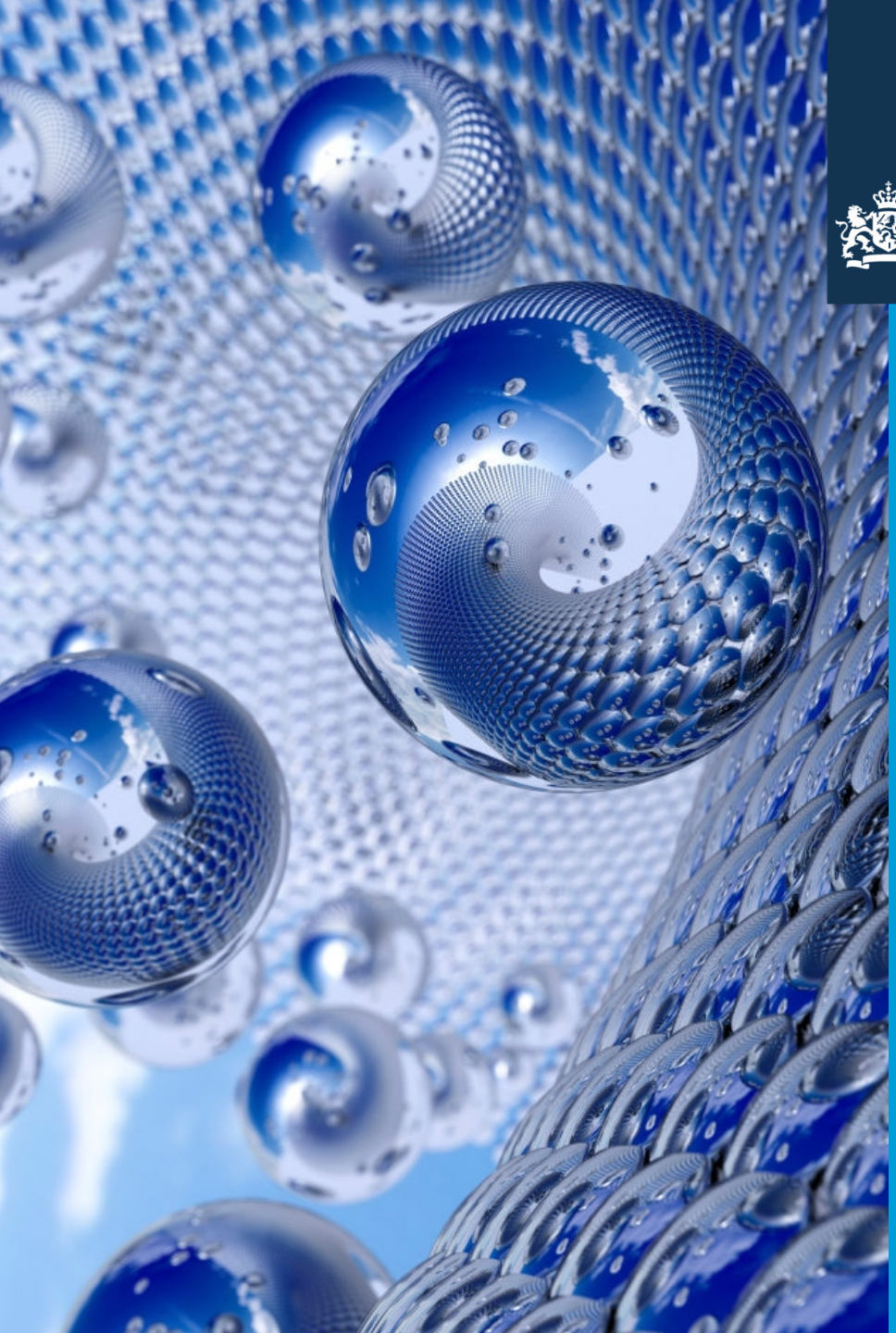

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Towards Health-based ‘Nano Reference Values’

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Dutch Nano Reference Values (NRV): a **pragmatic** tool for workplace risk assessment

NRV Class	Description	Examples	NRV (2012) (8-hr TWA)
1	Rigid, biopersistent nanofibres for which effects similar to those of asbestos are not excluded	SW… metal oxi… asb… re not excluded by manufacturer.	0.01 fibres/cm³ (= 10,000 fibres/m³)
2A	Biopersistent granular nanomaterial in the range of 1 and 100 nm and a densitiy of > 6000 kg/m³	Ag, … Fex… SnO2	20,000 particles/cm³
2B	Biopersistent granular and fibre form nanomaterials in the range of 1 and 100 nm and a densitiy of <6000 kg/m³	Al2… ², ZnO, nan… k, C60, den… Nar… asb… re excluded	40,000 particles/cm³
3	Non-biopersistent granular nanomaterials in the range of 1 and 100 nm	e.g. fats, common salt (NaCl)	Applicable OEL for the non-nano form

Based on OEL for asbestos

Pragmatic values, based on urban background concentrations and particle size vs density (IFA, Germany)

The Dutch Nano Reference Values (NRV)

The Dutch NRV were developed in 2011 as a **pragmatic tool** for exposure assessment of nanomaterials at the workplace.

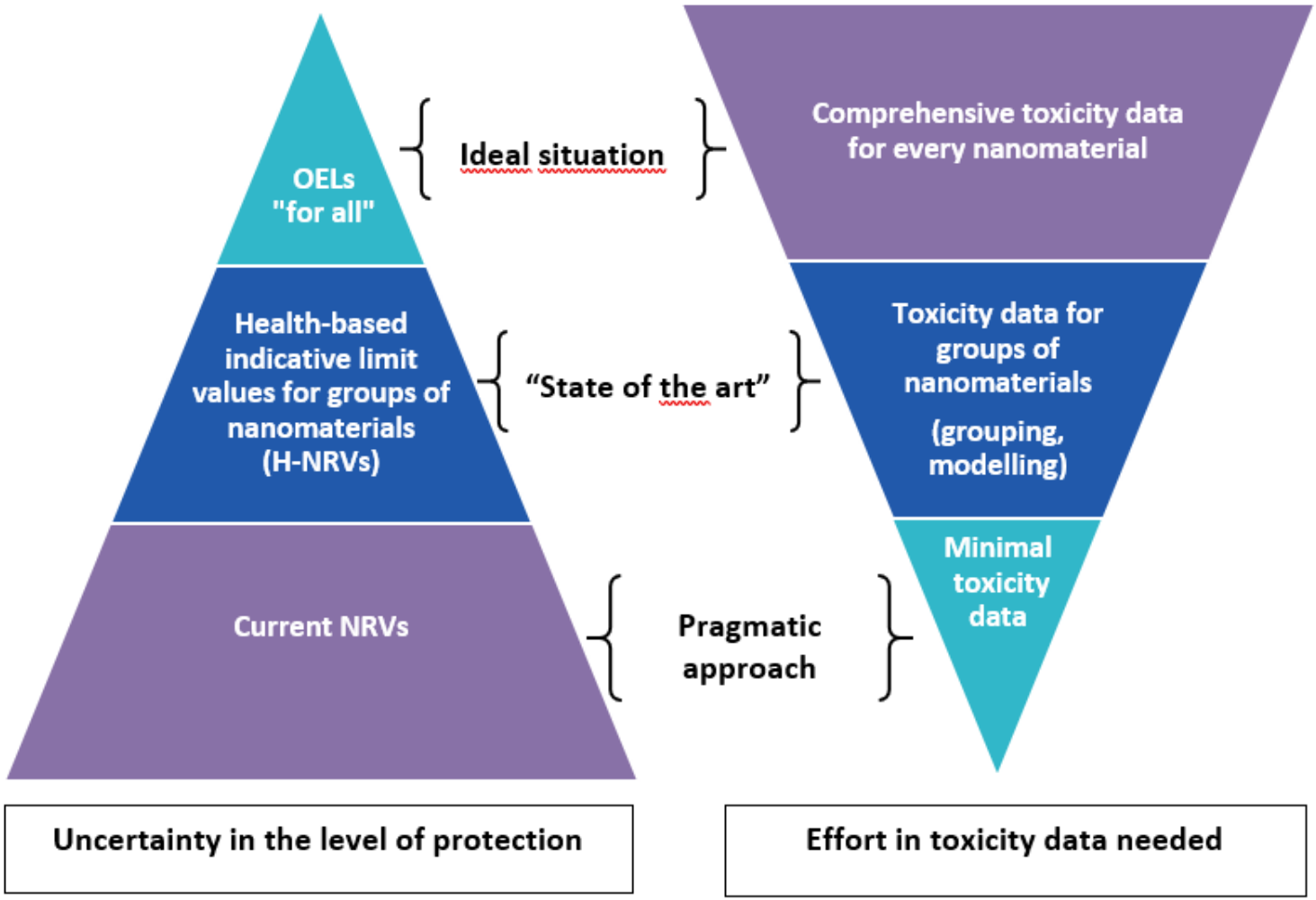
In NL, they are **accepted** as **benchmark values** in occupational risk assessment **in the absence of OELs** since 2012 (van Broekhuizen et al 2012; SER 2012).

They are also used in other countries.

Evaluation of NRVs (2017): NRVs may not always be protective (Buist et al 2017; Van Broekhuizen 2017)

>>> With the current state of knowledge, could we derive **health-based** NRVs?

The balance between effort and uncertainty…

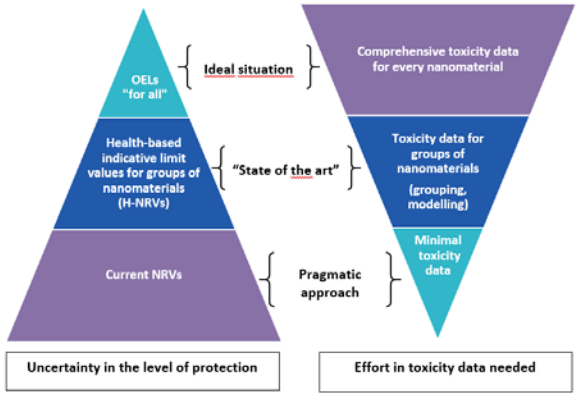


Goal of the current project

Use state of the art scientific knowledge on health effects caused by ENMs to advise on HNRVs, to better protect workers

Questions:

1) What ENM-categories should be distinguished to derive HNRVs?
2) What evidence would be needed to define values for these categories? and
3) How much effort would it take to achieve this?



What kind of data could be useful?

NM-specific data

- Recommended OELs (oa NIOSH, NRCWE)
- Human toxicity data (epidemiological studies)
- Animal toxicity data (oa CNT, TiO2, SiO2)

Grouping initiatives

- Grouping and read across (e.g. GRACIOUS)
- Adverse Outcome Pathways

Particle toxicity data

- e.g. Carbon Black, Diesel exhaust, ultrafine particles

>>> Can we use those data to derive health-based NRV for groups of nanomaterials?
If yes, how?

Expert panel approach (in kind contributions!)

Expert panel approach (in kind contributions!)

- **Online discussion meetings (4)**

  RIVM (lead), KLB, NRCWE, LEITAT, HSE, NIOSH, SCOEH

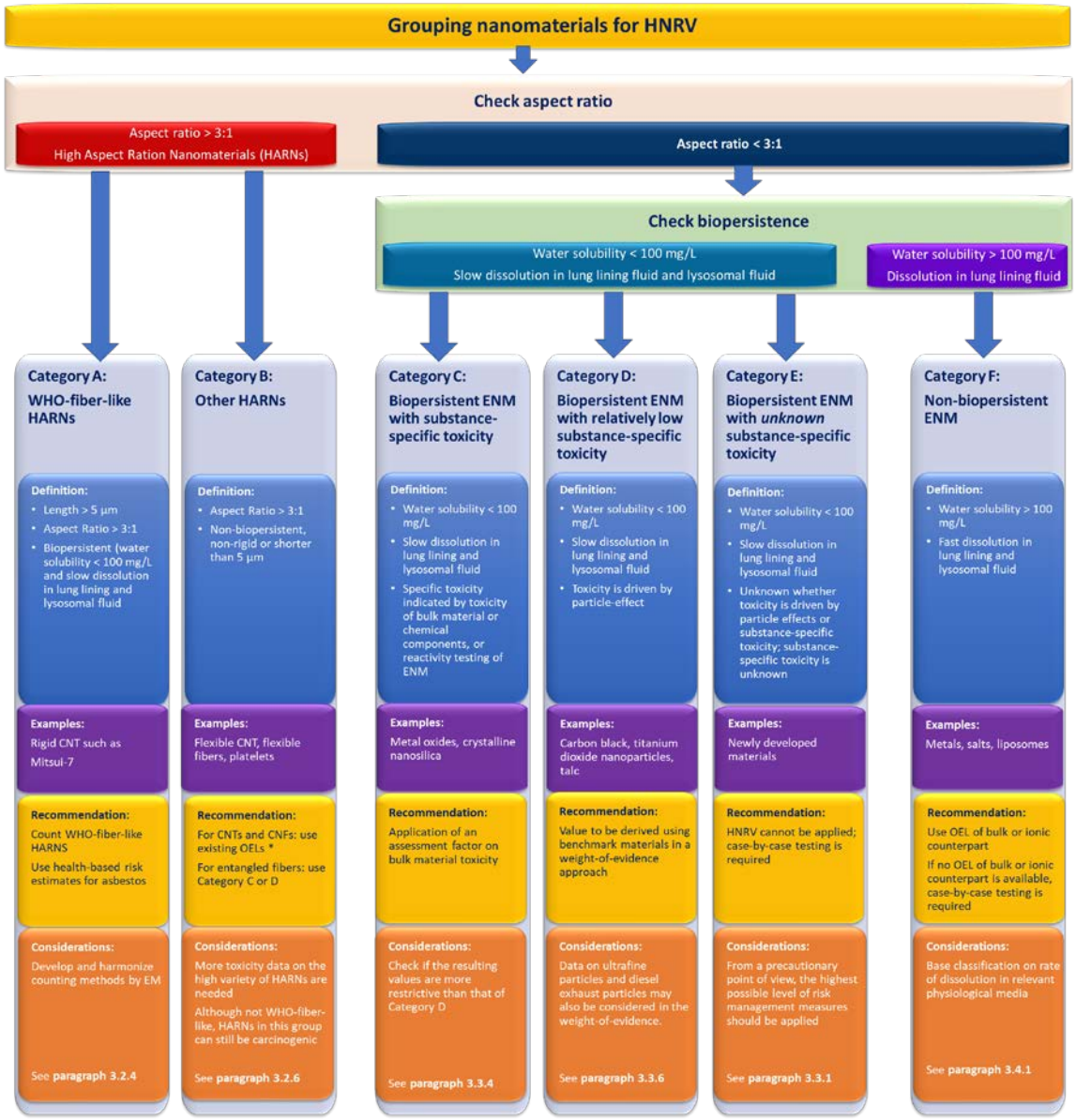
- **Written input (review panel: 2 rounds)**

  BAuA, IFA, VITO, NLIA, INSHT, SUVA, NIOSH, RIVM

Proposed HNRV categories:

A) WHO-fiber-like HARNs
B) Other HARNs
C) Biopersistent ENM with substance-specific toxicity
D) Biopersistent ENM with substance-specific toxicity
E) Biopersistent ENM with unknown toxicity
F) Non-biopersistent ENM

PGNPs: could be assigned to one of the categories based on type of process/material



Recommendations on further work (I)

Developing a harmonized methodology to **measure and count** nanofibers for category A.

– Methods are available (e.g., Meyer-Plath et al., 2020), but not yet standardized.

Derive cut-off values for dissolution rates in relevant physiological conditions as an estimate of biopersistence.

– Work is ongoing in international projects, e.g. in GRACIOUS

Recommendations on further work (II)

Derive a precautionary assessment factor which can be applied to bulk OELs in **subgroup C** (biopersistent nanomaterials with substance-specific toxicity).

– This needs evaluation of data on bulk- and nanoforms of the same substance

Derive a value for HRNV of category D (biopersistent nanomaterials with relatively low substance-specific toxicity).

– This needs combining of human and animal data in a weight-of-evidence approach

Generate more hazard data for the materials in **subgroup B** (non-WHO-fiber-like HARNs).

How could HNRVs be used in the workplace?

Recommendation to use available info in this order:

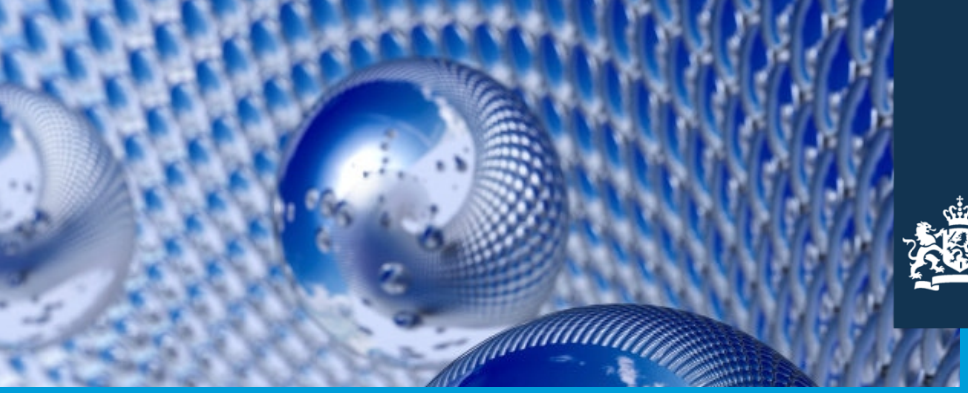
1) Nanomaterial-specific national statutory (legally binding) OEL

2) Nanomaterial-specific recommended worker exposure limit published by governmental institutes or scientific literature (e.g., TiO2 (ANSES), CNT (NIOSH REL))*

3) Self-derived, “company” OEL based on nanomaterial-specific toxicity data (e.g., REACH DNEL)

4) Use HNRV

*Overviews of more exposure limits for NM can be found in WHO 2017, Mihalache et al 2017



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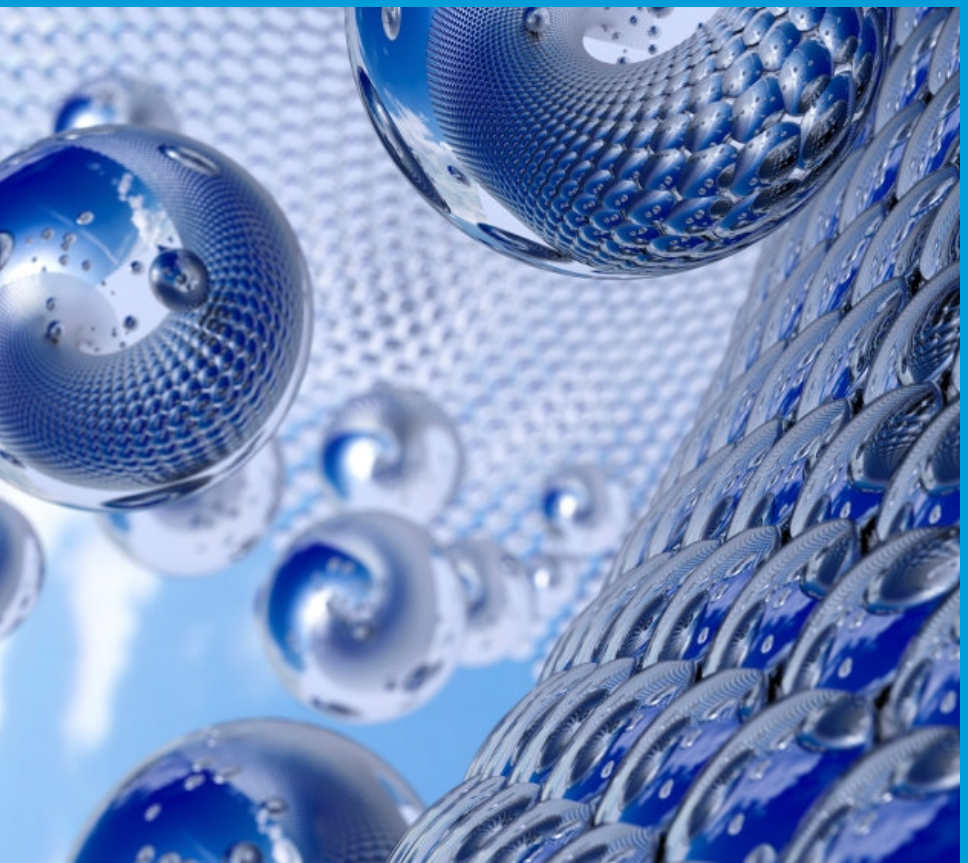
Thank you



Core Panel:
Delphine Bard, Pieter van Broekhuizen, Susan Dekkers, Ilse Gosens, Gemma Janer, Eileen Kuempel, Michael Riediker, Maaike Visser, Ulla Vogel

Review panel:
Renate Beisser, Flemming Cassee, Evelien Frijns, Thomas Gebel, Monique Groenewold, Laura Hodson, Ruth Jimenez, Michael Koller, Markus Mattenklott, Jurgen Mook, Eberhard Nies, Dirk Pallapies, Astrid Lund Ramstad

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