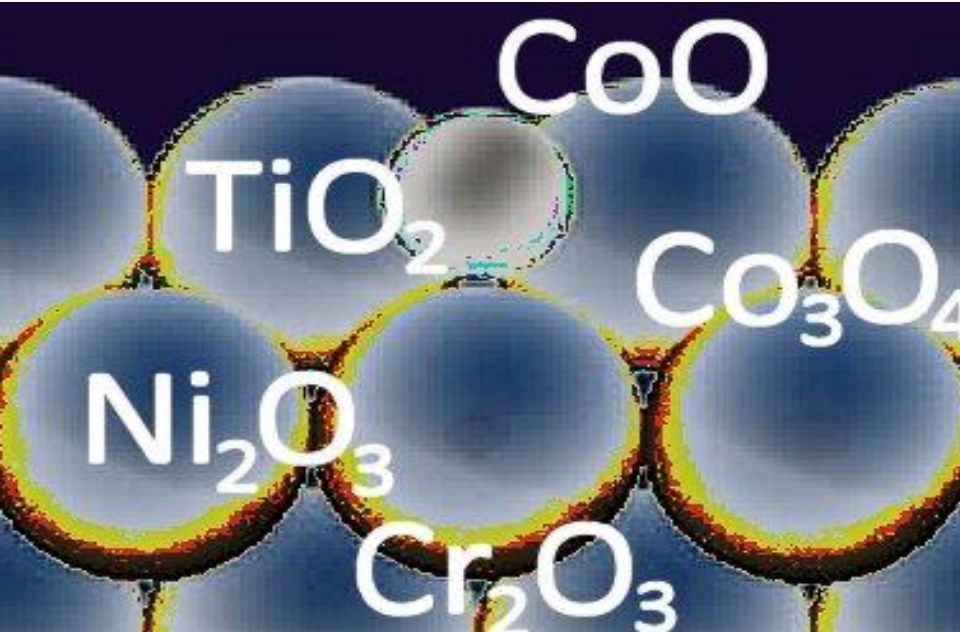National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

Development of a risk assessment strategy within the GUIDEnano project

Dr. Susan Wijnhoven

RIVM

Sustainable Nanotechnology Conference 2015

Development of a risk assessment strategy within the GUIDEnano project | March 10, 2015

GUIDEnano

Project Consortium

Universities & Research Centers

LEiTaT Technological Center | VENEZIA RICERCHE | cea liten | UNIVERSITY OF GOTHENBURG

TÉCNICO LISBOA | IOM | TNO innovation for life | 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

CID | PlasmaChem | LATI | inoTEX | Servià Cantó | NanoServices

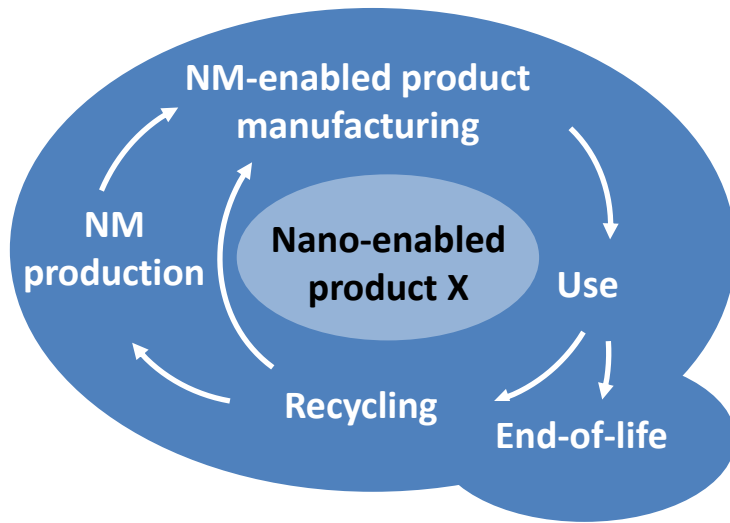GEOCHEM RESEARCH | Honeywell | HEMPEL Estd 1915 | Pinsent Masons | INNVENTIA

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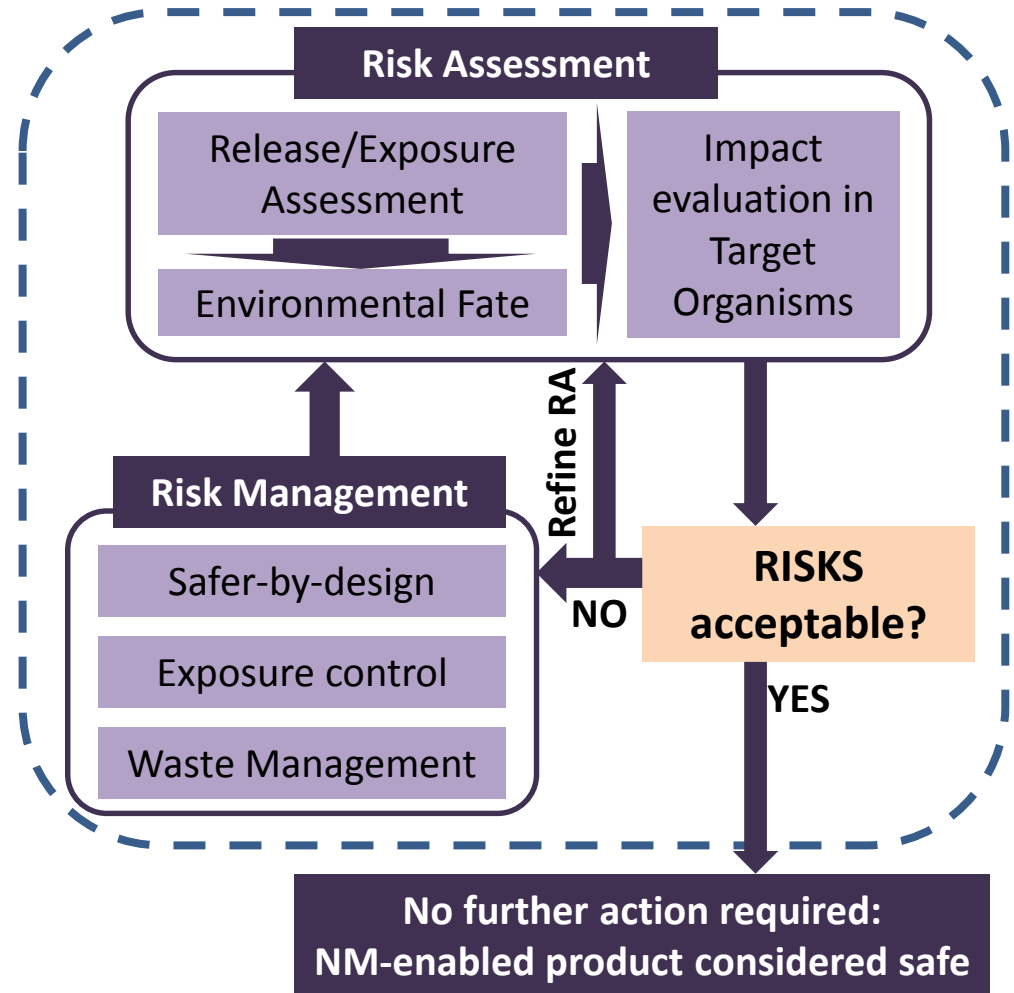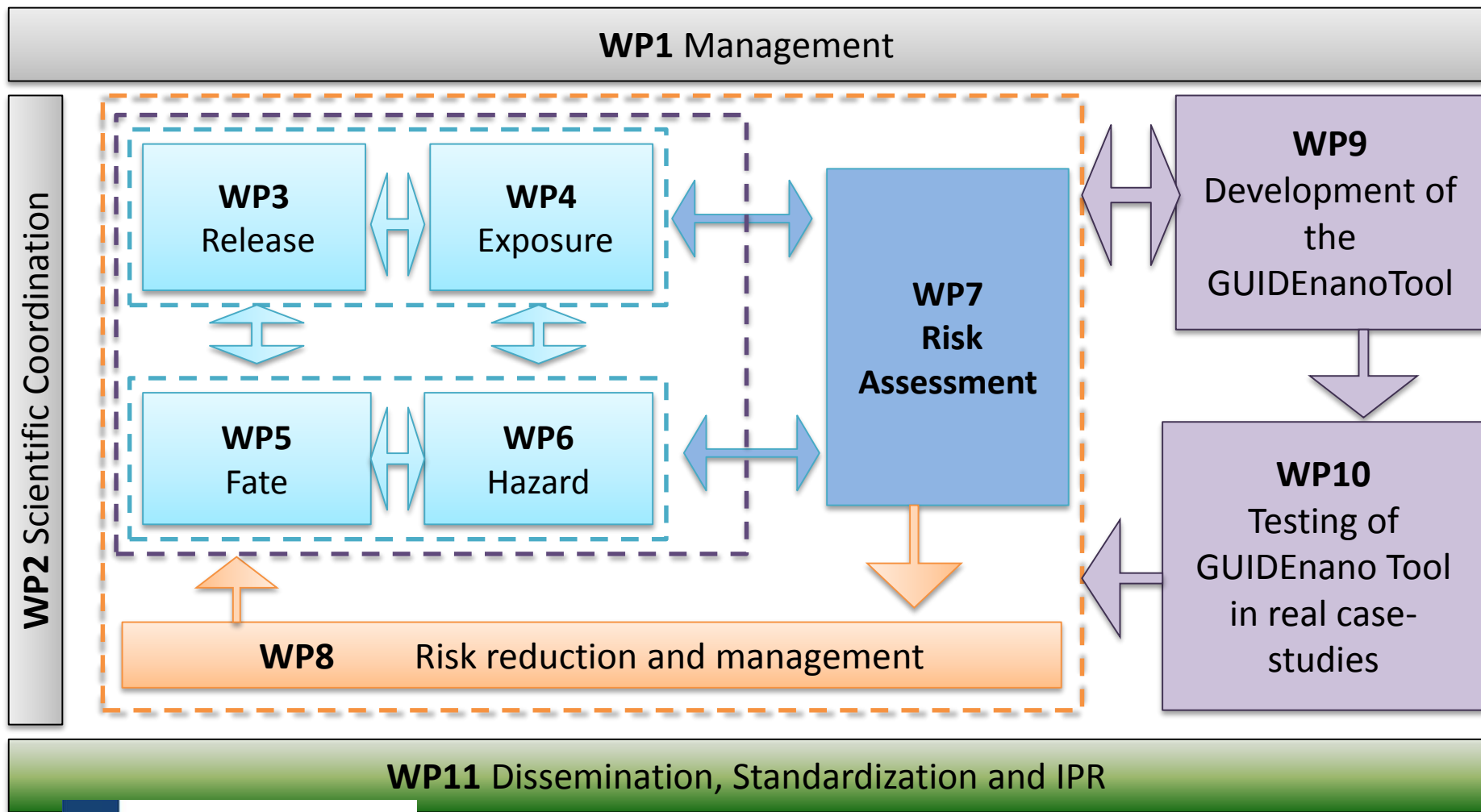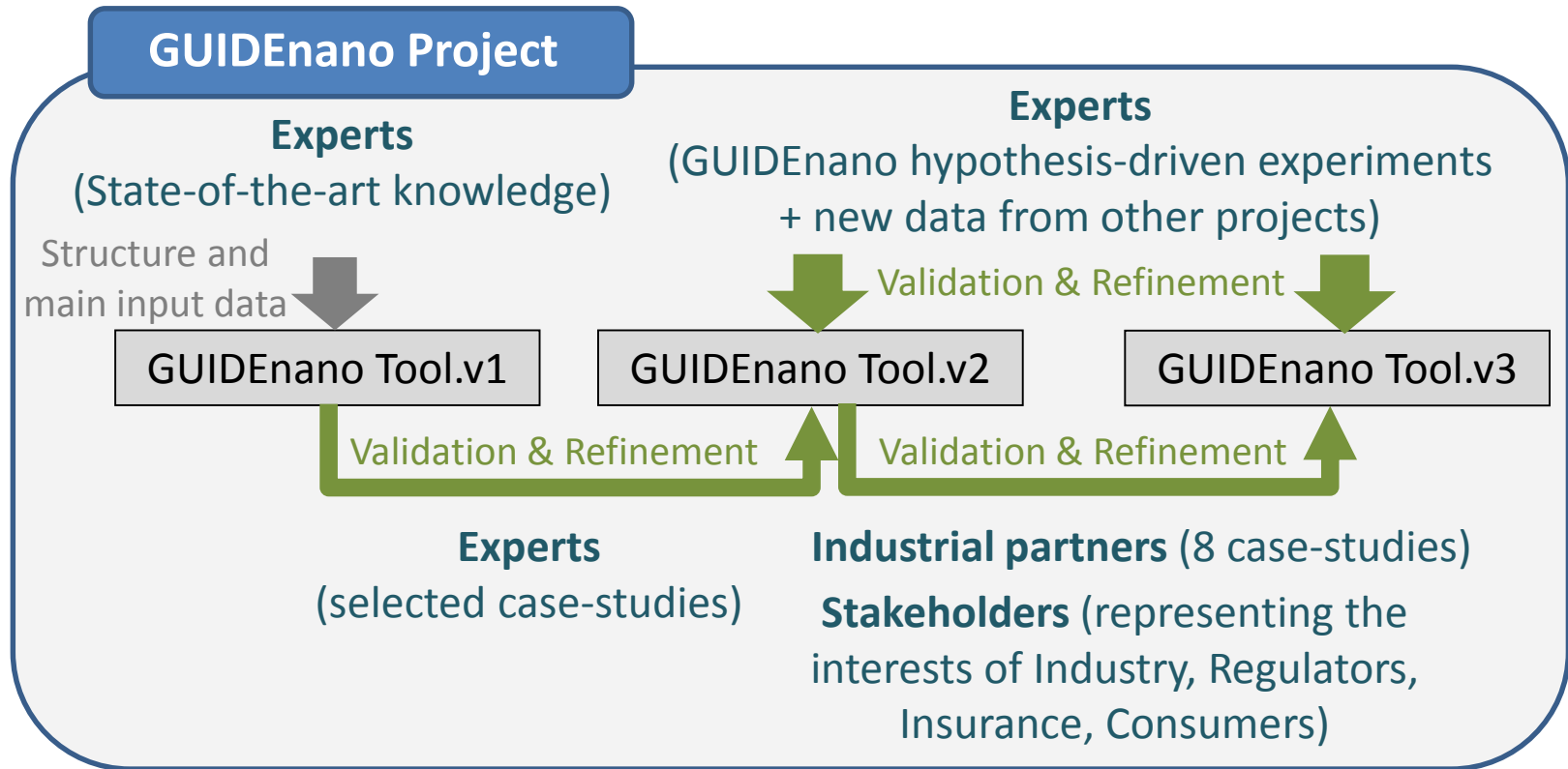
Interactive digital Guidance Tool

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GUIDE*nano*

THE TARGET
NM-enabled product Life Cycle

SCOPE OF THE GUIDANCE

Risk Assessment

Release/Exposure Assessment

Environmental Fate

Impact evaluation in Target Organisms

Refine RA

Risk Management

Safer-by-design

Exposure control

Waste Management

RISKS acceptable?

NO

YES

No further action required: NM-enabled product considered safe

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WP1 Management

WP2 Scientific Coordination

WP3 Release

WP4 Exposure

WP5 Fate

WP6 Hazard

WP7 Risk Assessment

WP8 Risk reduction and management

WP9 Development of the GUIDEnanoTool

WP10 Testing of GUIDEnano Tool in real case-studies

WP11 Dissemination, Standardization and IPR

Activity cards

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

NMs

WoE / Prioritization algorithm

Hazard endpoints values

Read-across Relevance / Quality score

Toxicity studies available to the user

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- 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

Risk Assessment

Hazard Assessment WP 6
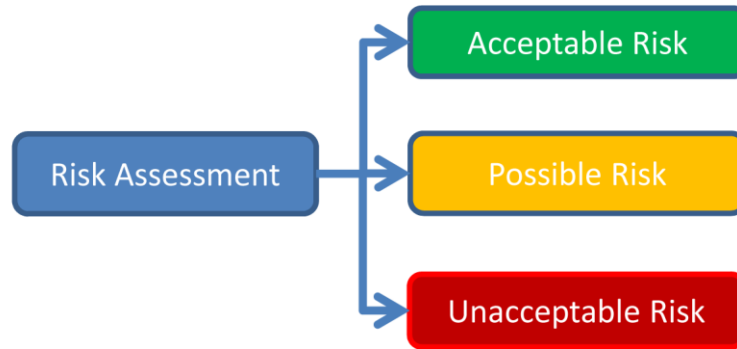
Exposure Assessment WP 3,4,5
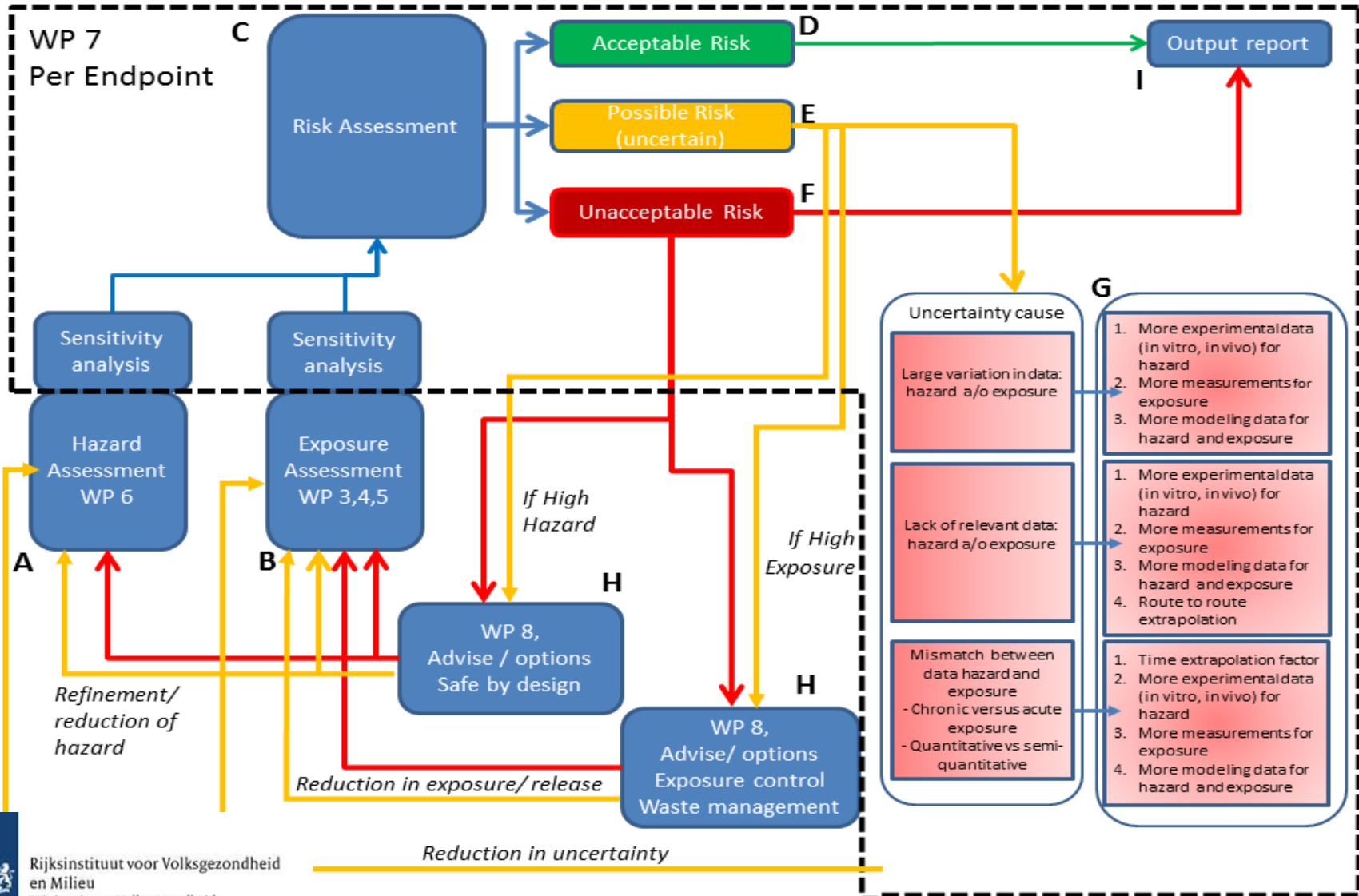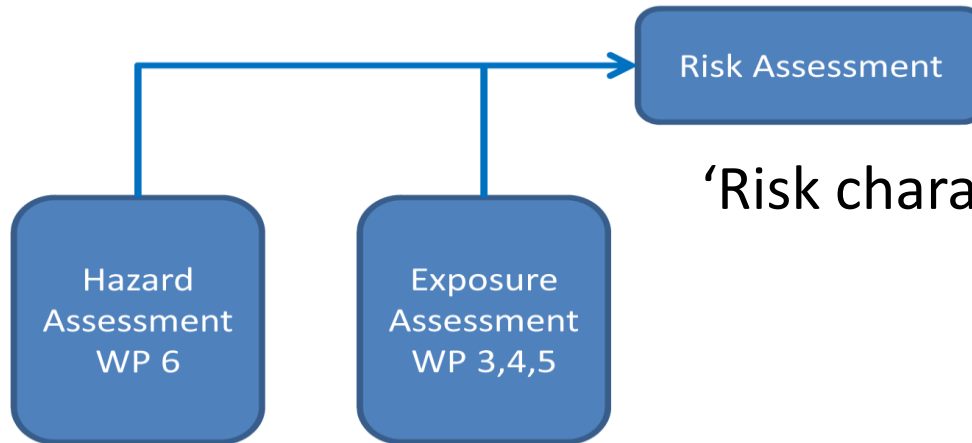
'Risk characterisation ratio' (RCR):

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

- Exposure:
  - relevant exposure routes/ duration
  - model output, exposure libraries, direct measurement data

- Hazard:
  - relevant endpoints with (if possible) quantitative exposure estimate with uncertainty

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- 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

Acceptable Risk

Risk Assessment

Possible Risk

Unacceptable Risk

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		

p

Yes

No
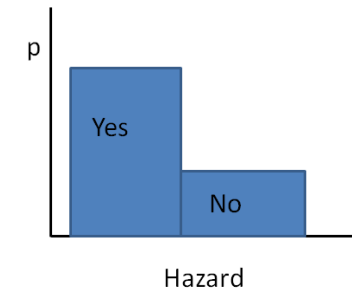
Hazard

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

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

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)

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~5% chance of risk

Relatively high chance of high exposure level

50% chance of risk

uncertainty
— high
— low

>95% chance of risk

RCR = Exposure / Hazard

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

Change from acceptable to "probability of risk"
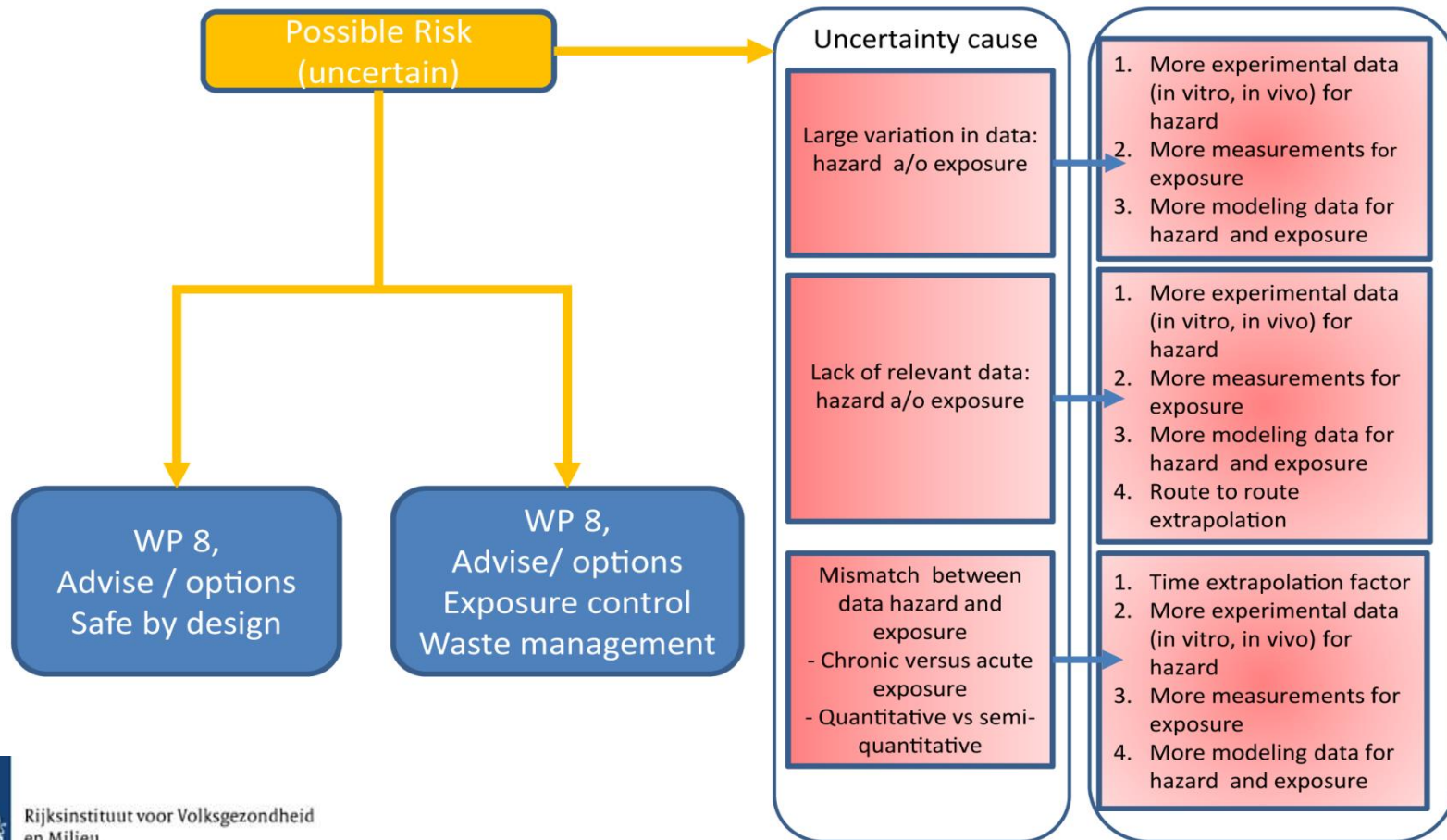
Defaults:

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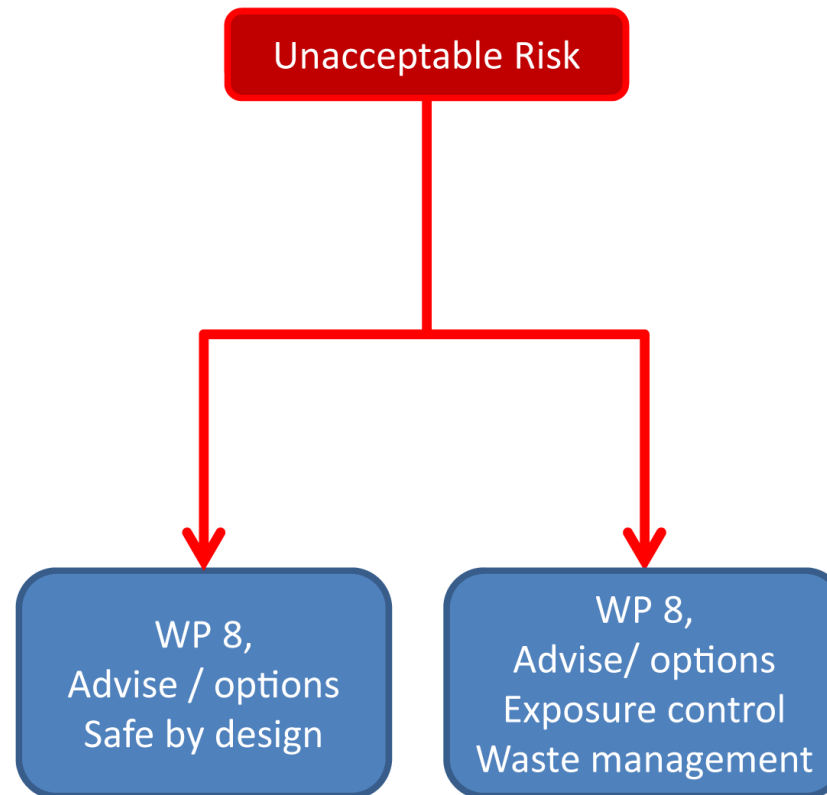
Unacceptable risk, high probability of risk: >75% probability on a ratio of > 1

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Possible risk: reduction of risk or reduction of uncertainty

Unacceptable risk: reduction of risk

- 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

- GUIDEnano project consortium
  - All partners
    - Gemma Janer (LEITAT)
    - Socorro Vazquez (LEITAT)
    - Margriet Park (RIVM)
    - Ralph Vanhauten (TW)
    - Lion Traas (TW)

  - WP7
    - Petra van Kesteren (RIVM)
    - Maria Luisa Cruz- Fernandez (INIA)
    - Derk Brouwer (TNO)
    - Thies Oosterwijk (TNO)
   - Joost Westerhout (TNO)
    - Manoj Vaghela (Pinsent Masons)

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
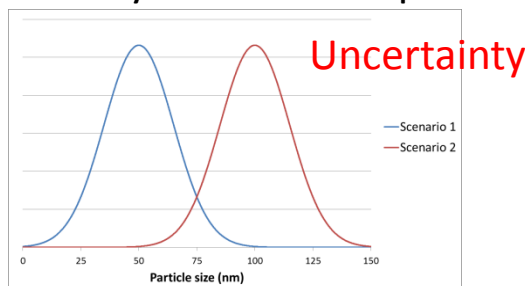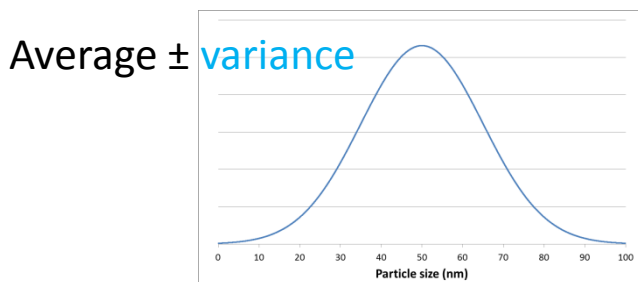
Uncertainty

Uncertainty when defining the appropriate reference scenario