

ICH M7 EWG Nitrosamine Sub-Group Work Plan

24 July 2026

Topic Adoption Date: *June 2024*

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

Last Face-to-Face Meeting: *Rio De Janeiro, Brazil, June 2026*

1 Key Milestones

1.1 Current Status of Key Milestones

Completion date	Milestone
<i>June, 2024</i>	<i>Outline of Concept Paper “3 June 2024” Endorsed by the Assembly on 4 June 2024</i>
<i>May, 2025</i>	<i>Final Concept Paper dated 24 April 2025 Endorsed by the Management Committee on 7 May 2025</i>

1.2 ICH MC Key Deliverables

MC Approval Date	Deliverable
<i>May, 2025</i>	<i>ICH M7 Addendum on Risk Assessment and Control of N-Nitrosamine Impurities</i>
<i>May, 2025</i>	<i>Compound specific monographs for some N-nitrosamines</i>
<i>May, 2025</i>	<i>Training materials</i>

1.3 Future Anticipated Milestones

Expected future completion date	Milestone
<i>June, 2028</i>	<i>Step 1 sign-off - Consensus reached on Draft Technical Document</i>

June, 2028	<i>Develop Step 2 Presentation</i>
August, 2028	<i>Step 2a/b sign-off - and Step 2 Presentation</i>
August, 2028	<i>Initiate Development of Training Materials</i>
August, 2028	<i>Step 3 - Initiate regional constituent review followed by discussion of comments</i>
December, 2029	<i>Step 3 - completed and signed off</i>
December, 2029	<i>Develop Step 4 Presentation</i>
March, 2030	<i>Step 4 Adoption of Final draft Guideline Document and Step 4 Presentation</i>
March, 2030	<i>Finalise Training Materials</i>

2. Timeline for Specific Tasks

Please provide in the table below short-term high-level specific tasks for work to be done within the Working Group between now and the next ICH meeting (recommended 4 – 10 tasks).

Beginning date	End date	Task / Activity	Details
June, 2026	Nov, 2026	ICH Party review of draft monographs for 5 key nitrosamines. Establish acceptable intakes (AIs) and develop monographs for 2 additional nitrosamines	ICH party review of 5 draft monographs due end August. Detailed monographs for 2 additional nitrosamines to be authored and reviewed by EWG in advance of Prague meeting.
June, 2026	Nov, 2026	Enhanced Ames test (EAT) protocol. Positive control & solvent recommendations, concentration limit considerations.	EWG to review positive control data as it becomes available; discuss/agree other protocol considerations, e.g. concentration limit, plate incorporation method.
June, 2026	Oct, 2026	Negative in vivo mutation assay outcomes and establishing an acceptable limit	Achieve alignment on recommendation for an acceptable limit for N-nitrosamines that are negative in an in vivo mutation assay.
June, 2026	Nov., 2026	Less-than-lifetime (LTL) framework	ICH reps holding discussions with constituents regarding EWG consensus opinion through end August. EWG to reach consensus on <i>Step 1</i> text in Prague.

June, 2026	<i>Nov., 2026</i>	Interpretation of EAT assay for establishing acceptable intakes	Achieve alignment on EAT interpretation and if EAT can be used as a stand-alone assay for hazard identification.
June, 2026	<i>Nov., 2026</i>	Assess OECD 488 in vivo mutation study design for nitrosamine hazard identification	Literature review of carcinogenicity studies ongoing to support recommendations on tissue selection. At Prague meeting discuss available data to advance the topic.
June, 2026	<i>Nov., 2026</i>	Use of in vivo mutation data as a surrogate for carcinogenicity data for nitrosamines	Data gathering and analyses ongoing to validate and achieve alignment on the approach within the EWG.
June, 2026	<i>Nov., 2026</i>	Develop methodology options for deriving Als using in vivo mutation as a point of departure	Evaluate case studies planned to advance this topic.
June, 2026	<i>Nov., 2026</i>	CPCA Framework	Data analyses ongoing to support discussions & agreements related to molecular weight adjustments and cutoffs.
September, 2026	<i>Nov 2026</i>	Quality discussions to kick off in Sept	Priority topics for discussion at Prague to be agreed.