# Workshop report
## Regulatory Risk Analysis Summit

**Date: 4-5 December 2019**
**Place: RIVM Bilthoven, The Netherlands**
**Participants: see Annex I**


## Summary

At Dec 4-5 2019, a Regulatory Risk Analysis Summit (RRAS) has been successfully organized at RIVM in Bilthoven. About 40 colleagues (from inside and outside Gov4Nano) with affinity for risk assessment of nanomaterials within different disciplines (food, chemicals, environment, medical devices, worker and cosmetics) participated in this interactive workshop. Issues concerning risk assessment of nanomaterials have been discussed in transdisciplinary groups and relevant research questions for funding agencies have been formulated. Also a 'value proposition' workshop has been organized to discuss the added value of a future NRGC for regulatory risk assessors.


## 1. Introduction

### 1.1 Background

Nanotechnologies are characterized by a legacy of already marketed and manufactured nanomaterials (NMs), nano-enabled products and continuously growing research activities, resulting in new materials, devices and applications across a multitude of sectors.
Methods and approaches for risk analysis are challenged by the novelty and uniqueness of nanomaterials. A growing set of risk data and information are needed to keep pace with innovation. Both material and product-specific regulatory frameworks worldwide, are introducing specific requirements for nanomaterials, although effective implementation is often challenged by a lack of guidance and data.
Risk assessors and risk managers, within regulatory and inspection bodies and industry, struggle to gain an overview of knowledge fragmented across a multitude of regulatory domains. As a result, commonly shared risk assessment questions and issues remain unresolved. In addition, present regulatory research agendas focus only on particular domains of application (e.g. REACH) and often do not consult regulatory risk assessors who deal directly with dossiers. This creates missed opportunities in building the appropriate weight of evidence to address regulatory information gaps.

### 1.2 Aim of the Summit

The **Regulatory Risk Analysis Summit** (RRAS) was organized to provide a forum to discuss risk assessment needs and expectations of stakeholders across disciplines and domains, and together find solutions to address the complexity of risk analysis for nanomaterials.


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- **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.

To that end policy makers, regulatory bodies, companies and other stakeholders involved in managing novel and emerging risks were invited. Participants were encouraged from a broad spectrum of disciplines and should have sufficient risk management, regulatory and policy experience to be able to contribute to discussions.

### 1.3 Why this RRAS in short:

*WHY*:

o Risk assessors and risk managers, within regulatory and inspection bodies and industry, struggle to gain an overview of knowledge fragmented across a multitude of regulatory domains. As a result, commonly shared risk assessment questions and issues remain unresolved. In addition, present regulatory research agendas focus only on particular domains of application (e.g. REACH) and often do not consult regulatory risk assessors who deal directly with dossiers

*WHO:*

o A transdisciplinary network consisting of 40 participants from 6 different regulatory domains: chemicals, workers, environment, food, cosmetics, medicine/ medical devices

*HOW:*

o Identify the regulatory risk assessment issues per domain and select top two
o Present the domain specific top two in a transdisciplinary group
o Select relevant issues that can be translated into research questions
o Write the research question for a funding agency
o Identify the role of a Nano Risk Governance Council to provide solutions for additional regulatory risk assessment issues

### 1.4 Link with the Gov4Nano project

The RRAS should be envisaged within a wider perspective than a forum to gather transdisciplinary regulatory issues and the need for scientific knowledge development to solve these issues. The outcomes of the summit will be brought forward to funding agencies to actively stimulate the uptake of issues by the scientific community. Moreover, a

monitoring scheme initiated and probably performed by the Nano Risk Governance Council (under development) will keep track on the uptake of the identified issues (See Figure 1).

Moreover, this RRAS is foreseen to be part of a longer term initiative to build greater interaction across domains and disciplines within regulation and will create a mechanism through which regulatory stakeholders can share priorities, learnings and good practice. A collaboration with the H2020 project REFINE (www.refine.eu) was established to give input on regulatory risk assessment issues in the nanomedicine domain. The Knowledge Exchange Conferences (KEC) in REFINE will take the outcomes of this RRAS into account.

## 2. Programme of the workshop

The programme of the RRAS is described in the scheme mentioned below. In the current report, the results of the plenary and break-out sessions with respect to regulatory risk assessment issues, and research questions based on these issues will be reported in detail.

**Day 1: 4 December 2019**

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| **12:00-13:00**<br>*T 0.12* | **Registration – walk-in lunch, meet and greet** |
| **13:00-13:10**<br>*T 0.12* | **Welcome to participants**<br>*Susan Wijnhoven* |
| **13:10-13:25**<br>*T 0.12* | **Questions to participants relating to risk of innovations (getting to know each other)**<br>*Harmen Kloosterboer/ Lya Hernandez* |
| **13:25-13:45**<br>*T 0.12* | **Goals of the next 2 days**<br>*Adrienne Sips* |
| **13:45-14:00**<br>*T 0.12* | **Introduction regulatory frameworks and requirements for nano in various disciplines**<br>*Phil Sayre/ Eric Bleeker* |
| **14.00-14.30**<br>*T 0.12* | **Interactive session: first impression of regulatory issues**<br>*Harmen Kloosterboer/ Lya Hernandez* |
| **14:30-15:00** | **Coffee / Tea break** |
| **15:00-16:30**<br>*T 0.12*<br>*T 0.08*<br>*T 0.04* | **Break out session** (per discipline/ regulatory framework)<br>• Recap of interactive session (before the break)<br>*Harmen Kloosterboer/ Lya Hernandez*<br>▪ Pitch of case studies (input from participants)<br>▪ Create a list of discipline-specific risk assessment issues |
| **16:30-17:00**<br>*T 0.12* | **Plenary session**<br>*Rob Aitken*<br>**Feedback on issues from the different disciplines** (workers, chemicals, environment, biocides, food, cosmetics, medicine/ medical devices) |
| **17:00-17:15** | **Short break** |
| **17:15-18.00** | **Reflection in conjunction with regulatory gap analysis and REFINE white paper**<br>*Susanne Bremer-Hoffmann/ Monique Groenewold* |
| **18:00-20:00** *PV Home* | **DINNER** |

**Day 2: 5 December 2019**

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|---|---|
| **08:30-09:00**<br>*T 0.12* | **Registration –meet and greet, coffee and tea** |
| **09:00-09:15**<br>*T 0.12* | **Welcome (back) and questions to participants**<br>*Harmen Kloosterboer/ Lya Hernandez* |
| **09:15-09:45**<br>*T 0.12*<br>*T 0.08*<br>*T 0.04* | **Break-out session: Wrap-up issues**<br>Make a top-2 of issues per domain |
| **09:45-11:00**<br>*T 0.12*<br>*T 0.08*<br>*T 0.04* | **Break out session**<br>Create a **transdisciplinary short list** based on a set of **criteria** and the issue has to be translated to a **research question** |
| **11:00-11:20** | **Coffee / Tea break** |
| **11.20-11.45**<br>*T 0.12* | **Plenary session**<br>*Rob Aitken*<br><br>**Feedback on transdisciplinary issues from break-out groups:** Presentation of issues and overlap |
| **11.45-12.00**<br>*T 0.12*<br>*T 0.08*<br>*T 0.04* | **Break out session part I:**<br>Translation of transdisciplinary issues into research questions: selection of issues to work on |
| **12:00-13:00** | **Lunch** |
| **13:00-14:00**<br>*T 0.12*<br>*T 0.08*<br>*T 0.04* | **Break-out session part II:**<br>Translation of transdisciplinary issues into research questions |
| **14:00-16:30**<br>*T 0.12* | **Value proposition workshop**<br>*Rob Aitken* |
| **16:30-17:00**<br>*T 0.12* | **Summary of the summit and follow up**<br>*Adrienne Sips* |
| **17:00** | **End of Regulatory Risk Analysis Summit 2019** |

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## 3. Results

In the workshop, the following risk assessment issues were discussed (word cloud based on the issues brought up by the participants).

**In one word, what issue do you hope will be addressed today?**


In order to facilitate fruitful discussions, the 40 participants were divided in the following 6 different groups based on their discipline (given by the participants during the registration for the event):

- Chemicals
- Worker
- Cosmetics
- Environment
- Medicines/ medical devices
- Food

The issues were divided into "Issues with respect to toxicity testing: exploratory research or validation of tests of NM's" and "Issues with respect to regulatory risk assessment of NM's". These were discussed in a plenary session afterwards, most of the issues discussed seemed to be potential relevant for all disciplines, although there appeared to be also some discipline-specific issues.

After that, a prioritization of the issues has been performed in transdisciplinary break-out groups. For this, the issues were divided in 4 categories; Definition/ harmonization/ equivalence, Exposure, Hazard, and Risk assessment.

A small impression of the issues is given in the table below, this is just a part of the issues mentioned in the summit.

In the next session of the workshop, the participants were encouraged to formulate research questions for the issues mentioned, these research questions should be ready to be sent to funding agencies. Research questions were formulated for the following main topics:

- Definition/ harmonization/ equivalence,
- Exposure,
- Hazard
- (Bridging the gap between science and regulation)

| | Nano-definition/ harmonization/ equivalence | Exposure | Hazard | Risk assessment |
|---|---|---|---|---|
| What parameters and methods to test definition/ harmonization/ equivalence? Data quality. | x | | | |
| Exposure: inside (human) body, outside (human) body, environment Exposure over lifetime, cellular uptake, exposure level, release, fate assessment (environment: focus on sinks sediment/ soil), transformations, data quality | | x | | |
| Hazard: how do you know a nanoform is safe + how do you make a nanoform safe? In vitro and in vivo test methods, alternative methods (in vitro and in silico to reduce animal testing): safety question includes exposure | | | x | |
| Develop validated risk management strategies and good practices towards reducing exposure to safe levels | | | | x |
| Collect high quality realistic exposure data to better understand exposure to relevant nanomaterials throughout the life cycle to improve and validate exposure models | | x | | |
| Development of reliable and regulatory accepted (non-animal) testing methods relevant for risk assessment purposes. E.g. Cellular uptake and transportation across barriers, AOPs | | | x | |
| How to demonstrate equivalence of NMs for risk assessment purposes within and across domains | x | | | x |

One example of a research question formulated during the meeting was

1. What is the minimal panel of parameters to determine equivalence/similarity for regulatory risk assessment (identity is covered in this) with respect to:

Phys-chem (intrinsic and extrinsic)
Biological interactions
Toxicokinetics(ADME)??

## Conclusion from the workshop.

In general, the RRAS has been highly appreciated among the participants. The information (at least the regulatory risk analysis issues) were maybe not that new but more a confirmation of what we already know. However, it was very valuable to discuss these issues transdisciplinary and with people within different stages of the decision making process (researchers, risk assessors, regulators).

The output of this workshop is a provisional list of transdisciplinary regulatory issues, from the perspective of regulatory risk assessors. Beside this list a provisional list of transdisciplinary research questions, addressing the regulatory issues was generated during the workshop.

The workshop also gave room for a Value Proposition session, identifying the needs of regulatory risk assessors dealing with nanomaterials or nanoproducts. The results of this workshop will be evaluated by IOM and will fuel in activities and reporting of Task 6.1 (stakeholder background analysis and force field analysis). Moreover, these results will form input into a brainstorm workshop on NRGC design (Feb 21st 2020, Schiphol).
During the workshop a.o. first results of task 7.1 (minimal data set) and the White Paper on Scientific Issues in the risk assessment of NanoMedicine, as developed in the H2020 project REFINE were shared. A structural collaboration with the REFINE project will be established. Outcomes of the RRAS will be presented in the next REFINE Knowledge Exchange Conference (June 25th).