ICH M7 EWG Sub-Group Work Plan
October 01, 2024

Topic Adoption date: *June 2024*

Rapporteur: *Dr. Krista Dobo, PhRMA*

Regulatory Chair: *Dr. Alisa Vespa, Health Canada, Canada*

Last Face-to-Face Meeting: *Not Applicable*

1. Key milestones

1.a. Current status of key milestones

Past completion date	Milestone
Jun. 2024	Concept Paper Outline of "3 June 2024"
Jun. 2024	New Topic endorsed by the Assembly on 4 June 2024

1.b. Key Deliverables

Approval Date	Deliverable
Jun. 2024	*<u>Stage 1 (2 years or less to reach Steps 1 and 2)</u>* *Principles for the design and use of in vitro assays (e.g., Ames test) to differentiate mutagenic and non-mutagenic nitrosamines* *Principles for defining AIs based on Structure Activity Relationships (SAR) (e.g., considering knowledge of structural features of the nitrosamine molecule)* *Application of less than lifetime (LTL) adjustments to AIs based on exposure, provided that sufficient scientific data is available.*
Jun. 2024	*<u>Stage 2 (initiate when data and literature available)</u>* *Principles for the design and use of in vivo mutation studies as follow-up studies to in vitro studies and/or in derivation of AIs* *Framework for deriving AIs based on read across methods*
Jun. 2024	*<u>Subsequent to Stage 2</u>* *A harmonised set of AIs for nitrosamines will be developed by the sub-group following the M7 maintenance process.*
Jun. 2024	*Development of training materials and examples to address relevant quality principles such as the application of M7 to nitrosamines risk assessment and control, particularly the finished dosage form.*
Sep. 2024	*Mutual Understanding Presentation Series (Oct -Dec 2024)*

1.c. Future anticipated key milestones

Expected future completion date	Milestone
Mar. 2025	*Final concept paper*
Mar. 2026	*Stage 1 Topics Step 1 –Sign off by topic leaders*
Mar. 2027	*Stage 2 Topics Step 1 – Sign off by topic leaders*
Apr. 2027	*Stage 1 & 2 Topics Step 2a/b – Endorsement*
May. 2027	*Step 3 Draft addendum (Stage 1 and 2 topics) released for comment – allow 6 months (end November 2027)*
Apr. 2028	*Step 3 Discussion of regional consultation comments and editing of draft addendum (Stage 1 and 2 topics)*
Apr. 2028	*Finalization of Step 3 experts draft addendum and Sign off (ICH Reg Members)*
May. 2028	*Step 4 – Adoption by ICH Assembly*
	Nitrosamine Monograph drafting to start subsequent to Addendum reaching Step 4

2. Timeline for specific tasks

Beginning date	End date	Task / Activity	Details
Oct. 2024	*Dec. 2024*	*Mutual Understanding Presentation Series*	*Through videoconferences (every other week) EWG will participate in a series of presentations to assure common understanding of most recent science related to nitrosamines.*
Jan. 2025	*Mar. 2025*	*Develop/finalize concept paper*	*EWG will meet 2X/month to develop and finalize the concept paper*
Mar. 2025	*May. 2025*	*Begin to develop text and build consensus on draft addendum sections*	*Based on Final Concept Paper (to be developed by end March)*