Aerosols and their considerations in different regulations

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Within the last few years, the official regulation of chemicals and chemical products has been intensified. In particular, consumer products have to be safe under conditions of foreseeable use and this is required by numerous regulations. Consequently, it is important to agree on relevant data needed for an informed and representative risk assessment.

In this context, the assessment of inhalation risk and safety assessment for aerosols i.e. aerosols generated from spray products needs specific attention. The dose to regional lung tissue is dependent on particle size, specific surface area and chemical solubility. Whereas the mucosal lining of the upper respiratory tract functions as a protective barrier the mucociliary activity has a major role in the clearance of inhaled particles/aerosols. Particles/droplets exceeding a diameter of 30 µm normally do not reach the lung. In contrast, smaller ones may reach the lower airways. The threshold of particle/droplet diameters small enough to reach the alveoli is set to 5 µm by German MAK (2012). The potential toxic effects from exposure to soluble aerosols include altered pulmonary function, irritation and altered gas exchange.

With respect to the regulatory requirement three different parts have to be considered:

1 – There is information about hazard testing and the specification of the test item. The toxicity data have to be obtained --preferably by guideline studies-- and described by dose parameters such as mg/kg bw/day for systemic effects and mg/cm² lung surface area for local effects. Within the test guidelines for chemicals the following specifications of the aerosol atmosphere are required:

- *Aerodynamic equivalent diameter*: used as an equivalent diameter to predict where in the respiratory tract the particles may be deposited
- *Concentration*: expressed as weight of the test substance per unit volume of air, e.g. mg/L.
- *Mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD):* quantities describing the median value of aerodynamic diameter and the geometric standard deviation of the aerosol mass size distribution
- *Inhalable diameter:* refers to maximum aerodynamic diameter of a particle which is considered to be inhalable for the organism under study, refers to particles which are capable of being deposited anywhere within the respiratory tract

For testing of pharmaceuticals with a focus on inhalation and nasal products the particle size for the drug substance itself has to be specified. A validated particle sizing method could be e.g. the laser diffraction; acceptance criteria should be employed. The following parameters are mentioned explicitly:

- *Particle size distribution in terms of the percentage of total particles in given size ranges.*
- *Median, upper,* and/or *lower particle size limits* and observed *range of variation*
- *Particle size distribution of batches* that showed acceptable performance in vivo
- *Intended use of the product*
- *Stability data*

For risk assessments and regulatory purposes a NOAEC (no observed adverse effect level) or LC50 (lethal concentration) is determined by standardized toxicity testing following the accepted guidelines.

2 – There is a special consideration of physico-chemical properties i.e. within the CLP (Regulation on Classification, Labelling and Packaging of Substances and Mixtures; EG No 1272/2008) a classification of “flammable aerosols” is foreseen under certain circumstances

3) – There is the special consideration of exposure which in connection with the toxicity data forms the basis for the final risk or safety assessment. Exposure is a topic in many regulations such as REACH (1907/2006/EC), the cosmetics regulation (1223/2009/EC), the biocides regulation (BPR) but also indirectly in the Aerosol-Dispensers-Directive (75/324/EEC) with obligation for marketing aerosol dispensers. Some of the guidances on exposure assessment such as “REACH Practical Guide on Exposure Assessment and Communication in the Supply Chains” provide the option for exposure modelling. On one hand the option to use the ConsExpo fact sheets is given but on the other hand the more specific “BAMA Indoor Air Model” that was developed by the British Aerosol Manufacturers' Association is described.

An overview of all these points where aerosols are mentioned explicitly in regulations will be given in the presentation.

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