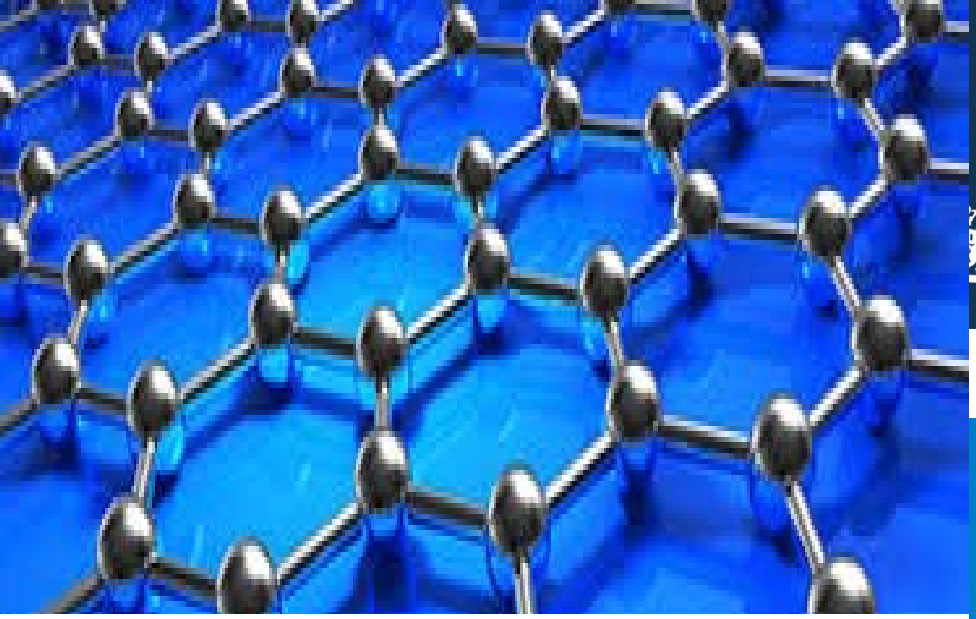

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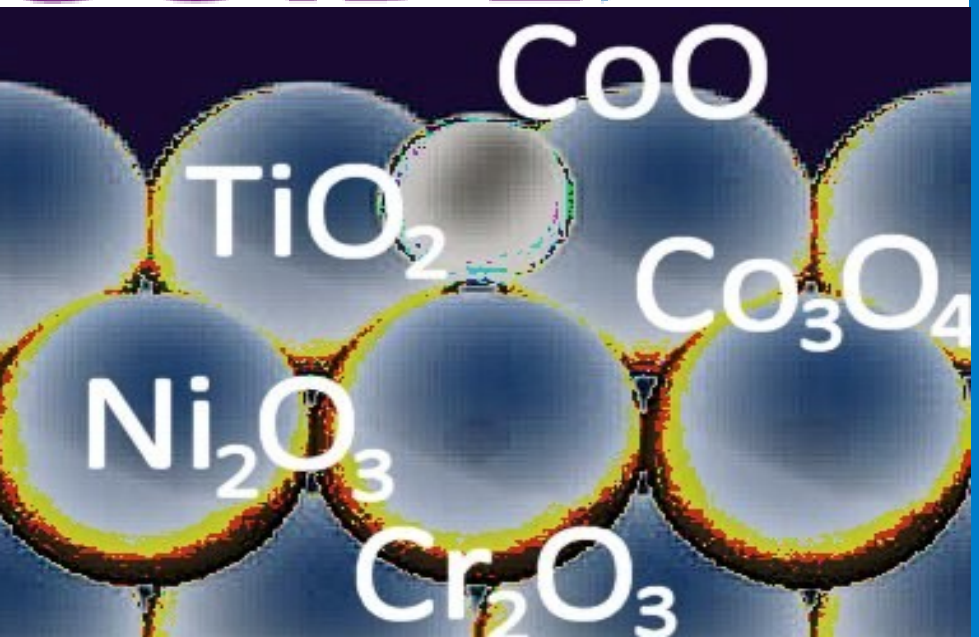

Development of a risk assessment strategy within the GUIDEnano project

Dr. Susan Wijnhoven

RIVM

Sustainable Nanotechnology Conference 2015

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Project Consortium

Universities & Research Centers

LEITAT Technological Center — managing your technologies — member of TECNIO

VENEZIA RICERCHE

cea liten

UNIVERSITY OF GOTHENBURG

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IOM

TNO innovation for life

INSTITUTO TECNOLÓGICO DEL EMBALAJE, TRANSPORTE Y LOGÍSTICA — ITENE

ICN Institut Català de Nanotecnologia

UNIVERSITY OF EXETER

Rijksinstituut voor Volksgezondheid en Milieu
Ministerie van Volksgezondheid, Welzijn en Sport

Finnish Institute of Occupational Health

UPPSALA UNIVERSITET

NERC SCIENCE OF THE ENVIRONMENT

INIA Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria

Industry

PlasmaChem

LATI

inoTEX®

Servià Cantó

NanoServices

INNVENTIA

GEOCHEM RESEARCH

Honeywell

HEMPEL Estd 1915

Pinsent Masons

Main Goal

Develop innovative methodologies to **evaluate** and **manage** **human and environmental health risks of NM-enabled products, considering the whole product life cycle**

Interactive digital Guidance Tool

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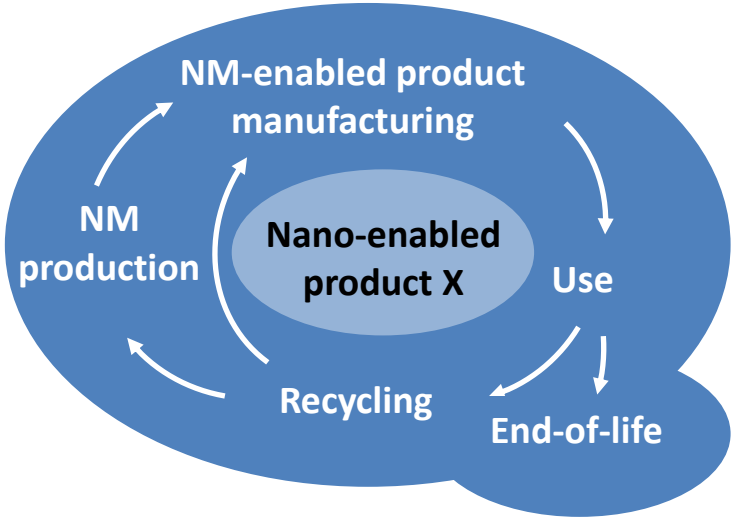
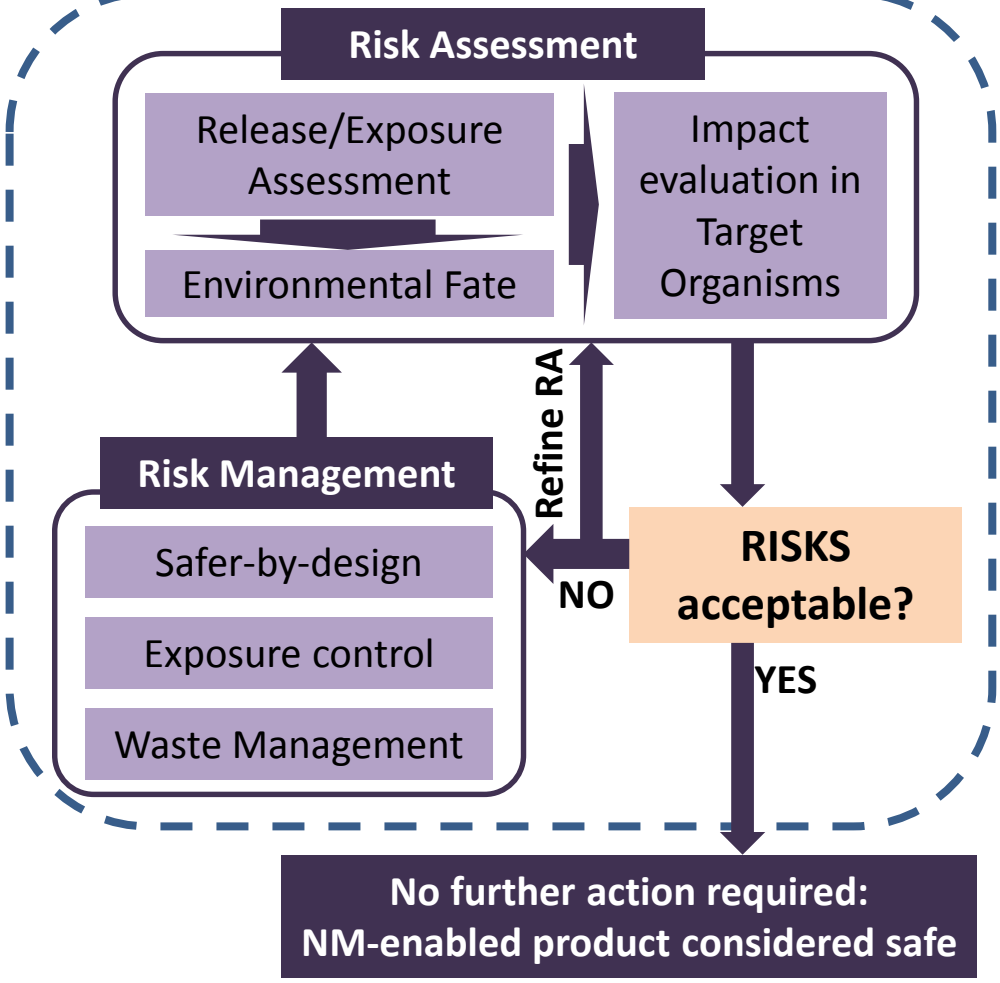
Target and scope

THE TARGET
NM-enabled product Life Cycle



SCOPE OF THE GUIDANCE



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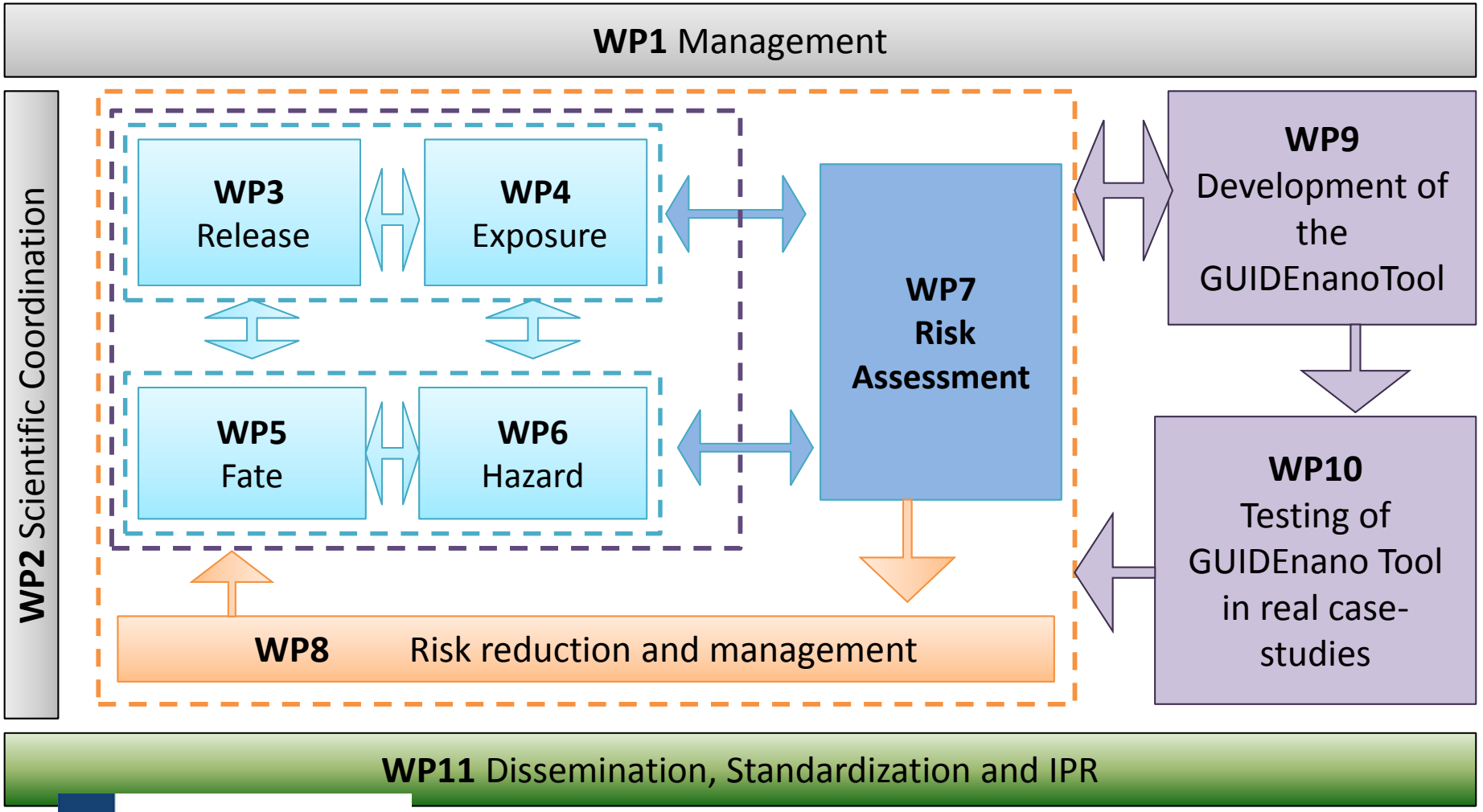
Organization in WPs



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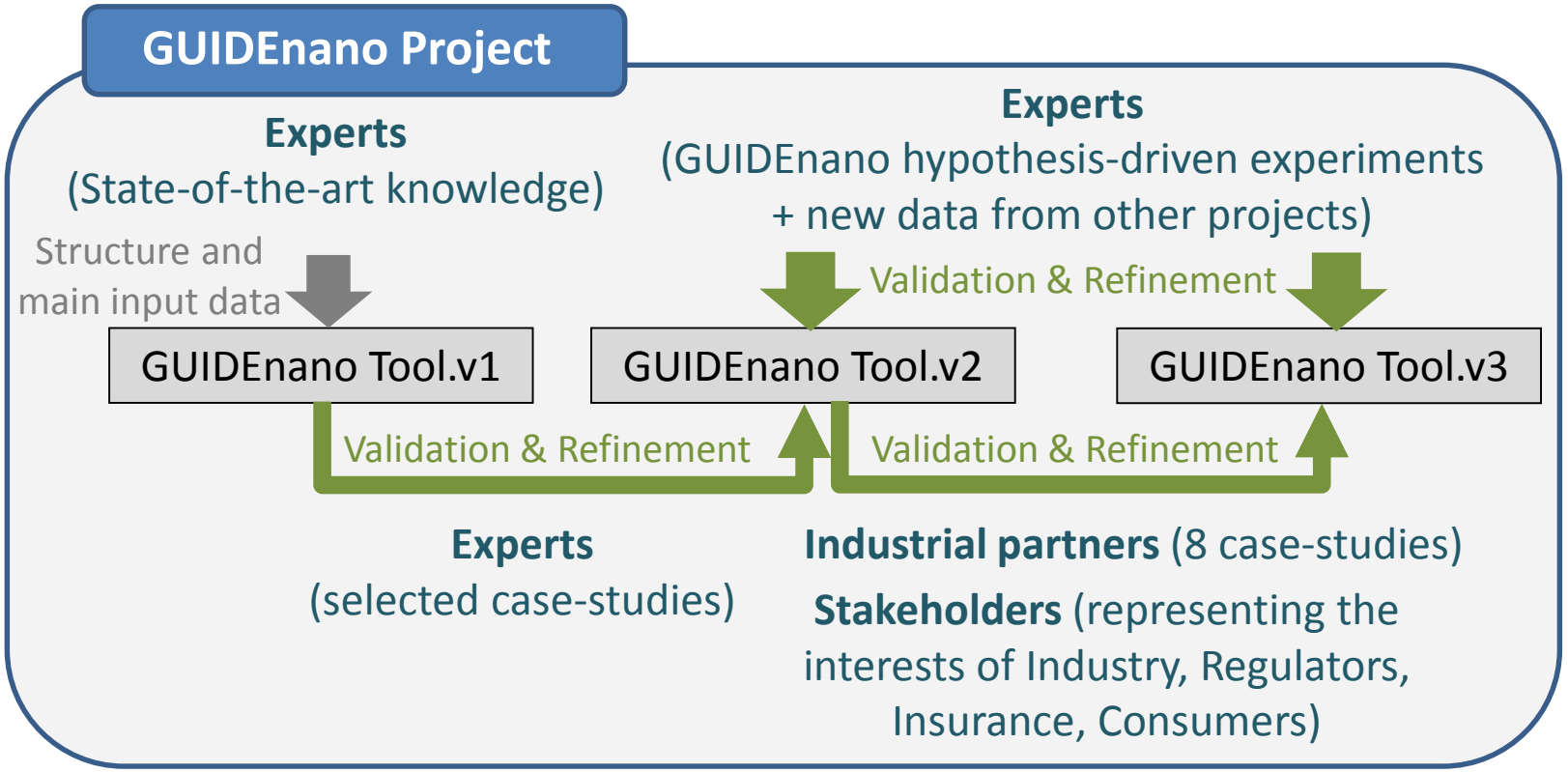
Project Timeline



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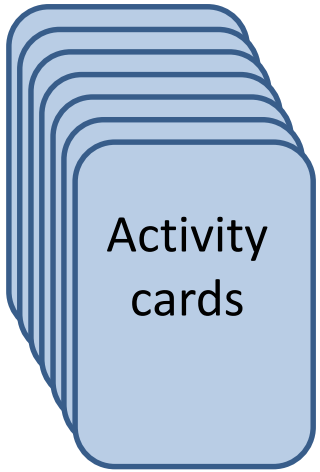
The Tool



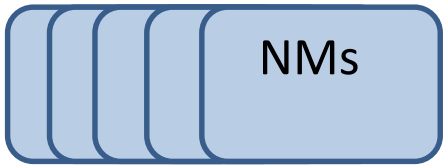
Default
Decision tree
Model

Release to relevant environmental / human compartments

Environmental fate modelling

Exposure levels and NM form in relevant environmental / human compartments

Read-across



Hazard endpoints values

WoE / Prioritization algorithm

Read-across Relevance / Quality score

Toxicity studies available to the user

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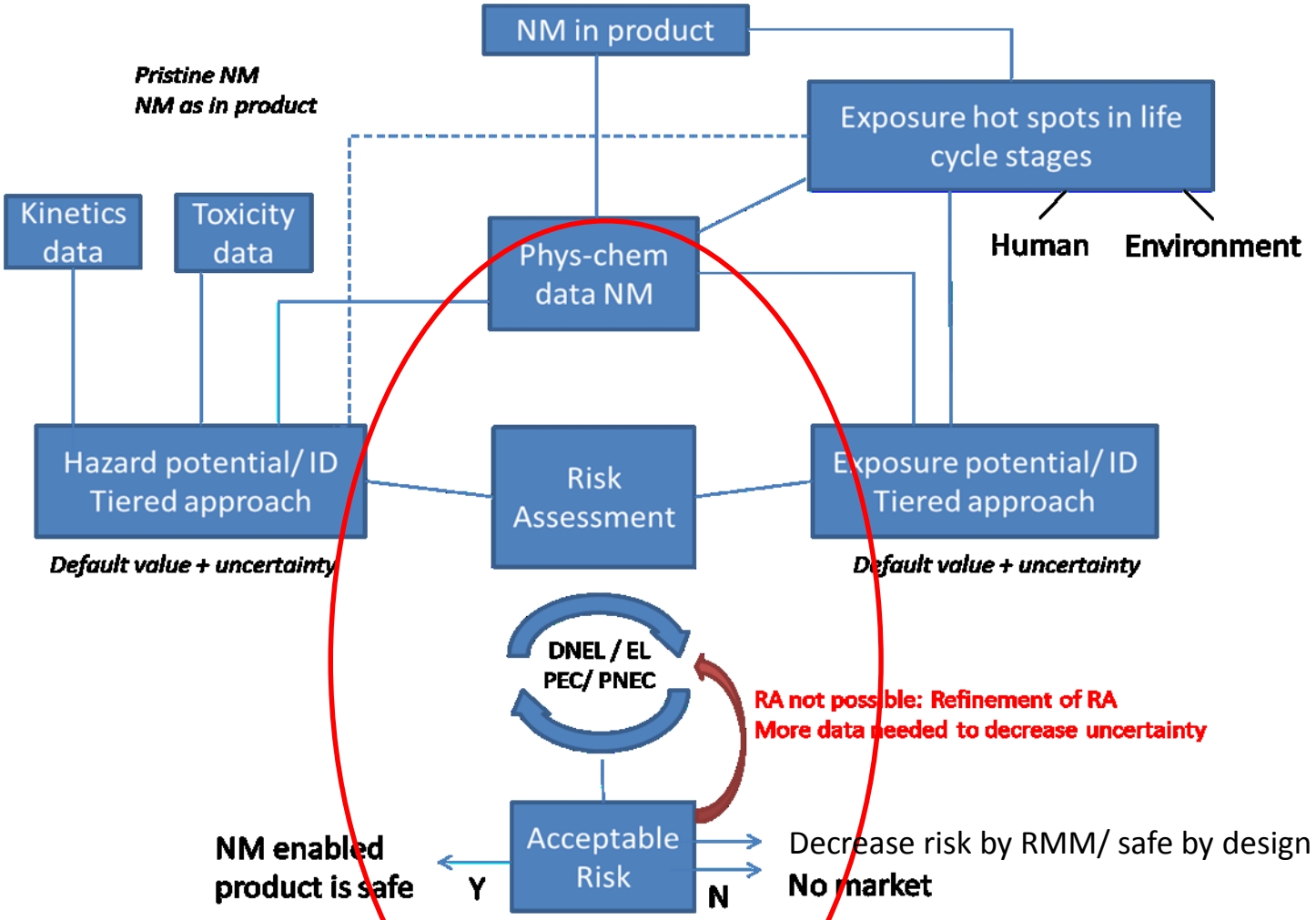
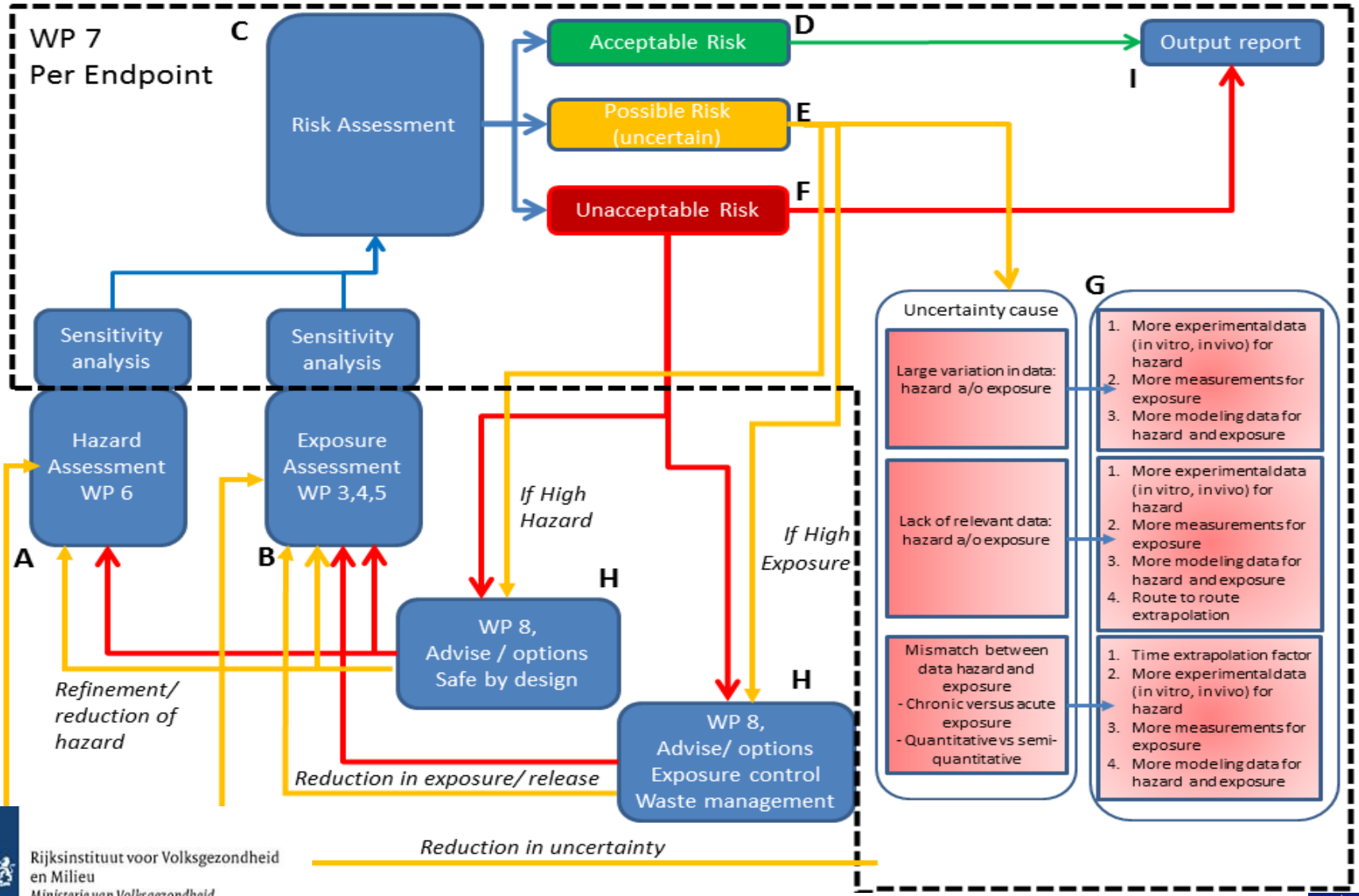
Risk assessment



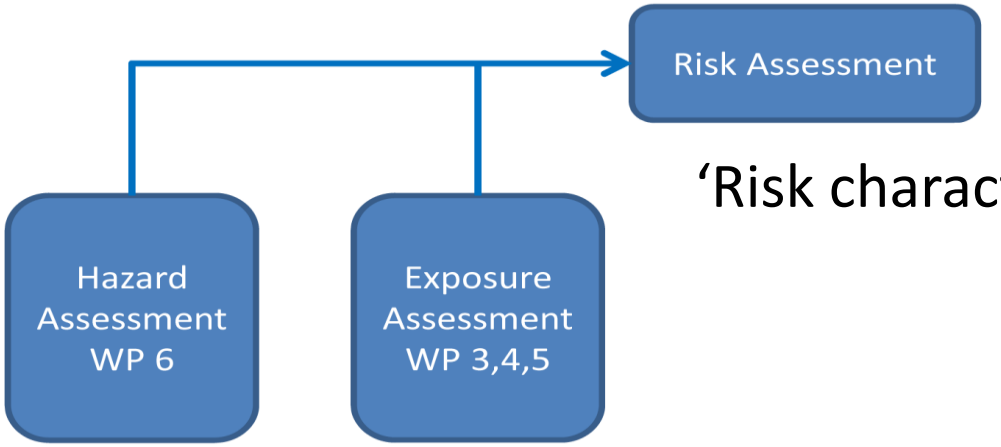
Risk assessment

- Risk assessment decision flow:
  - Divided in 4 main elements
    - Input and information requirements (exposure and hazard assessment)
    - Risk assessment (calculation of risk and classification into 3 categories)
    - Recommendation for follow-up actions (reduction of uncertainty, risk mitigation)
    - Output report

Risk assessment



Information requirements



'Risk characterisation ratio' (RCR):

$$\frac{exposure}{hazard\ value}$$

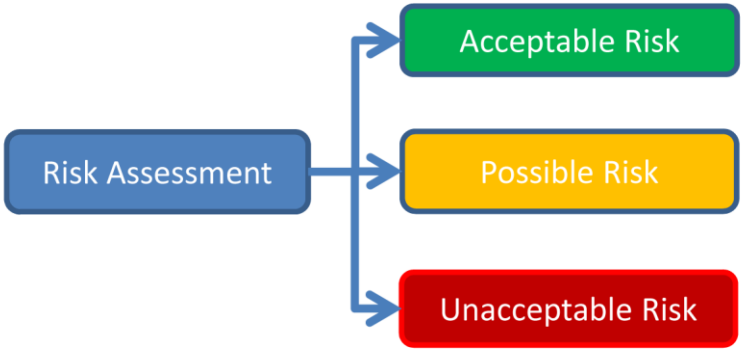
- Exposure:
  - relevant exposure routes/ duration
  - model output, exposure libraries, direct measurement data
- Hazard:
  - relevant endpoints with (if possible) quantitative exposure estimate with uncertainty

Hazard endpoints

- Identification of human hazard endpoints to be addressed for each exposure scenario

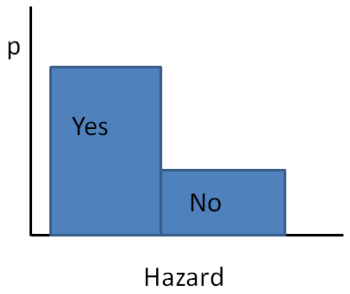
route	duration	endpoints to be evaluated	Endpoints		Quantitative ?
inhalation	single	1,3,4,6, 7	1	Irritation/corrosion	N
	repeated	1,2,3,5,6,7,8	2	sensitisation	N
dermal	single	1,3,4,6, 7	3	absorption/accumulation/elimination	Y
	repeated	1,2,3,5,6,7,8	4	acute toxicity	Y
oral	single	1,3,4,6,7	5	repeated dose toxicity	Y
	repeated	1,2,3,5,6,7,8	6	mutagenicity	N
			7	carcinogenicity	N/Y
			8	reproductive and developmental toxicity	Y

Risk assessment qualitative endpoints



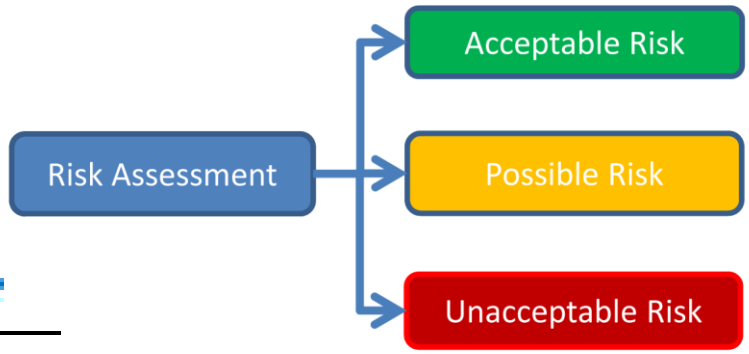
Yes/No answer with uncertainty value

Exposure		YES			NO		
Hazard		Low uncertainty	Medium Uncertainty	High uncertainty	Low uncertainty	Medium Uncertainty	High uncertainty
YES	Low uncertainty	Risk			No Risk		
	Medium Uncertainty				No Risk		
	High uncertainty				No Risk		
NO	Low uncertainty	No Risk	No Risk	No Risk	No Risk	No Risk	No Risk
	Medium Uncertainty				No Risk		
	High uncertainty				No Risk		



Uncertainty	Ratio Y/N
Low	70-90 / 10-30
Medium	50-70 / 30-50
High	50/50

Risk assessment quantitative endpoints

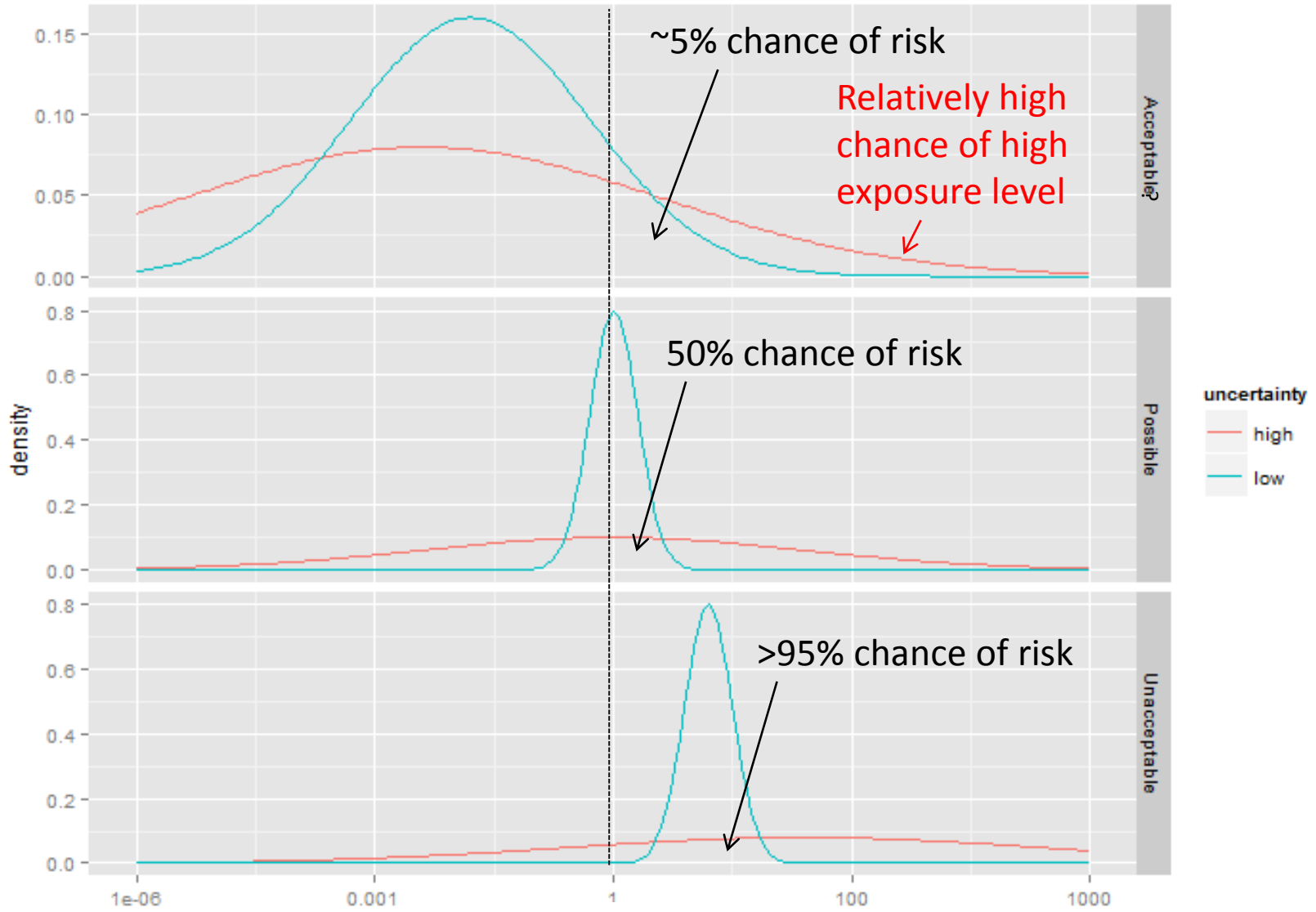


$$\frac{exposure}{hazard\ value}$$

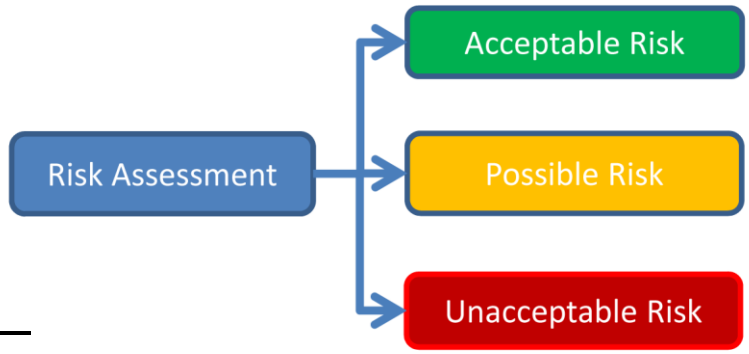
Exposure = certain amount per time in mass/ time
or surface area/ time or number of particles/ time

Hazard = lowest exposure level at which an adverse event can be expected ('DNEL', default, PNEC)

What risk is “acceptable”?



Risk assessment quantitative endpoints



$$\frac{exposure}{hazard\ value}$$

Change from acceptable to "probability of risk"

Defaults:

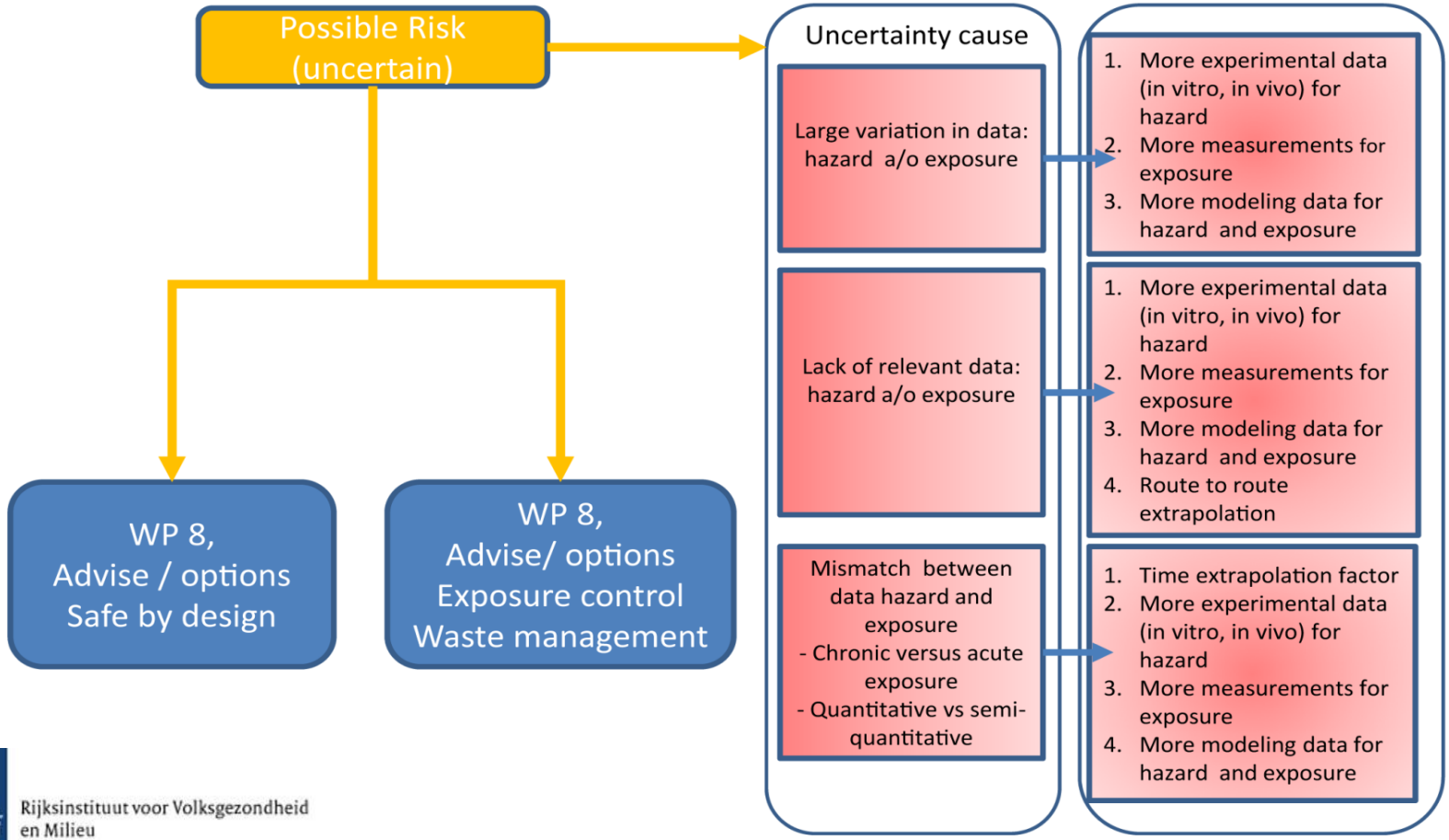
Acceptable risk, low probability of risk : <5% probability on a ratio of > 1.

Possible risk, medium probability of risk: 5-75% probability on a ratio of > 1.

Unacceptable risk, high probability of risk: >75% probability on a ratio of > 1

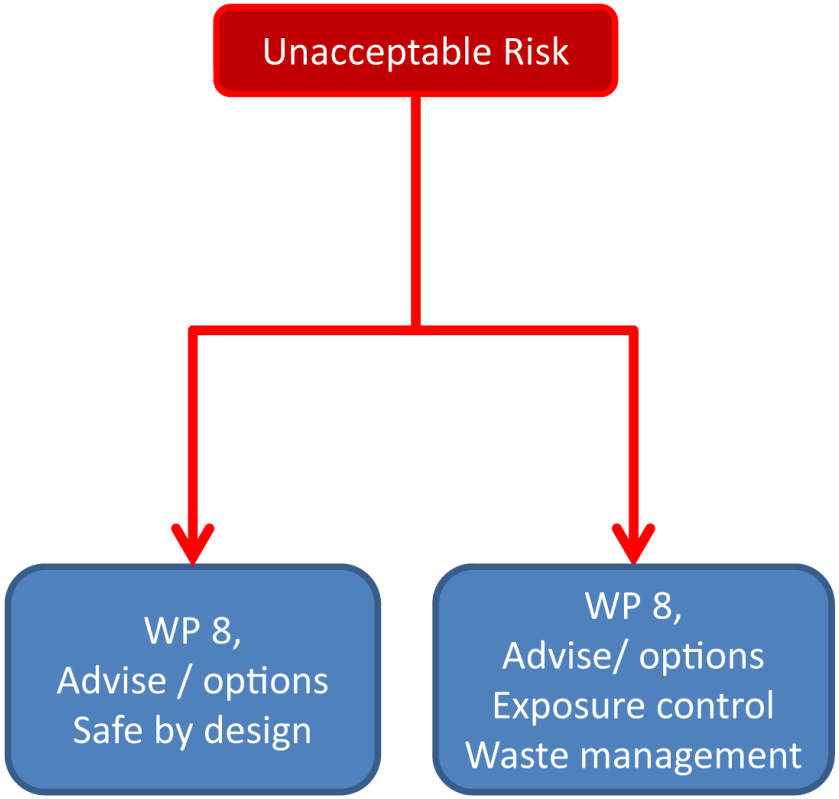
Follow up actions

Possible risk: reduction of risk or reduction of uncertainty



Follow up actions

Unacceptable risk: reduction of risk



Future work: risk assessment

- Continue with tool development
- Discuss and review definition of (acceptable) risk
- Further development of uncertainty/ sensitivity analysis
- Definition of content of output report
- Stakeholder analysis of tool
- Validation with case studies

Acknowlegdements

- GUIDEnano project consortium
  - All partners
    - Gemma Janer (LEITAT)
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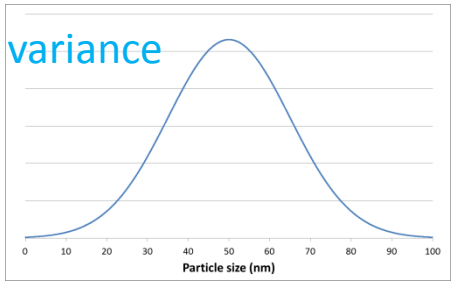
What is uncertainty?

Measured data can be summarized with an average value and standard deviation. This is the ***variance*** in the data.
Extrapolation of the data (e.g. from one scenario to the next, or from animals to humans) will introduce ***uncertainty***.
Model estimation of parameter values will also introduce ***uncertainty***.

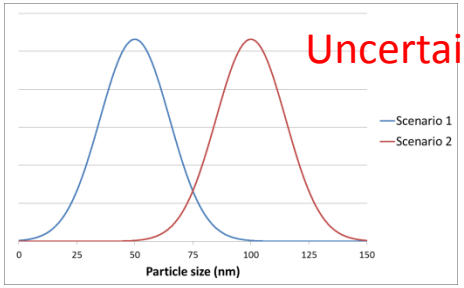
Introduced level of uncertainty		SCENARIO		
		IDENTICAL	COMPARABLE	DIFFERENT
SUBSTANCE	IDENTICAL	None	Low	High
	COMPARABLE	Medium	Medium/High	High/Very high
	DIFFERENT	High	High/Very high	Very high

- What is considered as "high" uncertainty? A 10-fold deviation? Or a 1000-fold deviation? The level of uncertainty needs to be quantifiable.

Average ± variance



Uncertainty



Uncertainty when defining the appropriate reference scenario