



## ICH Q3D(R1): Cadmium Inhalation PDE Revision (Step 2)

May 27, 2018

International Council for Harmonisation of Technical Requirements  
for Pharmaceuticals for Human Use



### ICH Q3D: Cadmium Inhalation PDE revision

## Legal Notice

- This presentation is protected by copyright and may be used, reproduced, incorporated into other works, adapted, modified, translated or distributed under a public license provided that ICH's copyright in the presentation is acknowledged at all times. In case of any adaptation, modification or translation of the presentation, reasonable steps must be taken to clearly label, demarcate or otherwise identify that changes were made to or based on the original presentation. Any impression that the adaptation, modification or translation of the original presentation is endorsed or sponsored by the ICH must be avoided.
- The presentation is provided "as is" without warranty of any kind. In no event shall the ICH or the authors of the original presentation be liable for any claim, damages or other liability arising from the use of the presentation.
- The above-mentioned permissions do not apply to content supplied by third parties. Therefore, for documents where the copyright vests in a third party, permission for reproduction must be obtained from this copyright holder.

## Outline

- This presentation will provide a summary of the proposed revision to the Cadmium Inhalation PDE in ICH Q3D.

## Guideline Objectives

- The objectives and scope remain the same as indicated in the ICH Q3D Guideline finalized in December 2014.
- The Guideline revision (R1) is focused on an error correction of the PDE for Cadmium by the inhalation route.

## Summary of Guideline Content

- The original PDE for cadmium by the inhalation route was identified as 2 µg/day in Table A.2.1 and the individual safety assessment in Appendix 3
- The ICH Secretariat was notified of an error in the PDE calculation
- Based upon the original approach used, the PDE should have been 0.2 µg/day, a level 10-fold below that identified in the finalised Guideline

## Summary of Guideline Content

- The Expert Working Group re-evaluated the data supporting the cadmium inhalation PDE and concluded that a modifying factors approach, similar to that used for calculating the oral and parenteral PDEs, was appropriate for the inhalation PDE.

## Summary of Guideline Content

- The revised calculation is based on a Permitted Exposure Level of  $5 \mu\text{g}/\text{m}^3$  developed by the United States Department of Labor Occupational Safety and Health Administration.
- The PDE calculation is as follows:

$$\text{For continuous dosing} = \frac{5 \mu\text{g}/\text{m}^3 \times 8 \text{ hr/d} \times 5 \text{ d/wk}}{24 \text{ hr/d} \times 7 \text{ d/wk}} = \frac{1.19 \mu\text{g}/\text{m}^3}{1000 \text{ L/m}^3} = 0.00119 \mu\text{g/L}$$

$$\text{Daily dose} = \frac{0.00119 \mu\text{g/L} \times 28800 \text{ L}}{50 \text{ kg}} = 0.685 \mu\text{g/kg}$$

$$\text{PDE} = 0.685 \mu\text{g/kg} \times 50 \text{ kg} / 1 \times 10 \times 1 \times 1 \times 1 = 3.43 \mu\text{g/day}$$

## Guideline for Implementation

- The guideline revision will be implemented immediately upon finalisation.

## Conclusions

- The PDE originally identified for cadmium by the inhalation route (2 µg/day) was incorrect due to a calculation error.
- The EWG re-evaluated the relevant data and concluded that a modifying factors approach was appropriate in determining the revised PDE.
- The revised PDE is identified as 3 µg/day.