

Challenges in organisation & research of risk governance of Nanotechnologies

Monique Groenewold, RIVM 6TH SAF€RA Symposium Safety in the new economy and energy transition May 19, 2022



NANORIGO: Grant N°814530 RiskGONE: Grant N°814425 Gov4Nano: Grant N°814401

Content

- Short introduction Risk Governance
- State of the art in EU research on Nano Risk Governance
 - NMBP-13 projects: expected impact and results
- Changing policy ambitions: green deal and Chemical Strategy for Sustainability, new demands for nanotechnology
- Regulatory Research needs: results of two Gov4Nano summits

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Risk governance

Governance refers to the actions, processes, traditions and institutions by which authority is exercised and decisions are taken and implemented.

- Involves Multi-disciplinary sciences and
- multi-stakeholder approaches
- A FRAMEWORK for risk governance is based on a defined and structured **process** to addressing **risk** in a comprehensive and holistic manner
 - Identification
 - Assessment (hazard, exposure, vulnerability)
 - Evaluation of acceptability, decision-making
 - Management and regulatory-relevant recommendations
 - Communication of risks

There exist already many 'frameworks' and tools, primarily for risk and safety assessment of nanotechnology

Environment In tem ational 95 (2016) 36-53 Contents lists available at ScienceDirect		nature nanotechnolog		ARTICLES https://doi.org/10.1038/s41565-018-0120-4	
Environment International		A framework for sustainable nanomaterial			
ELSEVIER journal homepage: www.elsevier.com/loc Review article Frameworks and tools for risk assessment of manufacture	-	selectio hazard,		caLIBRAte nano risk governance	
Danail Hristozov ^{a,*} , Stefania Gottardo ^b , Elena Semenzin ^a , Agnes Oom Martie van Tongeren ^d , Bernd Nowack ^e , Neil Hunt ^f , Andrea Brunelli ^a , Lang Tran ^d Antonio Marcomini ^a Nano Today (2014) 9, 546–549	en ^c , Peter Bos ^c , Willie Peijnenbur		ateri News	me Events Nano-Risk Governance Portal NanoSafety Cluster Week Partners Results Resc	
Available online at www.sciencedirect.com ScienceDirect journal homepage: www.elsevier.com/locate/nanotoday		GoNano	actio han idera bsta Are you cons dily c cal.IBR hpul • /	t involved: Test risk governance models ind involved in activities concerning R&D, production, marketing, use, risk assessment and management, inspection, insuraler, Ate invites you to get involved in the project and test one of the models identified as potentially suitable:	
NEWS AND OPINIONS	RISK GOVERNANCE AND RESEARCH & INNOVATION PRIORITIES IN NANOTECHNOLOGIES First Briefing report with A focus on food, health and the energy sector		d cor • L • E • S	 GUIDEnano LICARA nanoscan LICARA nanoscan BAUA Sprayexpo 2.3 Stoffenmanager Nano ANSES CB Nanotool Control banding nanotool Precautionary Matrix ISO / TS 12901-2 ConsExpo Nano SimpleBox4Nano (SB4N) SUNDs The caLIBRAte framework will link different nano-specific models and methods into a system-of-systems (SoS), which companie assessment, prioritisation and management of occupational, consumer and environmental risks associated with production and models will be aligned to support decisions along the research and innovation value chain, from basic research to market launch 	
A unified framework for nanosafety is needed			• F • / • (
Janeck J. Scott-Fordsmand ^{a,*} , S. Pozzi-Mucelli ^b , L. Tran ^c , K. Aschberger ^d , S. Sabella ^e , U. Vogel ^f , C. Poland ^c , D. Balharry ^g , T. Fernandes ^g , S. Gottardo ^d , S. Hankin ^c , M.G.J. Hartl ^g , N.B. Hartmann ^{d,1} , D. Hristozov ^b , K. Hund-Rinke ^h , H. Johnston ^g , A. Marcomini ^b , O. Panzer ⁱ , D. Roncato ^j , A.T. Saber ^f , H. Wallin ^f , V. Stone ^g			• S The cal assess		

So, what else do we need? Framework for nanotechnology risk governance

- 1. Integrate important concepts, principles and tools
- Access to data and guidance on how to obtain high quality data / outcome of knowledge-based risk assessment
- 3. Access to **tools** for risk assessment and risk management
- 4. Provide recommendation on **responsible** and transparent communication between **stakeholders**
- 5. Support to identify future scientific and regulatory research needs: address **current as well as future challenges**

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Societal challenge

- Nanotechnology has high economic potential and thereby impacts a broad range of industries and applications
- Interaction of engineered nanomaterials with the living environment is complex and is marked by uncertainty and ambiguity
- Urgent need to develop appropriate risk governance structures, to ensure full potential trough trust of all stakeholders



- €8.6M budget
- 01/19 to 12/22
- 32 partners
- 15 countries
- Coordinated by RIVM (NL)
- Grant agreement No. 814401



- €4.7M budget
- 01/19 to 02/23
- 28 partners
- 14 countries
- Coordinated by Aarhus (DK)
- Grant agreement No. 814530



- €5M budget
- 01/19 to 02/23
- 22 partners
- 17 countries
- Coordinated by NILU (NO)
- Grant agreement No. 814425

Setting the scene: the need for Gov4Nano



Agile and adaptable: meeting the changing needs of society





The process to Gov4Nano and the aims





Key building blocks for Nano Risk Governance



- **Cover all domains**: chemicals, biocides, consumers, food, medicine
- **Connect** key organizations and stakeholders (EU and global)
- Integrate important concepts, principles and tools
- Access to data and guidance on how to obtain high quality data
- Access to tools for risk assessment and risk management
- Support to identify future scientific and regulatory research needs
- Address current & future challenges
- Responsible and transparent
 communication between stakeholders







Outcome

- Proof of concept of an effective risk governance process
- Operational Nanotechnology Risk Governance Framework
- Nano Risk Governance Portal
- Blue print for an organization for Nano Risk Governance





Nano Risk Governance Framework

- All domains: chemicals, biocides, consumers, food, medicine
- Connecting key organizations and stakeholders (EU and global)
- Decision making framework
- Future-proof based on International Risk Governance Council
- Integrates scientific data and operational tools
- Participative and pro-active role for stakeholders
- Based on existing risk governance infrastructure



https://irgc.org/risk-governance/irgc-risk-governance-framework/



Nano Risk Governance Framework

Validated framework and tools



Software Architecture



Stakeholder involvement









Nano Risk Governance Framework – under construction





Organisation for Nano Risk Governance

- The main purpose is: fostering safe and sustainable development and use of nanomaterials in Europe.
- Put the framework into practice
- Overarching, independent, trustworthy body
- Bridge between knowledge generators and decision makers
- Services for all stakeholders



A new concept: the EU Nano Risk Governance House



Ambition: To foster safe and sustainable development, use and disposal of (products containing) nanomaterials in Europe



Nano Risk Governance Portal

- Infrastructure integrates academic, industry and regulatory information
- Support decision making framework & council
- Validated state-of-the-art tools
- NANoREG, caLIBRAte, NanoCommons & NanoReg²
- QA/QC processes and decision tree
- Process for collection and harmonisation of data
- Covers applicability and acceptance (regulatory or industrial)



Tools

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- Prospective early Risk screening tool (PERST)
- Library for dose equivalence
- Dosimetry model to connect in vitro data with in vivo exposure (for LCA and RA)
- MCDA
- Tool for underwriters

"Tools" to support Governance: Innovation risk management, SIA, Ethics, EH&S, SbD, LCA, Risk-Benefit, Decision Support, Data, Communication ...

RiskGONE

- Risk-Benefit Assessment Guidelines (RA, EIA, LCA, Econom)
- TG documents from experimental WPs
- SOPs
- 1-way and 2-ways communication tools
- Decision trees

Gov4Nano

- Further validation of inclusion of external (emerging) tools, R&D* of previously validated governance tools (a.o. NAMs) to further support revised Stage-Gate SIA/SbD and Nano-Risk Innovation Governance Management Tool
- New Tools
 - TRAAC
 - SbD nano-riskbenefit procedure
 - Data-use in tools

Main needs from stakeholders



Nano Risk Governance portal – under construction





Portal & tools -Scientific support for guidelines

- Collaboration with Malta Initiative to join (EU) forces
- Nano-specific adaptations of OECD TG/GD
- Dedicated regulatory risk research & experimental work
- Specific endpoints to be addressed: surface chemistry, solubility, reactivity and dustiness of nanomaterials, ecotoxicity and in vitro cytotoxicity and in vitro genotoxicity

The Malta Initiative

The Malta Initiative – A European Action to Develop OECD Test Guidelines for Nanomaterials

• A joint route towards standardisation, testing guidelines and guidance documents.













Testing and Assessment

Section 1 Physical Chemical Properties	Section 2 Effects on Biotic Systems	Section 3 Env. Fate and Behaviour	Section 4 Health Effects
TG on determination of the (volume) specific surface area of manufactured nanomaterials (EU) WNT 1.3	Adaptation of OECD TGs 201 V2 and 203 for the determine ecotoxicity of CNANO(2021)7 ENV/CBC/NANO(2021)7	TG on dissolution rate of nanomaterials in aquatic environment (DE) WNT 3.10 TG for nanomaterial removal from wastewater	GD on the adaptation of <i>in vitro</i> mammalian cell based genotoxicity TGs for testing of manufactured nanomaterials (EU)
TG on particle size and size distribution of manufactured nanomaterials (DE) WNT 1.4 GD on determination of solubility and disso-	ENVICE	GD on assessing the apparent accumulation potential for nanomaterials (ES) WNT 3.12	Applicability of the key event based TG 442D for <i>in vitro</i> skin sensitisation testing of nanomaterials (CH) WNT 4.133 TG on toxicokinetics to accommodate testing of nanoparticles (NL/UK) WNT 4.146 Integrated <i>in vitro</i> appro- fate or orally ingenerations fate or orally ingenerations fate or orally ingenerations (IT) WPM-ENVICECINANO(2021)8 GD on the determination of concentrations of nanoparticles in biological samples for (eco)toxicity studies (UK) WNT
Iution rate of nanomaterials in water and relevant synthetic biological media (DK/DE) WNT 1.5 GD on identification and quantification of the surface chemistry and coatings on nano- and microscale materials (DK/DE) WNT 1.6 TG on determination of surface hydrophobicity of manufactured nanomaterials (EU) WNT 1.7 TG on determination of the dustiness of manufactured nanomaterials (DK/FR) WNT 1.8		GD to support implementation of TG 312 for nanomaterial safety testing (CA/DE) WN T 3.14	
		GD on environmental abiotic transformation of nanomaterials (AT) WNT 3.16	
		Scoping review for a tiered are the for reliable bioaccu. assess. of Main NO(2021)9 rganisms minimising user (CBC/NANO vertebrate tests (UK) WPM ENVICECINANO vertebrate tests	
		Assessment of the durability of NMs and their surface ligands in env. surroundings (biodurable/ biodegradable) (SA/Korea) WPMN	



Data management – overall picture





Data management plans



Quality/fitness for re-use scoring of datasets







Interoperability and automation

Data management from concept to implementation......



FAIR databases are key – Findable, Accessible, Interoperable and Reusable



A free flow of high-quality, FAIR, NanoEHS data is essential for effective risk governance

- Science-based decision making
- Reuse of existing data
- Harmonisation of data templates



NANOEHS--GO FAIR IMPLEMENTATION NETWORK

www.go-fair.org/advancednano/





Systematic approach for efficient and effective Nano Risk Governance

- infrastructure for stakeholder engagement & collaboration
- networks for harmonization, improved data quality, international collaboration
- coordination and prioritization research needs for regulatory risk assessment
- monitoring system
- Access to high quality data & tools for decision making
- Improved standardisation and validation process



- Implementation
 FAIR principles
- Risk governance portal and platforms: knowledge & information sharing

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1. NEW POLICY AMBITIONS: EU Green Deal

The European Green Deal is about **improving the well-being of people**. Making Europe climate-neutral and protecting our natural habitat will be good for people, planet and economy. No one will be left behind.

The EU will:



Become climate-neutral by 2050



Protect human life, animals and plants, by cutting pollution



Help companies become world leaders in clean products and technologies



Help ensure a just and inclusive transition





EU Strategies: providing direction and goals







Potential to provide technical solutions for pressing global challenges, i.e. for energy revolution, digitalisation, or health care



Risk Governance of Advanced Materials

Considerations from the joint perspective of the German Higher Federal Authorities BAuA, BfR and UBA

by: Kathrin Schwirn, Doris Völker German Erwironment Agency, Dessau-Roßlau Andrea Haase, Jutta Tentschert, Uhike Bernauer German Federal Institute for Risk Assessment, Berlin Rolf Packoff, Volker Bachman Federal Institute for Occupational Safety and Health, Dortmund and Berlin

publisher: German Environment Agency



So PACE of development and application of (advanced) nanomaterials is stimulated by GD policy ambitions – MODERN INNOVATION POLICY





URGENCY for solutions



pubs.acs.org/est

Policy Analysis

Outside the Safe Operating Space of the Planetary Boundary for Novel Entities

Linn Persson,* Bethanie M. Carney Almroth, Christopher D. Collins, Sarah Cornell, Cynthia A. de Wit,* Miriam L. Diamond, Peter Fantke, Martin Hassellöv, Matthew MacLeod, Morten W. Ryberg, Peter Søgaard Jørgensen, Patricia Villarrubia-Gómez, Zhanyun Wang, and Michael Zwicky Hauschild

January 2022

Cite This: https://doi.org/10.1021/acs.est.1c04158







Technological solutions, regulatory perspective







2. New technology development, new nanomaterials

Circular knowledge translation: Increasing relevance of flowing diverse bodies of knowledge into lab activities early and often



Circular knowledge translation. Created by Wojciech Chrzanowski, Goretty Dias, Steven Maguire, and Elicia Maine, 2021.

Nanotechnology for a Sustainable Future: Addressing Global Challenges with the International Network4Sustainable Nanotechnology. Pokrajac et al. ACSnano; December 2021 DOI: (10.1021/acsnano.1c10919)

3. NEW CHEMICALS RISK ASSESSMENT

PARC: HE-partnership programme (2022-2029) – coordinated by ANSES, France -



New techniques; new analytical methods

Machine learning & AI

New Alternative Methods: NAMs

Etc.





3 developments affecting RA of nano







EU Strategies: Chemicals Strategy for Sustainability

OBJECTIVES

- •better protect citizens and the environment
- boost innovation for safe and sustainable chemicals

ACTIONS relevant for risk assessment nanomaterials banning the most harmful chemicals in consumer products – only essential use account for mixture effects boosting SSbD •establishing a simpler "one substance one assessment" process for the risk and hazard assessment of chemicals playing a leading role globally by championing and promoting high standards





EU Strategies: Chemicals Strategy for Sustainability



Figure: The toxic-free hierarchy – a new hierarchy in chemicals management





Nano dossier: keeping pace with policy ambitions

EXAMPLES	FOCUS
Elaboration on toxicological endpoints	Additional toxicological endpoints: immunotox, ED, neurotox, respiratory effects, specific organs
Elaboration on specific populations	Vulnerable groups, e.g. children
Harmonization, standardization	Development of standardized methods
Innovation in chemicals risk assessment	New techniques, digitization (like AI), etc.
Do no harm to man and its environment	Safe, sustainable, circular
Transregulatory	One substance, one assessment
Safe-by-Design	Safe-and-Sustainable-by-Design





Needs beyond toxicological knowledge

- Knowledge and information sharing: *how to organize?*
- Innovation supportive regulations: *how to connect?*
- Innovation in risk governance: how to adapt?
- Co-creation: how to operationalize?
- Dialogue:

do we have the skills and competences for it?





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Transregulatory risk assessment summit (2019 & 2022)

To provide a forum to discuss knowledge needs for risk assessment, and to translate these needs into research questions for the scientific Community

- Share lessons: facilitating mutual learning amongst experts and stakeholders in an interdisciplinary and inter-domain fashion.
- **Identify priorities**: ensuring most urgent scientific information needs and regulatory issues are integrated in policy research agenda, in support to regulatory oversight and compliance.
- **Promote harmonization**: finding common solutions to relevant topics such as data gaps, test guidelines and harmonization of methods.
- Identify operational research agendas: translate nano-specific issues in inputs for research agendas, funding mechanisms and other incentives to support and further develop risk analysis approaches, knowledge and data.







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What do regulatory risk assessors want and need?

Ideal situation

- Regulatory requirements are in line with risk assessment needs
- Integration of knowledge among regulatory domains
- Consultation of regulatory risk assessors
- Structural inventory of knowledge gaps/needs
- Structural funding despite urgency of needs
- Monitoring system to ensure efficiency of process







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GONE

Results RRAS and follow up survey I

Research question to pursue (challenge)	Regulatory risk assessment issues to overcome (scope)
Develop case studies on prediction/measurement of the toxicokinetic behaviour, including transformation of NMs inside the	Lack of knowledge on which <u>physico</u> -chemical characteristics are essential for risk assessment purposes within and across domains (definition)
 body (internal exposure) testing methods measured data , considering 	Lack of guidance in dealing with toxico-kinetics of nanomaterials (exposure)
issues of data quality and reliability	Lack of understanding of the exposure pathways inside (human) body and outside (human) body (exposure)
Use- to the extent possible- lessons learned from other nanomaterials	Lack of insight in reliability of in silico, in-vitro and in-vivo models toxico-kinetics and hazard (hazard)
	Limited availability of exposure/ release case studies, including measurements and guidance on exposure data, toxicokinetic data (risk assessment/ risk management)
	Data quality and reliability for the purpose of characterization and testing is questionable (definition)



ADME









Results RRAS and follow up survey II

Research question to pursue (challenge)	Regulatory risk assessment issues to overcome (scope)
Identify the minimal panel of parameters to determine equivalence/similarity in the different areas of regulatory risk assessment (identity is covered in this), with respect to:	Lack of knowledge on which physico-chemical characteristics are essential for risk assessment purposes within and across domains (definition).
with respect to: Phys-chem (intrinsic and extrinsic), Biological interactions, Toxicokinetics (ADME). 	Lack of harmonised understanding of equivalence of nanomaterials in regulatory context (e.g. parameters and methods to test equivalence) (definition)
Speed up the adoption of described parameters	Lack of grouping strategies (when are NM similar?) (definition)
Identify parameters and criteria for grouping and read across (equivalence)	

Equivalence



Similarity







Results RRAS and follow up survey III

Research question to pursue (challenge)	Regulatory risk assessment issues to overcome (scope)
Identify the usefulness of currently available non-nanomaterials exposure	Lack of validated exposure models (exposure)
models for nanomaterials (external exposure).	Limited availability of exposure/ release case studies, including measurements and guidance on exposure data,
If useful, validate the models for nanomaterials with measured data: share data, generate new data, incentives	toxicokinetic data (risk assessment/ risk management)



NAN RIGO

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Main conclusion RRAS and survey

- RRAS results are confirmed by follow up survey amongst more risk assessors from different domains
- RRAS results support recommendations from the ProSafe White Paper (2017)
 - Recommendation 6: Where possible, calls for nanosafety projects should be far more specific in giving clear instructions to ensure that data and results generated are of a type and form which allows their use in topics of regulatory relevance, such as choice of materials, test methods to be applied, SOPs and data management. The NanoSafety Cluster could play a role in defining such conditions.
- Risk assessors expressed the need for more informal transregulatory exchange of views and issues

REF: ProSafe (2017) The ProSafe White paper: Towards a more effective and efficient governance and regulation of nanomaterials. last visited July 2020







2nd Regulatory Risk Assessment Summit (2022)



Keeping pace with European ambitions for safe and sustainable nanomaterials and products:

Main Actions

- banning most harmful chemicals in consumer products (unless essential) including PFAS;
- "one substance one assessment" for risk and hazard assessment of chemicals;
- account for the cocktail effect of chemicals when assessing risks from chemicals;
- boosting production and use of safe and sustainable by design chemicals;
- global role by promoting high standards and not exporting chemicals banned.
- 1. One substance one assessment
- 2. New endpoints for risk assessment (nano)









Summary

> Research needs

- -Physico-chemical properties
 - stability of the nanomaterials
 - surface chemistry/reactivity
- -Human health endpoints

ECHA-NMEG

Environment: emission scenarios, relevant PECs <u>Human health</u>: dermal absorption, irritation & corrosion (skin/eye), reproduction/development toxicity, carcinogenicity/long-term toxicity

- dispersion stability in biological media and related dosing in toxicity testing
- dermal exposure route
- endocrine disruption, immunotoxicity, neurotoxicity, reprotoxicity
- -Environmental endpoints
 - Iong-term testing (including interference of fee_d)
 - biotic and abiotic degradation/transformation persistence
 - interactions with natural (particulate) matter (adsorption/desorption, heteroaggregation)
 mobility



Innovation Policy Ambitions Green Deal Scientific/RA challenges

> Share lessons learned

Open to finding solutions with other regulatory communities and domains





Thanks to all partners and people in NMBP-13 projects

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