CURRENT TO NEAR-FUTURE RISK ASSESSMENT AND MANAGEMENT METHODS FOR MANUFACTURED NANOMATERIALS.

Professor Keld Alstrup Jensen, Ph.D., cand.scient.

kaj@nrcwe.dk

National Research Centre for the Working Environment
Materials and Product Innovation and Current Practice in Risk assessment and Management

**Cooper Stage-Gate® Idea to launch model**

- **Idea screen**
  - Gate 1
  - Discovery and ideas

- **Scoping Screen**
  - Gate 2
  - Scoping Stage 1

- **Go to development**
  - Gate 3
  - Build business case

- **Go to test**
  - Gate 4
  - Research and development

- **Go to Launch**
  - Gate 5
  - Go to test

- **Post-Launch review**
  - Gate 6
  - Build business case

**Insure**

- **EHS**

**Material, product and safety knowledge**

**E|S|E**

NANOSAFE 2018; November 6-9, 2018.
CNT as an Example!

Observed filaments/first structural data
Radushkevich and Lukyanovich Zurn Fisic Chim (1952)
Hillert and Lange Z Kristallogr (1958)
Baker et al. Carbon (1973); J. Catalysis (1973)

Patents CNT production 1980ies

Naming and TEM images

Antifouling
Ca. 2007-2009

www.amcoat.no (closed)

Industrial Production

<table>
<thead>
<tr>
<th>Year</th>
<th>Tonnes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>65</td>
</tr>
<tr>
<td>2007</td>
<td>271</td>
</tr>
<tr>
<td>2009</td>
<td>500-1000</td>
</tr>
<tr>
<td>2014</td>
<td>1750-2500</td>
</tr>
</tbody>
</table>

Application area | Uses in 2015
--- | ---
Electronics | Printed electronics (conductive ink)
Coatings | Conductive coatings (displays and touch screens)
 | Anti-fouling coatings
 | High-durability epoxy-paints
Energy | Li-ion batteries
Materials | Antistatic thermoplastics
 | Conductive textiles
 | Thin heating mats
 | High performance sports goods
 | Small windmills
Biomedical | Microscopy probes

CNT as an Example!

Observed filaments/first structural data:
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2004-2009

2009-2013

2013
Bayer closes Large new plant

2017
Danish Worker Authorities start process for setting nano-OEL

**CNT as an Example!**

- **Observed filaments**/first structural data:
  - Radushkevich and Lukyanovich
  - Hillert and Lange

**Patents CNT production 1980ies**

**Naming and TEM images**

**Application area**
- **Electronics**
  - Printed electronics (conductive ink)
- **Coatings**
  - Conductive coatings (displays and touch screens)
  - Anti-fouling coatings (high durability epoxy paints)
- **Energy**
  - Li-ion batteries
- **Materials**
  - Antistatic thermoplastics
  - Conductive textiles
  - Thin heating mats
  - High performance sports goods
  - Small windmills
- **Biomedical**
  - Microscopy probes

**www.amcoat.no (closed)**

**Industrial Production**

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<tr>
<td>2014</td>
<td>1750-2500 tons</td>
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</tbody>
</table>

**2004-2009**
- Serious scientific health concern (e.g., Lam et al. Tox Sci. (2004), Poland et al. Nature (2008); Ma-Hock et al. Tox Sci (2009))

**2009-2013**

**2013**
- Bayer closes large new plant

**2017**
- Danish Worker Authorities start process for setting nano-OEL

**Could this R&D and Launch process have been better, safer (and cheaper for the companies and society)?**

**Jensen et al. Environmental project No. 1805 (2015)**
Principal Risk Assessment
and Risk Management

Establishing the context

Risk Identification

Risk Analysis

Risk Evaluation

Risk Treatment

Monitoring and Review

Communication and Consulting

ISO/IS/31000 (2009)
Current situation in the REACH risk assessment approach

- REACH Tier 1 estimates
- ECETOC TRA
- EMKG EXPO Tool
- ConsExpo
- (Risk of Derm)
- Stoffenmanager
- Advanced REACH Tool
- ...

- No official exposure limits or DNEL’s for NM
- No proper emission potentials for NM
- No default exposure scenarios in the tools
- Lack of product categories for nanoparticles
- Gaps in application domains

Reliable risk assessments with REACH model is impossible or should be done with GREAT care!

NANOSAFE 2018; November 6-9, 2018.
Current situation in the REACH risk assessment approach

- REACH Tier 1 estimates
- ECETOC TRA
- EMKG EXPO Tool

No data and lack of validated REACH RA tools ⇒
Need for precautionary nano-specific Risk Assessment and – Management approaches

Reliable risk assessments with REACH model is impossible or should be done with GREAT care!
Is that critical? - Opinions among stakeholders

<table>
<thead>
<tr>
<th>Adequacy of current regulation for nano-risk governance</th>
<th>Industry Representatives</th>
<th>Academic Public Researchers</th>
<th>Policy makers Regulators Insurers</th>
<th>Users Society Representatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Importance of nano-risk assessment procedures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Importance of specific disposal procedures for NMs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usefulness of DS (decision support) web-tools for nano-risk governance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Color scale (from 1-very low to 5-very high)

Unpublished caLIBRAte results
Horizon scanning / Early Warnings
Pre-risk assessment
Risk assessment
Risk management and decision
Communication and consultation
Monitoring

Context and concerns
ID of risk scenarios
Evaluation

Analysis
Characterization
Evaluation

Emerging Risk Management Framework [CEN Workshop Agreement 16649 (2013)]

Idea screen
Scoping Screen
Go to development
Go to test
Go to Launch
Post-Launch review

Gate 1
Gate 2
Gate 3
Gate 4
Gate 5
Gate 6
Discovery and ideas
Scoping Stage 1
Build business case
Research and development
Testing and Validation
Launch
Horizon Scanning/Monitoring

Cooper Stage-Gate® Idea to launch model

NANOSAFE 2018; November 6-9, 2018.
From Emerging Risk Management to Nano-risk (innovation) Governance

Building and maintainence of confidence in the risk assessment for trustworthy risk communication and governance

Cooper Stage-Gate® Idea to launch model

Qualitative / Semiquantitative predictive

Quantitative predictive / Test Data Driven
Further development in NMBP-13 and NMBP14 projects.

Nano-Risk (Innovation) Governance Platform

Communication and Knowledge Transfer
- Regulation
- Guided Practice
- Horizon scanning
- Regulatory foresight
- Monitoring
- Safe Innovation Approach (SIA) Tools Portal
  H2020 NANOREG2

Risk Assessment and Management Models
- Simulation
- Risk- benefit
- Decission support
- Exposure Data
- Process emission
- Risk Management
- Dustiness
- PhysChem (Eco)toxicology
- Data bases & libraries

Users: industry, service providers, regulators, NGO's etc.
From Risk Assessment to Emerging Risk Management (Governance)

Horizon scanning / Early Warnings
Pre-risk assessment
Risk assessment
Risk management and decision
Communication and consultation
Monitoring

Context and concerns
ID of risk scenarios
Analysis
Characterization
Evaluation

Emerging Risk Management Framework [CEN Workshop Agreement 16649 (2013)]

Ability to ID a new risk
Different?; Unsafe?; Regulation? ...

Share ideas and views on how to best deal with innovations
Discuss implementation of the RP concept
Identify tools needed to support RP
Identify the needs of regulatory risk assessors to be prepared for innovations

NANOSAFE 2018; November 6-9, 2018.
Nano-Risk Radar: Horizon Scanning and Monitoring

- **Web-based tool**

- Regular automatic search for "Nano-safety" related topics from online sources based on user-defined query.

- Analyses content using natural language processing techniques

- Ranks the results according to their relevance in graphical summary – The Radar

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News: Google News, BBC

Regulatory bodies: ECHA, EPA...

Blogs: Wordpress.

Research database: Sciencedirect, Nature...

Review and Analysis

R&D info service: Cordis...

Jovanovic, Chakravarty, Jelic; R-Tech (Germany) Klimek et al. *Scientometrics* (2016)
From Risk Assessment to Emerging Risk Management (Governance)

Emerging Risk Management Framework [CEN Workshop Agreement 16649 (2013)]

- Horizon scanning / Early Warnings
- Pre-risk assessment
- Risk assessment
- Risk management and decision
- Communication and consultation
- Monitoring

- Context and concerns
  - ID of risk scenarios
  - Evaluation
- Analysis
- Characterization
- Evaluation

- Ability to ID a new risk
- Applicable data or methods and tools
- Applicable data knowledge
- Knowledge
  - Applicable methods, tools, data

Different?; Unsafe?; Regulation? ...

Methods, Measurement, Read-across, Grouping, ..

Efficacy of RMM, "risk-knowledge", ..

Methods, Systems, Data-bases, ..
When should nano-risk assessment procedures be performed?

<table>
<thead>
<tr>
<th>Event Description</th>
<th>Industry Representatives</th>
<th>Academic Public Researchers</th>
<th>Policy makers Regulators Insurers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idea screening; Early planning stage of R&amp;I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scoping screening; Basic research</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Go to development; Applied research/proof of concept</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Go to test; Production/engineering/testing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Go to launch; Go to market</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post launch review; On the market</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In all stages</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Unpublished caLIBRAte results

Color scale (Number of counts)

0 | Max
Conceptual innovation risk governance framework

Stage-gate innovation funnel:
- Idea screen
- Scoping screen
- Go to development
- Go to test
- Go to launch
- Post-launch review

Discovery and ideas → Scoping → Build business case → Research and development → Testing and validation → Launch → Horizon Scanning/Monitoring

Decision support

Safe-by-design

Pre-risk assessment

Predictive risk assessment

Regulatory risk assessment

Monitoring

Control banding and “simple” predictive models

New or innovative test methods and tools (HTS; NANOCLASSIFIER…)

NANOSAFE 2018; November 6-9, 2018.
So, do we have the data and the tools?
Several different nano-specific tools

<table>
<thead>
<tr>
<th>No.</th>
<th>Model name</th>
<th>Application area</th>
<th>Owner</th>
<th>Model</th>
<th>Description</th>
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<tr>
<td>1</td>
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<td>CB</td>
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<td>ISO TS 12901 CB tool</td>
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<td>CB</td>
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<td>Work</td>
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<td>5</td>
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<td>6</td>
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<td>Work</td>
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<td>QEA</td>
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<td>Work</td>
<td>IOM</td>
<td>QEA</td>
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<tr>
<td>10</td>
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<td>FOPH (CH)</td>
<td>Risk Cat</td>
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<tr>
<td>11</td>
<td>LICARA NanoScan</td>
<td>Env/Cons/Work</td>
<td>EMPA/TNO</td>
<td>Risk Benefit</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>SUNDS</td>
<td>Env/Cons/Work</td>
<td>UNIVE / GD</td>
<td>RA / RM</td>
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<tr>
<td>13</td>
<td>GuideNano</td>
<td>Env/Cons/Work</td>
<td>LEITAT</td>
<td>RA / RM</td>
<td></td>
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<td>14</td>
<td>nano-QSAR</td>
<td>Human/Env.</td>
<td>Tomas Puzyn</td>
<td>QHA</td>
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<tr>
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<td>RIVM</td>
<td>QEA</td>
<td></td>
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<tr>
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<td>Env</td>
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<td>19</td>
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<td>Env</td>
<td>UNIVE</td>
<td>QEcotox</td>
<td></td>
</tr>
</tbody>
</table>

SUN Decision Support

Iterative procedure for safe nano-enabled product design

TIER 1
- Synthesis
- Formulation
- Use
- End of Life
- LICARA nanoSCAN

TIER 2
- Risk Control (RC) module
- Socio-economic Assessment (SEA) module
- Integration and uncertainty estimation

CENARIOS Risk management system
- Ranking of technologies/measures for ecological and human health risk reduction
- Benefit/Risk Analysis to compare nano-enabled products

D. Hristosov (Green Decision)
Conceptual framework

- Activities
- Compartment / Fate
- Exposure
- Hazard
- Materials
- Similarity
- Risk assessment and management
Several different nano-specific tools

Common for all!
Often restricted to specific application domains
Users often have challenges in finding input data
Limited use and low general knowledge about them
NOT VALIDATED

Conceptual innovation risk governance idea

Building and maintainence of confidence in the risk assessment for trustworthy risk communication and governance

Testing and Validation is key to build the foundations

Quantitative predictive / Test Data Driven
Ongoing in H2020 caLIBRAte: Validation by sensitivity and performance testing

Pouring 700g CuO under a fume hood

ASSESSMENT BY TIER 2
NanoSafer v 1.1

Result of assessment

<table>
<thead>
<tr>
<th>Estimated hazard level</th>
<th>Estimated time-resolved exposure index</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2</td>
<td>500.0</td>
</tr>
</tbody>
</table>

Near-field Acute: 0.0025
EB1: Very low exposure potential

Near-field Daily: 0.0000
EB1: Very low exposure potential

Far-field Acute: 0.0002
EB1: Very low exposure potential

Far-field Daily: 0.0000
EB1: Very low exposure potential

NF = 1.5 μg m⁻³ < M_{NF real work environment} (9.2 μg m⁻³)

Toxicity

<table>
<thead>
<tr>
<th>Exposure</th>
<th>0.76-1.00</th>
<th>0.51-0.75</th>
<th>0.25-0.50</th>
<th>0.00-0.25</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1.00</td>
<td>RL5</td>
<td>RL5</td>
<td>RL5</td>
<td>RL5</td>
</tr>
<tr>
<td>0.51-1.00</td>
<td>RL5</td>
<td>RL5</td>
<td>RL4</td>
<td>RL4</td>
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<td>0.26-0.50</td>
<td>RL5</td>
<td>RL4</td>
<td>RL4</td>
<td>RL3</td>
</tr>
<tr>
<td>0.11-0.25</td>
<td>RL4</td>
<td>RL4</td>
<td>RL3</td>
<td>RL2</td>
</tr>
<tr>
<td>&lt; 0.11</td>
<td>RL4</td>
<td>RL3</td>
<td>RL2</td>
<td>RL1</td>
</tr>
</tbody>
</table>

RL1: Very low toxicity and low exposure potential

OEL_{nano} = OEL_{real work environment}
EXP_{Acute} = \frac{C_{Acute}}{2 \cdot OEL_{nano}}
EXP_{8 hour} = \frac{C_{8 hour}}{OEL_{nano}}

Specific density of the nanomaterial (g/cm³)
Specific surface area of the nanomaterial [SSA]: m²/g

(From AS Fonseca)
**Sensitivity analysis** and performance testing

Refinement and next generation methods

Operational database and structure development

Primary test databases

Filling data gaps and new case studies

Final comprehensive databases

**Year**

1

Conceptual framework development

Stakeholder consultation

Interviews and surveys

Alignment with Cooper Stage Gate® and stakeholder needs

Sensitivity analysis and performance testing

Refinement and next generation methods

Sensitivity analysis and calibration

Model development and testing

Collecting models

Collecting of existing data

Database development

2

Development of guidance documents

User testing of models

Model integration into the SoS Framework

Implementation and stakeholder training

3

Demonstration using database case studies

3.5

Implementation and stakeholder training

Primary test databases

Final comprehensive databases

Year 1

Year 2

Year 3

Year 3.5

Publication
Nano-Risk (Innovation) Governance Platform

Communication and Knowledge Transfer

- Monitoring
- Horizon scanning

Nano-Risk Assessment and Management Tools Portal

- Risk-benefit
- Decision support

Safe Innovation Approach (SIA) Tools Portal

H2020 NANOREG2

Users: industry, service providers, regulators, NGO's etc.

Data bases & libraries
- PhysChem
- (Eco)toxicology
- Dustiness
- Process emission
- Risk Management
- Exposure Data

Risk Assessment and Management models

Tool 1, Tool 2, Tool 3, Tool 4, Tool 5, Tool 6

Further development in NMBP-13 and NMBP14 projects
Nano-Risk (Innovation) Governance Platform

Users: industry, service providers, regulators, NGO’s etc.

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Risk Assessment and Management models

Data bases & libraries

PhysChem (Eco)toxicology
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Further development in NMBP-13 and NMBP14 projects

https://laughingsquid.com/
Thank you for your attention

www.nanocalibrate.eu
www.researchgate.net/profile/Keld_Jensen

calibrate@nrcwe.dk
kaj@nrcwe.dk