaterial mechanisms of interactions with living systems and the environment: a universal framework for safe nanotechnology), SUN (Sustainable Nanotechnologies) and GUIDEnano (Interactive digital Guidance Tool).

NanoMILE's objectives are to formulate an intelligent and powerful paradigm for the mode(s) of interaction between manufactured nanomaterials (MNMs) and organisms or the environment. This includes the development of a single framework for the classification of MNM's safety and the creation of a universally applicable framework to enable informed consent/ decisions concerning nanosafety.

SUN's objectives are to give clear answers to regulatory questions regarding nano-EHS risks, open new possibilities for innovators to design greener nanotechnologies and develop and validate new methods and tools for prediction of long-term exposure, effects and risks for humans and ecosystems (services). This includes developing implementable practices for risk prevention and management, and guidance for safe disposal and recycling. This project's approach aims to protect innovation by providing industries with data and prospective tools to streamline effective decision making about safer products and processes.

GUIDEnano's objectives are to develop innovative methodologies to evaluate and manage human and environmental health risks of nanomaterial-enabled products, considering the whole product life cycle.

Overall, these three projects aim to provide knowledge and/or tools to support industry in its decision-making on how to produce safe nanomaterials.

Dr. Marco Monopoli presented "Long range challenges in nanosafety ensuring responsible development of new technologies". In this presentation, he explained the core mission for research being to identify and classify new nano-biological mechanisms and paradigms, not presented by chemicals (e.g. biodistributions, where do particles go/why, long term accumulation effects), identify and classify new mechanisms of impact in the inanimate environment (e.g. partitioning in environments, where do particles go/why, anomalies in biomagnification), inform regulatory testing programmes, and new implementation of the existing REACH regulation appropriate for nanomaterials. He explained the QualityNano Research Infrastructure which, in terms of research, seeks to develop novel analytical approaches and tools to enhance understanding of health and safety issues in nanotechnology and push beyond the state of the art in nanomaterials processing, labeling and identification and characterization in situ. A strong networking activities component for QualityNano aims to support and integrate the European nanosafety community. The Transnational Access component of QualityNano is dedicated to providing users from the European nanosafety community access to nanomaterials processing, characterization and exposure assessment facilities.

Dr. Hermann Stamm gave 2 presentations: "Activities at the European Commission's Joint Research Centre on Nanomaterials Safety" and "Nanomaterials in European Regulations". He explained the mission of JRC as providing customer-driven scientific and technical support for the conception, development, implementation and monitoring of EU policies. The JRC functions as a reference center of science and technology for the European Union and is close to the policy-making process. It serves the common interest of the Member States, while being independent of special interests, whether private or national. JRC's key activities in nanotechnolgy include general scientific advice, policy support (e.g. nanomaterial definition, safety assessment and analysis), safety assessment of nanomaterials (bridge the gap between available scientific results and regulatory data needs, and development of standardized protocols for toxicity testing), nanomaterials in food and consumer products (methods for detection and tracing and validating analytical methods), and quality assurance tools (Reference Materials and Representative Nanomaterials for Testing). An important issue in JRC's Institute for Health and Consumer Protection (IHCP) is in vitro nanotoxicology including the syntheses of nanomaterials, their characterization, uptake, cell response and cell interaction. JRC was highlighted as having has a strong interaction with the Nanosafety Cluster in the EU. Dr. Stamm concluded with comments on a regulatory view of research needs: implementation of a definition (methods to determine the size distribution of nanomaterials (how to deal with agglomeration and aggregation when measuring particle size)); implementation of nano-ingredient labelling (methods to detect, identify and quantify nanomaterials in complex matrices); methods for safety testing (adaptation and development of testing methods for (eco)toxicity testing; computational and in vitro test methods (high throughput testing); characterisation of nanomaterials during test and life cycle; grouping of nanomaterials and data for regulatory purposes (OECD WPMN, research projects (e.g. MARINA, NANoREG, etc.))

Dr. Jose Mauro Grangeiro highlighted the validated toxicological tests applied at LABIO, which include ISO 10993-5 and ISO/TC 229/WG 3 N 497, the European Pharmacopoea with the Monocyte Activation Test (MAT), the OECD TGs such as cytotoxicity (TG 129), ocular irritation and corrosion (TG 437 (BCOP), TG 438 (chicken eye), TG 460 (fluorescein)) and the OECD TGs for skin irritation and corrosion (TG 430, TG 431, TG 435, TG 439), phototoxicity (TG 432), skin sensitization (TG 429, TG 442A and 442B) and genotoxicity (TG 487). LABIO has concerns with the classical assays interferences, such as the effect of nanoparticles on assays (e.g. MTT/XTT, Neutral Red Uptake (NR), Crystal Violet Dye and Exclusion). Research includes study of metabolic parameters including ATP, ROS, apoptosis/necrosis, mitochondrial activity (membrane potential) and cytokines studies. LABIO is considered highly qualified to carry out regulatory studies in nanotechnology.

Dr. Valtencir Zucolotto presented the Nanotox network as previously presented at SIBRATEC meeting at Brazilia. He emphasized the interaction of Nanotox with industries in several areas of nanomedicine, and ecotoxicity.

Prof. Nelson Durán presented the activities of the NanoDialogues Programme, commissioned by MCTI and undertaken jointly between Dr Steve Hankin (IOM, UK) and Prof. Durán, and a draft report on the initiatives and actions aimed at regulating nanotechnology in Brazil and the European Union. The NanoDialogues Programme supports the Brazilian Government's actions to appropriately address the regulation of nanotechnology, to demonstrate that Brazil's scientific community is aware of the issues about nanotechnology safety and is taking a coordinated and valued approach to addressing the issues, thereby mitigating risks from the development of nanotechnology in Brazil. This specifically includes Brazil seeking cooperation and collaboration with international research and the development of regulation for nanomaterials, to inform the approach that should be taken domestically. In Brazil, several actions are being conducted relating to nanotechnology regulation, including the Nanotechnology Advisory Committee (CCNano), Interministerial Committee for Nanotechnology (ICN), the Working Group on Regulation (GT-Reg) and Nanotoxicology Networks. Given that the development of regulation applicable to nanomaterials is well advanced in the European Union, at a Community-wide level and by individual Member States, a Sector Dialogue with the European Union on the Regulation of Nanotechnology-based Products was established and is intended to support (underpin) the process leading to the development of a nanotechnology regulatory framework or frameworks in Brazil. The draft report's contents include an introduction to nanotechnology regulation

and the challenges, a commentary on the regulation of nanomaterials in Europe, metrology to support nanotechnology risk assessment and regulation, standardization activity, aspects related to governance as prelude to nanomaterials regulation, a Roadmap of actions related to nanotechnology regulation in Brazil, and Appendices providing details of Brazil's Nanotechnology Laboratory & Network Infrastructure, and an overview of the EU-Brazil Missions. The final steps for the NanoDialogues Programme are consideration report by MCTI with response to feedback prior to embarking on implementing the recommendations and the report's roadmap indicating relevant players and a proposed sequence of actions.

VISIT TO INSTITUTES IN CAMPINAS, SP: NANOSTRUCTURES SYNTHESIS AND ITS INTERACTION WITH BIOSYSTEMS (NANOBIOSS) AND NANOTOXICOLOGY NETWORK (CIGENANOTOX) (CHEMISTRY INSTITUTE, UNICAMP) AND NATIONAL NANOTECHNOLOGY LABORATORY (LNNANO), CNPEM, 25 SEPTEMBER 2014.

The European Mission was received by Prof. Oswaldo L. Alves, Coordinator of NanoBioss and Prof. Nelson Durán (Vice-Coordinator of NanoBioss and Coordinator of CIGENANOTOX network). Prof. Lauro Kubota (Head of Chemistry Institute) and Prof. Carlos Ramos (Vice-Head of Chemistry Institute) gave a welcome at the Institute of Chemistry at Universidade Estadual de Campinas (State University of Campinas). Prof. Alves showed the activities and facilities at the NanoBioss Laboratory, and in particular studies on the interactions of nanomaterials and protein corona.

Dr. Georgios Katalagarianakis gave an introduction to the European Union and NANoREG and presented Dr. Sergio Moya who gave a presentation on "Nanoafety Cluster in Europe". The objectives of the cluster are: to facilitate the formation of a consensus on nanotoxicology in Europe; to provide a single voice for discussions with external bodies; to avoid duplicating work and improve efficiency; to improve the coherence of nanotoxicology studies and harmonize methods; to provide a forum for discussion, problem solving and planning R&D activities in Europe; to provide industrial stakeholders and the general public with appropriate knowledge on the risks of nano particles and nanomaterials for human health and the environment. Common nanosafety research themes are: nanomaterial identification and classification; exposure, transformation and the life cycle; hazard mechanisms, biokinetics, and vulnerable populations; and risk prediction and management tools. The research priorities of the NanoSafety Cluster for the next 10 years are described below

RESEARCH PRIORITIES AND ROADMAP

TIIME	MATERIAL	EXPOSURE	HAZARD	RISK
2015	Reference methods and nano-biointeractions	Laboratory and computer simulations	Systems biology approaches available for hazard research	Improved risk communication and tools for risk assessment
2020	Data sets on reference ENM	Database on release	Understanding the association between material characteristics and hazard	Models and standars available
2025	Key metrics for harmful impact	Laboratory tests and models available for exposure assessment	A tool for safety assessment	A tool for the integration of safety by design strategies. Quidance, tools, and automatisation

Dr. Steffi Friedrichs together with Dr. Aart Dijkzeul discussed NANoREG with NanoBioss and the possibilities of interaction with Brazil, similarly to that discussed in Curitiba.

After these presentations, the European Mission visited some of the laboratory facilities at the Institute. The European Mission also visited the National Laboratory of Nanotechnology (LNNano) and National Bioscience Laboratory (LNBio) at the Brazilian Center of Research in Energy and Materials (CNPEM). At the LNNano, Prof. Fernando Galembeck presented the CNPEM and the LNNano facilities and research in particular the use of biomass for new nanomaterials.

Dr. Diego S.T. Martinez presented "Nanotoxicology & Nanosafety: LNNano/CNPEM". Studies at the Nanotoxicology Laboratory at LNNano are related to protein corona and the toxicity of nanomaterials from biomass toxicity in soil (acute ecotoxicity).

Dr. Rodrigo V. Portugal presented "A Cryo-Electron Microscopy Facility for Single Particle Analysis at the National Center for Energy and Materials Research" and he gave an explanation of all the equipment of LNNano with an emphasis on high resolution microscopy.

Dr. Georgios Katalagarianakis gave comments on the visit of European Mission to Brazil with Drs. Steffi Friedrichs and Sergio Moya complementing the presentation with information on NANoREG and the NanoSafety Cluster in Europe.

The Mission visited LNBio in order to see the laboratory infrastructure given the important work studying nanomaterial interactions with biological systems in close collaboration with LNNano.

SUPPLEMENTARY SPECIALIST VISITS, 26 SEPTEMBER 2014.

Prof. Flavio Plentz, Dr. Danail Hristozov and Dr. Hermann Stamm visited EMBRAPA (Prof. Luiz Mattoso, Head of the Institute of NanoAgro (São Carlos, SP) and the Nanotox network (Prof. V. Zucolotto, Physics Institute of São Carlos, University of São Paulo, São Carlos, SP).

Dr. Anna Tempesta and the other members of the European Mission visited the University of São Paulo (SP) the NAP-PP and received by Prof. Koiti Araki.

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