Serious magic-nano like lung oedemas caused by a liquid stain protection product: - (Developing) and using two new tests as a combined screening tool for aerosol product(s)

Co-operative study by Monika Fischer\textsuperscript{1)}, Dorothee Walter\textsuperscript{1)}, Clemens Dasenbrock\textsuperscript{1)}, Wolfgang Koch\textsuperscript{1)}, Kathrin Begemann\textsuperscript{2)}, Matthias Greiner\textsuperscript{2)} and \textit{Axel Hahn}\textsuperscript{2)}
• BfR reports about 'Magic-nano' like cases series
• Lessons learned about spray aerosols
• The 'Carrier' effect and consequences
• The 'Eta Test' for solid particles
• The 'Isolated Perfused Lung –IPL-'
• The both tests as screening tools
• Questions
BfR 'Magic-nano' and a similar case series

2006 case series (6 weeks):
153 reports with 8 severe lung oedemas

'Liquid Stain Protection Product'

Since 2003 single case reports: Severe lung oedemas
<table>
<thead>
<tr>
<th>Year</th>
<th>Age</th>
<th>Mode of Use/Application</th>
<th>Main Symptoms/signs</th>
<th>PSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>Adult</td>
<td>Spraying?</td>
<td>Coughing (heavy), nausea</td>
<td>minor</td>
</tr>
<tr>
<td>2004</td>
<td>Adults</td>
<td>Stone-terrace sealing with paint-brushing in hot sun (Spain)</td>
<td>Coughing (heavy), pronounced dyspnea, breathlessness</td>
<td>severe</td>
</tr>
<tr>
<td>2005</td>
<td>Adult</td>
<td>Spraying</td>
<td>Coughing (heavy), dyspnoea, sore throat, hoarseness</td>
<td>minor</td>
</tr>
<tr>
<td>2005</td>
<td>Adult</td>
<td>Spraying</td>
<td>Coughing (heavy), dyspnoea, sore throat, hoarseness</td>
<td>moderate</td>
</tr>
<tr>
<td>2005</td>
<td>Adult</td>
<td>Spraying</td>
<td>Coughing (heavy), dyspnoea</td>
<td>minor</td>
</tr>
<tr>
<td>2008</td>
<td>Adult</td>
<td>Spraying?</td>
<td>Coughing (heavy), pronounced dyspnea, breathlessness, pneumonitis, lung oedema?</td>
<td>severe</td>
</tr>
<tr>
<td>2008</td>
<td>Adults</td>
<td>Storefront sealing working (spraying?, several workers?)</td>
<td>Coughing (heavy), pronounced dyspnea, breathlessness</td>
<td>moderate</td>
</tr>
<tr>
<td>2009</td>
<td>Adult</td>
<td>Spraying</td>
<td>Coughing (heavy), sore throat, pronounced dyspnea, breathlessness, lung oedema</td>
<td>severe</td>
</tr>
<tr>
<td>2011</td>
<td>Adult</td>
<td>Paint-brushing for 30 min</td>
<td>Coughing (heavy), pronounced dyspnea, breathlessness, pneumonitis, lung oedema</td>
<td>severe</td>
</tr>
<tr>
<td>2011</td>
<td>Adult</td>
<td>Removal of product spots (grinding?, polishing, solvent)</td>
<td>Coughing (heavy), nausea</td>
<td>minor</td>
</tr>
<tr>
<td>2011</td>
<td>Adult</td>
<td>Removal of product spots (grinding?, polishing, solvent)</td>
<td>Coughing (heavy), dyspnoea, sore throat</td>
<td>moderate</td>
</tr>
</tbody>
</table>

More serious problems obviously after spaying-turnout!
Lessons learned 2006: Particle-distribution in Different Sprays

Spray specimens: Commercial Insecticides, impregnants, hair, furniture, etc. (Pilot studies in exposure chambers of German Environmental Agency (UBA), German Institute for Material Testing (BAM))
Lessons learned 2006: Origin of aerosol particles

The aerosols are always a mixtures of **liquid** and **solid** particles

But:
Only the counting of solid particles is relevant (false pos. results!)

![Image of aerosol particles and 'Colimator']
Lessons learned 2007: The ‘Magic-nano’ Findings

‘Carriers’
Solid particles < 100nm with coatings of ‘toxic’ compounds

- Solid carrier particles can ‘bridge the lung’ with alveolar toxic compounds:
  Hydrophobic chemicals like different fluorinated hydrocarbons (often semi-volatile)
- Liquid particles can not (aggregation!)
1. Step: Development of a 'Carrier Mass Test': Eta-Test

\[ \eta_{\text{alv}} = \frac{m_{\text{alv}}}{M} \]

\[ \eta_{\text{thor}} = \frac{m_{\text{thor}}}{M} \]

EAPCCT Congress Malta
2. Step: Development of an Isolated Perfused Lung (IPL) Model

IPL Model (Type 829/2) Hugo Sachs Elektronik, March-Hugstetten, Germany

Rats (Crl:CD (SD)), Charles River Laboratories, Sulzfeld, Germany
Isolated Perfused Lung (IPL) Model
IPL Lung Findings (Spray Exposure)

1. Normal
2. Heptane
3. Leather spray
4. ‘Magic nano’
5. ‘liquid stain protection product’

Effect more severe
IPL Parameters (Tidal volume, Compliance, Resistance)

Rat-lung, spray formulation **without** acute toxic effects

During exposure

After exposure

Rat-lung, spray formulation **with** acute toxic effects

During exposure

After exposure
IPL other Pathophysiological Parameters

Tidal volume, Lung weight

Respiratory gases (O₂, CO₂)
Conclusion

The developed promising test battery of two successive test had to be continuous future tested based by

1. Model substances and

2. further human intoxications with aerosols.

Using the Eta-test and the IPL-test as screening method for new developed sprays or formulations may help

1. to avoid animal inhalation studies in the future in line with the "3-Rs” principles and

2. provides manufactures with more product safety before the commercial launch
Thanks to all the co-authors of the Study:

Monika Fischer, Dorothee Walter, Clemens Dasenbrock, Wolfgang Koch, ITEM, Fraunhofer Institut, Hannover, Germany
Kathrin Begemann, Matthias Greiner, Horst Spielmann, BfR

- Hartmut Giese, Bundesministerium Umwelt
- Helmut Bake, Umweltbundesamt
- Tin Winn, Bundesanstalt Materialforschung

Esther Feistkorn

Thank you!

Eta + IPL