

WPMN INFORMATION SHARING SEMINAR ON IN VIVO INHALATION TOXICITY SCREENING METHODS FOR MANUFACTURED NANOMATERIAL

Washington DC, USA on 21 Sept 2015

DRAFT SUMMARY RECORD:
ENV/CHEM/NANO/RD(2015)4

Co-Chairs:

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Karin Wiench (BASF, BIAC)

- This seminar was proposed by Japan with support from BIAC in OECD WPMN 14 last February.
- United States proposed to host this seminar back-to-back with the Inhalation Test Guideline meeting.
- It was held on 21 September 2015 at US EPA headquarters in Washington, D.C. United States.
- Participants were from France, Germany, Japan, Korea, the Netherlands, United Kingdom, United States, European Chemicals Agency (ECHA), industry (BIAC), environment and animal welfare NGOs and the Secretariat to the WPMN.

The list of participants is available in Annex II of the Draft Summary Record.



Agenda

Opening

Recent development and application of Short Term Inhalation Study (STIS)

Lan Ma-Hock, Head of Inhalation Toxicology, BASF SE, Germany

Il Je Yu, Institute of Nanoproduct Safety Research, Hoseo University, Korea

David Warheit, Chemours, USA

Coffee Break

Recent development and application of Intratracheal Administration Study (ITAS)

Yasuo Morimoto, Institute of Industrial Ecological Sciences, University of
Occupational and Environmental Health (UOEH), Japan

Shoji Fukushima, Director, Japan Bioassay Research Center, Japan Industrial
Safety & Health Association, Japan

Yutaka Oshima, Chemical Evaluation and Research Institute (CERI), Japan

Discussion

Closing

Recent Development and Application of Short Term Inhalation Study

- It was stated that Short Term Inhalation Study covers the following key elements;
 - Inflammation potency at the respiratory tract;
 - Potential reversibility or progression of the effects; and
 - Deposition and clearance kinetics
- Applications of short term inhalation study were presented as a screening tool for grouping approach or as a range finder for sub-chronic study.
- It was pointed out that this method have an advantage over acute inhalation study (TG403).
- It was also pointed out that screening methods be used for "bridging" the results to previous performed subchronic inhalation studies.
- Rationale for choosing recovery period was discussed; importance of long post-exposure period and pragmatic approach as a screening tool.

Recent Development and Application of Intratracheal Administration Study

- Comparing with 4 weeks inhalation studies, instillation was considered being appropriate to be used as a screening tool to rank pulmonary toxicity of nanomaterials .
- It was shown that instillation of MWCNT was indicative for outcome after inhalation exposure.
- Based on the results of multiple intratracheal administration studies, single administration was considered appropriate for hazard.
- The most appropriate protocol for nanomaterials was suggested for anesthesia, administration device, procedure, instillation volume, and concentration of the formulation.
- Sample preparation and distribution (unevenness) within the lung after intratracheal administration in comparison with inhalation were discussed.

Discussion on Harmonization and Standardization of the Methods

- At the very beginning phase, it was clarified that "harmonization and standardization" did not necessarily mean development of a regulatory-accepted new test guideline.
- There was general agreement among the attendees that even for a screening tool, certain standardization is essential, so that the data collected by academia and industry were reproducible and interpretable.
- The representative of regulatory bodies would welcome harmonized and standardized screening tools collecting more hazard information on different nanomaterials
- Regarding standardization of intratracheal instillation, more effort on technical details is necessary before standardization process can be initiated.

Suggestions for Guidance and Framework of Discussed Screening Methods

- It was suggested to achieve a standardized protocol within ISO.

The majority of the attendees consider ISO as one possible option to standardize technical details.

- However, OECD was considered a more appropriate platform for application and the interpretation of the screening data.

A guidance for use of screening tools i.e. in an integrated testing strategy and on interpretation of screening data (i.e. for hazard ranking, but also to predict possible long-term toxicity) may be helpful for risk assessors and regulators.

Technical Discussion

- Inhalation and intratracheal administration have their legitimacy as screening tools.

[Inhalation]

- Inhalation study can be used for regulatory purposes.
- However, inhalation study required elaborate equipment and thus cannot be performed easily.

[Intratracheal Administration]

- Instillation bypasses the upper respiratory tract and cause bolus effects.
- However, the available data indicated that it reveals reliably the quality of the changes caused by the test substance, providing appropriate dose is used.