nanoCare

Bundesministerium
für Bildung
und Forschung

NanoCare

A German Initiative on the Health Aspects
of Synthetic Nanoparticles:

Establishing an Information- and Knowledge-Base for
Innovative Material Research

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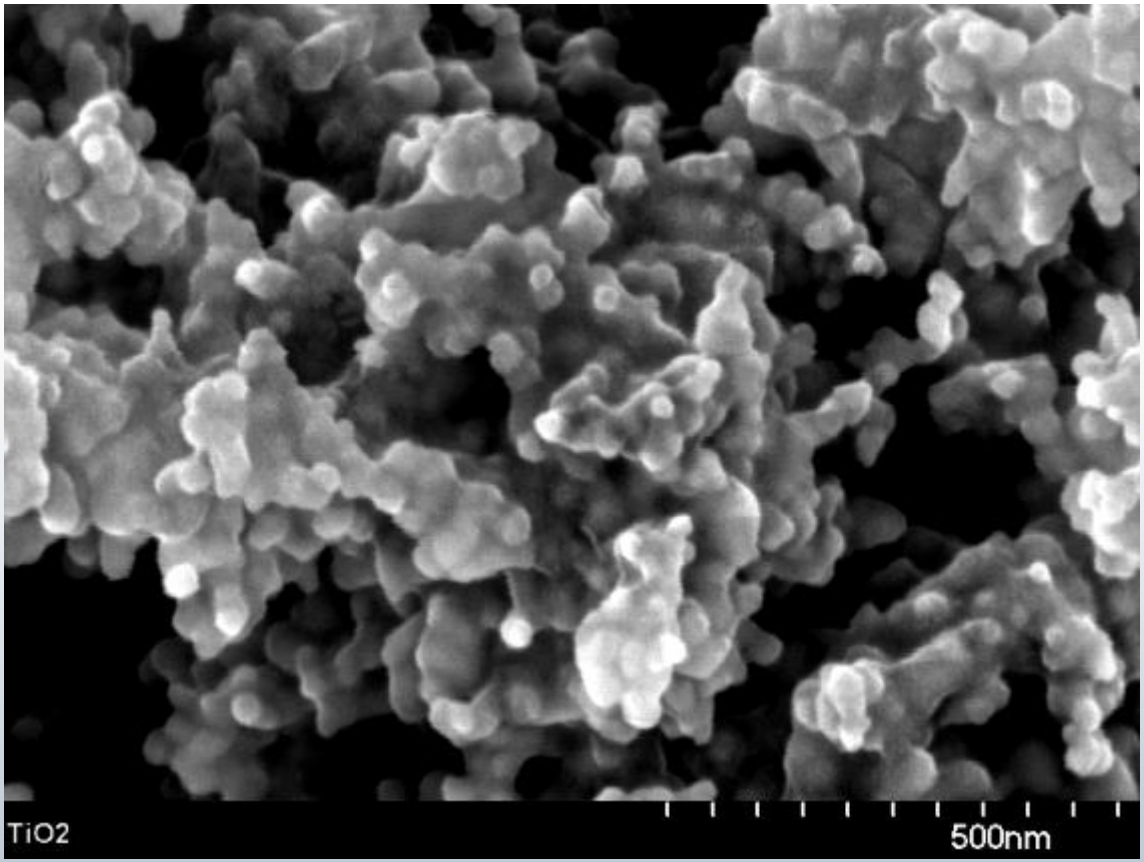
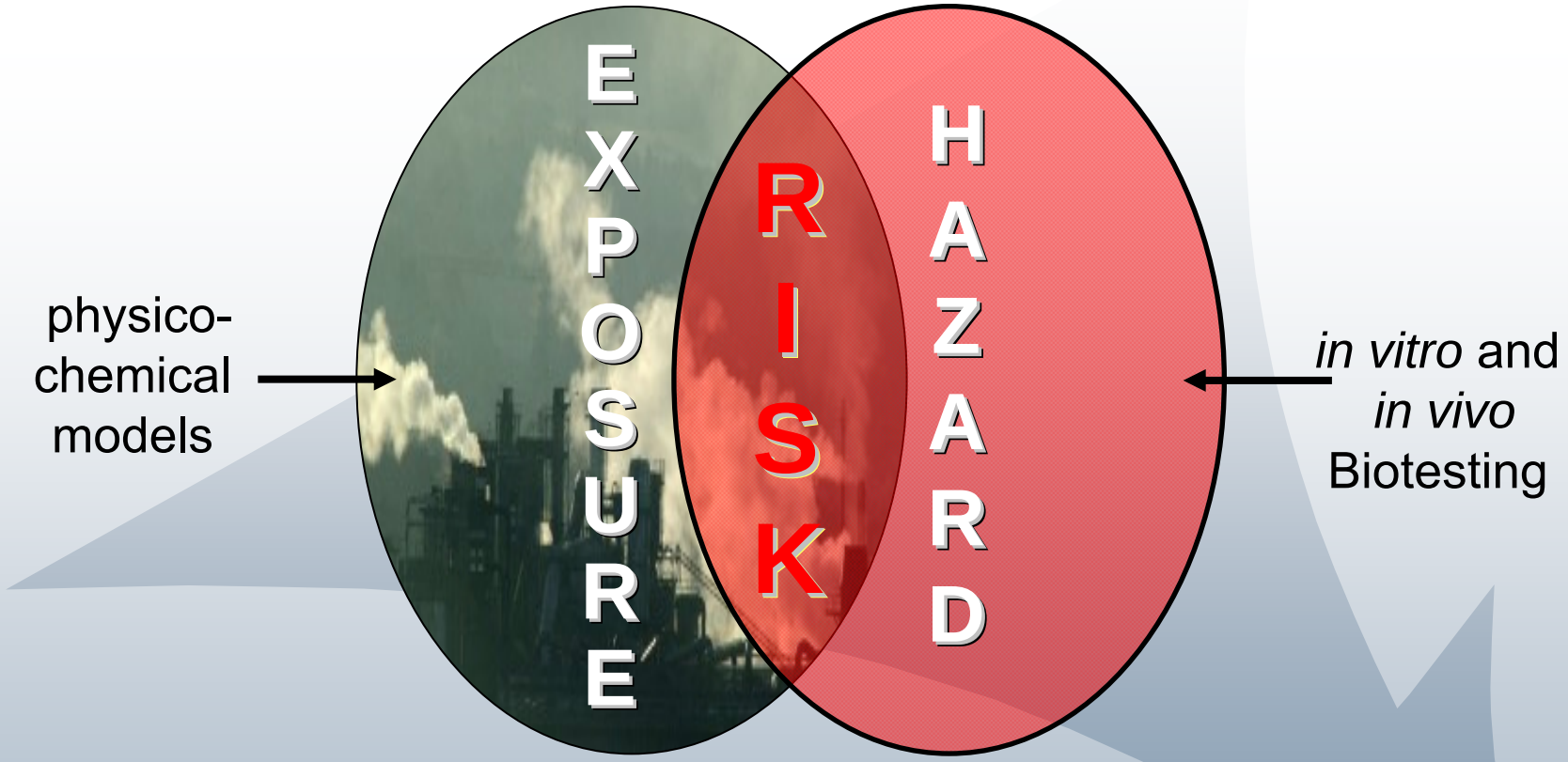
Introduction

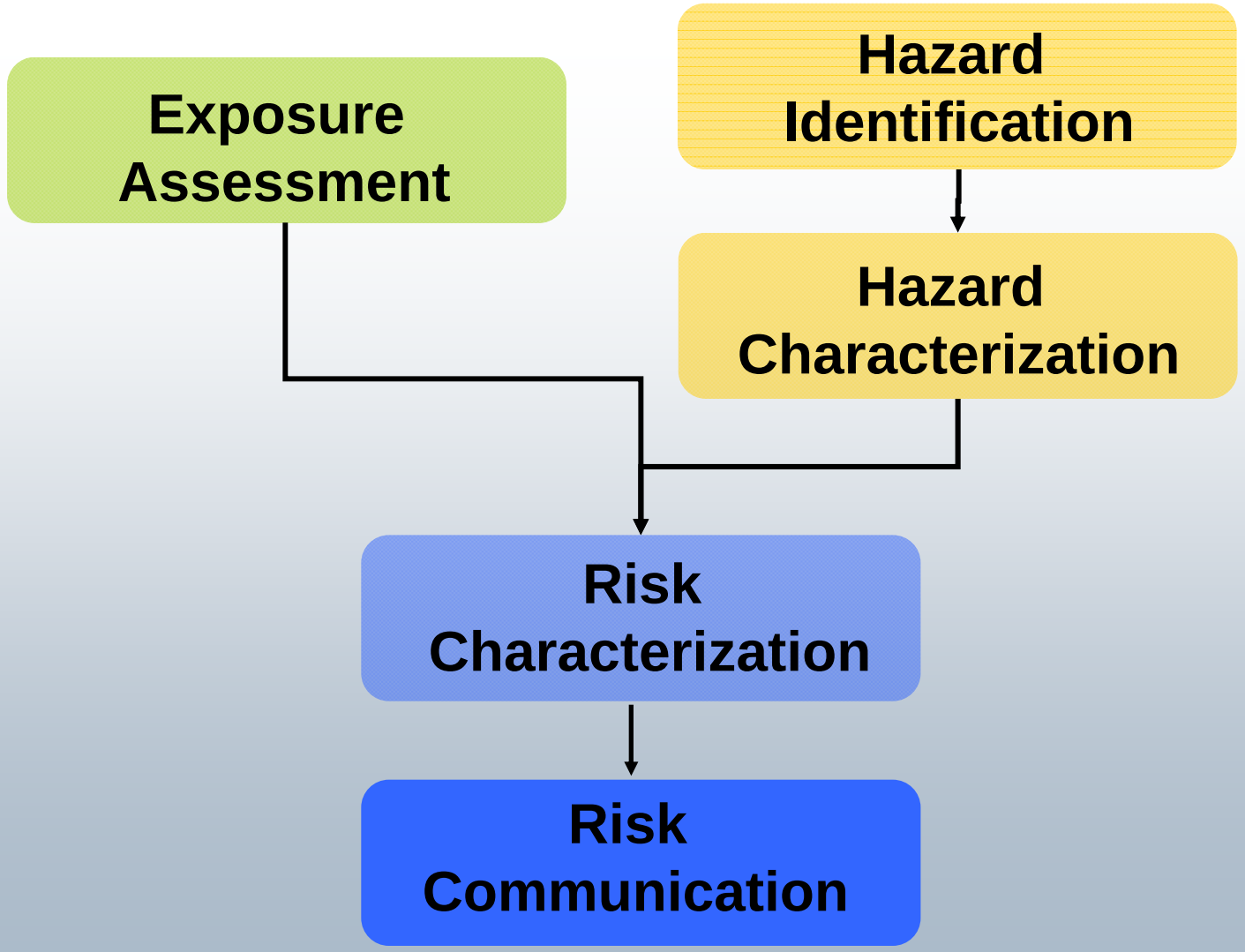


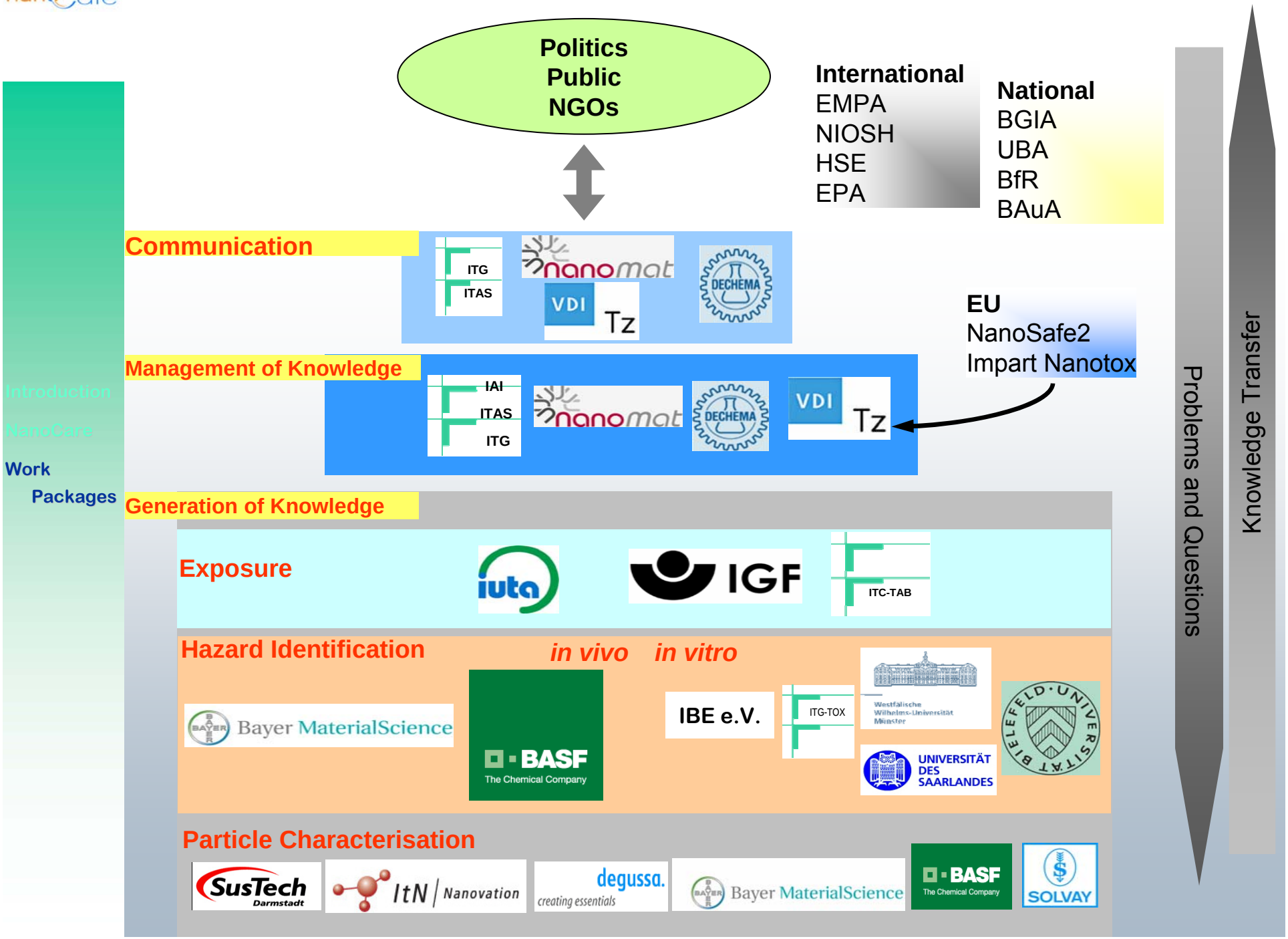
Information- and Knowledge-Base on
Health Aspects of Synthetic Nanoparticles

Conventional Approach for Toxicological Risk Assessment



Risk Assessment




nanoCare
Politics
Public
NGOs
International
EMPA
NIOSH
HSE
EPA
National
BGIA
UBA
BfR
BAuA
Communication
ITG
ITAS
nanomat
VDI
Tz
DECHEMA
EU
NanoSafe2
Impart Nanotox
Management of Knowledge
IAI
ITAS
ITG
nanomat
DECHEMA
VDI
Tz
Introduction
NanoCare
Work
Packages
Generation of Knowledge
Exposure
iuta
IGF
ITC-TAB
Hazard Identification
in vivo
in vitro
Bayer MaterialScience
BASF
The Chemical Company
IBE e.V.
ITG-TOX
Westfälische Wilhelms-Universität Münster
UNIVERSITÄT DES SAARLANDES
BIELEFELD UNIVERSITÄT
Particle Characterisation
SusTech
Darmstadt
ItN Nanovation
degussa.
creating essentials
Bayer MaterialScience
BASF
The Chemical Company
SOLVAY
Problems and Questions
Knowledge Transfer

Tasks

from Particles to Effects

Data Generation and Risk Communication

Generation of Knowledge

- Particle synthesis
- Particle characterisation
- Occupational Exposure
- Hazard identification *in vitro* and *in vivo*

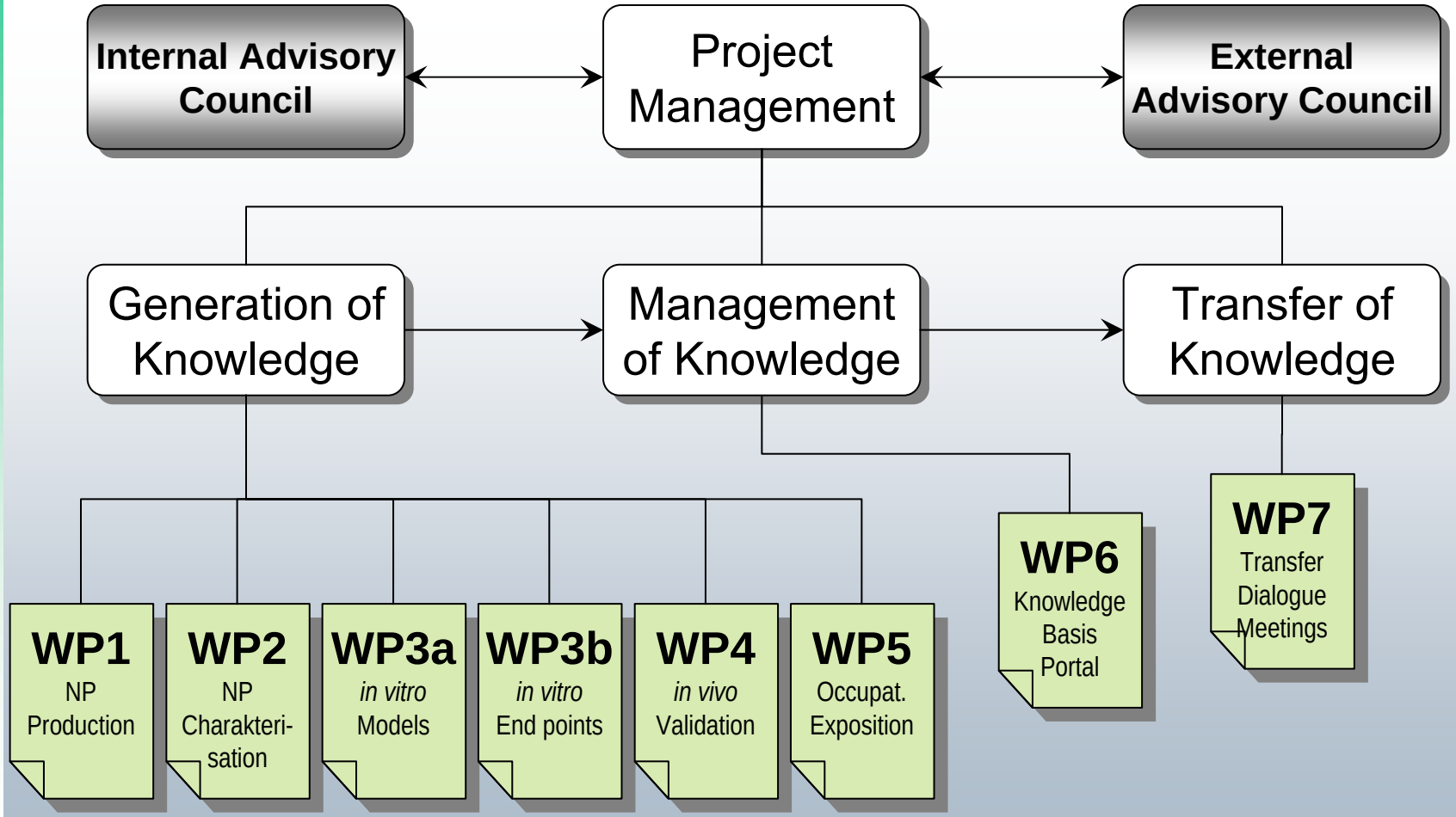
Management of Knowledge

- Data acquisition and -structuring
- Knowledge base and portal

Transfer of Knowledge

- Publication
- Communication (Dialogue Meetings)

Organization



Work Packages

WP 1: **Particle Production**

Directed modification of the investigated particles with regard to their size, surface charge and surface chemistry. Additional parameters are various surface coatings and alteration of hydrophobicity

WP 2: **Particle Standardisation and Characterisation**

Method of synthesis: precursors and modifications will be the same for all involved labs. The comparability of the results is ensured.
All facilities and methods have to be standardised.
Important property: agglomeration- and aggregation behaviour as well as the stability of agglomerates and aggregates

Work Packages

Introduction
NanoCare
Work Packages

WP 3a: ***in vitro* Models – Cell Cultures**

Selection of valid cells/cell types for the investigations
e.g. lung cells, epithelial cells, co-cultures

WP 3b: ***in vitro* Models - biological Endpoints**

Selection of valid biomarkers (effect identification) for a significant effect monitoring within these cellular systems

WP 4: **Validation *in vivo***

Examination of the *in vitro*-results within animal experiments - Extrapolation *in vitro - in vivo*

WP 5: **Occupational Exposure**

Number, agglomeration behaviour and distribution of nanoparticles at work places
Adjustment and development of new measuring methods

Work Packages

WP 6: **Data Preparation, Interpretation – Knowledge Base**

Analysis of the produced results and of relevant results from the literature

Maintenance of the knowledge base for internal use as well as the creation of interpreted data sets for public domain

WP 7: **Knowledge Transfer - Communication and Dialogue**

Internal dialogue and knowledge transfer for structuring of the research results

Dialogue and expert meetings; web portal

Publications in scientific journals as well as in the internet

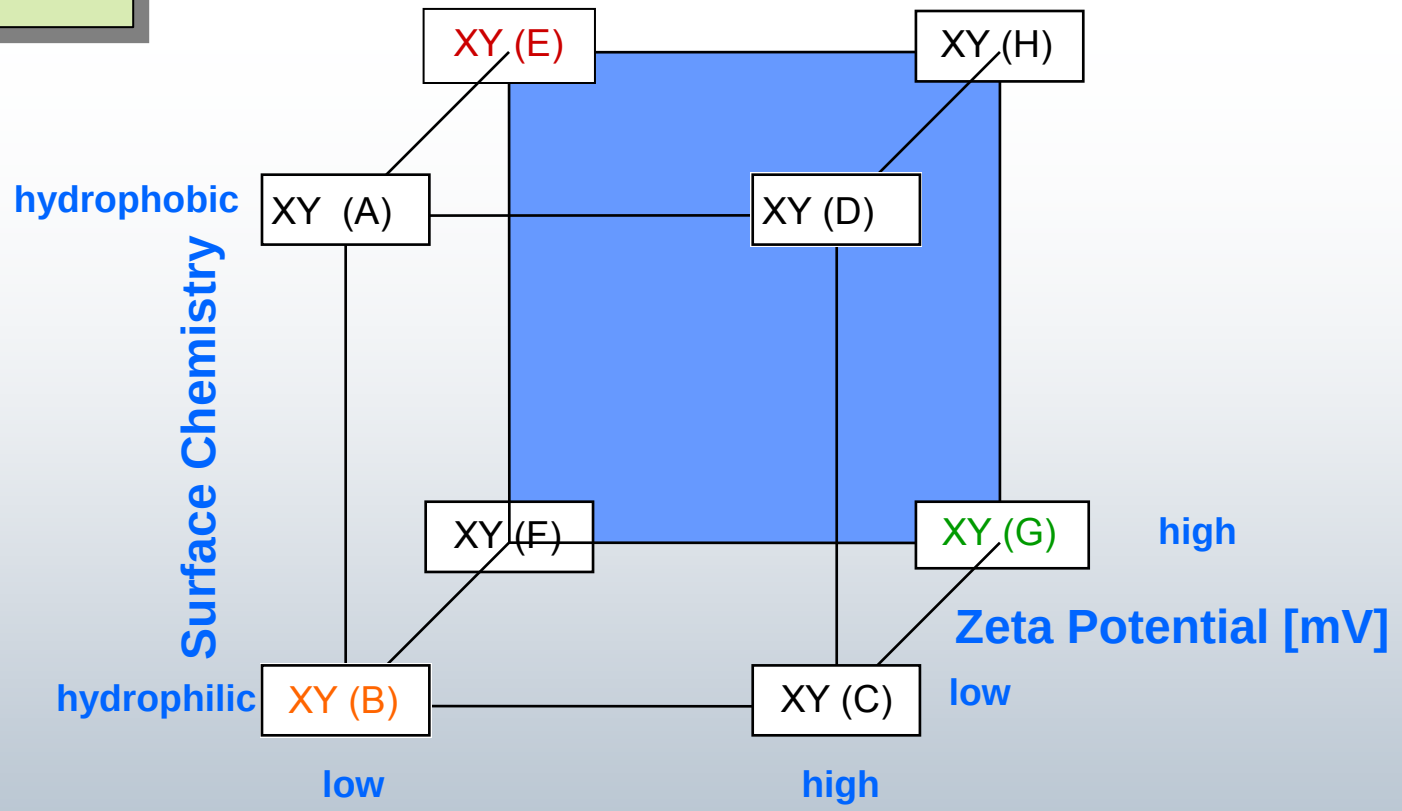
WP 8: **Coordination and Management of the Project**

Coordination of the WPs and the meetings

WP1
Production of Nanoparticles

Critical Parameters

Hypothetic Material XY



Effective Particle Size d50 (nm)

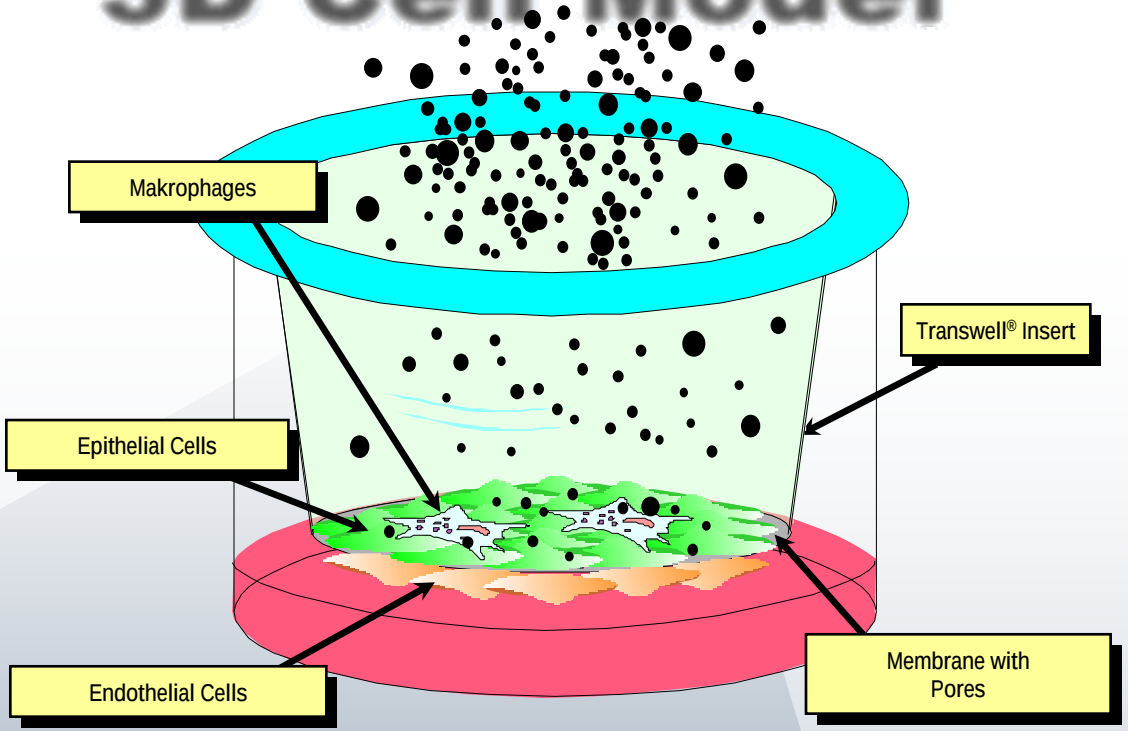
WP2
Characterisation of Nanoparticles

Particle Characterisation

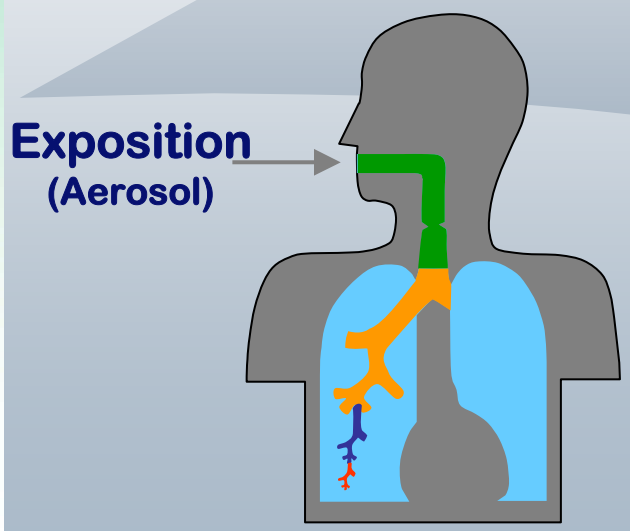
Information	*Method*
Particle Morphology (primarry and agglomerated)	TEM
	SEM
Particle size distribution (primarry and agglomerated)	TEM
	Light scattering, AUC
Chemical composition (core, surface, bulk, purity, modifications, stabilization)	TOF-SIMS
	XPS
	ICP-MS
	AAS
	Zeta-potential
Surface area	BET
Cristallinity and Homogenicity	XRD, EDX (TEM)
Solubility in media	special methods

WP3a
in vitro Transport

3D Cell Model



Uptake Mechanisms



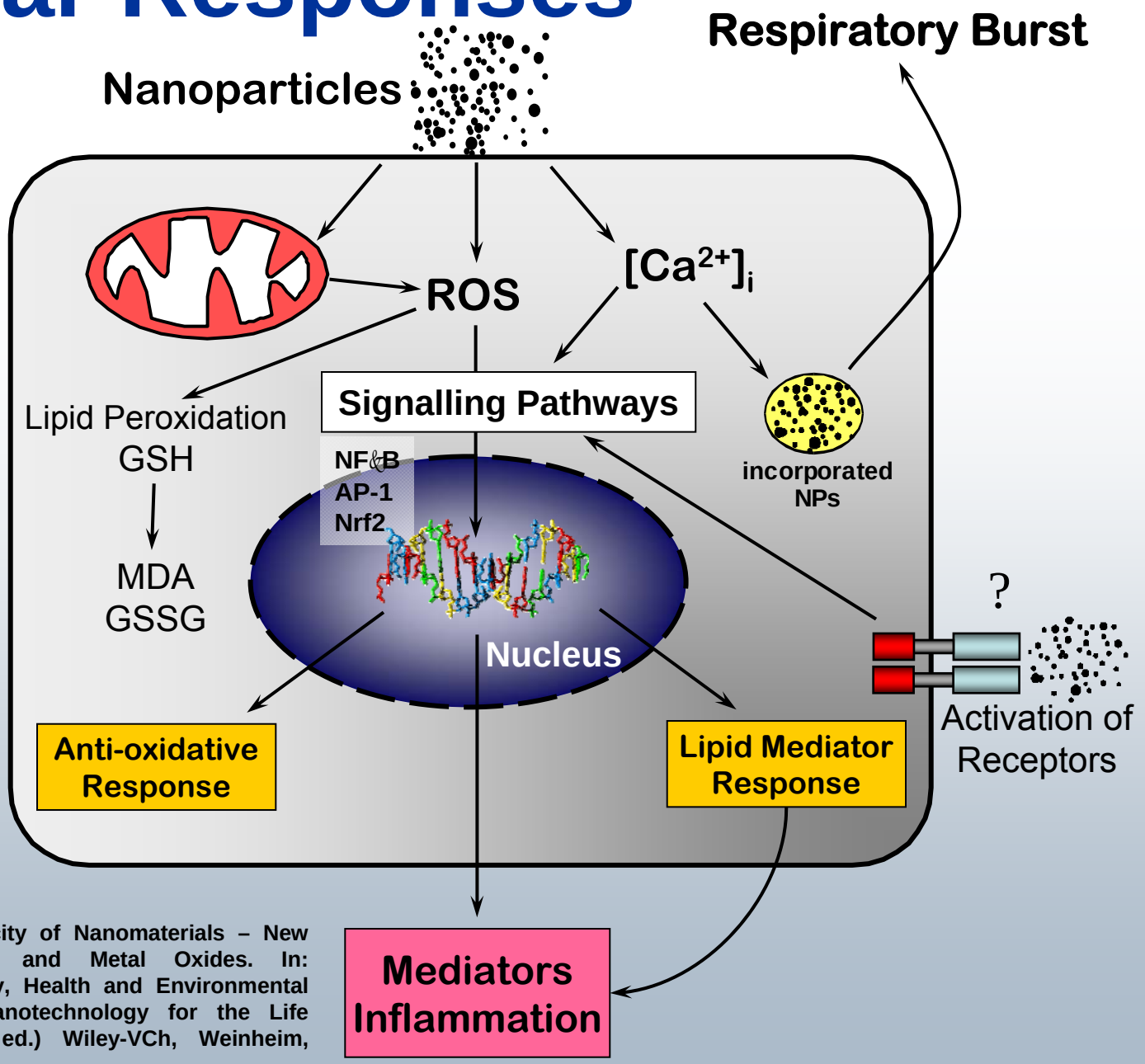
Possible adverse Effects

Hazard Identification

Risk Characterization
Risk Communication

Cellular Responses

WP3b
in vitro
End Points



Krug et al. (2006) Toxicity of Nanomaterials – New Carbon Conformations and Metal Oxides. In: Nanomaterials – Toxicity, Health and Environmental Issues, Series title: Nanotechnology for the Life Sciences (Kumar, C., ed.) Wiley-VCh, Weinheim, pp. 153-185.

WP4
in vivo Validation

Atmosphere Generation and Characterisation

- Head/Nose only
- Spray Generator
- Analysis of concentrations
- Particle size measurement
  - Impactor
  - OPC (optical particle counter)
  - SMPS (scanning mobility particle sizer)

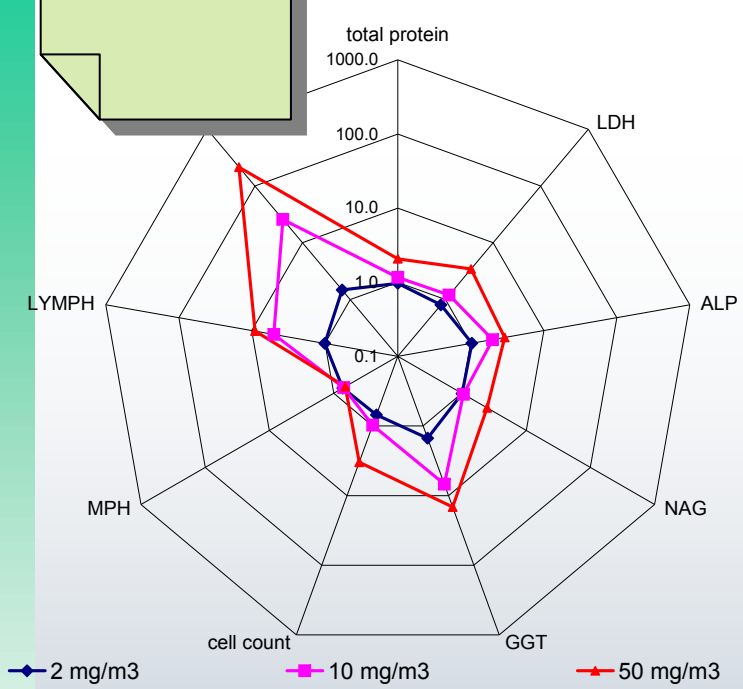
WP4
in vivo
Validation

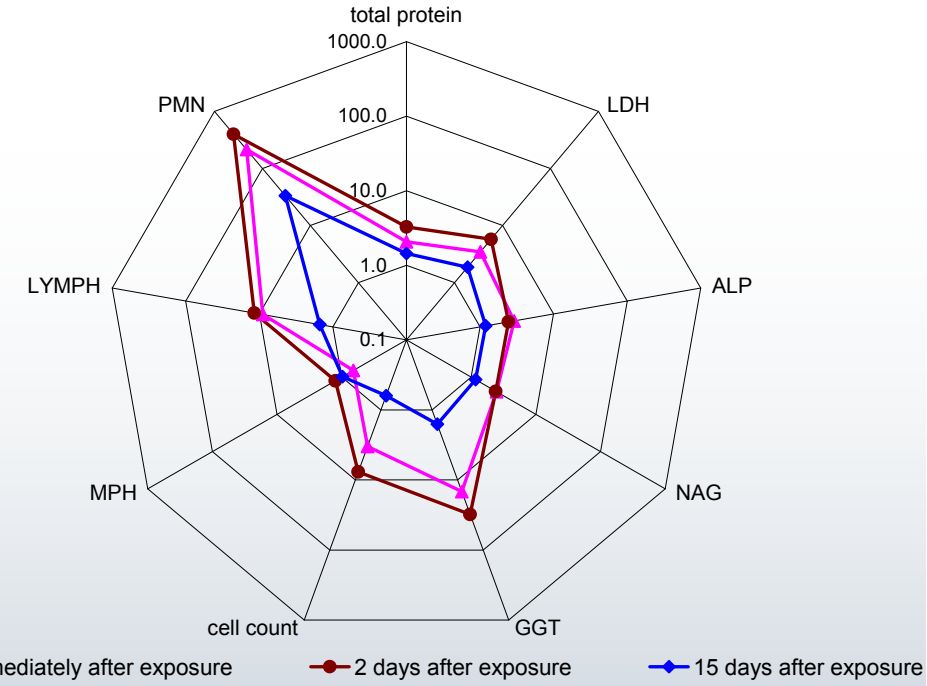
Biological Parameters

1. Histopathology of the lung
2. Cell proliferation in the lung
3. Total Protein in BALF
4. Lactate dehydrogenase (LDH)
5. Alkaline phosphatase (ALP)
6. γ-Glutamyltransferase (GGT)
7. N-acetyl-β-Glucosaminidase (NAG)
8. Total cell count
9. Macrophage (MPH)
10. Polymorph nuclear granulocytes (PMN)
11. Lymphocyte (LYMPH)
12. Carboxymethyllysin (CML)
13. Malondialdehyd (MDA)
14. 8-OHdG
15. Apolipoprotein A1
16. ß-2 Microglobulin
17. Calbindin
18. CD40
19. CD40L
20. Clusterin
21. C-Reactive Protein
22. Cystatin
23. EGF
24. Emdothelin-1
25. Eotaxin
26. Factor VII
27. FGF-basic
28. FGF-9
29. Fibrinogen
30. GCP-2
31. GM-CSF
32. Growth Hormone
33. GST-α
34. GST-1 Yb
35. Haptoglobin
36. IFN-γ
37. IgA
38. IL-1α
39. IL-1ß
40. IL-2
41. IL-3
42. IL-4
43. IL-5
44. IL-6
45. IL-7
46. IL-8
47. IL-10
48. IL-11
49. IL-12p70
50. IL-17
51. Insulin
52. IP-10
53. KC/GROα
54. Leptin
55. LIF
56. Lipocalin-2
57. MCP-1
58. MCP-2
59. MCP-3
60. MCP-5
61. M-CSF
62. MDC
63. MIP-1α
64. MIP-1ß
65. MIP-1γ
66. MIP-2
67. MIP-3ß
68. MMP-9
69. Myoglobulin
70. OSM
71. Osteopontin
72. RANTES
73. SCF
74. Serum Amyloid P
75. SGOT
76. TIMP-1
77. Tissue Factor
78. TNF-α
79. TPO
80. VCAM-1
81. VEGF
82. von Willebrand factor

WP4
in vivo
Validation

Biological Parameters





Concentration-Effect Diagram

- Rats exposed to 2, 10 and 50 mg/m^3
- Immediately after the last exposure
- Relative increase vs. control

➢ Reflect different levels of local inflammation in inhalation studies

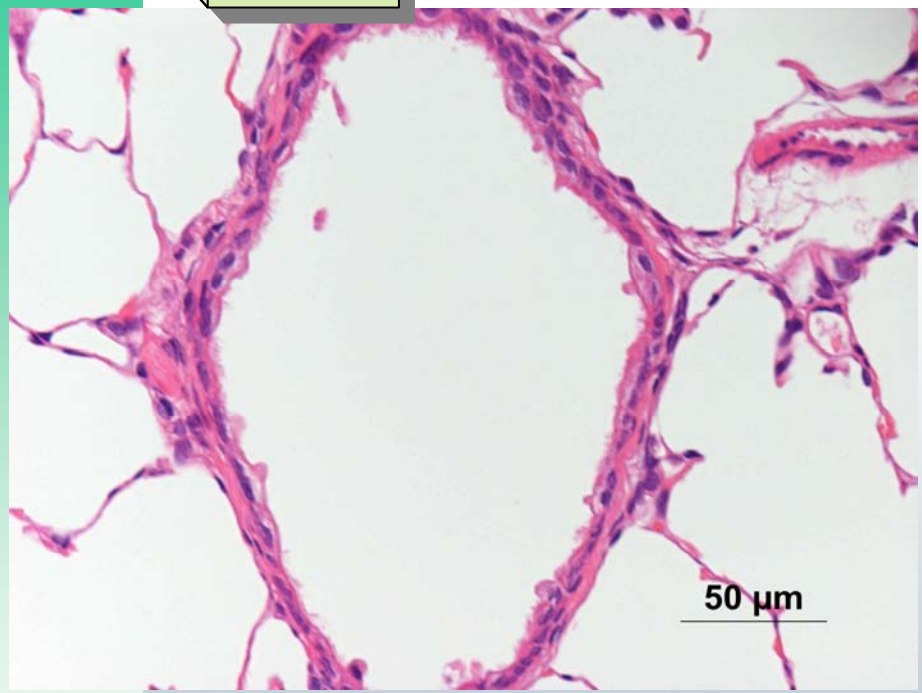
Time-Effect Diagram

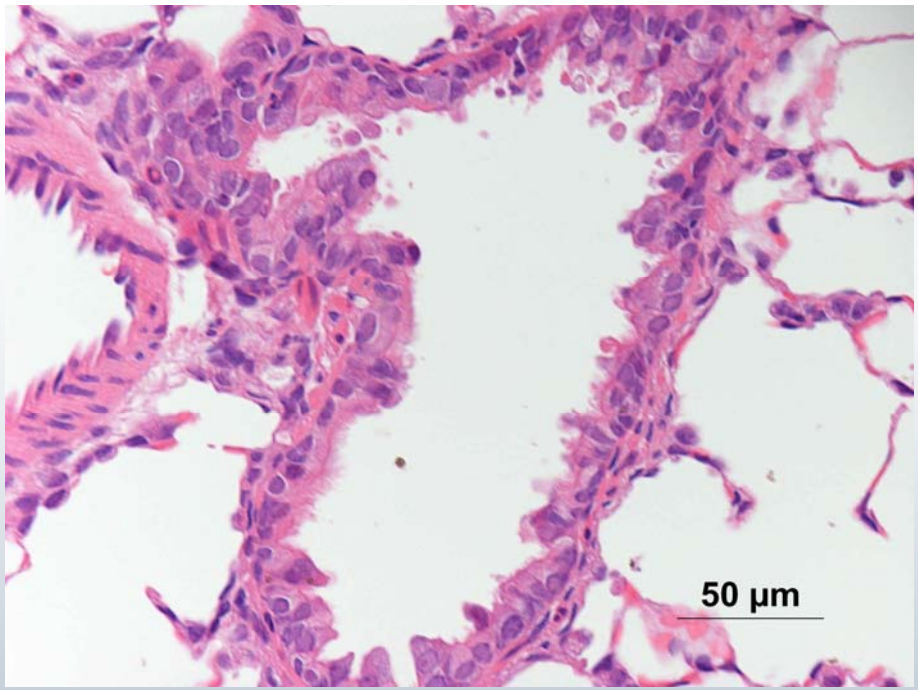
- Rats exposed to 50 mg/m^3
- Immediately, 2 and 15 days after exposure
- Relative increase vs. control

➢ Most prominent changes occurred 2 days after the last exposure.

WP4
in vivo
Validation

Biological Parameters



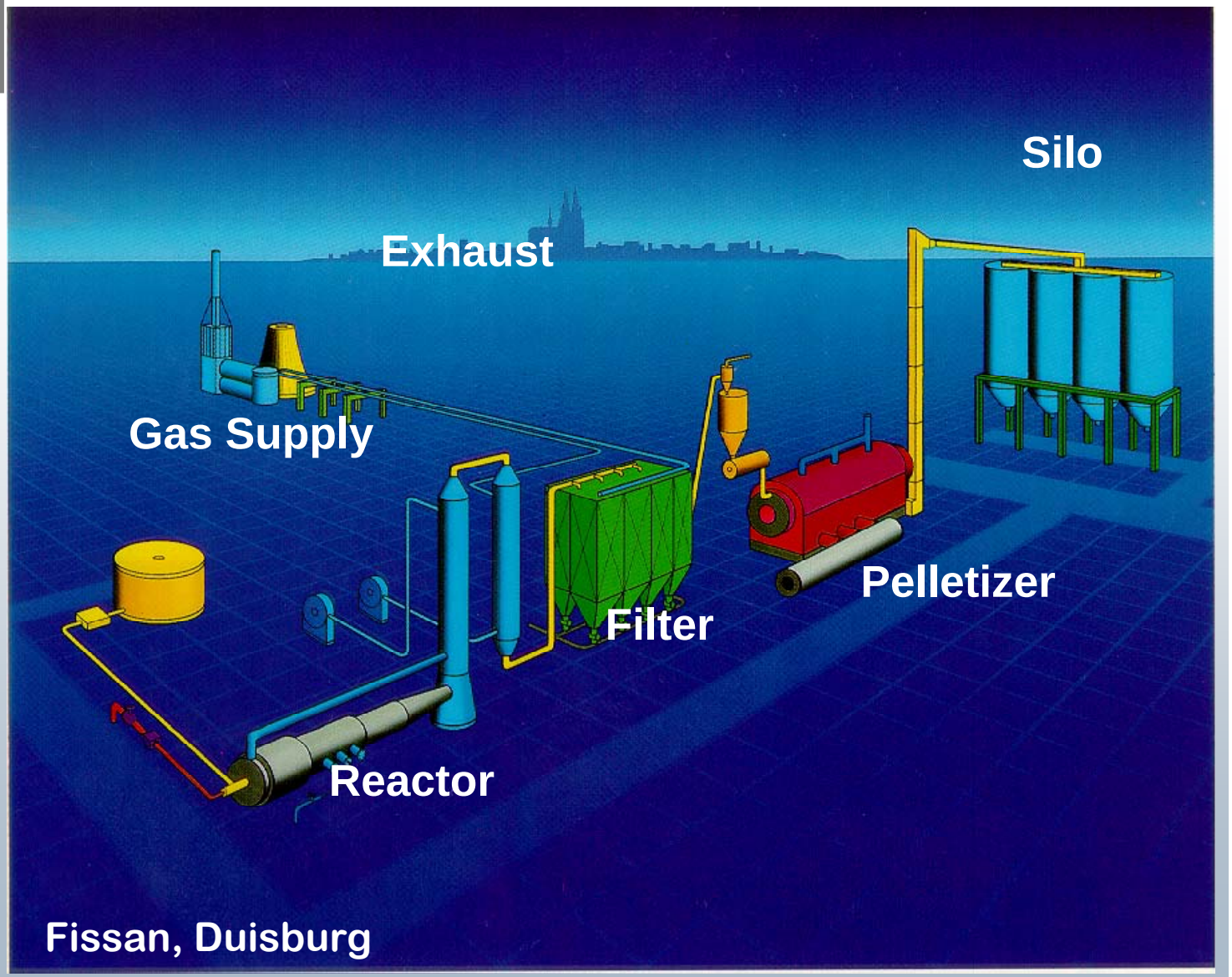


Major findings immediately after end of exposure:

- Diffuse alveolar histiocytosis
- Hyperplasia and epithelialization in the region of the terminal bronchioli
- Particle loaded macrophages
- All findings are regarded as adaptive changes

WP5

Occupational Exposure



Measurements conducted at NP-workplaces by IUTA

Main measurement techniques employed:

- SMPS and FMPS
- ESP and REM/TEM + EDX

Number of areas investigated

	Locations			
NP material	Reactor	Processing	Handling/other	Publications
Carbon Black	3	3	3	Kuhlbusch et al., 2004 Kuhlbusch and Fissan, 2006
TiO_2	2	2	2	
Al_2O_3	1	1	1	
other			1	
scheduled	3	3	3	

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Introduction

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Work Packages

European Activities

will be available in English

Thank you for your Attention