



iNTeg-Risk

Early Recognition, Monitoring and Integrated Management
of Emerging, New Technology Related, Risks



Grant agreement number: CP-IP 213345-2

Nanotechnologies and SMEs - a case study

1st iNTeg-Risk Conference

June 3, 2009

Stuttgart, Germany



Industrie Service



Production of
nanoscale structures in
unprocessed form

Intermediate products
with nanoscale features

Finished goods
incorporating nanomaterials
(„nano-enabled“ products)

NT companies worldwide

- **North America: > 1,050 (~ 975 in the USA, ~ 75 in Canada)**
- **Europe: > 300 (~ 100 in Germany)**
UK & Germany: largest SME activities and big business investment
- **Asia-Pacific: > 250 (~ 90 in China, followed by South Korea, Japan, Australia)**



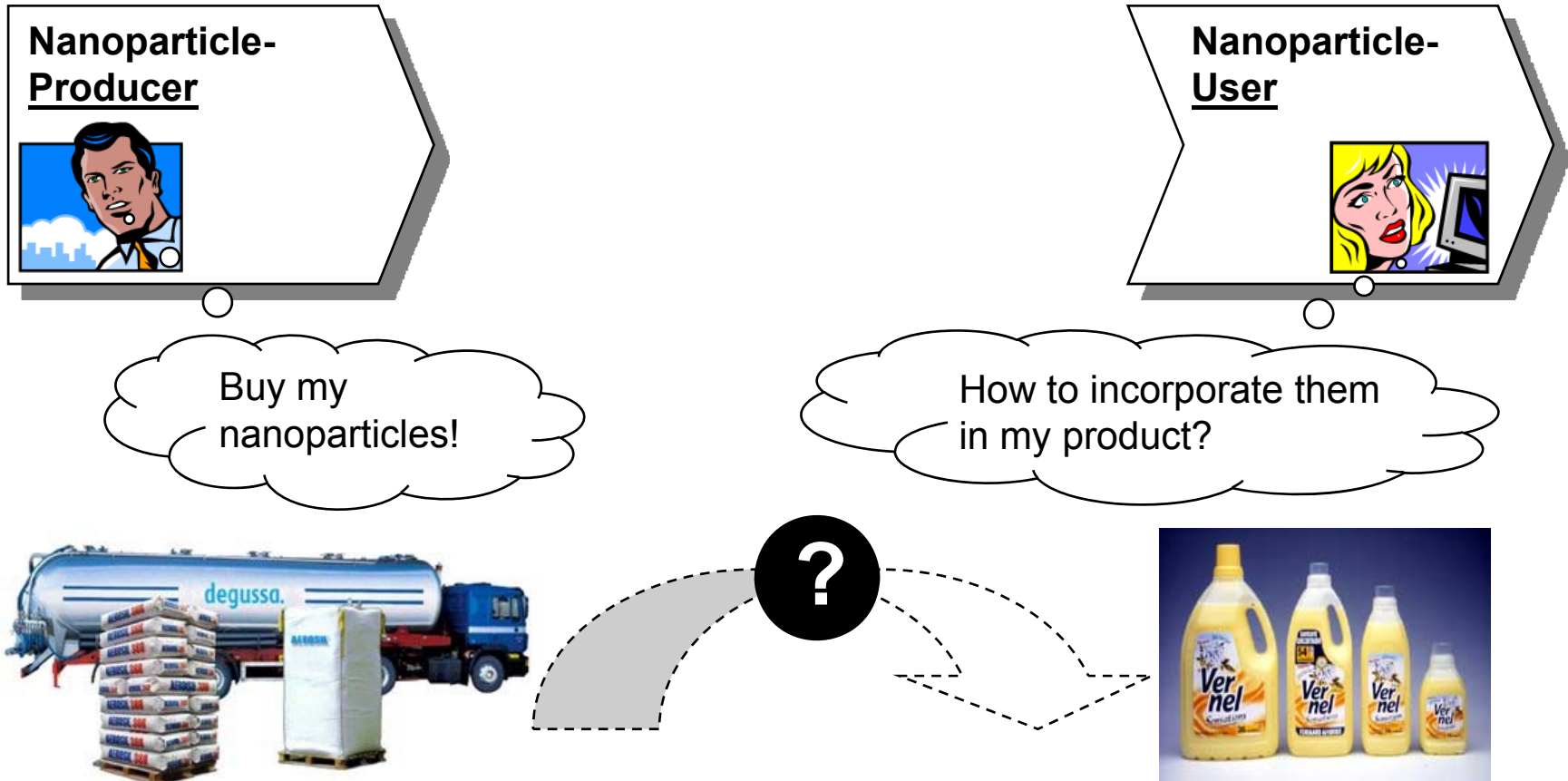
1. What we do and the kind of nanorisks we need to manage
2. How we manage these nanorisks (hands on approach)

Question: How can the functionality of nanoparticles unfold in real world products?



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Value chain

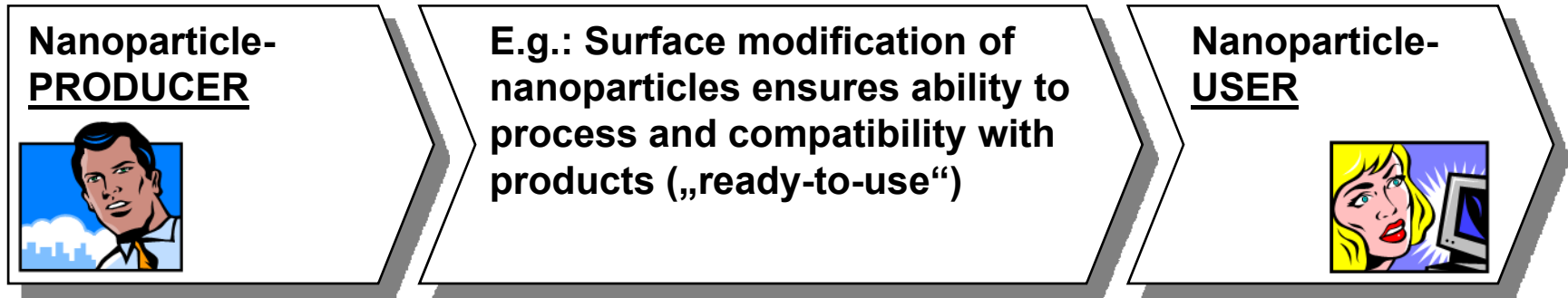


Names Degussa and Vernel used as illustrative examples only

*Combining existing strengths with new technology
to tackle a specific part of the nanoparticle processing value*



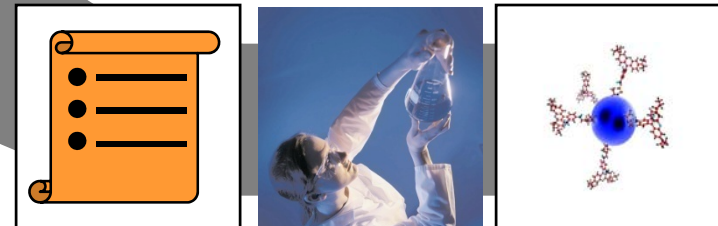
Value chain



Dispersion device



Surface modifier

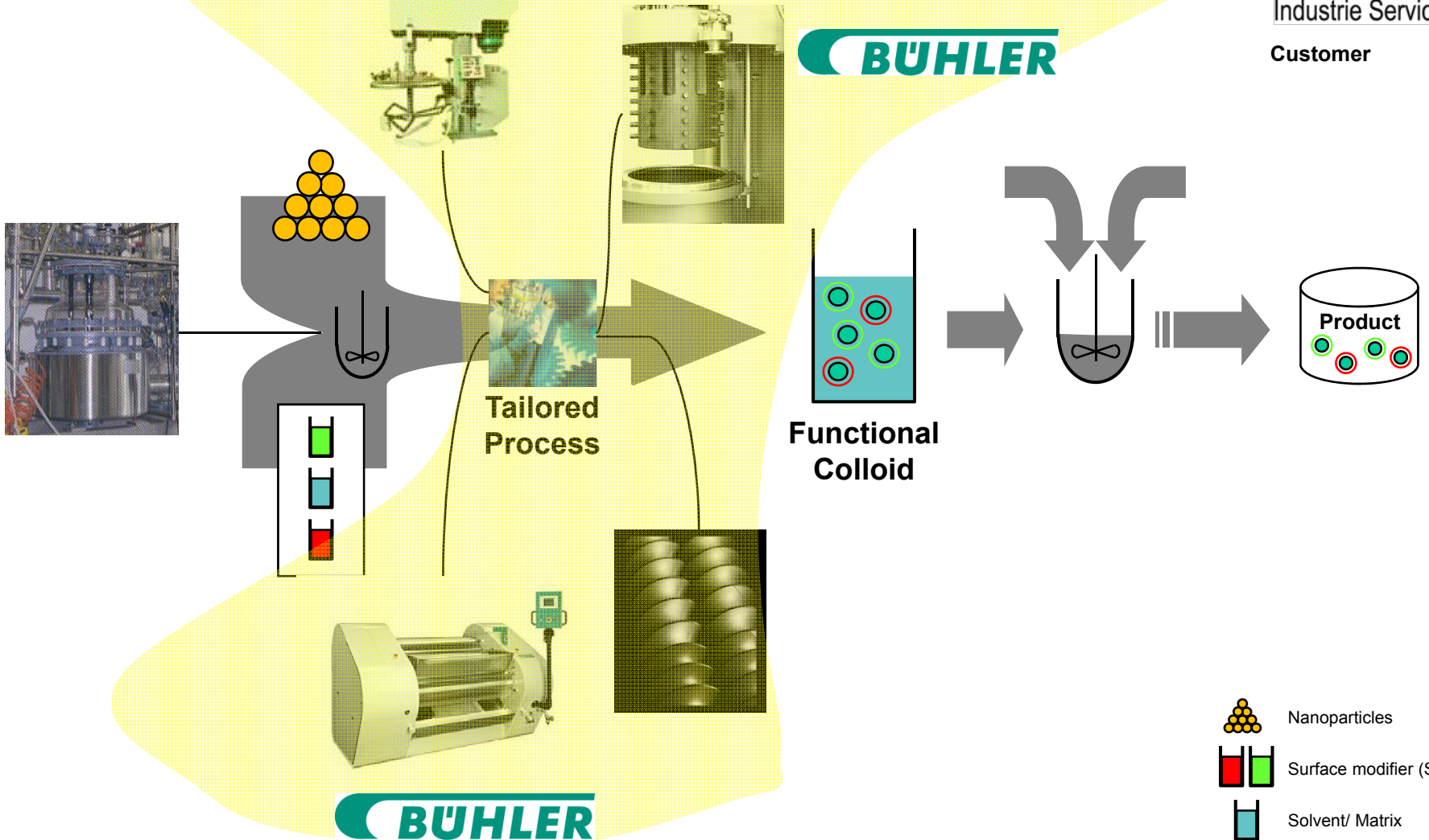


Typical processes needed in the nanoparticle processing value chain



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Customer

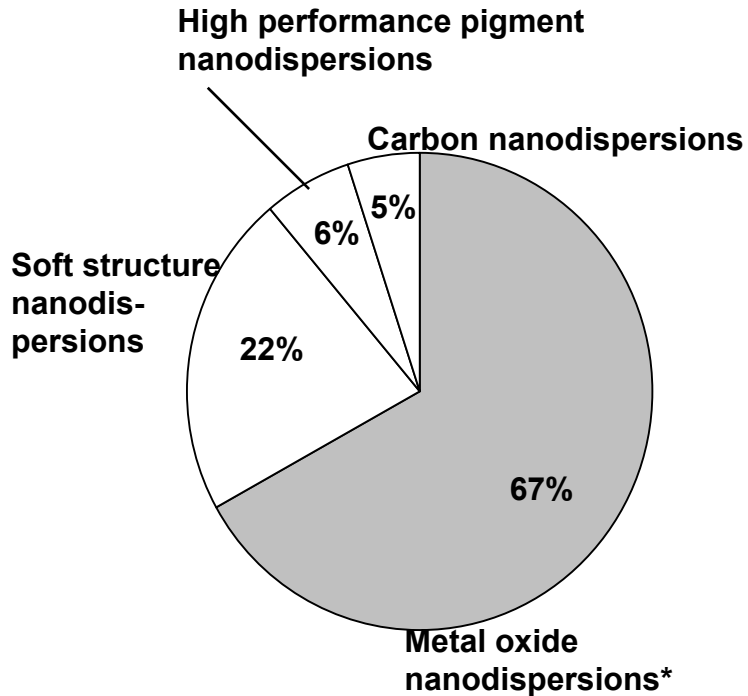


Buhler PARTEC main fields of activity

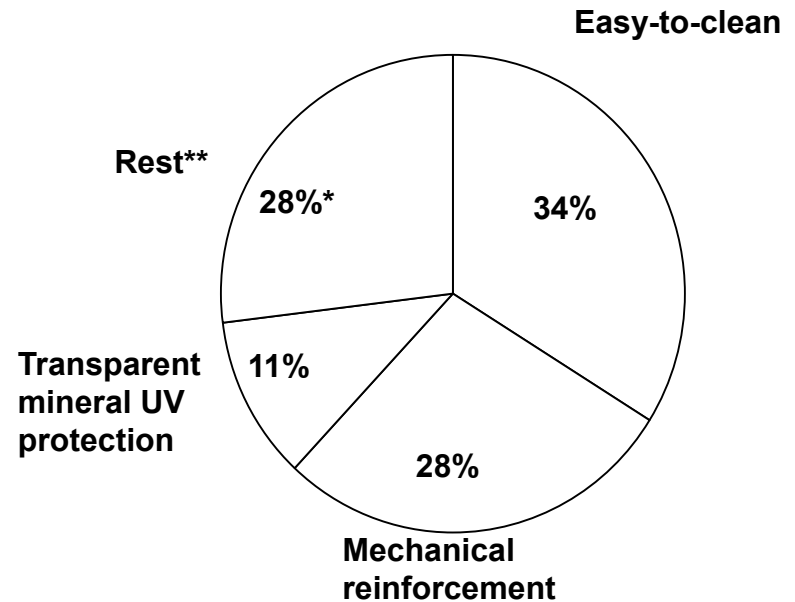
Revenue breakdown by type of business



By material



By application



* Mainly ZnO, TiO₂, Al₂O₃, ZrO₂ and also SiO₂

** Emerging applications

The Problem

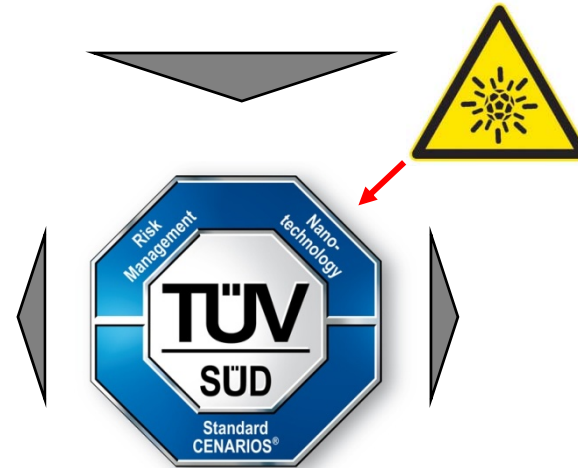
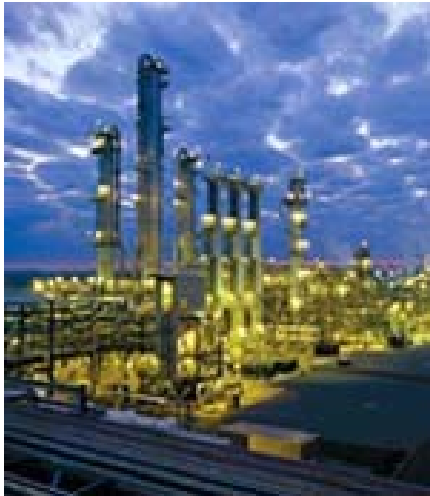


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Corporate Buhler as equipment and plant manufacturer does not intrinsically have a HSE department



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1. What we do and the kind of nanorisks we need to manage

2. How we manage these nanorisks (hands on approach)

*Risk management ≠ risk elimination, but
the management to keep the risks
As Low As Reasonably Practicable*

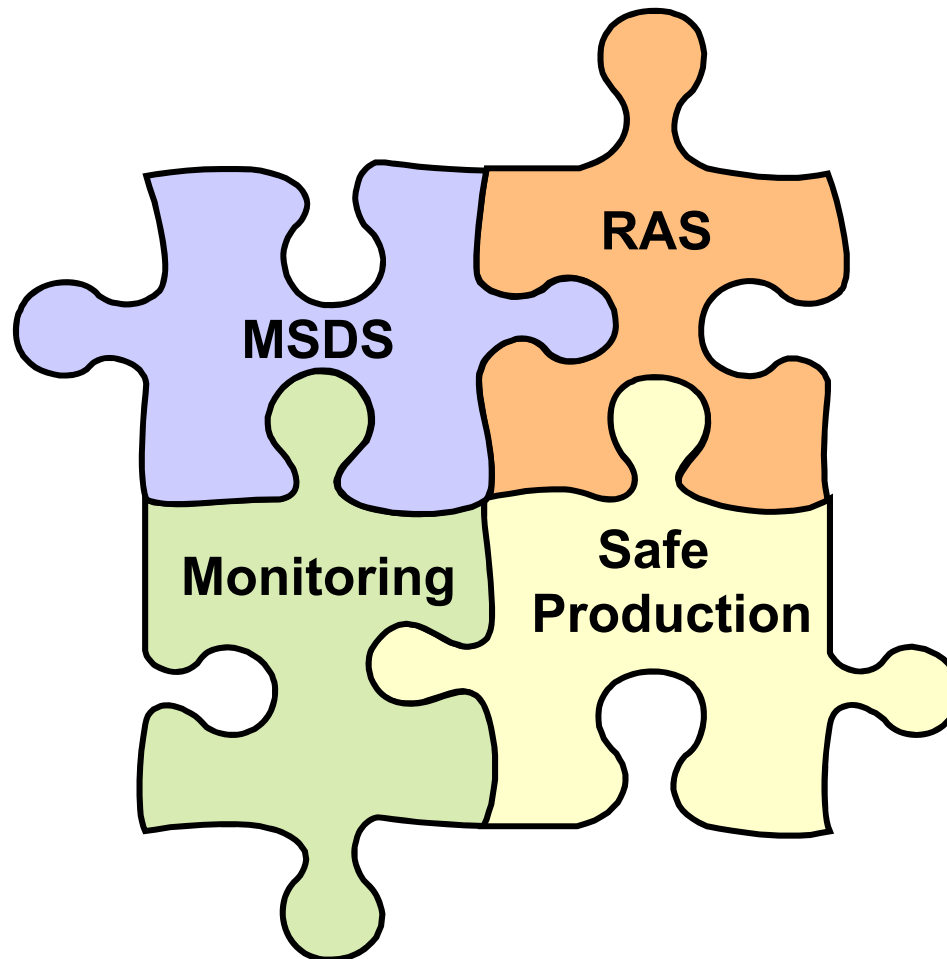


RISKS ARE ALARP
=
RISK MANAGEMENT
≠
RISK ELIMINATION

Our risk management system is based on 4 elements



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How we practice our nanospecific risk management



1st quarter

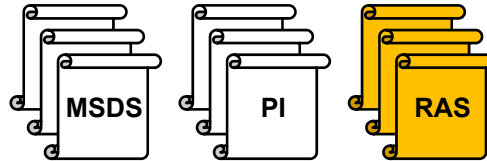
2nd quarter

3rd quarter

4th quarter

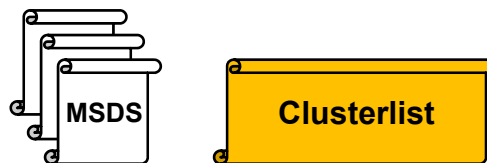
QM / ISO 9001

BUHLER PARTEC production Uzwil, CH

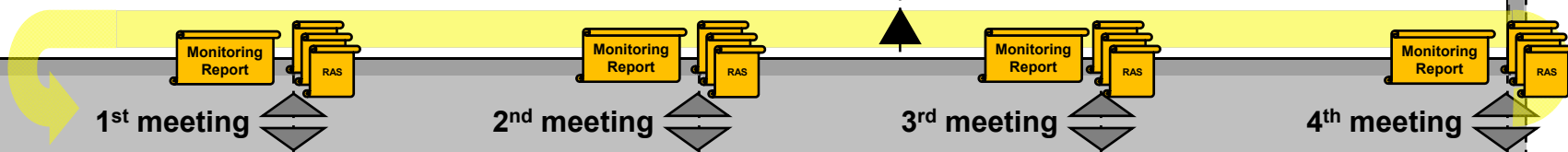


- 1st Certification Sept. 2007
- Recertification Aug. 2008

BUHLER PARTEC R&D Saarbrucken, D



BUHLER PARTEC management team



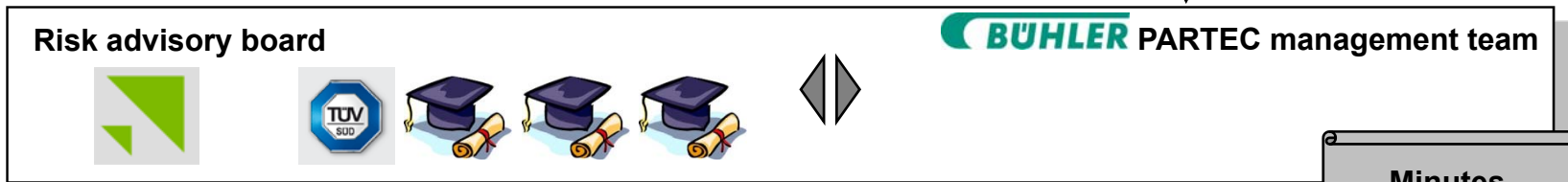
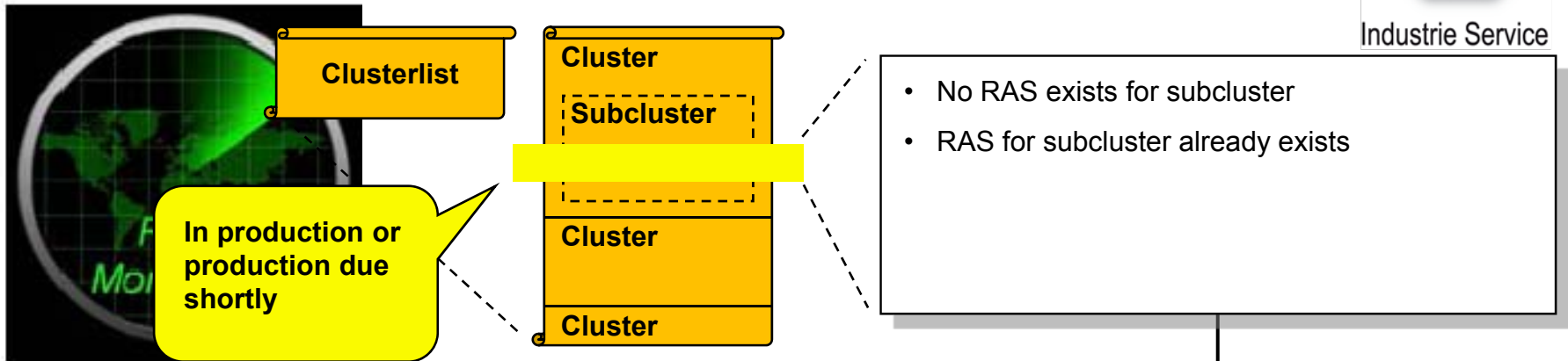
Risk advisory board



The RAS define the input for the monitoring radar,
 the Clusterlist defines the input for the foresight monitoring radar



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A

Risk appraisal critical

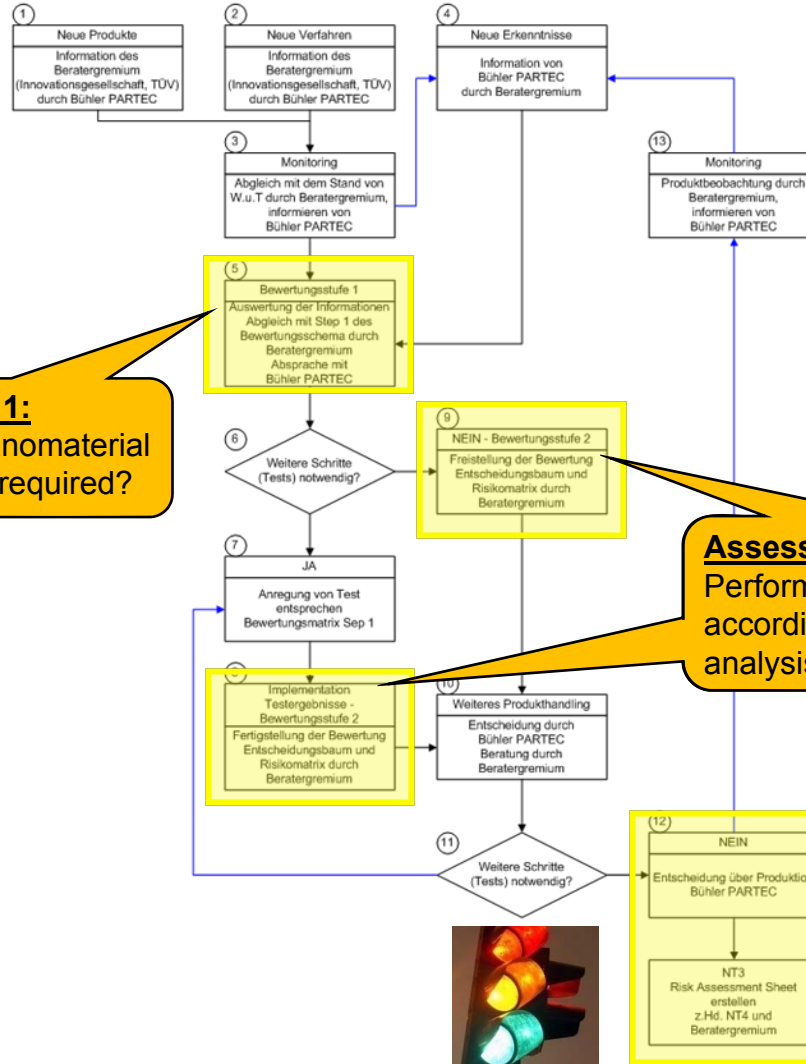
- Issue RAS immediately for new product
- Complete RAS immediately with new product

B

Risk appraisal non critical

- Threshold rule applies
- No RAS if quantity less than 1'000 kg
- No RAS if revenue < 50 kCHF

RAS are issued with a two step assessment process



Assessment 1:
Are further nanomaterial specific tests required?

Assessment 2:
Perform HSE risk assessment according to conventional risk analysis methods



Consideration of the state of science & technology in order to decide whether additional tests are required



Risk advisory board

Material: Carbon Nanotubes | Organismus:

Filter anwenden | Filter löschen

Resultate (sortiert nach absteigendem "Journal Impact Factor" der Quelle)

- 1 Florence Mouchet, Perine Landais, Emmanuel Flahaut, Eric Pinelli, Laury Gauthier
Assessment of the potential in vivo ecotoxicity of Double-Walled Carbon Nanotubes | Artikel in wiss. Journal (Einzelstudie) von/in: *Nanotoxicology* (Impact Factor: not yet rated). Datum: 01.06.2007
Okotoxikologie, Carbon Nanotubes, in vivo, Amphibien
- 2 Tonya K. Leeuw, R. Michelle Reith, Rebecca A. Simonette, Mallory E. Harden, Paul Cherukuri, Dmitri A
Single-Walled Carbon Nanotubes in the Intact Organism: Near-IR Imaging and Bioco
Artikel in wiss. Journal (Einzelstudie) von/in: *Nano Letters* (Impact Factor: 9.96). Datum: 16.08.2007
Okotoxikologie, Carbon Nanotubes, in vivo, Drosophila
- 3 Arnaud Magrez, Sandor Kasas, Valérie Salicico, Nathalie Pasquier, Jin Won Seo, Marco Cello, Stefan C
Cellular Toxicity of Carbon-Based Nanomaterials
Artikel in wiss. Journal (Einzelstudie) von/in: *Nano Letters* (Impact Factor: 9.96). Datum: 20.05.2006
Toxikologie, Carbon Nanotubes, in vitro, menschliche Lungenzellen
- 4 Leah A. Mitchell, Jun Gao, Randy Vander Wal, Andrew Gigliotti, Scott W. Burchiel and Jacob D. McD
Pulmonary and Systemic Immune Response to Inhaled Multiwalled Carbon Nanotube
Artikel in wiss. Journal (Einzelstudie) von/in: *Toxicological Sciences* (Impact Factor: 3.598). Datum: 01.07.2007
Toxikologie, Carbon Nanotubes, in vivo, Maus
- 5 Milena De Nicola, Daniele Mirabile Gattia, Stefano Bellucci, Giovanni De Bellis, Federico Micciulla,
Effect of different carbon nanotubes on cell viability and proliferation
Artikel in wiss. Journal (Einzelstudie) von/in: *Journal of Condensed Matter* (Impact Factor: 2.038). Datum: 30.08
Toxikologie, Carbon Nanotubes, in vitro, menschliche Zellen
- 6 Jae-Kap Lee, Michael W. Anderson, Fraser A. Gray, Phillip John
Explosive oxidation of HPHD diamond particles
Artikel in wiss. Journal (Einzelstudie) von/in: *Diamond & Related Materials* (Impact Factor: 1.935). Datum: 11.0
Physikalisch-chemische Gefahren, Carbon Nanotubes, Testansatz nicht spezifiziert, Organismus nicht

A
B
C
D
E
F
G

Electrical, etc), carbon nanotubes (CNTs) are being assessed applications, the impact of CNTs on the environment must NTs in the amphibian larvae (Ambystoma mexicanum). Acut ototoxic effects were analysed by scoring the micronucleated ay. The results obtained in the present study demonstrate er, although black masses of CNTs were observed inside thically including mechanistic and environmental investigati onum

Datensatz: 1 von 6 | Gefiltert | Suchen

α = Expected/estimated damage

β = Portability/analogy of data

keine Tests nötig

stoffspezifische Tests nötig

stoff- und risikospezifische Tests nötig

vermuteter bzw. nachgewiesener Schaden (α)

sehr hoch

hoch

mittel

keiner / gering

PC-Daten	in vitro	in vivo Tier	in vivo Mensch

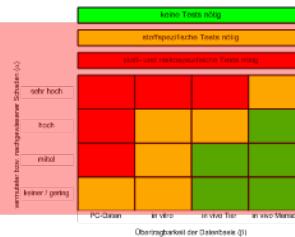
Übertragbarkeit der Datenbasis (β)

- 1 Base of knowledge**
PC data, in vitro or in vivo data, longtime experiences
- 2 Transferability of the database**
in vivo: principle of similarity (similarity to hb)
in vitro: exposition relevant information, general information
- 3 Comparison of publications**
How many publications are available? Are the results similar?
- 4 Rating of the publication**
Reputation of journal and author(s)
- 5 Transferability to the product**
Are the possible incorporation paths discussed properly?

Assessment of β = Assessment of relevance

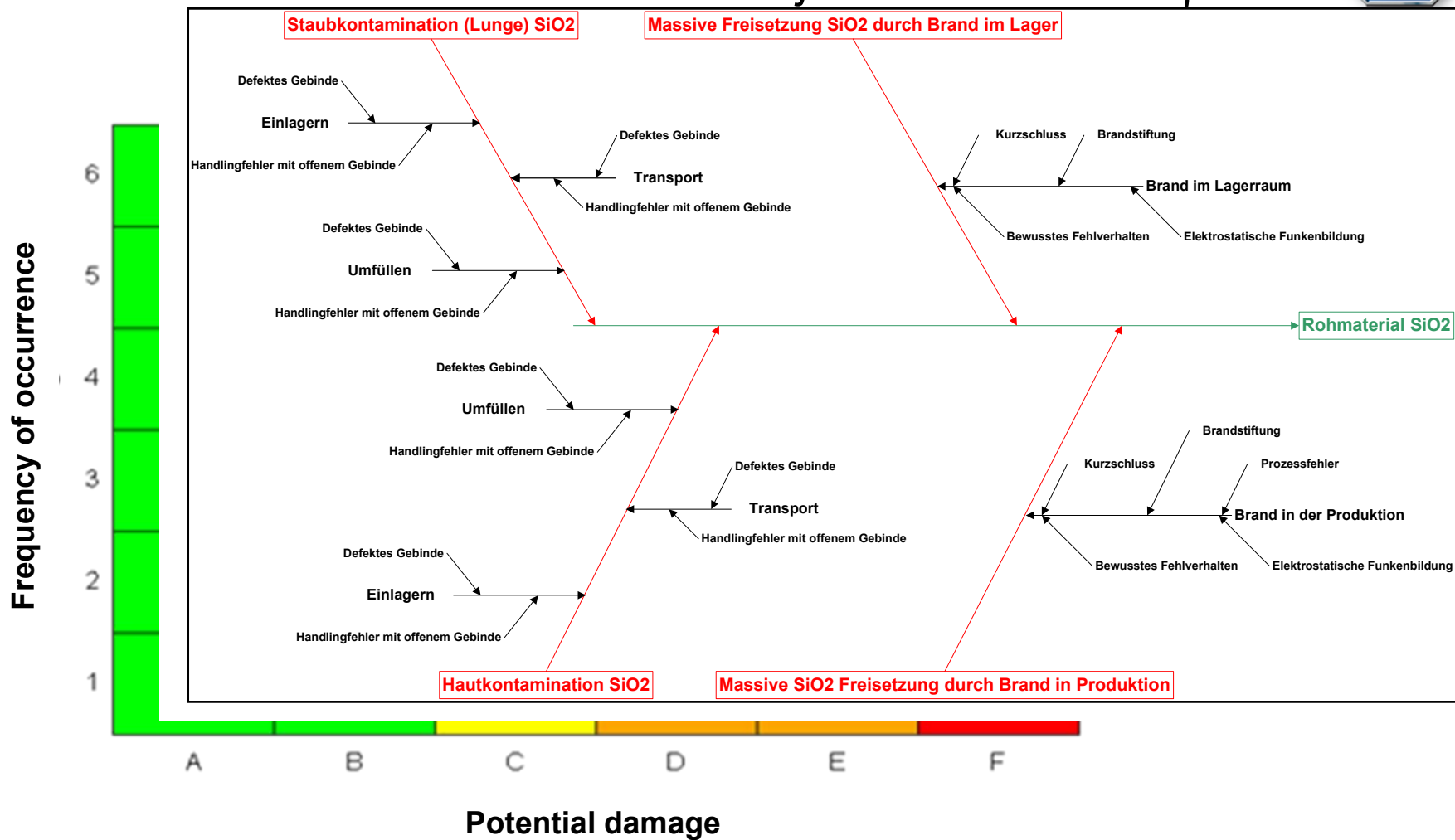
Criterion	Appraisal		
	fulfilled	Limited	Questionable
1 β_a Portability	$\beta_1 \rightarrow \beta_1$ $\beta_2 \rightarrow \beta_2$ $\beta_3 \rightarrow \beta_3$	$\beta_4 \rightarrow \beta_3$ $\beta_3 \rightarrow \beta_2$ $\beta_2 \rightarrow \beta_1$	$\beta_4 \rightarrow \beta_2$ $\beta_3 \rightarrow \beta_1$ $\beta_2 \rightarrow \beta_1$
2 β_b Consistent expert opinion	$\beta_4 \rightarrow \beta_4$	$\beta_1 \rightarrow \beta_1$ $\beta_2 \rightarrow \beta_2$ $\beta_3 \rightarrow \beta_3$ $\beta_4 \rightarrow \beta_4$	
3 β_c Accredited source		$\beta_4 \rightarrow \beta_3$ $\beta_3 \rightarrow \beta_2$ $\beta_2 \rightarrow \beta_1$	

β



β_a

2nd Assessment: Conventional risk analysis using the root cause method and same in conjunction with α and β



The issue is tackled the less you know

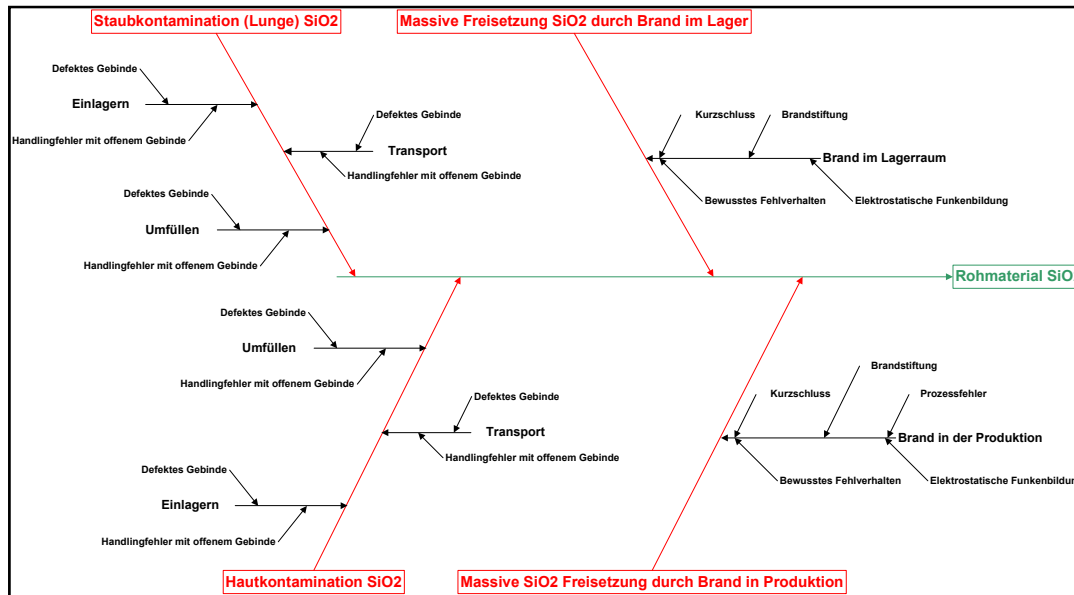
Auswirkung auf Menschen	Analogieschluss	Schadenspotenzial	Art der Schädigung	Inkorporationsweg	Schadensausmass
β		Schadenspotenzial bekannt $\alpha = 2, 3 \text{ od. } 4$	Schwere Schädigung $\alpha = 3 \text{ od. } 4$	Inhalation	F
				Ingestion	E
				dermal	E
				nicht möglich	A
				Inhalation	D
				Ingestion	C
				dermal	C
				nicht möglich	A
				Inhalation	B
				Ingestion	A
keine Schädigung $\alpha = 1$		keine Schädigung $\alpha = 1$	Schädigung $\alpha = 2$	Inhalation	D
				Ingestion	A
				dermal	A
				nicht möglich	B
				Inhalation	A
				Ingestion	A
				dermal	A
				nicht möglich	E
				Inhalation	D
				Ingestion	A



definition

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Root cause analysis for incorporation path



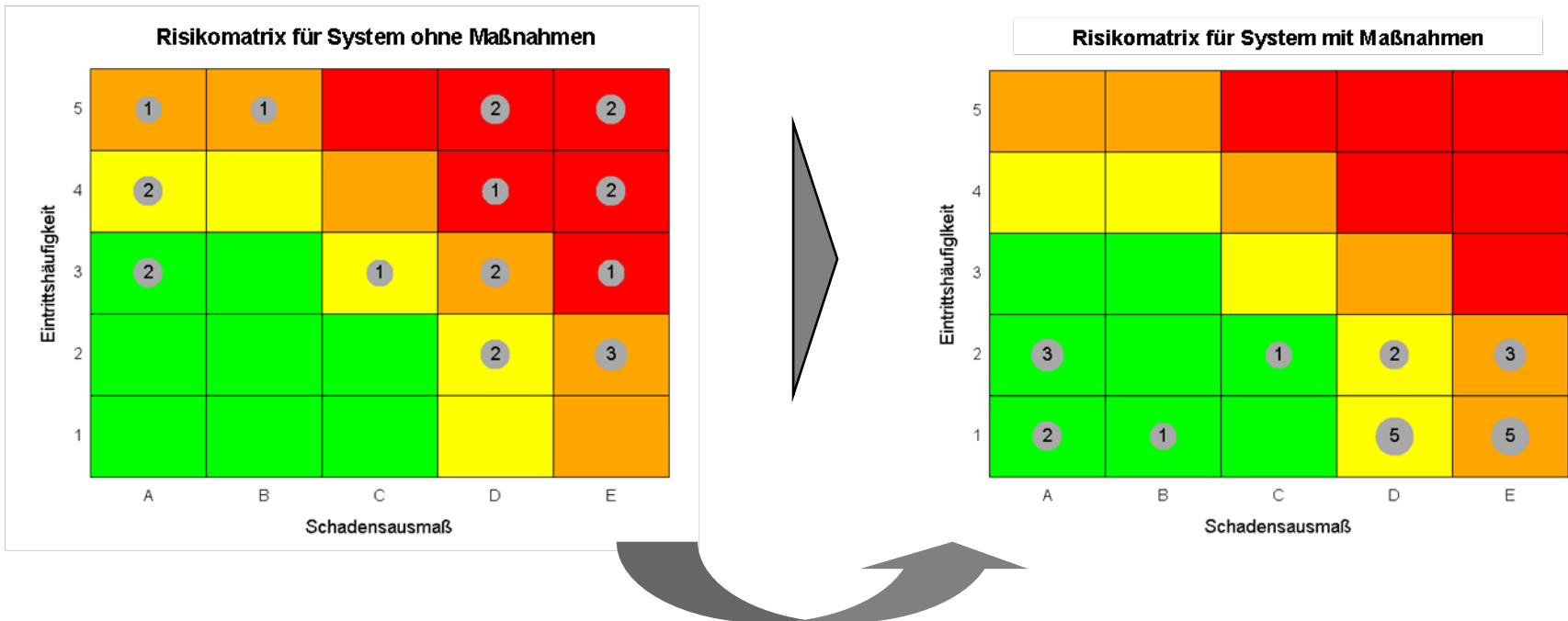
Auswirkung auf Menschen	Analogieschluss	Schadenspotenzial	Art der Schädigung	Inkorporationsweg	Schadensausmass
$\beta = 4$	Auswirkungen auf Menschen ausreichend untersucht (in vivo Mensch)	Schadenspotenzial bekannt $\alpha = 2, 3 \text{ od. } 4$	Schwere Schädigung $\alpha = 3 \text{ od. } 4$	Inhalation	F
				Ingestion	F
				dermal	E
				nicht möglich	A
				Inhalation	D
				Ingestion	D
				dermal	C
				nicht möglich	A
				Inhalation	A
				Ingestion	A
keine Schädigung $\alpha = 1$		keine Schädigung $\alpha = 1$	Schädigung $\alpha = 2$	Inhalation	D
				Ingestion	C
				dermal	C
				nicht möglich	A
				Inhalation	F
				Ingestion	F
				dermal	E
				nicht möglich	A
				Inhalation	D
				Ingestion	C

Consideration of safety systems and containment barriers rounds off the picture of the risk assessment matrix



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Safety systems

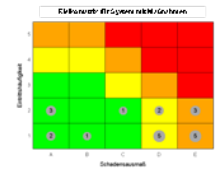
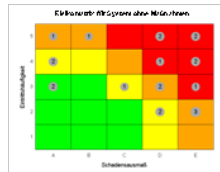
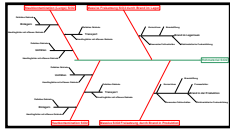
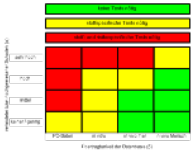


Barriers

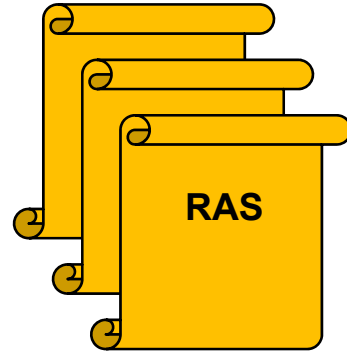
The RAS (Risk Assessment Sheet) is the central document



- 4 RAS issued in first year
- Typically documents with 20 pages



Criterion	Appraisal		
	Fulfilled	Limited	Questionable
Portability	(1) → (1) (2) → (2) (3) → (3) (4) → (4)	(4) → (3) (3) → (2) (2) → (1)	(4) → (2) (3) → (1) (2) → (1)
Consistent expert opinion	(1) → (1) (2) → (2) (3) → (3) (4) → (4)		
Accredited source	(4) → (3) (3) → (2) (2) → (1)		



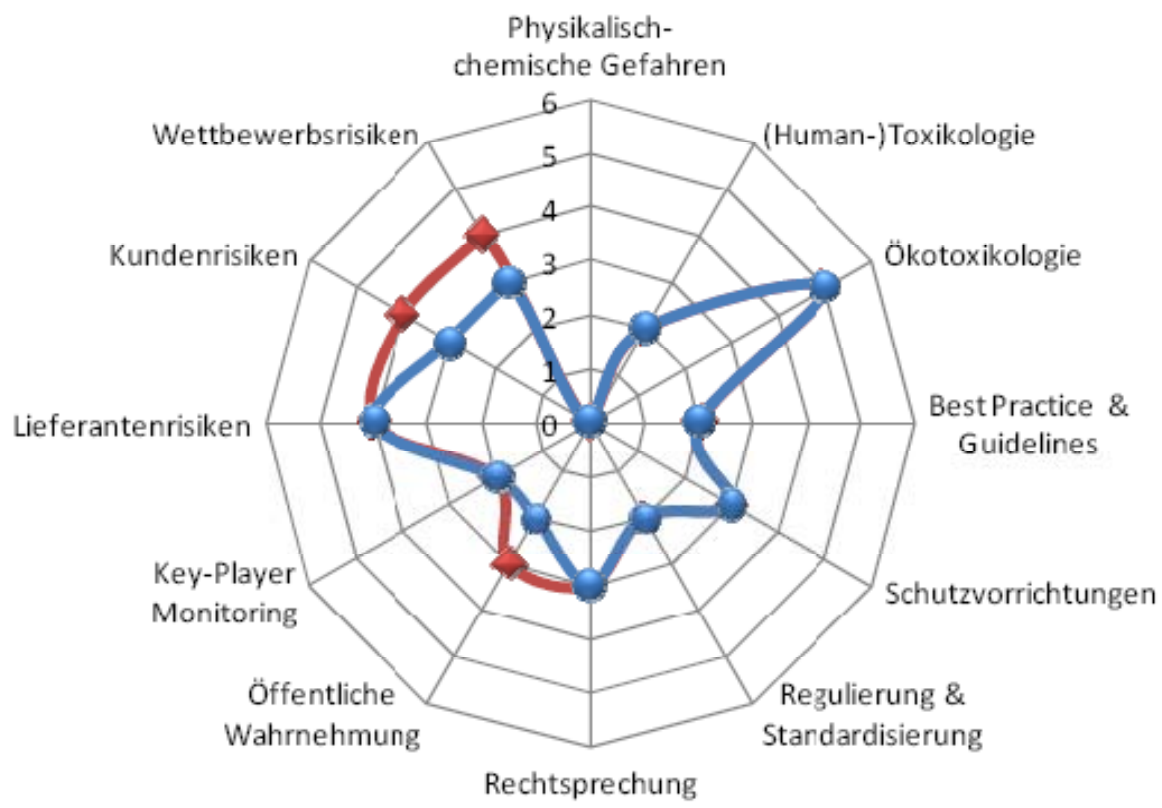
Is also used in the context of EU REACH as risk analysis



The monitoring systems manages changes required for the RAS and acts as an early warning system for future products



Indu:



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RAS

s

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What is interesting here for iNTeg-Risk?

- Risk assessments in situations of uncertainty**
- Judgements of similar situations**
- Monitoring risks – what are relevant parameters?**