Final Business Plan
ICH Q3E: Guideline for Extractables and Leachables (E&L)
Dated 30 June 2020
Endorsed by the Management Committee on 10 July

1. The issue and its costs

What problem/issue is the proposal expected to tackle?

There is a current lack of alignment, consensus and clarity among existing guidelines, pharmacopoeial and other standards addressing extractables and leachables (E&L).

A new guideline on the assessment and control of E&L is proposed. ICH has developed guidelines covering many aspects of impurities. This includes process and product related substances (Q3A, Q3B), residual solvents (Q3C) and new guidelines covering elemental (Q3D) and mutagenic (M7) impurities. However, E&L impurities are excluded from the scope of the general ICH impurity guidelines.

The scope of the proposed new quality guideline will include:

- Chemical, biological and biotechnicological products, as well as drug-device combination drug products.
- All associated dosages forms and take into account the extracting/leaching conditions, the route of administration, drug indication and patient exposure.

What are the costs (social/health and financial) to our stakeholders associated with the current situation or associated with "non action"?

This lack of alignment leads to variability in both application and interpretation of standards by industry and among regulators. These differences with respect to key areas such as quality and safety assessment impact the global development of new medicines.

2. Planning

- *What are the main deliverables?*

  The primary deliverable is a new quality guideline; ICH Q3E, Guideline for Extractables and Leachables (E&L).

- *What resources (financial and human) would be required?*

  The Expert Working Group would include up to approximately 30 Quality and Safety experts. We anticipate the need for Rapporteur supporter to assist with general project management, drafting and associated activities to complete the new guideline.

- *What is the time frame of the project?*

  We anticipate the need for seven to eight face-to-face meetings and multiple interim

teleconferences to complete the new guideline.

- *What will be the key milestones?*

Final concept paper and business plan endorsed	July 2020
First EWG Meeting	November 2020
Second EWG Meeting	June 2021
Third EWG Meeting	November 2021
Fourth EWG Meeting	June 2022
Fifth EWG Meeting	November 2022
Step 1 sign-off, *Step 2a/b* endorsement	November 2022
Public Consultation Period	January-June 2023
Step 4	November 2024

- *What special actions to advance the topic through ICH, e.g. stakeholder engagement or training, can be anticipated either in the development of the guideline or for its implementation?*

  The following are potential special actions that may be taken to advance development of the guideline:

  - Presentations at major technical conferences to promote engagement in the ICH guideline during the consultation phase
  - Engagement with external, technical experts as consistent with appropriate ICH procedures and requirements.

  The following are potential special actions that may be taken to advance or promote implementation of the guideline:

  - Creation of formal training materials related to the Q3E guideline and their distribution at inter-agency engagement activities and ICH-supported technical workshops.
  - Development of example case studies that illustrate E&L study conduct, assessment and control for selected therapeutic modalities..

3. The impacts of the project

- *What are the likely benefits (social, health and financial) to our key stakeholders of the fulfilment of the objective?*

An ICH harmonized guideline addressing the gaps and inconsistencies would remove much uncertainty currently associated with this topic. Such a guideline would assist both applicants and regulators by providing focus on critical aspects, and improving transparency in requirements for medicinal products including drug delivery device components.

This new guideline is expected to deliver a number of benefits for regulatory authorities, industry by aligning on key areas:

- Lack of aligned E&L guidance framework: There is a current lack of alignment, consensus and clarity among existing guidelines, pharmacopoeial and other standards addressing E&L.
- Lack of guidance alignment regarding: the conduct of E&L studies; the design of a science and risk-based E&L control strategy; processes to address material and component selection and characterization; risk assessment; and lifecycle

management (including post-approval changes) for container-closure systems, manufacturing systems, and drug delivery device components.
- Thresholds: Development of harmonized thresholds for reporting and identifying E&L and qualifying leachables in context of route of administration, drug indication and patient exposure, with an emphasis on science-based and risk-based approaches.
- Safety Assesment: Establishment of limits that are relevant to route of administration, drug indication and patient exposure.
- Control options: This would include options to mitigate and control process-derived leachables including considerations such as distance along the production stream and processing conditions analogous to ICH M7.
- Alignment with existing ICH guidelines: The guideline would employ principles (e.g., control approaches) consistent with those described within other ICH impurities guidelines (Q3A-D, M7) to create a complementary guideline.
- Pharmacopoeial standards: The guideline will provide a key opportunity for national and regional pharmacopoeias to align.

- *What are the regulatory implications of the proposed work – is the topic feasible (implementable) from a regulatory standpoint?*

  Development of an ICH guideline provides a clear opportunity to harmonize current expectations with a clear definition of scope and focus on critical quality and safety aspects.

  The topic is feasible (implementable) from a regulatory standpoint because there is adequate technical and regulatory expertise and extensive experience to develop a guideline.

- *Will the guideline have implications for the submission of content in the CTD/eCTD? If so, how will the working group address submission of content in the dossier? Will a consult be requested with the ICH M8 working group?*

  It is anticipated that any documentation related to E&L assessment would be incorporated into the relevant existing CTD/eCTD quality modules. Thus, the guideline would have no implications for the submission of content in the CTD/eCTD. Information may be provided within the guideline on the level of detail and documentation that could be submitted within those sections. The consult with the ICH M8 group is not currently anticipated.

4. Post-hoc evaluation

- *How and when will the results of the work be evaluated?*
  At the conclusion of each stage, we will determine whether deliverables and their timelines were met by comparison against our concept paper and business plan.