A common European approach to the regulatory testing of nanomaterials

Responsible Development of Nanotechnology

"Safe-by-Design" and Innovation

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NANoREG's Safe-by-Design concept

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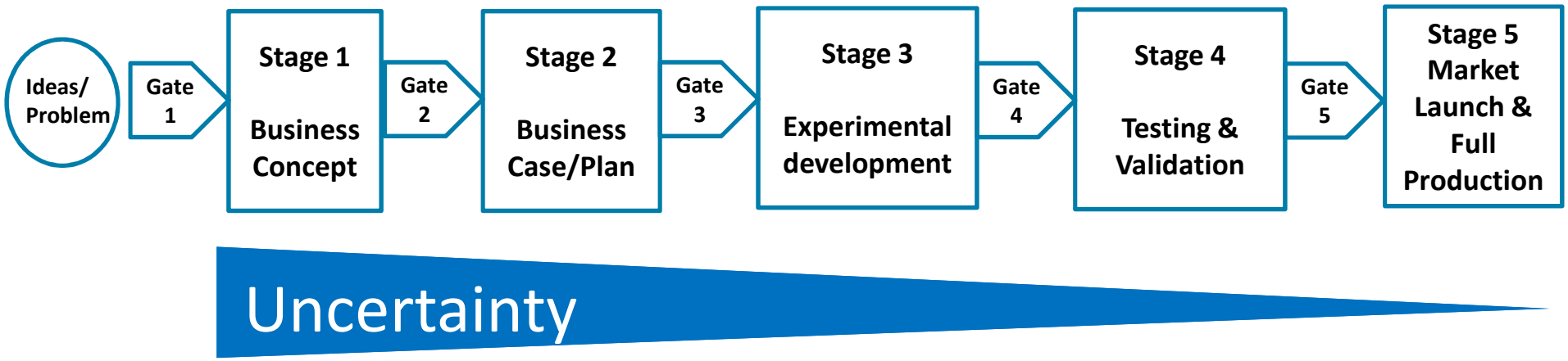

Safe-by-Design (NANoREG I)

FROM POTENTIAL RISKS TO MANAGED RISKS
of Nanomaterials and nano inspired Products

Participation of industry in NANoREG:

Safety in Value Chain Case Studies

Interested? → Contact Helena Gouveia, ISQ/PToNANO

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NANoREG's Safe-by-Design concept

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- The idea of Safe-by-Design (SbD) is not new, similar concepts for other purposes (e.g. QbD) have been used for years by the industry.
- There is no generally accepted definition of SbD. The understanding of SbD is diffuse and sometimes misleading.
- NANoREG's SbD concept is intended and designed as an extension of current industrial innovation processes.
- The SbD concept focusses on the **timely identification** and management of **uncertainties** and **potential risks** during an innovation project.
- The SbD concept could be used by any industrial enterprise along nanomaterials' or nanoproducts' value chains.

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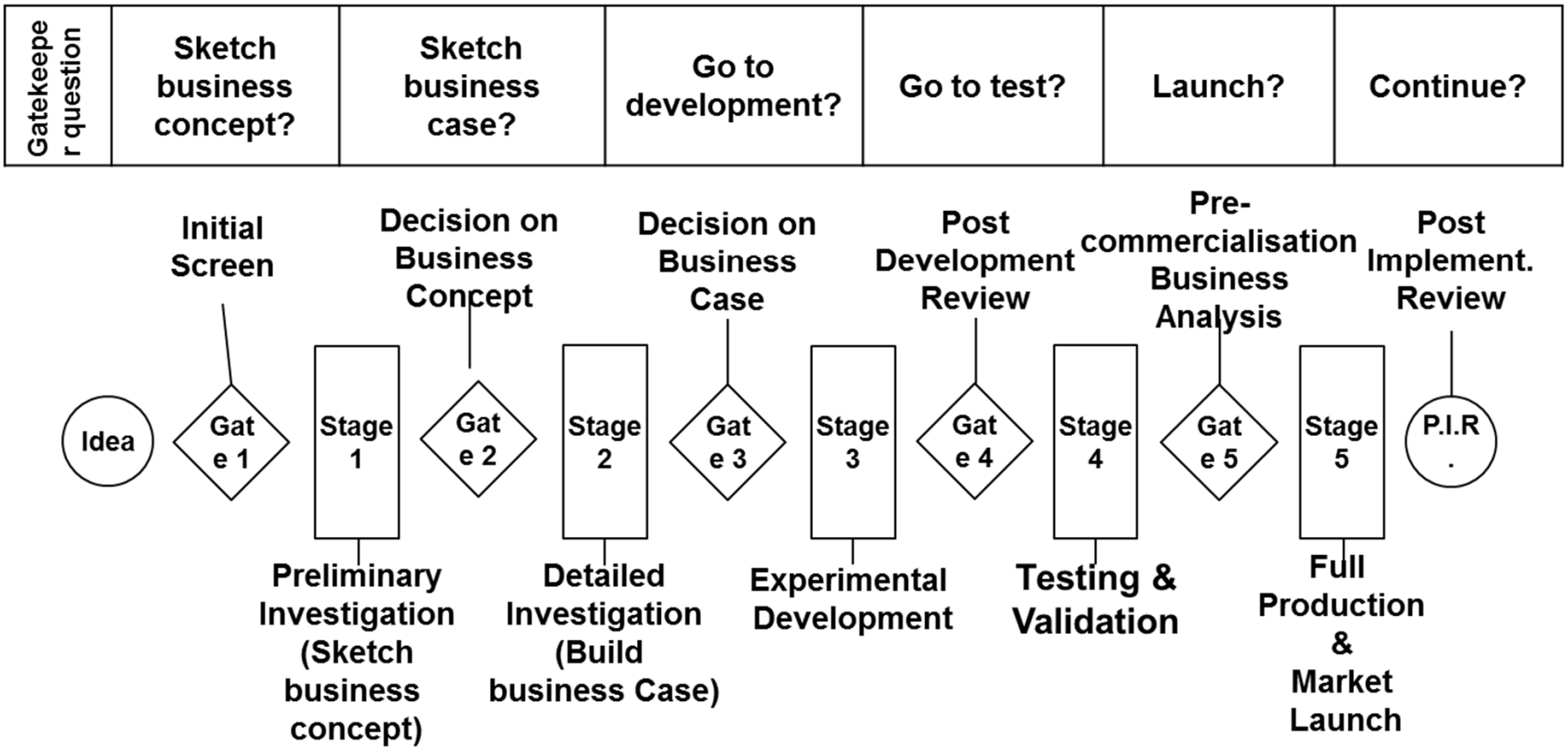
Innovation models used by Industry, e.g. the stage gate model are the backbones of NANoREG's SbD



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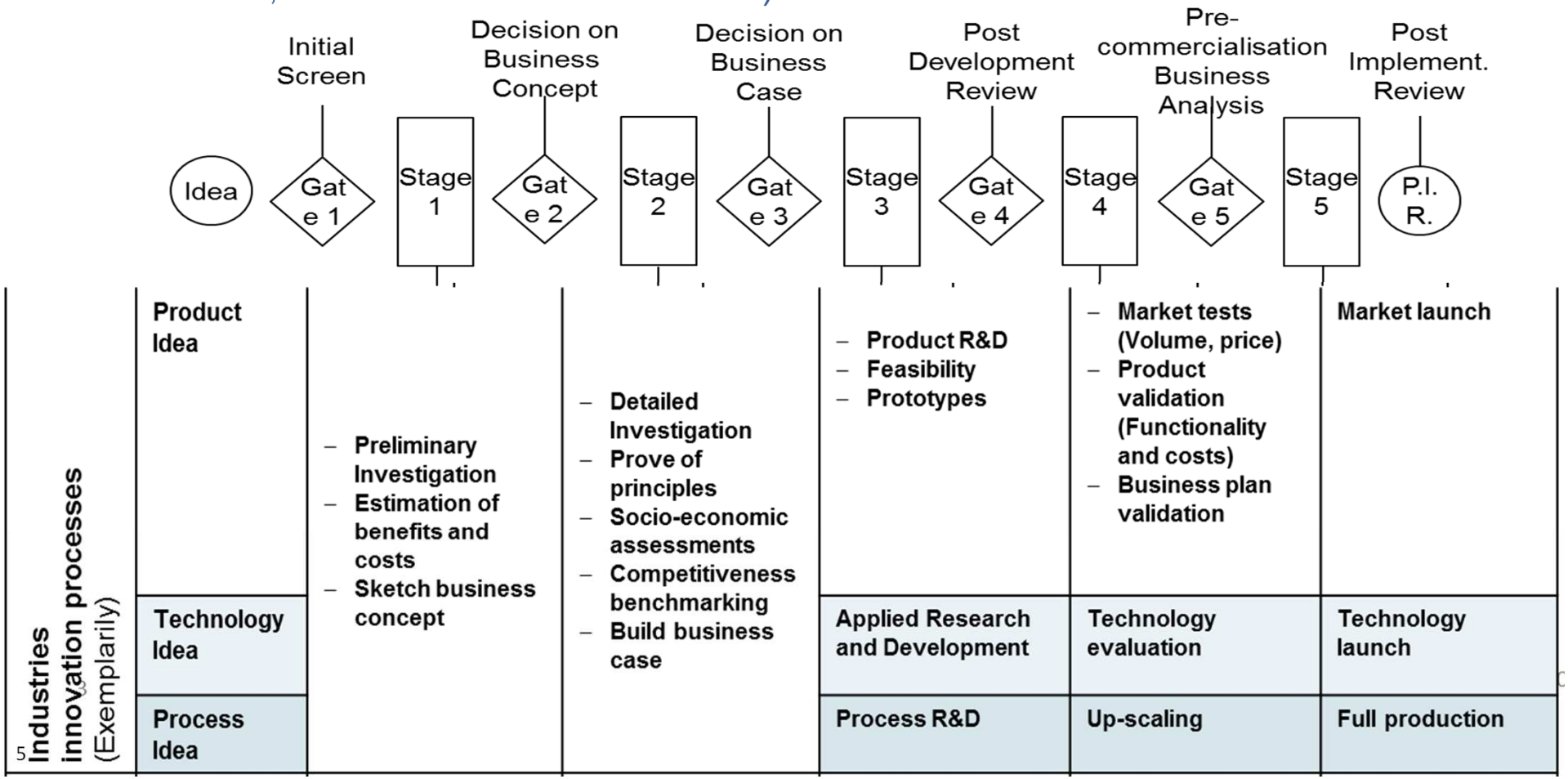
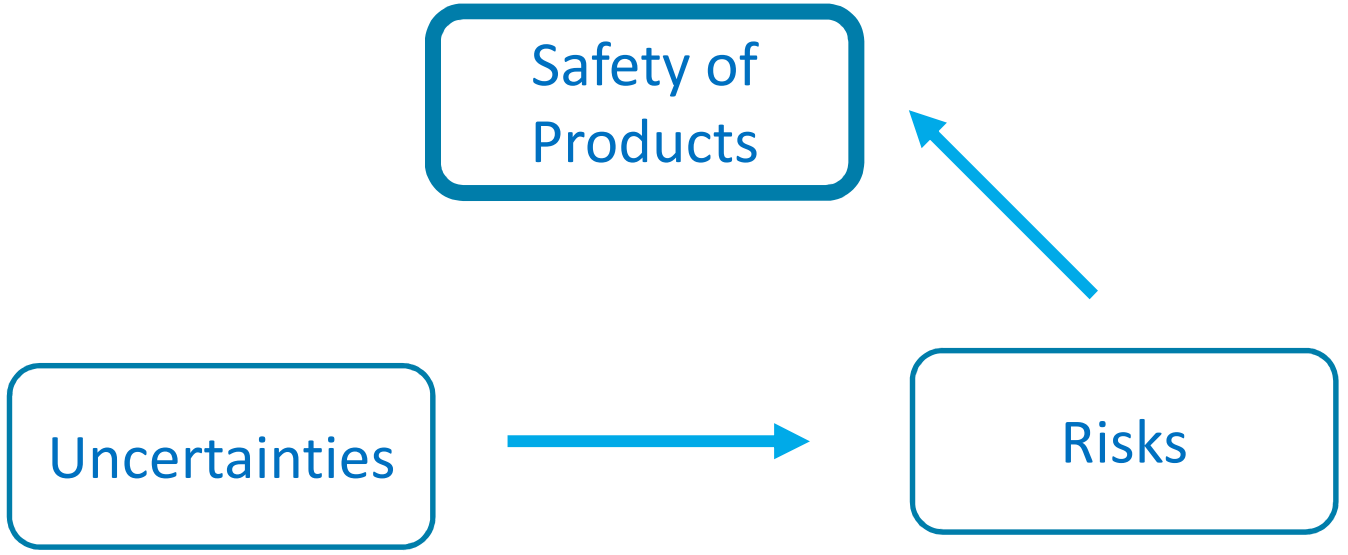
Risks and Risk analysis (RA) in the stage gate model

In some companies, the stage gate processes are already supplemented by some sort of risk analysis (environmental, health and safety {EHS}, economic, technical and other risks).



Uncertainties, Risks and Safety



Identification of risks at the earliest time.
Reduction of uncertainties

Identifying risks, typical situations and WC scenarios in the life cycle of a product.
Reduction of risks
Elimination of risks

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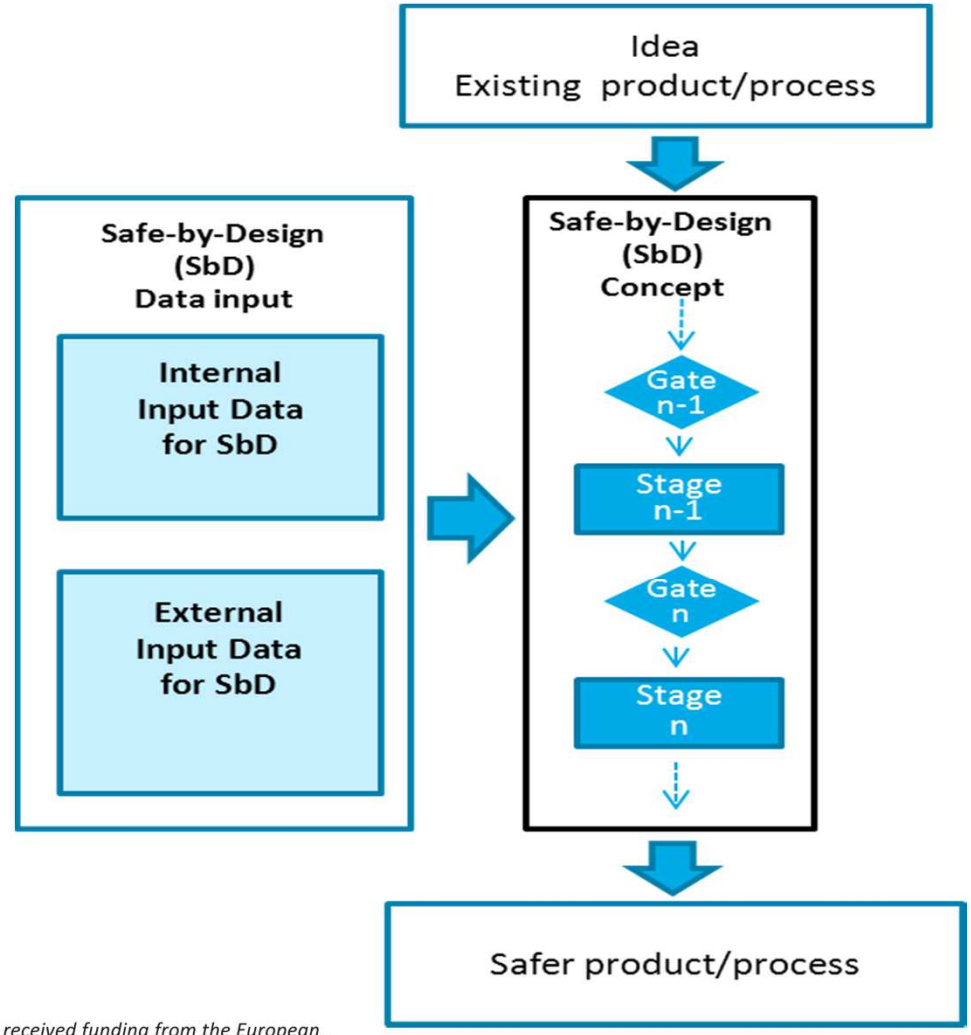
Two processes:

- ✓ The stable Safe-by-Design process
- ✓ The variable data, According the Progress in science and knowldedge



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NANoREG's Safe-by-Design concept

The NANoREG's SbD can be seen as nano-related add-on for existing industrial safe innovations processes encompassing different activities and tools.

SbD supplements the risk analysis starting in stage 1 and continuing into the risk management in stage 5.

Thus, every activity carried out during a "normal" risk analysis is also carried out within a SbD-process.

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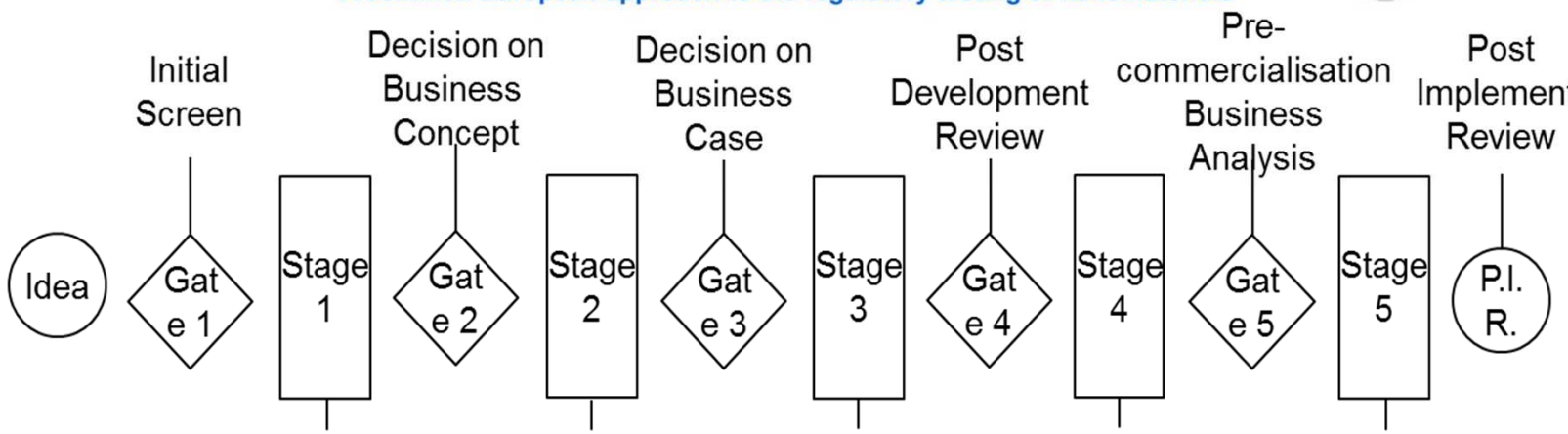

Safe-by-Design process integration in industries innovation process	No Safe-by-Design activities	- Reduction of nano related uncertainties - List of potential nano related risks - Analysis of alternatives	- Theoretical nano related risk analysis - Nano related risk mitigation - Grouping principles - Read across	Experimental nano related risk analysis	Nano related risk assessment before launch	Update nano related risk assessment after launch	
		Occupational and product safety Consumer safety Environmental safety			Nano related risk management	Occupational health management during production	
		Organized Dossier shared by stakeholders (Robust nano safety data) (Pre-regulatory information) Role of regulators along the GATES			Reach Dossier		

Practical recommendations
Risk assessment in the stage gate

- ✓ During stage 1 potential risk situations and scenarios are formulated as well as risks identified and listed for gate 2.
- ✓ During stage 2 a theoretical (i.e. only using subjective and existing objective data) risk assessment is carried out and risk treatment options are prepared for gate 3.
- ✓ During stage 3 the risk assessment and risk treatment options are updated with the development results for gate 4.
- ✓ During stage 4 the risk assessment and risk treatment options are updated with the results of market testing and upscaling for gate 5.
- ✓ During stage 5 the risk assessment and risk treatment options are updated with the feedback from the market introduction for gate 6, the post launch review (PLR).

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Costs in the risk analysis

Costs of measures to reduce uncertainties in a stage have a direct impact on the remaining risks: the higher the costs, the lower the remaining risk. However, the costs of uncertainty and risk reduction have to be balanced with the costs of the remaining uncertainties and risk to find the most efficient solutions (e.g. a reduction of the remaining risk to zero is usually inefficient because of exponentially increasing costs).

	Investment to reduce uncertainties	Benefit of investment	Remaining risk potential	Remark
Stage 1	small	large	small	Small investments have large benefits
Stage 2	medium	medium	medium	
Stage 3	large	small	large	Large investments have small benefits

How does SbD work

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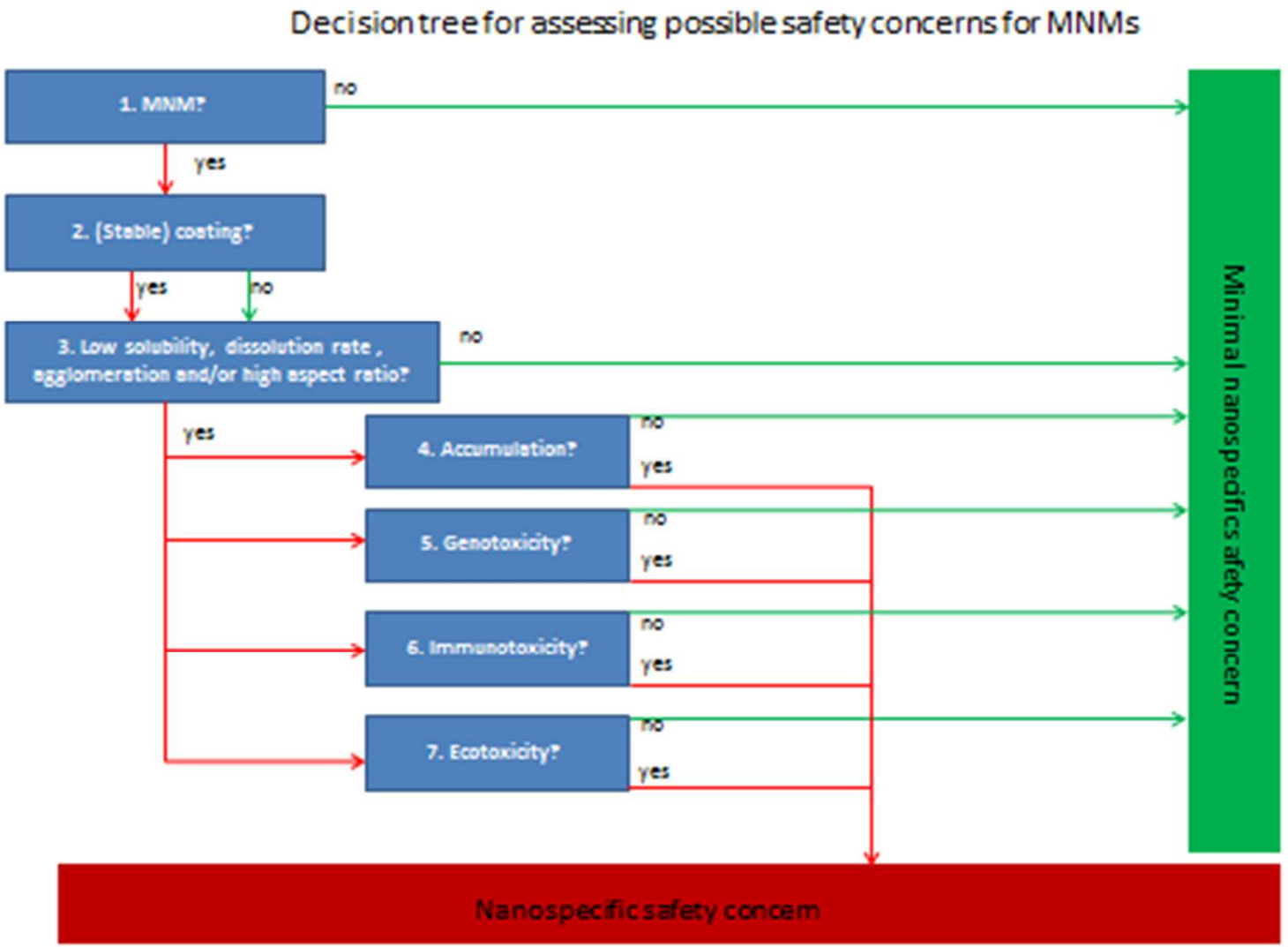

Benefits for industry

- SbD can be integrated in existing industrial innovation processes of enterprises (no new processes)
- Less uncertainty, lower cost and less time result in a more stable material respectively product.
- Uncertainties are detected at the earliest time and can be reduced by alternative solutions.
- Reduced uncertainty needs smaller risk margins!
- Projects with large uncertainties respectively with unacceptable risks may be timely recycled timely or can become a different orientation.
- Less “surprises” (i.e. unforeseen events) during the development process and market introduction
- The strict separation of data allows an easy check and up-date of data and thus to perform a new risk analysis
- Be prepared to meet todays and future regulatory requirements
- SbD delivers a good balance between safety, functionality and costs

Summary: money, time, and resources can be saved

Benefits for regulatory authorities

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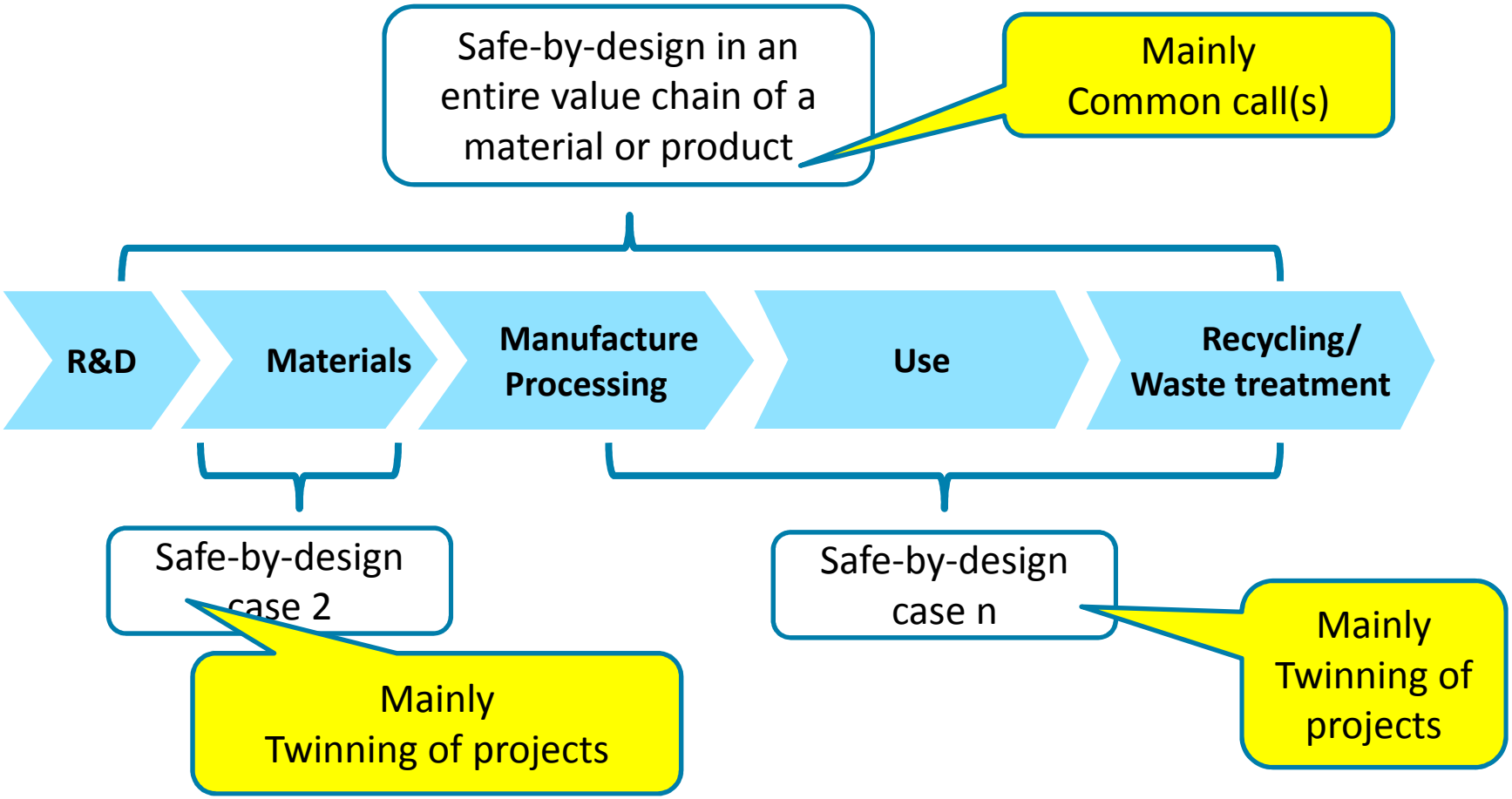
- SbD delivers transparent data for all stages of the innovation process
- The SbD process delivers organized dossiers and data formats shared by all stakeholders
- SbD uses ISO and OECD Standards as well as their Guidance Manuals and the NANoREG's Guidance Document
- The strict separation of data allows an easy check and up-date of the data and thus a new risk analysis
- Be prepared to meet todays and future regulatory requirements
- SbD delivers a good balance between safety, functionality and costs
- Application of the precautionary principle to reduce uncertainties and risks at the earliest possible date.

Summary: higher transparency, better process understanding

Outlook

ProSafe:
Common projects calls and twinning of projects



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Principle of proportionality

Obviously, a full-fledged risk management process like a full-fledged stage gate process is only carried out for:

- major projects,
- not for minor alterations.

Hence, the process design must make sure that small but risky alterations (such as label changes) are subjected to an appropriate risk management process.

On the other hand, there must not be too much red tape esp. for smaller and riskless projects.

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Thank you for your attention

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Health risk

When looking for potentials for health risks one can consider:

1) aspects specific for nanomaterials like solubility (if a particle readily dissolves into its molecular form, then it no longer needs to be treated as a nanomaterial) or stability of the coating of a particle (if the coating readily dissolves of the core then one needs to know to consider whether the coated particle and the uncoated particle may exhibit the same kinetics and toxicity)

2) markers for increased risk probability like accumulation in tissue and organs or in environmental compartments

3) unacceptable toxicity like genotoxicity as a first marker for carcinogenicity or inflammation as a first marker for many pathological conditions

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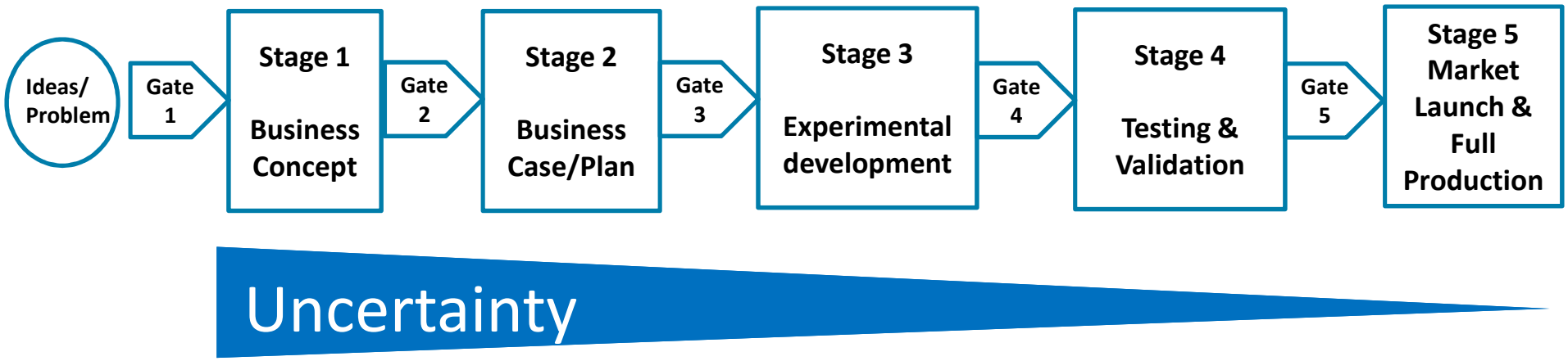

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FROM POTENTIAL RISKS TO MANAGED RISKS
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ProSafe:

Implementation of safe-by-design concept in industrial innovation processes

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