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

Standard Operating Procedure of the ICH Working Groups

Version 8.0

Approval by the ICH Management Committee on 6 June 2019

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

ICH Secretariat, Route de Pré-Bois 20, 1215 Geneva, Switzerland

Telephone: +41 (22) 710 74 80 - admin@ich.org, http://www.ich.org

SOP of the ICH WGs

Document History

Version number	Action	Date
v8.0	The ICH Management Committee endorsed Version 8.0 of the SOP of the ICH WGs which contains revisions regarding the management of the size of ICH WGs; the replacement of a WG's Regulatory Chair in the event of their resignation; the process to appoint a Rapporteur; the development of Work Plans by WGs; clarifications on WG quorum; and other clarifications including on templates and forms in the SOPs of the WGs.	**June 2019**
v7.0	The ICH Management Committee endorsed Version 7.0 of the SOP of the ICH WGs which contains revisions to Annex 5 to reflect the new maintenance procedure of Q4B Annexes.	**November 2018**
v6.0	The ICH Management Committee endorsed Version 6.0 of the SOP of the ICH WGs which includes edits to provide clarity regarding Discussion Groups, the management of WG size, the process for endorsement of activities of WGs and training materials, and the appointment process of Regulatory Chairs.	**October 2018**
v5.0	The ICH Management Committee endorsed Version 5.0 of the SOP of the ICH WGs which includes edits for consistency with the revisions to the Assembly Rules of Procedures regarding managing the size of the Working Groups, as well as other minor edits.	**June 2018**
v4.1	The ICH Management Committee endorsed Version 4.1 of the SOP of the ICH WGs with a minor edit to the Business Plan template in Annex 10.	**March 2018**
v4.0	The ICH Management Committee endorsed Version 4.0 of the SOP of the ICH WGs.	**November 2017**
v3.1	The ICH Secretariat made some minor editorial changes post approval/publication to update cross-references.	**June 2017**
v3.0	The ICH Management Committee endorsed Version 3.0 of the SOP of the ICH WGs which includes several procedural clarifications from Version 2.0 on the attendance of support staff to face-to-face meetings, sign-off procedures, and the maintenance procedure. Additionally, Version 3.0 includes provisions to clarify the relevant expertise of prospective Working Group experts, a procedure for appointing experts to Working Groups, appointment of Ad-hoc Observers to Workings Groups, and a policy on the publication of papers or presentations related to the work of an ICH Working Group.	**May 2017**
v2.0	The ICH Management Committee endorsed Version 2.0 of the SOP of the ICH WGs following inclusion of Table 2 to clarify the endorsing party for ICH work, clarification on the endorsement procedure for a Concept Paper, a section on confidentiality, updates to Annex 6, and other editorial changes.	**November 2016**

v1.0	The ICH Management Committee endorsed Version 1.0 of the Standard Operating Procedure of the ICH Working Groups with revisions to be included that were provided both prior to and during the meeting in Lisbon.	**June 2016**

Table of Contents

Glossary

5-year Strategic Plan: A 5-year planning tool for the ICH Association to assess current ICH topics and their anticipated time for completion and assess when new harmonisation activities should begin.

Business Plan: Outlines the costs and benefits of harmonising a topic that was previously proposed by a Concept Paper and focuses on regulatory feasibility (See Annex 10).

Concept Paper: Describes the perceived problem and the issues to be resolved by a harmonisation project (see Annex 9).

Deputy Topic Leader: Co-participant of a Working Group who represents the views of their Member during any ICH interactions and supports the work of the Topic Leader.

Discussion Group: A type of technical Working Group established to discuss specific scientific considerations or views and which follow similar rules to EWG/IWG.

Expert: Representative appointed to participate in an ICH Working Group on behalf of an ICH Member.

Expert Working Group (EWG): An EWG is charged with developing a harmonised Guideline that meets the objectives in the Concept Paper and Business Plan. ICH Members nominate representatives and, unless otherwise specified by the Management Committee, the official membership is limited to two representatives per ICH Member per working group and one representative per ICH Observer, if nominated.

Federal Register: A daily publication of the US federal government that issues proposed and final administrative regulations of US federal agencies.

Formal ICH Procedure: The Formal ICH Procedure that consists of 5 Steps. See definition of Step Process.

Founding Industry Member: An Industry Member who was an original member of the former ICH Association, known as the International Conference on Harmonisation, and founded the new ICH Association established on October 23, 2015.

Founding Regulatory Member: A Regulatory Member who was an original member of the former ICH Association, known as the International Conference on Harmonisation, and founded the new ICH Association established on October 23, 2015.

ICH Assembly: Overarching body of the ICH Association that consists of all Members of the Association and adopts decisions related to the harmonisation of guidelines.

ICH Coordinator: Nominated by ICH Members to assist in the efficient operation of ICH harmonisation activities. A Coordinator acts as the central point of contact with the ICH Secretariat and facilitates conversation between the ICH Management Committee and/or Assembly and the ICH Working Groups as needed.

ICH Management Committee (MC): Oversees operational aspects of the ICH Association on behalf of all Members of the Association.

ICH Member: A legislative or administrative authority or international organisation who meets all qualifications for membership according to the ICH Articles of Association Article (11) & (12) and has applied and been accepted to join the ICH as a voting Member of the Assembly. ICH Members actively support the compliance with ICH Guidelines, appoint experts in Working Groups, and support the aims of the ICH Association.

ICH Observer: Attendees of ICH Assembly meetings who may provide input on ICH harmonisation activities but who do not have voting rights.

ICH Secretariat: The staff responsible for the day-to-day management of ICH, including preparations for and documentation of meetings of the ICH Assembly and its Working Groups.

ICH Standing Observer: The World Health Organization and the International Federation of Pharmaceutical Manufacturers & Associations who attend meetings of the Assembly and Management Committee but do not have any voting rights. ICH Standing Observers may appoint experts to Working Groups.

ICH Standing Regulatory Member: A legislative or administrative authority that has the responsibility of the regulation of pharmaceutical products for human use and has been a Member of the Steering Committee of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use immediately prior to the establishment of the new ICH Association.

Implementation Working Group (IWG): A Working Group established for the purposes of developing a Q&A document following the implementation of a guideline.

Informal Working Group: A Working Group established for the purposes of developing a Concept Paper and Business Plan for a harmonisation activity.

Informal Working Group Leader: An expert from an informal Working Group that is designated to lead the efforts of the informal Working Group.

New Topic Proposal: A Proposal for a new ICH harmonisation activity.

Plenary Working Party (PWP): A type of technical group associated with a Working Group (WG) following the formal ICH Procedure (further to approval of its Concept Paper), the membership of which would include that of the WG as well as up to one expert per ICH Member or Observer who is either unable to participate in the WG due to size limitations, or who is unable to devote the necessary level of effort to participate actively in WG activities, but still wants to follow the progress of the WG.

Quorum: The minimum number of Members of the Assembly that must be present at any of its meetings to make the proceedings of that meeting valid.

Rapporteur: Is a representative of one of the ICH Members, who is designated by the Assembly when a new topic is formally adopted. The Rapporteur is responsible for leading the scientific discussions in a working group (EWG/IWG) and reconciling the divergent views with a view to reaching consensus. The Rapporteur, in collaboration with the Regulatory Chair, ensures that the group keeps an up-to-date action plan and timetable, with clear deliverables and deadlines. The Rapporteur shall regularly present reports to the Assembly, focusing in particular on the timelines and milestones.

Regulatory Chair: A representative of one of the ICH Regulatory Members, who is designated by the Management Committee from amongst the Regulatory Members of the Management Committee when a new topic is formally adopted. The Regulatory Chair provides regulatory oversight throughout the ICH 5-Step Process ensuring its timely execution and adherence to the Concept Paper and Business Plan, including scope and timelines. The Regulatory Chair should report in a timely manner any issues that may have an impact on the expected deliverables to the Management Committee. The Regulatory Chair (in charge of the process) works in close collaboration with the Rapporteur (in charge of the subject-matter).

Sign-Off: The procedure where the experts of an ICH Working Group provide their signature (scan or electronic signature) to show their endorsement of either a draft or final Guideline. Expert sign-off occurs during *Step 1* and *Step 3* of the formal ICH process.

Standards Developing Organisation (SDO): An organisation whose primary activities are developing technical standards.

Step Process: The formal ICH Procedure that consists of 5 Steps: *Step 1*: Consensus Building, *Step 2a*: Confirmation of Member Consensus of the Technical Document, *Step 2b*: Adoption of Draft Guideline by Regulatory Members, *Step 3*: Regulatory Consultation and Discussion, *Step 4*: Adoption of an ICH Harmonised Guideline, and *Step 5*: Implementation.

Technical Coordinator: Provides support to their respective ICH Coordinators and facilitates actions of the ICH Management Committee by applying their scientific knowledge.

Topic Leader: Co-participant of a Working Group who leads in the representation of the views of their Member during any ICH interactions with support of the Deputy Topic Leader.

Work Plan: A work plan is developed by a Working Group and is used to establish milestones and develop a timeline for completion of activities. Additionally, a Work Plan will include an agenda for any face-to-face meetings.

Introduction

This Standard Operating Procedure (SOP) is intended to provide an overview of the standard processes for the harmonisation activities that take place under the ICH Association and to provide guidance for the Working Groups (WGs) that carry out these activities.

ICH Working Groups are comprised of experts representing ICH Members and Observers. In accordance with the ICH Assembly Rules of Procedure 1.6, ICH Members and Observers should be referred to by the official names used by the ICH Association as listed on the ICH website under Members & Observers page. Only these names shall be used in ICH when referring to these entities. In addition, national, and other flags, emblems, or anthems are not to be used in the ICH.

The ICH harmonisation activities fall into six categories outlined in Table 1 below. These activities include 1) the formal ICH procedure, 2) Q&A procedure, 3) revision procedure, 4) the maintenance procedure, 5) error correction, and 6) Guideline withdrawal. This SOP begins with an overview of the activities that occur prior to initiating a harmonisation activity followed by a detailed overview of each harmonisation process.

Table 1 Summary of ICH Harmonisation Processes

Type of Harmonisation Procedure	Technical Group	Type of Work Conducted
Formal ICH Procedure	EWG	Development of a new Guideline
Q&A Procedure	IWG	Creation of Q&As to assist in the implementation of existing Guidelines
Revision Procedure	EWG	Revision/modification of existing Guidelines through amendments to the content of a Guideline or addition of Addenda or Annexes
Maintenance Procedure	EWG	Updating existing Guidelines; Addition of standards to existing Guidelines and/or recommendations
Error Correction	EWG/IWG and/or ICH Secretariat	Correction of errors in ICH documents
Guideline Withdrawal	ICH Assembly	Withdrawal of an ICH Guideline

In general, the ICH Management Committee (MC) is responsible for the oversight of the ICH Working Groups and for presenting recommendations to the ICH Assembly on various issues. The ICH Assembly is responsible for the adoption of new topics for harmonisation; the endorsement and adoption of the final Guidelines, Q&A documents, revised Guidelines etc.; and the endorsement of a new harmonisation activity of an existing WG which is outside of the scope of its Concept Paper. Some decisions may be taken through written procedure by electronic means such as email whereas other decisions are reserved for face-to-face meetings. A summary of the various ICH Harmonisation Activities, the endorsing party, and the venue for endorsement is provided in Table 2 on the next page.

Table 2 Endorsement/Adoption Procedure for ICH Harmonisation Activities

ICH Harmonisation Activity	Endorsing Party	Venue for Endorsement[1]
1. Selection of new ICH topic for harmonisation/endorsement of Concept Paper Outline	Assembly	Face-to-face (F2F) Mtg.
2. Final Concept Paper	MC	Electronic or F2F Mtg.
3. Business Plan	MC	Electronic or F2F Mtg.
4. EWG/IWG Regulatory Chair	Regulatory MC Members	Electronic or F2F Mtg.
5. EWG/IWG Rapporteur	Assembly	Electronic or F2F Mtg.
6. EWG/IWG Membership	MC	Electronic or F2F Mtg.
7. EWG/IWG Observers	MC	Electronic or F2F Mtg.
8. *Step 2a* – Confirmation of Technical Document	Assembly	Electronic or F2F Mtg.
9. *Step 2b* – Adoption of Draft Guideline	Regulatory Members of the Assembly	Electronic or F2F Mtg.
10. *Step 4* – Adoption of ICH Harmonised Guideline	Regulatory Members of the Assembly	Electronic or F2F Mtg.
11. Decision to develop a new Q&A document[2]	Assembly	F2F meeting
12. Decision to conduct public consultation for Q&A document	MC (may elevate to Assembly if necessary)	Electronic or F2F Mtg.
13. Decision to revise an ICH Guideline	Assembly	F2F meeting
14. Guideline Withdrawal	Assembly	F2F meeting
15. Options paper	Working Group/MC	N/A
16. Points to Consider	Assembly	Electronic or F2F Mtg.
17. Proof of Concept	Working Group/MC	N/A
18. Implementation Package	Assembly	Electronic of F2F Mtg.
19. Training Materials	Topic Leaders	Electronic or F2F Mtg.
20. New harmonization activity of an existing WG which is outside of the scope of its Concept Paper.	Assembly	Electronic or F2F Mtg.

The ICH MC is responsible for oversight of the ICH Working Group process and operations (Article 36 (2)(f)) and is therefore, responsible for developing this SOP and approving any revisions. A proposed

[1] A tele/web conference may in exceptional cases be used in place of a written procedure (an electronic endorsement).

[2] Note: the Q&A process follows the same process for development of a new ICH Guideline with the exception that public consultation may or may not occur.

revision to the SOP can be brought forward by any ICH Member by notifying the ICH secretariat or the ICH coordinator of the respective region. Revisions to the SOP may be discussed among the MC or the ICH Coordinators may work together to develop a recommendation for the ICH MC's consideration. Once the MC provides its endorsement for any revisions to this document, the ICH Assembly should be informed of the approved revisions.

1. ICH Harmonisation Activities before Step 1

1.1. Selection of New Topics

1.1.1. Topic Nomination and Review

A topic proposal can be submitted by any ICH Member or Observer. New topic proposals should be submitted to the Management Committee (MC) by completing all sections of the New Topic Proposal Template (see Annex 8). The MC will confirm the deadline for submission of new topic proposals during each November biannual meeting of the Assembly. The MC will review any topic proposals received, and prioritize proposals that are to be recommended for endorsement by the Assembly. The MC will provide a recommendation to the Assembly during each June meeting to endorse any recommended topics and their prioritization. The Assembly will be asked to make a decision during the June face-to-face meeting to either endorse or reject a topic proposal. If the Assembly chooses to endorse the topic that is being proposed for harmonisation, it will also be asked to endorse the outline for the Concept Paper. If a new topic proposal and Concept Paper outline are endorsed by the Assembly, an informal Working Group (WG) will be established to develop the Concept Paper and a Business Plan, if requested.

In principle, the agreement of all ICH Members of the Assembly is necessary for initiating any ICH harmonisation activities. However, in exceptional cases when Assembly consensus cannot be achieved, the Assembly will proceed to voting where a decision to endorse a new topic proposal will be adopted by majority. Refer to the ICH Rules of Procedure of the Assembly section 3.6 and 3.6.1 for a more detailed discussion of the Assembly decision making process and decisions on selection of ICH topics.

1.1.2. Scheduling and Timing for Planning Approach

New ICH Guideline topic proposals will be considered in the context of the work plan once per year. The MC will review new topic proposals ahead of each June biannual ICH Assembly meeting. The deadline for submission of new topics will be confirmed by the ICH MC at the preceding November biannual meeting. The Assembly will be provided with a copy of the topic proposals that will be considered at the next Assembly meeting no later than one month prior to the meeting. The MC will provide its recommendations to the Assembly during the June biannual Assembly meeting.

The Assembly should discuss the necessity to develop a new ICH Guideline, to revise an existing ICH Guideline, or to develop a Q&A document. Any changes to the content of an existing ICH Guideline are considered as a revision of the Guideline. This includes an addendum of a new paragraph and/or

partial replacement of the sentence but does not mean adding an identified list of standards (i.e. level of residual solvents) and/or correction of a typographical error.

1.2. Establishment of an informal Working Group

An informal Working Group (WG) is formed prior to an official ICH harmonisation activity with the objectives of developing and finalizing a Concept Paper, as well as developing a Business Plan if the Concept Paper outline is endorsed (although as per section 1.4, it is highly encouraged that the Business Plan is developed in parallel with the Concept Paper). In general, the MC oversees all operations of an informal WG. If an ICH Member proposed a selected topic, that Member will be provided the opportunity to lead the informal WG. Otherwise, the MC will designate a Member to lead the informal WG. The ICH Regulatory Members of the MC may appoint, in line with the principles in section 1.5.2, a Regulatory Chair from the Regulatory Members of the MC. As a principle, informal WGs should work by e-mail and tele/web conference and should not need to meet face-to-face. In exceptional cases, an informal WG may be allowed to meet face-to-face with the approval of the MC.

1.2.1. Informal Working Group Membership

ICH Members nominate experts to informal WGs as per the principles described in section 1.5.1.2. At a minimum, every Founding Regulatory Member should nominate at least one expert to each informal WG. Any experts nominated to the informal WG should have expertise relevant to the subject matter.

The ICH Secretariat will issue a call for expression of interest to eligible ICH Members and Observers to nominate experts to the informal WG. This call for expression of interest will also provide an alternative option to nominate experts to a Plenary Working Party which would later be established once the WG is formed following approval of the Concept Paper. ICH Members and Observers will be invited to express their interest within a three-week period, after which it may not be possible to accommodate additional requests to nominate experts to the informal WG due to size constraints. The MC will review the expert nomination requests at the end of the three-week period and will confirm the expert nominations from Members and Observers in line with the principles described in section 1.5.1.2. The MC reserves the right to allow additional members to join or limit the size of an informal WG; however, to support the efficiency and effectiveness of WG operations, as a rule a WG should not exceed 30 participants.

In line with the principles described in section 1.5.1.2, requests received to nominate experts after the three-week period from Members/Observers not represented in the WG and seeking to join the WG will be reviewed by the MC as part of a biannual review process; however, those ICH Members and Observers that have an interest in the WG which is being established, are encouraged to appoint any experts during the initial formation of the informal WG. Furthermore, in line with section 1.5.1.2, requests for expertise issued by the WG should be reviewed by the MC on ad-hoc basis.

The Topic Leaders/Deputy Topic Leaders will participate in the informal WG discussions and be the point of contact for any consultation carried out between meetings by correspondence, fax, e-mail etc. It is the responsibility of the Topic Leader/Deputy Topic Leader to officially represent a consolidated view from their Member during any ICH interactions (e-mails and tele/web conferences). An expert from the Member responsible for originally proposing the topic should be nominated Group Leader and will lead the efforts of the informal WG.

To support the work of the informal WG, each Member may appoint additional support staff to assist with the preparation of that Member organisation's contributions to the WG. Their names would be submitted to the ICH Secretariat for inclusion on emails for the informal WG. These additional staff would work outside of the ICH WG sessions in their support of ongoing operations of the informal WG. Additionally, a Member's position should be presented solely by the experts nominated to the WG; additional staff should not opine on technical aspects of the WG discussions. In displaying the composition of the WG, there should be a clear distinction between the experts of the WG and the support staff. Support staff should operate in a limited capacity so as not to impede progress of the WG. To keep the size of the meetings manageable, support staff should not attend face-to-face meetings, except for in exceptional circumstances and when appropriate justification can be provided. Any requests for support staff to attend a face to face meeting should be discussed with the Group Leader. Additionally, the Secretariat should be consulted to determine if there is enough space to accommodate the additional attendees.

The entire membership of an informal WG shall be copied on e-mails and invited to participate in tele/web conferences.

As per section 4.4 of the Rules of Procedures of the Assembly, the presence of at least one expert from each Founding Regulatory Member and if nominated, one expert from each Founding Industry Member and Standing Regulatory Member nominated to the informal Working Group, is required to constitute a quorum. Each Regulatory Member and Industry Member appointed to the informal WG is expected to actively participate in and contribute to the work of the informal WG on a continuous and regular basis until the work is completed to ensure continuity. The absence of an Observer from an informal WG meeting will not prevent the meeting from taking place.

1.3. Developing a Concept Paper for a Selected Topic

A Concept Paper is developed by an informal WG after a topic proposal has been selected to go forward in the harmonisation process. The Concept Paper provides further context surrounding a proposal and should be completed in accordance with the Concept Paper Template (see Annex 9).

The Concept Paper should be a maximum of two pages. If necessary, further documentation and reports may be annexed to the Concept Paper. The Concept Paper should ideally be completed within two months (60 days) following the endorsement of the topic proposal by the Assembly to allow for approval at a MC teleconference.

The informal WG may consult the MC as needed to resolve any issues that may arise during development of the Concept Paper. The MC will work with the informal WG to ensure that a Concept Paper is developed in line with the topic proposal and Concept Paper outline endorsed by the Assembly. The Concept Paper should identify any considerations for special subpopulations (e.g. pediatrics) and how the proposed Guideline may need to be tailored to meet the needs of a particular population. The final Concept Paper will be submitted to the MC for endorsement and the Assembly will be notified once a final Concept Paper is endorsed.

When complete consensus cannot be achieved on the Concept Paper within the agreed time frame, the informal WG will make a report to the MC indicating the extent of agreement reached and

highlighting the points on which differences between the Members remain. Experts from all ICH Members represented on the informal WG will have the opportunity to explain their position to the MC. The MC may then:

- Provide guidance to the informal WG on how to proceed;
- Allow an extension of the time frame, if the WG can give assurances that consensus could be reached within a short, specified period;
- Provide a recommendation to the Assembly to suspend or abandon the harmonisation project and disband the informal WG; or
- Elevate the decision on how to proceed to the Assembly.

1.4. Development of a Business Plan

A Business Plan should be developed in alignment with the Business Plan Template (see Annex 10). It is highly encouraged that the Business Plan is developed in parallel with the Concept Paper. The Business Plan will be submitted by the informal WG for review and approval by the MC no later than 30 days following endorsement of the Concept Paper by the MC, or if needed, a longer time period that is requested by the WG and approved by the MC. The informal WG will work through e-mail, tele/web conference and, exceptionally, face-to-face meetings to develop a Business Plan.

The Business Plan submitted to the MC will be reviewed for either feedback to or revision by the WG, or approval by the MC. This review will be handled by the MC through tele/web conference, at the next face-to-face meeting, or by email. The MC will report the decision to approve the Business Plan to the Assembly and following that, an Expert Working Group (EWG) or Implementation Working Group (IWG) will be established to initiate harmonisation activities.

If in working to develop the Business Plan, consensus among the informal WG cannot be achieved on the Business Plan within the agreed time frame, the informal WG should consult the MC indicating the extent of agreement reached and highlight the points on which differences between the Members remain. Experts from all ICH Members represented on the informal WG will have the opportunity to explain their position to the MC. The MC may then:

- Allow an extension of the time frame, if the WG can give assurances that consensus could be reached within a short, specified period;
- Provide guidance to the WG on how to proceed; or
- Provide a recommendation to the Assembly to modify the scope of the harmonisation project or to suspend or abandon the harmonisation project and disband the informal WG.

1.5. Establishment of the EWG/IWG[3]

Following the endorsement of a Concept Paper and Business Plan, an Expert Working Group (EWG) or Implementation Working Group (IWG) will be established depending on the type of work to be

[3] Any Working Groups established prior to the formation of the new ICH Association in October of 2015 will maintain their current membership until their work is completed with the exception of any new Members who may appoint new experts or observers to a working group under this SOP. Additionally, the status of any working group expert will be updated if a party

undertaken. An EWG will be established for the development or revision of new or existing Guidelines and an IWG will be established for the development of a Q&A document.

In general, the MC oversees all operations of a WG including the appointment of new experts. The timing of the establishment of the EWG or IWG should align with the priorities of the ICH in accordance with the 5-year strategic plan. If a harmonisation project is abandoned at any time the EWG or IWG should be dissolved. The membership of all active EWGs/IWGs including nominating party, name of representative and role (regulatory chair, rapporteur or expert) is made publicly available via the ICH website.

1.5.1. EWG/IWG Membership

The ICH Members nominate representatives to EWGs and IWGs. In cases where the time between the establishment of an informal WG and an EWG is relatively short (less than a year), the informal WG will be automatically converted into an EWG, with Members and Observers invited to modify their nominated experts if they wish.

Otherwise, the ICH Secretariat will issue a call for expression of interest to eligible ICH Members and Observers to nominate experts to the WG. This call for expression of interest will also provide an alternative option to nominate experts to a Plenary Working Party. ICH Members and Observers will be invited to express their interest within a three-week period, after which it may not be possible to accommodate additional requests to nominate experts to the WG due to size constraints. The MC will review the expert nomination requests at the end of the three-week period and will confirm the expert nominations from Members and Observers in line with the principles described in section 1.5.1.2. Additional requests from Members/Observers not represented in the group and seeking to nominate experts following the initial establishment of the WG, will be reviewed by the MC as part of the biannual review process as described in section 1.5.1.2; however, those ICH Members and Observers that have an interest in the Working Group which is being established, are encouraged to appoint any experts during the initial formation of the Working Group. Requests received from the WG for additional expertise should be reviewed by the MC on an ad-hoc basis. For more information on the establishment of ICH WGs, see the ICH Assembly RoP Section 4.1

The Founding Regulatory Members are required to appoint an expert to all EWGs and IWGs. Founding Industry Members, Standing Regulatory Members and other Assembly Members are not required to appoint technical experts in all EWGs/IWGs. Information on the appointment of experts by the ICH Regulatory and Industry Members is provided in the Assembly Rules of Procedure (RoPs 4.3.4 & 4.3.5 respectively).

The Industry Member should provide information to the MC, via the ICH Secretariat about how it or its affiliate members will be affected or regulated by the Guideline in question in line with Article 12(2)(d) (see Annex 13). The Management Committee may invite further clarification on this point.

---

has since become an ICH Member or Observer. EWGs and IWGs established following the endorsement of this SOP in June 2018 will be established in accordance with the procedure outlined in this document.[4] The membership of Working Groups established prior to 6 June 2019 will not be modified for alignment with these rules, but requests received after June 2019 for new / additional experts to Working Groups established prior to 6 June 2019 will follow the limitations described in this section.

1.5.1.1. *Appointment of Observers to a WG*

Any ICH Observers who would like to participate in an EWG or IWG should submit a request in writing to the ICH Secretariat, for consideration of the ICH MC, with an explanation of their anticipated contribution to the WG (see Annex 12). The ICH Observers may nominate an alternate member to the WG, who shall be added to the email list, which may replace the representative for the Observer if he or she is unable to participate. Any experts nominated to an EWG or IWG should have expertise relevant to the subject matter.

Observers approved to participate in either an informal WG or a EWG/IWG may have their participation revisited in view of new Members seeking to participate since preference would need to be given to Members.

If an ICH Observer applies and is granted Membership by the MC, then that Observer's experts will also become Members of the WG (s) they are currently participating in. As such, it is expected that the Members' experts assume the role of an expert in the WG following the decision made by the MC to grant Membership to the Observer.

1.5.1.2. *Managing the Size of ICH Working Groups*[4]

Further to section 4.1.2 of the Assembly RoP, with the exclusion of the Rapporteur (or the Group Leader in the case of informal WGs and Regulatory Chair, the Membership of a WG shall be limited to maximum two representatives per ICH Founding Regulatory Member per WG (one expert shall be designated as Topic Leader and the other as Deputy Topic Leader), and one representative which shall be designated as Topic Leader, per Standing Regulatory Member, Regulatory Member, Founding Industry Member, Industry Member, Standing Observers and ICH Observer per WG. Furthermore, Founding Industry Members, Industry Members, Industry Standing Observer and Industry Observers of ICH may collectively as a group nominate up to 3 additional experts, by coordinating amongst themselves the nomination from a pool of designated industry experts amongst their associations. In this coordination, efforts should be made to identify the best possible experts across concerned industry sectors while at the same time make efforts to have experts from regions outside of the 3 Founding Members to achieve appropriate diversity in representation of industry perspectives. The additional experts that would be appointed in this process would subsequently report to the appropriate Founding Industry Member / Industry Member / Industry Standing Observer for their respective industry sector(s). If Industry collectively as a group cannot reach an agreement on which expert(s) to appoint, the additional industry expert position(s) would remain unfilled.

Standing Regulatory Members, Regulatory Members, Industry Members, Standing Observers and ICH Observers, which are limited to one representative per WG, may nominate an alternate expert. The alternate expert may be copied on emails and may listen during teleconferences of the WG but would not participate in the discussion. In the event that the expert cannot participate in the WG, the alternate expert would replace the expert.

[4] The membership of Working Groups established prior to 6 June 2019 will not be modified for alignment with these rules, but requests received after June 2019 for new / additional experts to Working Groups established prior to 6 June 2019 will follow the limitations described in this section.

The MC reserves the right to allow additional members to join a WG or limit the size of the WG. However, as a general rule, to support the efficiency and effectiveness of WG operations, a WG should not exceed 30 participants. In respect of this, only experts should be included in the formal count of the size of the WG, in which the following types of participants would not be counted: Rapporteur/informal WG Leader; Regulatory Chair; Rapporteur Supporter (if not an expert); Editor (if not an expert); Additional Staff or Member/Observer Alternates (for more information, see section *1.5.1.4)*.

Requests for additional expertise should be made from the WG (i.e. through the Rapporteur/informal WG Leader) and should be reviewed by the MC on an ad-hoc basis. To address such requests, the MC may allow a Member who already has a representative in the WG to appoint an additional expert or an *ad-hoc* expert (in line with section 1.5.1.4).

The ICH MC shall review twice a year requests from Members/Observers not represented in the WG and seeking to appoint experts. When reviewing requests to appoint experts to a WG that is already large (≥25 experts), the ICH MC should consult with the Rapporteur regarding the appointment of additional Members or Observers for feedback from the group's perspective, on both the possible added value of the expertise proposed as well as concerns around the size of the WG and the impact to the efficiency of the WG operations. The MC may furthermore determine not to allow additional experts to join a WG in view of the stage of the work. For example, additional experts may not be allowed to immediately join a WG which is very close to reaching *Step 1* as it may be disruptive to the process. Furthermore, additional experts may not be allowed to join a WG which is about to reach *Step 3/Step 4*, as the work may be too advanced.

In the event that the MC must decide amongst Members or Observers who should be permitted to appoint experts to a WG, preference should generally be given to Regulatory Members since they are expected to implement ICH Guidelines followed by Standing Observers as they have a right appoint experts versus Observers who require approval of the MC. Additionally, special consideration may be given to Industry Members who would be most regulated by the Guideline. If the MC must decide among Observers, priority should be given to Observers referred to in Article 17(1)(a) and particularly those authorities that have indicated their intention to apply for membership in ICH in order to facilitate their subsequent membership which is in the interest of global harmonization. For further information on limiting the size of a WG and prioritization among Members and Observers, see ICH Assembly RoP Section 4.1.3.

1.5.1.3. *Participation in ICH WGs*

The Topic Leaders/Deputy Topic Leaders will participate in the EWG/IWG discussions and be the point of contact for any consultation carried out between meetings by correspondence, e-mail etc. It is the responsibility of the Topic Leader/Deputy Topic Leader to officially represent a consolidated view from their Member, during any ICH interactions (e-mails, tele/web conferences and face-to-face meetings).

To support the efficiency and effectiveness of WG operations, an expert should not be appointed to work in more than one WG at a time. However, in exceptional cases the MC can decide that an expert may serve on more than one WG if the merits outweigh the adverse impacts on the work process for the other experts on the WG.

It is encouraged for an expert on a given WG to serve as a liaison across WGs when appropriate due to similarities in the scope of technical issues and to ensure complementarity across topics (e.g. liaison for M2 and E2B).

1.5.1.4. *Additional Experts and Support Staff*

Additional experts, which should be approved by the MC as per section 1.5.1.2, may contribute to the discussion but the official voice of each delegation rests with the Topic Leader, and in the case of Founding Regulatory Members, their Deputy. ICH Regulatory Members may nominate additional support staff to the EWG/IWG mailing list for information only.

To support the work of the WG, each Member may appoint additional support staff to assist with the preparation of that Member organisation's contributions to the WG. Their names would be submitted to the ICH Secretariat for inclusion on emails for the WG. These additional staff would work outside of the WG sessions in their support of ongoing operations of the WG. Additionally, a Member's position should be presented solely by the experts nominated to the WG; additional staff should not opine on technical aspects of the WG discussions. In displaying the composition of the WGs, there should be a clear distinction between the experts of the WG and the support staff. Support staff should operate in a limited capacity so as not to impede progress of the WG. To keep the size of the meetings manageable, support staff should not attend face-to-face meetings, except for in exceptional circumstances and when appropriate justification can be provided. Any requests for support staff to attend a face to face meeting should be discussed with the Rapporteur. Additionally, the Secretariat should be consulted to determine if there is enough space to accommodate the additional attendees.

The entire membership of a WG shall be copied on e-mails and they may also be invited to participate in tele/web conferences.

Further to a WG's request for additional expertise limited to a specific item, the MC may exceptionally allow the appointment of an additional expert, possibly to serve in a consulting capacity on an *ad-hoc* basis to address (and limited to) a specific technical issue or set of issues within the scope of the MC endorsed Concept Paper. The WG membership should however remain at or below 30 participants. The specific expected duration of participation and the specific issues that will be covered during the expert's participation should be agreed with the Rapporteur and the MC. The additional expert may exceptionally attend face-to-face meetings and teleconference only when the agreed scientific issues will be discussed, subject to the approval by the MC. The Rapporteur should inform the ICH Secretariat of the role of the additional expert and the specific technical issue.

To ensure the continued smooth operation of the EWG/IWG and adhere to the limits on the number of each Member's representatives the involvement of additional experts should be managed, firstly by the Member's Topic Leader / Deputy Topic Leader for that WG and also by the active management of the Rapporteur and Regulatory Chair as needed. As noted above, where appropriate, additional experts may contribute to the discussion but the official voice of each delegation rests with their Topic Leader / Deputy Topic Leader and they are not expected to participate outside the scope of their agreed-upon role. If participation to a meeting would be necessary, this would be expected only when the specific technical issue the Additional Expert is consulted on will be covered in discussion.

In the case that external expertise may be helpful, and subject to MC approval, a WG may consider inviting a limited number of liaisons from an entity (e.g. a scientific or technical expert from a university or research institute) to participate in the WG on an *ad-hoc* basis to provide additional technical expertise. MC approval would be obtained for the liaisons' participation for each topic or issue to be addressed.

1.5.1.5. *Ad hoc Observers*

In exceptional circumstances, and when the MC considers it important for the benefit of the ICH, and with approval of the WG Rapporteur and the Regulatory Chair, the MC may permit an *ad-hoc* Observer from a regulatory authority to appoint an *ad-hoc* observer to attend a face-to-face meeting of a WG on a *per* meeting basis.

1.5.1.6. *Editor and Content Manager*

An editor should be identified during the formation of an EWG or IWG. It is the responsibility of the editor to ensure that Guidelines, Q&As, and Technical Documents are formatted according to the ICH style guide. A content manager may also be identified as appropriate. It is the responsibility of the content manager to create the structure of the WG's dedicated section of the online working area, to upload the documents within the structure, and to maintain the WG's section to be up-to-date. Ideally, the editor and the content manager should be nominated from one of the already existing experts; however, in exceptional cases the MC reserves the right to decide if an additional expert should be nominated to the WG for the sole responsibility of editing any documents or handling the online working area.

1.5.2. Appointment of the Regulatory Chair and Rapporteur

The ICH Regulatory MC Members officially designate a Regulatory Chair from the Regulatory MC Members. In line with Section 9.3 of the MC RoP, when setting-up a new working group, eligible Members should put forward a candidate. If a Working Group is established from an informal Working Group which had a Regulatory Chair, the Regulatory Chair will continue his/her role, unless otherwise specified by the MC. If a Working Group had been operating without a Regulatory Chair and chooses to nominate one, the Coordinator from the member that holds the role of Rapporteur will work with the Rapporteur to identify if there would be any potential candidates from the MC Regulatory Members with experts represented on the working group. The Rapporteur will liaise with the experts from the MC Regulatory Members on the Working Group to identify potential volunteers and the coordinators of the regulatory MC members will be notified. Potential candidates would be made aware, by the Rapporteur, that the names of potential candidates will be submitted to the Regulatory Members of the MC and that the final decision of who will serve as the regulatory chair will be made by the regulatory members of the MC. Experts should consult with their Coordinator prior to volunteering for this role. If an expert volunteers to serve as the Regulatory Chair, the nomination will be forwarded to the Regulatory Members of the Management Committee for a final decision. If there are no volunteers for the role, the coordinators of the regulatory MC Members would work together to identify a potential candidate. Where more than one candidate has volunteered for the role, the Regulatory Members of the MC will take a decision based on consideration of each candidate's experience (e.g., project management skills, past experience with ICH consensus-building, knowledge of ICH procedures).

In the event that a Regulatory Chair, for whatever reason, is unable to continue in this position, the Member, which the Regulatory Chair is a representative of, will be responsible for putting forward a new candidate. Prior to submitting the new candidate to the Regulatory MC Members for their approval, the Rapporteur and his/her Coordinator should be consulted. In the case where the Member is not putting forward a new candidate, the process described above will be applied to appoint a new Regulatory Chair from another Regulatory MC Member.

The Assembly officially designates a Rapporteur, preferably among the Topic Leaders designated by the ICH Members when a new ICH topic is formally adopted. In general, the party who proposed the topic would assume the role of Rapporteur; however, if this party is unable to fill this role, then another topic lead from the working group could be nominated as Rapporteur. For further information on the appointment of the Rapporteur, as well as the replacement of a Rapporteur that is stepping down from his/her role, refer to the Assembly RoP section 4.2.

In general, the Regulatory Chair and the Rapporteur should be from different regions. In principle, in order to effectively perform the role of Regulatory Chair and Rapporteur, the Regulatory Chair and Rapporteur should not be nominated as an expert to another active WG and by the same token should not serve as Regulatory Chair or Rapporteur on more than one WG.

In exceptional cases, both a Rapporteur and a Co-Rapporteur may be appointed. Whenever possible, Co-Rapporteurs should be from different regions and should not both be from a Regulatory or Industry Member. If an Industry Member is appointed to be the Rapporteur for a WG, a Regulatory Member will need to replace the Industry Member following completion of *Step 2b*; however, the Industry Member will still be invited to participate in the WG discussions going forward.

Members who have nominated experts as either a Regulatory Chair or Rapporteur may nominate one additional representative to the WG. Additionally, a Member serving as the Rapporteur may nominate someone to serve as a Rapporteur Supporter to assist in the going operations of the WG. It is not excluded that another member could also offer to appoint a Rapporteur Supporter with approval from the Rapporteur. While this role can be filled by someone who is serving as one of the nominated experts, it may also be filled by someone who is not an expert on the WG. The Rapporteur Supporter may be responsible for activities such as note taking, scheduling of meetings, agenda development, capturing agreements and outcomes of EWG/IWG discussions, etc. The Rapporteur Supporter may attend teleconferences and face-to-face meetings of the WG at the recommendation of the Rapporteur; however, will not opine on technical issues or participate in the decision making of the WG if they are not also a nominated expert to the WG.

1.5.2.1. *Roles and Responsibilities of the Regulatory Chair*

The role of the Regulatory Chair is to ensure timely execution of the ICH process and adherence to the Concept Paper and Business Plan, including scope and timelines. The Regulatory Chair should work in close collaboration with the Rapporteur.

<u>Responsibilities of the Regulatory Chair include:</u>

1. Ensuring timeframes are met and work is within the scope of the EWG/IWG mandate;
2. Collaborating with the Rapporteur in developing a Work Plan that is consistent with the scope and time frame of the approved Concept Paper and Business Plan;

3. Regularly reporting to the MC on progress of the EWG/IWG regarding timeliness, adherence to scope and conflicting views if they arise and ensuring that all expert perspectives are reflected in the documents presented to the MC and Assembly;
4. If conflict arises, working with the Rapporteur to achieve consensus within the EWG/IWG by reconciling divergent views. If the Regulatory Chair and the Rapporteur fail to achieve consensus, the Regulatory Chair will elevate the issue to the MC for resolution as early as possible;
5. Addressing the behavior of any expert within the EWG/IWG that is disruptive or is not constructive, in consultation with the Regulatory Chair's Coordinator (see Annex 2 - Ground Rules for Good Practices of ICH Working Groups); and
6. Deciding when it is necessary to document significant differences of position or conflicting views among members of the EWG/IWG and will work on this task with the assistance of the Rapporteur.
7. Regulatory Chairs of WGs with a Plenary Working Party (PWP) are also expected to lead the activities of the PWP as described in section 1.7.

In exceptional circumstances, the MC reserves the right to replace a Regulatory Chair when it is considered necessary for a WG to progress according to plan.

1.5.2.2. *Roles and Responsibilities of the Rapporteur*

When a new ICH Topic is formally adopted, the Assembly appoints the Rapporteur preferably from among the Topic Leaders designated by the ICH Members. In exceptional cases, a Co-Rapporteur may also be appointed to assist the Rapporteur. Whenever possible, Co-Rapporteurs should be from different regions and they should not both be from a Regulatory or Industry Member. If the Rapporteur is a representative from one of the Industry Members, the Rapporteur role will then have to be transferred to a Regulatory Member after *Step 2b* is reached. In general, to ensure the independence and efficiency of the two key leadership roles of a WG, the role of the Rapporteur and Regulatory Chair should be assumed by two different Members. In general, a single Regulatory Member should not assume the role of both the Regulatory Chair and Rapporteur except in exceptional cases and with explicit agreement of the Assembly.

The role of the Rapporteur is to serve as the scientific co-chair, to facilitate and manage scientific and technical activities of the EWG/IWG, reconciling scientific differences of opinion, in order to produce an ICH document with the scientific and technical content that is in accordance with Assembly decisions/expectations. The Rapporteur shall work in close collaboration with the Regulatory Chair.

<u>Responsibilities of the Rapporteur include:</u>

1. Develop a detailed Work Plan in collaboration with the Regulatory Chair that will achieve the technical objectives outlined in the ICH MC-approved Concept Paper and Business Plan and contains clear technical deliverables and associated deadlines; the updated work plan, approved by the whole EWG, shall be provided ahead of the Coordinator/MC tele/web conference for MC consideration.
2. Maintaining a record of participation of the ICH Members nominated to the WG;

3. Responsible for day-to-day management including organising (scheduling and hosting) teleconferences of the WG, setting deadlines, assigning work to the members of the EWG/IWG and assuring all ICH Members' views are incorporated into documents and presentations as appropriate.
4. The Rapporteur shall seek to reconcile scientific and technical differences among EWG/IWG members.
5. The Rapporteur shall make sure that the views of the different members are reflected in an appropriate and fair manner in any outcomes of the EWG/IWG work.
6. The Rapporteur shall regularly present reports to the Assembly, on the technical and scientific aspects of the document under development.
7. Upon reaching Step 2b or 4, the Rapporteur shall ensure the development of a presentation for review by EWG/IWG members, and provision to the ICH Secretariat to be included in a library of presentations and implementation materials made available on the ICH public website. This presentation should follow the format and Guidelines as specified in the guide documents (available from the ICH Secretariat).
8. Rapporteurs of WGs with a Plenary Working Party (PWP) are also expected to lead the activities of the PWP as described in section 1.7.

The appointed Rapporteur should enjoy the confidence of the Assembly and of the MC. Should a Rapporteur no longer enjoy the confidence of the Assembly, it should appoint a new Rapporteur. In exceptional circumstances, the MC may provide a recommendation to the Assembly to replace a Rapporteur when it is considered necessary for a WG to progress according to the plan.

1.5.3. Meetings of the EWG/IWG

Any face-to-face meetings of a WG will be subject to decision by the MC. WGs shall not systematically meet in conjunction with every Assembly meeting if not justified. In order to minimize organisational and logistical costs of the ICH process, WGs should meet face-to-face only when necessary and justified and when sufficient discussion materials are available. Interim face-to-face meetings (i.e., WG meetings outside the regular ICH Assembly meetings, see Annex 3) should be exceptional, and only when there is an absolute necessity in order for the topic to meet its assigned objectives in time. WGs are encouraged to communicate through e-mail to progress draft Guidelines between face-to-face meetings and through tele/web conferences.

ICH does not cover the cost of travel or accommodation for WG participants. Participation is at the expense of the Member, Observer, or expert concerned.

For logistical purposes, it is essential that in preparation for any official biannual face-to-face meeting, each ICH Member and Observer communicate the names of its representatives to the ICH Secretariat, and that the host organisation is informed of each Member/Observer delegation well in advance of the meetings. The ICH Secretariat shall keep a record of experts' nominations.

1.5.4. Meeting Attendance

The presence of at least one expert representative from each Founding Regulatory Member and if nominated, one expert from each Founding Industry Member and, if nominated, one expert from each Standing Regulatory Member is required to constitute a quorum (section 4.4 of the Rules of

Procedures of the Assembly). However, all Regulatory Members and Industry Members who have appointed expert representatives to the WG are expected to actively participate in and contribute to the work of the WG on a continuous and regular basis until the work is completed to ensure continuity. Section 4.3.7 of the ICH Rules of Procedure of the Assembly also outlines the criteria and expectations for participation of Observer experts appointed to a WG. It should be noted that the absence of an Observer from a WG meeting will not prevent the meeting from taking place.

The requirement for continuous and regular participation is intended to ensure both the benefit of continued contribution of the Member representative's expertise, and to minimize the harm or disservice to the WG's already-challenging process from disruptions or lost time for the other experts due to needed repetition and revisiting of the same issues, discussions, or decisions for the benefit of the expert who was repeatedly absent. If a Member's expert representative is absent from a WG meeting where a decision was made, that Member shall not request that the WG revisit decisions made in that Member's expert's absence. If an appointed expert is absent from two consecutive meetings of a WG (either face-to-face or through teleconference) and it appears that expert will continue to be absent, the ICH Member should appoint another qualified expert.

If an ICH Member's expert has been absent from two consecutive meetings, and if no other qualified expert from that Member participates in the subsequent meeting of the Working Group, the Regulatory Chair and Rapporteur should notify the ICH Secretariat. The ICH Secretariat will notify the Coordinator and MC Member of the respective Member. In the event that the issue cannot be resolved, the Rapporteur and Regulatory chair will provide a report to the MC on the impact of that expert's absence from the WG and may provide a recommendation on how to proceed to the MC. The MC will make a decision on how to proceed; however, in principle that Member will lose its right to appoint an expert to that WG after two subsequent absences. As an exception, this does not apply to the Founding Regulatory Members as they are required to have appointed experts in all WGs, (4.3.1 of the Rules of Procedure of the Assembly) their presence is also required for the quorum of the WG (4.4 of the Rules of Procedures of the Assembly). See the ICH Rules of Procedure of the Assembly section 4.3 for more details of the expectations for expert participation in WGs and the consequences of failure to maintain participation on a continuous and regular basis.

1.5.5. Confidentiality

Members and Observers appointed to a WG or PWP have a responsibility to maintain confidentiality of the issues discussed within their WG/PWP and other confidential information of the kind covered by the obligation of a professional society. Members and Observers are entitled to share such confidential information with persons within their respective organisation and third parties provided that the recipients (i) must have access to the confidential information to fulfil their duties within their organisation and (ii) executed a confidentiality agreement or arrangement that has corresponding confidentiality obligations or that such persons or third parties are otherwise bound to confidentiality obligations. The representatives of the Members, Standing Observers and Observers shall not use the confidential information for any purpose other than as necessary to enjoy their rights or perform their obligations within the Association. For the avoidance of doubt, confidential information includes draft documents and proposals pending Assembly approval, in addition to other information not in public domain. See the ICH Rules of Procedure of the Assembly section 7.3 for more details on maintaining confidentiality.

If Members are requested to provide information about the discussions within the WG/PWP publicly or to anyone who is not a representative of the ICH or an ICH Member, they should not disclose this information but refer the requester to the ICH Secretariat. An expert should not publicly disclose orally or in writing the details of the ongoing discussions nor should they disclose the position of the individual parties without prior approval from the WG/PWP Members and informing the ICH MC.

ICH experts are permitted to present on the development of an ICH guideline at a public meeting or conference. The slides for such presentations should be shared with and cleared by the entire membership of the ICH working group in advance of the presentation. If the presentation is to be conducted in a language other than English, the slides should be shared in the original language along with at least a summary in English for each slide explaining the content of the slide. The positions of individual parties should not be disclosed. Additionally, if there are issues that the working group has not yet reached consensus on, these issues should not be discussed in detail in a public forum. Following finalization of the guideline at *Step 4*, clearance of slides for outside presentations is not required.

In an effort to promote transparency of the ICH Association, a list of the Members who participate in each of the Working Groups as well as their expert representatives will be published on the ICH website. The following disclaimer should be included whenever expert names are published to make it clear that experts are representatives of the Member they represent and that they do not necessarily represent their personal views but the views on behalf of their Member organization:

"Working Group and Plenary Working Party members are appointed by their nominating ICH Member or Observer party and are responsible for representing the views of that party, which may not necessarily reflect their personal views. Working Group and Plenary Working Party experts do not respond personally to external inquiries but are directed to forward any inquiries they receive to their nominating party or the ICH Secretariat for a response on behalf of either their ICH party or the ICH Association as appropriate. For questions to the ICH Secretariat, please use the contact form on the ICH website."

1.6. Development of Work Plan by Working Groups

Once a Working Group (WG) is established, the WG will be responsible for developing a detailed Work Plan prior to initiation of any work activity. The development of a Work Plan is led by the Rapporteur with input from the entire WG. The Work Plan should follow the template provided in Annex 11 and include anticipated milestones, a timeline for the completion of activities, a summary of any issues, and a justification for a face-to-face meeting, if requested. The details of a Work Plan should focus on the process steps that will be required to carry out any identified tasks, it is not necessary to provide substantive technical information in the context of the Work Plan. The Work Plan should be updated as needed. This should be done prior to the biannual face-to-face meeting and other key teleconference such as the Coordinators teleconference that takes place approximately 3 months prior to each biannual meeting. The Work Plan for each WG will be posted on the ICH Public Website and an updated Work Plan will be shared with the Assembly ahead of each biannual meeting.

1.7. Plenary Working Party

As per section 4.1.4 of the Assembly RoP, a Plenary Working Party (PWP) may be established for each Working Group (WG) following the Formal ICH Procedure, further to approval of its Concept Paper. The PWP includes the WG membership, plus additional experts from other ICH Members and Observers who do not have an expert in the WG and wish to follow more closely the work on a particular guideline topic.

1.7.1. Establishment of PWP

A PWP is established based on need and interest, with up to one (1) expert per Member and Observer who either (1) is unable to participate in the WG due to size limitations, or (2) is unable to devote the necessary level of effort to participate actively in WG activities, but still want to follow the progress of the WG. In the latter scenario, ICH Members and Observers will be given the alternative option at the time of establishment of a WG to nominate an expert to the PWP rather than the WG.

For WGs established after 6 June 2019, and prior to the reaching of *Step 2a/b,* the PWP will be automatically established based on interest and need. Requests to nominate experts to these PWP should be sent to the ICH Secretariat in writing further to which the expert will automatically be added to the PWP. If *Step 2a/b* has already been reached, and in view of the advanced stage of work of the WG, the MC should approve the establishment of a PWP.

Requests to appoint experts to a PWP for a WG established prior to 6 June 2019 should considered by the MC which should approve the establishment of a PWP for these WGs.

1.7.2. Activities of the PWP

In the case where a PWP has been established, the following activities should be integrated into the Formal ICH Procedure (described in section 2.1):

1. **PWP one-month consultation period prior to *Step 1* sign-off:** When the WG has reached consensus on their *Step 1* document, it should be shared with the PWP with a consultation period of one month, during which the PWP experts may review the document and send questions, make comments or recommendations for revision. A teleconference of the PWP may be held to discuss the document and feedback received. The WG may incorporate recommendations as appropriate.
2. **PWP participation to *Step 1* sign-off:** After the feedback from the PWP has been addressed, and when the WG has reached consensus on the *Step 1* document (i.e. including after any revisions that may have been made further to the consultation with the PWP), the *Step 1* sign-off will be initiated as per section 2.1.1.1. experts participating in the PWP will be invited to sign-off in recognition of their contribution to the discussion, but as it is not a requirement to reach *Step 1*, the progression of the *Step 1* document from the WG to the Assembly will not be delayed.
3. **PWP Workshop between *Step 2b* and the *Step 3* public consultation period:**
    i. The PWP, with leadership from the Rapporteur, Regulatory Chair and others on the WG, may convene teleconferences or workshops in their respective region to reach out and engage external industry stakeholders (i.e. regulated

industry and related entities engaged in pharmaceutical development and manufacturing that are not directly involved in ICH).

ii. Workshops at this stage may for example be used as a venue to inform external industry stakeholders about their region's process for gathering further comments on the *Step 2b* document.

4. **PWP one-month consultation period after *Step 3* public consultation period and prior to *Step 3* sign-off:** Following the public consultation period and after the WG has reached consensus on a revised version of the *Step 2b* document, the document should be shared with the PWP with a timeframe of one month, during which time the PWP experts may review the document and send questions, make comments or recommendations for revision. A teleconference of the PWP may be held to discuss the document and feedback received. With approval from the MC, the PWP may hold workshops as described in item 3.i in conjunction with the ICH meeting after the Assembly meeting. The WG may incorporate recommendations as appropriate.
5. **PWP participation to *Step 3* sign-off**: Similarly, to item 2 above, after the feedback from the PWP has been addressed, and when the WG has reached consensus on the *Step 3* document (including after any revisions that may have been made further to the consultation with the PWP), the *Step 3* sign-off will be initiated as per section 2.1.5. Experts participating in the PWP will be invited to sign-off in recognition of their contribution to the discussion, but as it is not a requirement to reach *Step 3*, the progression of the *Step 3* document from the WG to the Assembly will not be delayed.
6. **PWP Workshop after *Step 4***: The PWP may hold workshops as per item 3.i above. Workshops at this stage may for example be used as a venue to inform external industry stakeholders about their region's process for training and regulatory implementation of the *Step 4* document.

PWPs work primarily through tele- and web-conferences, however exceptional requests for face-to-face meetings, as determined necessary by the Rapporteur in consultation with Regulatory Chair, may be submitted to the Secretariat for MC consideration. PWP face-to-face meetings would be expected to be of limited duration, perhaps following on immediately after the end of the WG face-to-face meeting.

In addition to their responsibilities described in section 1.5.2.1 and 1.5.2.2, the Rapporteur and Regulatory Chair should lead the PWP. However, they may jointly appoint one of the regulatory experts of the WG to the role of "supporting Regulatory Chair" to take the lead for the meetings of the PWP (including liaising with the ICH Secretariat) thus assisting the Regulatory Chair. Furthermore, the duties of the Rapporteur regarding the PWP include:

- Coordinating with the PWP on the timeframe of the PWP one-month consultation periods which occur prior to Step *1* and *3* sign-off and which should be organised in consideration of the experts participating in the PWP (e.g. avoiding major national holidays), without unreasonably causing delays to the progress of the Guideline development;
- Collecting and managing the feedback from the PWP experts during the PWP consultation prior to *Step 1* and *3* sign-off.

2. ICH Process for Each Harmonisation Activity

This section provides an overview of the process for each harmonisation activity including the formal ICH procedure, the Q&A procedure, and the procedures for revision, maintenance, and error correction of ICH documents.

2.1. Formal ICH Procedure by EWG

The Formal ICH Procedure is a step-wise procedure that is used to develop a harmonised Guideline for implementation within each Member's region and consists of 5 steps. This procedure is used for new Guidelines and is initiated following the endorsement of a Concept Paper by the MC.

Each Member is responsible for following any internal processes that are required for that Member to provide their endorsement for, or adoption of, an ICH product. For example, the review of a final Guideline by a Member's legal counsel may need to occur before that Member can endorse the Guideline in the Assembly. To facilitate this process, a WG should aim to have a draft document prepared for internal review one month in advance of a face-to-face meeting. In the event that significant changes are made to a document during a biannual face-to-face meeting and the WG is requesting endorsement or adoption by the Assembly, a Member's internal approval procedure should be considered, and sufficient time be allowed for these processes. However, each Member should work to complete any additional internal approval during the course of the face-to-face meeting so as not to delay the decision of the Assembly, particularly in instances where adoption of a final Guideline is being requested.

For EWGs with associated PWPs, refer to section 1.7.2 for the additional activities of a PWP which should be integrated with the formal ICH Procedure.

2.1.1. *Step 1*: Consensus Building – Technical Document

In *Step 1* of the formal ICH Procedure, the EWG works together to prepare a consensus draft of the Technical Document based on the objectives set out in the Concept Paper. The Rapporteur prepares an initial draft of the Technical Document in consultation with the experts appointed to the EWG. The initial draft and successive revisions are discussed among the EWG and circulated with comments. Each Member with experts appointed to the EWG is responsible for providing any comments within the allotted timeframe.

To the extent possible, the EWG will work by e-mail and teleconferences. Face-to-face meetings of the EWG will normally only take place at the time and venue of the biannual Assembly meetings. Additionally, face-to-face meetings of the ICH EWG need to be agreed, in advance, by the MC.

The EWG should consult the MC if any issues arise during *Step 1* that could delay the timeline, or if there are any issues that may make it difficult for the EWG to reach consensus.

The EWG Regulatory Chair and Rapporteur will provide an interim report, representative of the Working Groups views, at each meeting of the Assembly. The interim report should provide an overview of the recent progress and accomplishments of the Working Group, planned next steps, and requests to the Assembly, if any (see template for report to the Assembly - available from the ICH Secretariat).

2.1.1.1. *Step 1 Experts Sign-Off*

When the EWG reaches consensus on the Technical Document, the ICH Secretariat will organise a *Step 1* Experts Sign-Off by the Topic Leaders of the EWG (see Annex 14). In the event that the Topic Leader is not present, the Deputy Topic Leader, Coordinator, or ICH Assembly Member representative may sign in place of the Topic Leader. The experts may provide their signature either through physical or electronic means according to the instructions provided by the ICH Secretariat. The consensus text approved by the ICH Members' experts in the EWG is signed-off by those experts as *Step 1 Technical Document*. Once all Members of the EWG sign-off on the Technical Document, the *Step 1 Technical Document* with expert signatures is submitted to the Assembly to request endorsement under *Step 2a* of the ICH process. After *Step 1* has been reached, the WG should provide, to the MC, an estimate of the length of time for the public consultation period in each region.

In exceptional circumstances where the EWG cannot come to full consensus on all aspects of the Technical Document, the Regulatory Chair with support of the Rapporteur will provide a report to the MC indicating the extent of agreement reached and highlight points where there are differences among Members. Experts from all ICH Members represented on the EWG will have the opportunity to explain their position to the MC.

The Regulatory Chair, with support of the Rapporteur, will propose a potential resolution to the MC (such as preparing a Technical Document that includes the different alternatives which are supported by the experts or minority opinions).

The MC may then:

- Allow an extension of the timetable, on the basis that the EWG can give assurances that consensus could be reached within a short, specified period;
- Request the EWG to develop a Technical Document, intended to inform further MC discussion and decision making, that identifies and analyzes different alternatives reflecting those positions which are supported by a minority as well as those supported by the majority of EWG experts;
- Provide guidance to the EWG/IWG to proceed with a certain course of action or elevate the decision to the Assembly; or
- Decide to recommend to the Assembly to suspend or abandon the harmonisation project and disband the EWG/IWG.

If consensus is reached following work under the extended timetable or further analysis of alternatives, then the EWG will proceed with the *Step 1 Experts Sign-off*.

2.1.2. *Step 2a*: Confirmation of consensus on the Technical Document

In *Step 2a*, the MC will provide a recommendation to the Assembly on the decision to endorse the final Technical Document, based on the report of the EWG that there is sufficient scientific consensus on the technical issues for the Technical Document and recommendation to proceed to the next stage of regulatory consultation.

The consensus text is endorsed by the Assembly as a *Step 2a Final Technical Document* either during a face-to-face meeting or through a written approval procedure that is organised by the ICH Secretariat. Ideally, an EWG would provide the Technical Document one month in advance of a face-to-face meeting where endorsement will be requested; however, an advanced draft may also be provided, with a revised version submitted closer to the meeting, or during the meeting, if necessary. Edits to the new version should be tracked so that any revisions can be clearly identified.

Irrespective of whether or not an Assembly Member has appointed technical experts in a Working Group, all Members will be invited to endorse *Step 2a* as ICH Members.

In the unlikely situation where consensus cannot be reached, the Assembly will proceed to voting where a decision to endorse the *Step 2a* Final Technical Document will be adopted by majority. If the majority votes to endorse *Step 2a* then the Assembly's endorsement will be captured in the Assembly Meeting Minutes. Refer to the ICH Rules of Procedure of the Assembly section 3.6 for a more detailed discussion of the Assembly decision making process.

2.1.3. *Step 2* for Testing (Optional)

Step 2 for Testing is an optional step where the proposed Implementation Guide, standard, or specification is tested by an ICH Member against the ICH requirements (e.g. business, technical, system and functional requirements) to confirm technical adequacy. An Observer may also participate in the testing; however, this is not required. The ICH Secretariat will publish a consensus document on the ICH website for review of the proposed implementation guide, standard, or specification by the public. The document will only be published in English and it will not be required to be translated by ICH into other languages. Testing is intended to be conducted by the ICH regions, however, comments will be considered from external parties. *Step 2* for Testing may be repeated if considered necessary. The duration of *Step 2* for Testing is flexible and may be set based upon the timescale allowed by the project of concern (e.g. Standards Development Organisation (SDO) ballot timelines or target for ICH *Step 2).*

Step 2 for Testing is particularly relevant to an EWG that develops an ICH Implementation Guide as part of an SDO project where the ICH Step Process is aligned with SDO processes. *Step 2* for Testing is conducted to assess technical feasibility of proposed SDO solutions prior to ICH *Step 2* because there is a greater ability to influence the degree of modification of technical solutions at this stage of development rather than at later stages.

Step 2 for Testing is distinguished from general feasibility testing in the sense that feasibility testing can be conducted at any time during the development of a technical standard in an informal way.

2.1.4. *Step 2b*: Adoption of the Draft Guideline

On the basis of the Final Technical Document, the ICH Regulatory Members will take the actions they deem necessary to develop the "draft Guideline". The consensus text of the draft Guideline is endorsed by the Regulatory Members of the ICH Assembly as *Step 2b* Draft Guideline either during a face-to-face meeting or through a written approval procedure that is organised by the ICH Secretariat.

Each ICH Regulatory Member will be invited to endorse the *Step 2b* Guideline as an ICH Member irrespective of whether or not that Member has appointed technical experts to the WG.

In the unlikely situation where consensus cannot be reached, the Regulatory Members of the Assembly will proceed to voting where a decision to endorse the *Step 2b* draft Guideline will be adopted by majority. If the majority votes to endorse *Step 2b*, then the Assembly's endorsement will be captured in the Assembly Meeting Report. Refer to the ICH Rules of Procedure of the Assembly Section 3.6 for a more detailed discussion of the Assembly decision making process.

The draft Guideline will be made public on the ICH website after *Step 2* is reached.

2.1.5. *Step 3*: Regulatory Consultation and Discussion

Step 3 is divided into three phases including i) regional consultation, ii) discussion of regional comments, and iii) *Step 3* Experts Sign-Off by the regulatory experts.

Regional regulatory consultation

At this step, the *Step 2b* draft Guideline leaves the ICH process and becomes the subject of normal wide-ranging regulatory consultation in each of the Member's regions. For example, for EC, Europe it is published as a draft CHMP Guideline, in Japan it is translated and issued by MHLW/PMDA, Japan for internal and external consultation and in the USA it is published as draft guidance in the Federal Register with a request for public comment. Swissmedic, Switzerland refers input to the EU consultation and Health Canada, Canada solicits its own public comments on draft ICH Guidelines.

Each region's public consultation period may range from 30 days up to 6 months for more technical Guidelines, or longer than 6 months when the circumstances warrant it. Prior to entering *Step 2b*, each Member should report the planned length of their consultation period to the WG and the ICH Secretariat.

Following the close of all the regional comment periods, the Regulatory Members review and exchange information on the comments they have received from the public in the various regions, and consider what further revisions to the *Step 2b* draft Guideline might be needed in order to arrive at a single, harmonised Guideline. There is also an opportunity for Industry Associations and Regulatory Authorities in other regions to comment on the draft consultation documents, which are published by the ICH Secretariat on the ICH website.

Discussion of regional consultation comments

After obtaining all regulatory consultation results, the EWG that organised the discussion for consensus building will be resumed – including both Industry and Regulatory expert representatives. If the Rapporteur was designated from an Industry Member until *Step 2b*, then a new Rapporteur will be appointed from a Regulatory Member and approved by the Assembly following Step 2b. The same procedure described in Step 1 is used to address the consultation results. Although an Industry Member cannot serve as a Rapporteur following Step 2b of the Formal ICH Process, Industry Members are expected to continue to participate in the WG until a final harmonised Guideline is developed. The draft document to be generated as a result of the *Step 3* phase is called *Step 3 Experts Draft Guideline*.

Finalisation of Step 3 Experts Draft Guideline

If the experts from the ICH Regulatory Members reach consensus on a revised version of the *Step 2b* Final Draft Guideline after consideration of the consultation results, the ICH Secretariat will organise a *Step 3* sign-off (see Annex 15). The *Step 3 Experts Draft Guideline* is signed by the EWG experts of the ICH Regulatory Members either through a physical signature or electronic means according to the instructions provided by the ICH Secretariat. The *Step 3* Document with regulatory EWG signatures is submitted to the Assembly to request adoption at *Step 4* of the ICH process.

This *Step 3* Document with regulatory EWG signatures is named *Step 3 Draft Guideline*, and this sign-off is called the *Step 3 Experts Sign-off*. In the event that an EWG reaches consensus on a revised version of the *Step 2b* Final Draft Guideline between ICH biannual meetings, the ICH Secretariat will organize a postal (electronic) sign-off at the expert level. For these WGs who will not be attending the next biannual face-to-face meeting of the ICH Assembly, the electronic sign-off should be completed at least 2 weeks before an Assembly meeting, to ensure the Guideline can be adopted by the Assembly at the next meeting. If the sign-off is not completed ahead of the Assembly meeting, it is likely that the adoption of the Guideline will be done electronically after the ICH Assembly meeting.

Where complete consensus has not been achieved within the agreed time frame, the Regulatory Chair in support of the Rapporteur will make a report to the Regulatory Members of the MC indicating the extent of agreement reached and highlighting the points on which differences between the parties remain. Experts from all ICH Members represented on the EWG will have the opportunity to explain their position to the Regulatory Members of the MC. The Regulatory Members of the MC may then:

- Allow an extension of the time frame, if the EWG can give assurances that consensus could be reached within a short, specified period;
- Decide to recommend to the Regulatory Members of the ICH Assembly to abandon the current draft and resume the discussion from *Step 1*; or
- Decide to recommend to the Regulatory Members of the ICH Assembly to suspend or abandon the harmonisation project and to disband the EWG.

2.1.6. *Step 4*: Adoption of an ICH Harmonised Guideline

In *Step 4* of the ICH process, the Regulatory Members of the Assembly adopt a harmonised Guideline in consultation with the MC. This adoption is based on a recommendation by the MC and the consensus of the ICH Assembly Regulatory Members affirming that the Guideline is recommended for adoption by the Regulatory Members of the ICH regions. Ideally, the Guideline should be provided to the Assembly one month in advance of a face-to-face meeting where adoption will be requested, however, an advanced draft may also be provided, with a revised version, with changes clearly tracked, submitted closer to the meeting, or during the meeting, if necessary. In exceptional cases when Assembly consensus cannot be achieved, the Assembly will proceed to voting where a decision will be adopted by majority. Please refer to the ICH Rules of Procedure of the Assembly section 3.6 for a more detailed discussion of the Assembly decision making process.

2.1.7. *Step 5*: Implementation

Once *Step 4* is reached, the harmonised Guideline moves to the final step of the process and is implemented by each of the Regulatory Members in their respective regions. The harmonised

Guideline is implemented according to the same national/regional procedures that apply to other regional, scientific or regulatory Guidelines and requirements, as for example, in the EU, Japan, USA, Canada, and Switzerland.

Information on the regulatory action taken and implementation dates are reported back to the Assembly and are published by the ICH Secretariat on the ICH website.

2.2. Q&A Procedure by Implementation Working Group

The Q&A Procedure is followed when additional guidance is considered necessary to help with interpretation of a Guideline and ensure consistent implementation in the ICH regions. A need for additional guidance is generally identified when a large number of questions are received during the *Step 5* phase (regional implementation) after the Guideline has been finalised by the ICH. The Q&A process is intended to be a mechanism by which questions received from stakeholders are collected, analyzed, reformulated, and ultimately used as model questions for which standard answers are developed and posted on the ICH website. Incoming questions will not be answered individually but will serve to highlight areas that need additional clarification and will be used to develop a model question that will be answered in the Q&A document.

A Q&A document should only be developed following completion of a Guideline; however, in the course of Guideline development it may become apparent to an EWG that a Q&A will be necessary. In that event, an EWG may recommend to the Assembly that a Q&A be developed immediately following finalization of a Guideline.

2.2.1. Process for Q&A Development

The Assembly, in consultation with the MC, will need to endorse all Q&A activities. Proposals for development of a Q&A should be submitted by completing a new topic proposal template and following the process outlined in section 1.1.1 Topic Nomination and Review of this EWG/IWG SOP. The MC will review all Q&A recommendations following the same procedure that is used for the review of new topic proposals and provide a recommendation to the Assembly on the decision to endorse the development of a Q&A document.

Once the Assembly has endorsed the development of a Q&A document, an informal WG should be established to develop a Concept Paper. The same process applies for the establishment of an informal WG and review of a Concept Paper as in section 1.2 - Establishment of an informal Working Group and section 1.3 - Developing a Concept Paper for a Selected Topic, respectively, of this EWG/IWG SOP. Once a Concept Paper is endorsed by the Assembly, an Implementation Working Group (IWG) should be established to develop the Q&A according to section 1.5 Establishment of the EWG/IWG of this SOP. The Formal ICH Procedure outlined in section 2.1 of this SOP applies to the development of a Q&A document. For IWGs with associated PWPs, refer to section 1.7.2 for the additional activities of a PWP which should be integrated with the Formal ICH Procedure as applicable with the process described below.

The MC will be responsible for overseeing the operations of the IWG and resolving any obstacles that may arise or elevating decisions to the Assembly when necessary. A Business Plan is not required for all Q&A documents however, for major implementation activities it is recommended that the MC consider whether a Business Plan should be required.

When an IWG is established, the ICH Secretariat will create a mailbox for the IWG that will be accessible through the public ICH website. Any questions sent to the mailbox, or raised by any of the ICH Members, and/or by the ICH Observers, will be brought to the attention of the appropriate Working Group. The regional questions and issues should first be handled by the Regulatory Member of the concerned region then shared and evaluated within the IWG, if applicable. Once the IWG has completed its work, the mailbox for that IWG will be deactivated.

The IWG Rapporteur in collaboration with the Regulatory Chair will send the questions to the members of his or her IWG. Based on this information, the IWG will prepare model questions and their responses for presentation at the Assembly meeting. An answer developed in response to a question must fall within the original scope of the Guideline, the answer cannot introduce new issues that were not previously discussed in the harmonised Guideline.

Based on the level of guidance given by the answers, the IWG will assess whether the Q&A document should proceed to *Step 2b* and then be published for comments or if it should be signed off by the regulatory experts at *Step 3* and submitted to the Regulatory Members of the Assembly for adoption at *Step 4* and published as final.

- The document should go through public consultation and proceed to *Step 2b* if, by the answers provided, it sets forth substantial new interpretations of the Guideline(s).
- The document should not go through public consultation and proceed to *Step 3* sign-off if, by the answers provided, it sets forth existing practices or minor changes in the interpretation or policy of the Guideline(s).

The IWG will provide its recommendation on the decision to go through public consultation to the ICH MC. The MC may in some circumstances where the Q&A document is of policy significance, elevate the decision for Assembly endorsement.

The Assembly will need to endorse the Q&A document and its (Step) status either through written procedure or during a meeting of the Assembly. The document will then follow the normal path of a *Step 2b / Step 4* document as follows:

- For documents going through public consultation: Following agreement on the technical content of the Q&A through sign-off by the experts of the IWG as *Step 1* and the endorsement of the ICH Members of the Assembly at *Step 2a*, the IWG will proceed to *Step 2b*. In *Step 2b*, the Regulatory Members of the Assembly will endorse the Q&A document at *Step 2b*. The document will then be published for comments in the ICH regions.
- For documents that will not go through public consultation: Following agreement of the technical content of the Q&A within the IWG, the Regulatory experts of the IWG will sign the Q&A document as a *Step 3* Final Document and then the Regulatory Assembly Members will be invited to adopt it as final at *Step 4*.

The Final Q&A document will be posted on the ICH website within four weeks after it has been endorsed by the Assembly.

If an IWG is working on several answers in a single Q&A document and it becomes apparent that some of the answers may require considerably more time than others, an IWG may decide, with MC approval, to publish the answers sequentially in batches so that some of the answers will be more

readily available while the remaining answers are further deliberated. The IWG will assess, and obtain Assembly adoption at *Step 4*, for each batch of questions published.

2.3. Revision Procedure

The revision procedure is used when the scientific/technical content of an adopted Guideline is no longer up-to-date or valid and needs to be revised or modified. Additionally, the revision procedure can be used in cases when there is new information to be added to an existing Guideline. The formal ICH Step Process in section 2.1 of this EWG/IWG SOP should be followed for all revision activities in conjunction with the process outlined below.

The Assembly, in consultation with the MC, will need to endorse all revision activities. Proposals for the revision of a Guideline should be submitted by completing a new topic proposal template (see Annex 8) and following the process outlined in section 1.1 - Selection of New Topics of this SOP. The MC will review all Guideline revision proposals following this process and provide a recommendation to the Assembly on the decision to endorse the revision of an ICH Guideline.

If the Assembly endorses the revision of an existing Guideline on the basis of a Concept Paper outline, an informal Working Group should be established to develop the final Concept Paper and Business Plan. The same process applies for the establishment of an informal Working Group and review of a Concept Paper and Business Plan as in section 1.2 - Establishment of an informal Working Group, section 1.3 - Developing a Concept Paper for a Selected Topic, and 1.4 Business Plan respectively, of this EWG/IWG SOP. Once the Final Concept Paper is endorsed by the MC, an Expert Working Group (EWG) should be established to revise the Guideline in accordance with section 1.5 Establishment of the EWG/IWG of this SOP. The MC will be responsible for overseeing the operations of the EWG and resolving any obstacles that may arise or elevating decisions to the Assembly when necessary.

If an adopted Guideline needs to be revised, then the formal ICH Step process should take place. However, if minor errors are discovered following implementation of a Guideline or if it becomes apparent that the use of certain terminology is causing misinterpretation of a Guideline, the EWG who developed the original Guideline may be reconvened to discuss any necessary revisions. The EWG will work with the Coordinators and MC to determine if the proposed revisions warrant the ICH formal Step Process.

There are two approaches for revision of an existing ICH Guideline:

- The first approach involves amendments being made directly to the content of the existing Guideline e.g., in cases where the scientific/technical content is no longer up-to-date or valid.
- The second approach is where the existing text in the original Guideline is not modified, but instead an Addendum or Annex to that Guideline is developed. The latter approach is used where no amendments to the content of the existing Guideline are necessary but there is a need to provide further complementary guidance.

In addition, there are two types of addenda: 1) an Addendum, and 2) an Integrated Addendum. For an Addendum, the additional or new text is added at the end of the current ICH Guideline. In contrast, an Integrated Addendum is developed when the purpose of the Addendum is to clarify or augment specific section(s) of an ICH Guideline and text is inserted right after the relevant paragraph(s) within the original Guideline. Additionally, integration of the Addendum text into the original Guideline

should be used to avoid many cross references and for easier reading of the Guideline. The clarifying content added after specific sections of the Guideline should be formatted in a specific way to facilitate its distinction from the original text by the reader. The format of the Addendum (i.e. which of the two types just described) should be recommended in the Concept Paper.

The "Revision Procedure" is almost identical to the formal ICH procedure, i.e., five ICH steps. The only difference, compared to the ICH formal Step Process, is the final outcome. For a Guideline revision, the final outcome will be a revised version of a currently existing Guideline, whereas in the formal Step Process, the final outcome is a new Guideline.

In cases where an Addendum or Annex has been developed, upon reaching *Step 4,* the Addendum or Annex is added to the existing Guideline resulting in a revised Guideline.

The revision of a Guideline is designated by the letter R1 after the usual denomination of the Guideline. When a Guideline is revised more than once either through amendment to the original text or by addition of an addendum, the document will be named R2, R3, R4, (etc.) at each new revision.

If in the creation of a Q&A document it becomes apparent that a revision to the original Guideline is necessary, an EWG may provide a recommendation to the Assembly in consultation with the MC to establish an informal Working Group to discuss the type of modifications needed and develop a Concept Paper. To increase efficiency, the same members as those forming the IWG may develop both the Q&A document and revise the ICH Guideline.

In the case of Q4B, topic-specific Annexes are developed to provide information on how pharmacopoeial texts can be used at a national/regional level. Each Annex is issued as a stand-alone companion document to the Q4B Guideline, with each Annex assigned a number in sequential order e.g., Annex 1, Annex 2, Annex 3 etc. (see Q4B maintenance procedure in Annex 5).

2.4. Maintenance Procedure

This procedure specifically applies to the Q3C Guideline (residual solvents), Q3D Guideline (elemental impurities), Q4B Annexes, M7 (genotoxic impurities) and M2 Recommendations (see Annex 4).

Updates to the Q3C, Q3D, and M7 Guidelines (Parent Guideline or Addenda) and the Q4B Annexes are considered as revisions and are designated by the letter R.

M2 Recommendations constitute an exceptional case, because no *Step 2b* Document is required. However, the MC may request further clarification. In such cases, a *Step 2b* document may be necessary. Each new version of the M2 Recommendations is designated by a different version number.

The Maintenance Procedure also extends to any ICH Guideline which contains out-of-date information (e.g., out-of-date references, links etc…) which can be updated by the ICH Secretariat without the establishment of an EWG. Such updates require MC approval and are also considered revisions and assigned the letter R.

2.5. Error Correction

The ICH Secretariat may correct obvious typographical errors. In this case, no approval from the MC is required.

In some cases where more substantial corrections are needed (e.g., editorial mistakes, errors/inaccuracies), a technical expert discussion may be necessary. This case would therefore undergo the Revision Procedure.

All editorial mistakes (i.e., changes in the wording, the grammar in order to keep with consistency and clarity) and errors/inaccuracies (i.e., wrong meaning needing correction), even if minor, should be corrected by the WG and require approval by the MC and should be communicated to the Assembly.

Table 3 provides more details on the approval process for the correction of errors.

Table 3 Summary of Error Correction Procedure

Type of Error Correction	ICH Secretariat	Topic leaders from WG	Coordinators	MC	Assembly
Post sign-off and prior to publication of Guidelines/materials	Correction of minor typographical errors and other minor editorial changes				
Substantial corrections (e.g. editorial mistakes, errors/inaccuracies)		Approval	Approval	Informed	Informed
Prior and post to publication of materials (training materials and support documents, etc)		Approval	Informed	Informed	Informed
After publication of a Guideline		Approval	Informed	Approval	Informed
After publication of a Guideline	Correction of minor typographical errors and other minor editorial changes		Informed		

2.6. Guideline Withdrawal

Under exceptional circumstances an ICH Guideline may be withdrawn. Such actions require substantial justification and endorsement by the ICH Assembly in consultation with the MC.

3. Additional Activities during the Course of ICH Harmonisation

During the course of the ICH harmonisation activities outlined in the previous sections, the Management Committee (MC) or Assembly, as appropriate, may authorize a Working Group (WG) to carry out other tasks intended to provide additional information complementary to a topic that is undergoing one of the above categories of harmonisation. These activities are outlined below and include development of an Options Paper, a Points to Consider document, a Proof of Concept, or an Implementation Package.

3.1. Options paper

An Options Paper is used when experts on a WG have differing viewpoints and cannot come to consensus on how to proceed with a harmonisation activity. The Regulatory Chair should facilitate development of an Options Paper following a request from the MC. The Options Paper should clearly articulate the differing views of the Member's experts of the WG, and the advantages and disadvantages of proceeding with the proposed options. The MC will use the Options Paper to provide a recommendation to the Assembly on how to best proceed for a given harmonisation activity. All experts should sign-off on the Options Paper however, further endorsement is not necessary.

3.2. Points to Consider

A Points to Consider (PtC) document may be developed to provide additional clarity on an ICH document and/or to develop best practices following finalization of a Guideline. When proposing a new PtC document, a Concept Paper outline should be submitted to the ICH Assembly for approval. The Final Concept Paper should be submitted to the MC for approval. The PtC documents are not subject to regional implementation, but provide a best practice approach. The final document will need to be signed-off by the experts who developed the document and endorsed by the Assembly.

3.3. Proof of Concept

A Proof of Concept (POC) is used to test the viability of a specification during Guideline development such as enabling the transfer of regulatory information by electronic means. In the case of M2/M5/E2B(R3), the POC concerns testing the viability of using M2's message specifications to exchange information. A WG should request endorsement from the ICH MC before initiating any POC activities.

3.4. Implementation Package

An Implementation Package may be developed following adoption of a Guideline to provide instruction on how a Guideline should be implemented (e.g. how to use a particular standard). The same Expert WG that developed the Guideline should be maintained or reconvened to develop the

Implementation Package. The Implementation Package should include an Implementation Guide as the core document and this should describe how the standard will be implemented to meet ICH requirements. The Implementation Package should also include any associated technical files such as technical data standards, controlled vocabularies for field usage, or additional supporting documentation (e.g. orientation materials) needed to fully implement a particular standard.

Development of the Implementation Package should follow the formal Step Process outlined in section 2.1 Formal ICH Procedure by EWG of this SOP. Following completion of the Implementation Package, an Implementation Working Group may be established to maintain the standard and to address change requests.

Annex 1: Roles and Responsibilities

This Annex provides an overview of the roles and responsibilities of the ICH Management Committee (MC), Assembly, Coordinators, Technical Coordinators, and Observers in the context of the ICH Working Groups.

I. ICH Management Committee

The ICH MC is responsible for oversight of the Working Group (WG) process and operations to ensure the efficiency and timeliness of ICH Guideline completion and quality. The MC appoints a Regulatory Chair to each WG from one of the Regulatory MC Members represented on the WG. Additionally, the MC manages the size of a WG appropriately and reserves the decision to allow additional Members to join a WG. The MC is also responsible for approving final Concept Papers and Business Plans created in alignment with an Assembly approved Concept Paper outline.

The MC is responsible for submitting recommendations and proposals to the ICH Assembly for new topics and decisions on the endorsement of an ICH document at its step status. Additionally, the MC makes a recommendation to the Assembly on the adoption of final Guidelines, revisions to existing Guidelines, or withdrawal of a Guideline. The MC serves as a conduit between the EWGs/IWGs and the ICH Assembly. The MC should to the extent possible work with each WG to resolve any discrepancies or issues that may interfere with the harmonisation process. In instances when an issue cannot be resolved, the MC should elevate the decision to the ICH Assembly. For more information on the roles and responsibilities of the ICH MC refer to the ICH Rules of Procedure of the Assembly and the ICH Rules of Procedure for the Management Committee.

II. ICH Assembly

The ICH Assembly has the responsibility for approving new topics for ICH Guidelines and adoption, amendment or withdrawal of ICH Guidelines. Additionally, the Assembly will endorse each Guideline at its step status as follows:

- The Assembly will endorse the final Technical Document at *Step 2a*;
- The Regulatory Members of the Assembly will endorse the draft Guideline at *Step 2b*;
- The Regulatory Members of the Assembly will adopt the final harmonised Guideline at *Step 4*.

Each WG that attends a biannual face-to-face meeting will provide a report to the Assembly and update the Assembly on the status of the WG and provide any requests for endorsement or adoption of an ICH document as appropriate. Assembly endorsement at *Step 2* and adoption at *Step 4* may occur either through an electronic process or during a face-to-face meeting of the Assembly. However, if consensus cannot be reached when an electronic process is used, the matter should be postponed for decision to the next face-to-face Assembly meeting. Additionally, the Assembly will endorse a Concept Paper outline developed to support a new topic proposal during face-to-face meetings. For more information on the roles and responsibilities of the ICH Assembly refer to the ICH Rules of Procedure of the Assembly.

III. ICH Coordinators[5]

ICH Coordinators are designated by ICH Members and play a fundamental role in the efficient operations of the ICH Association. The role of a Coordinator is to act as the main point of contact with the ICH Secretariat and to ensure that ICH documents are distributed to the appropriate persons within their respective organisation. The Coordinator also serves as a point of contact for communication to the experts within their own organisation. Furthermore, an ICH Coordinator of a Member who is on the MC may support their respective MC Members in a subcommittee. The following lists specific responsibilities of the Coordinator and their role as a liaison, for teleconferences, and for biannual face-to-face meetings.

1) Liaison among experts, the Management Committee, and the ICH Secretariat[6]

The ICH Coordinator is the central point of contact and liaison among experts, the Management Committee if relevant, and the ICH Secretariat. The ICH coordinator serves in the following capacity:

- The main point of contact between their respective organisation's experts and the ICH Secretariat
- The initial point of contact between the Regulatory Chair/Rapporteur of its Member and the MC when there is an issue to be raised
- Conveying comments and requests from experts to the ICH Secretariat and MC as appropriate
- Notifying the ICH Secretariat of any change in membership of its organisation
- Ensuring proper distribution of ICH information, documents, and actions to the appropriate individuals from their Member delegation (MC Members, Topic Leaders, Experts, and any other representatives) within the area of their responsibility.

2) Tele/web conferences

a. <u>Before a teleconference or web conference the ICH Coordinator should:</u>
   - Notify the ICH Secretariat of any issues or topics to be discussed.
   - Consult with relevant experts on various topics and issues for discussion in order to be prepared to convey information as appropriate during the tele/web conference.

b. <u>During a teleconference or web conference the ICH Coordinator may:</u>
   - Give an oral report on the status and/or Member's position on an issue or topic under discussion as appropriate.
   - Take notes on actions for the responsible topics (e.g. if Co-Rapporteurs are designated from two Members, Coordinators from both Members will take responsibility for actions).

c. <u>After a teleconference or web conference the ICH Coordinators should:</u>
   - Review and comment on the draft report of the tele/web conference circulated by ICH Secretariat respecting the designated deadline.

[5] If an Assembly Member is not on the MC, the Coordinator for that Member will not be involved in matters related to the MC.

- Ensure proper follow up on actions by their respective Member within assigned deadlines.

3) Face-to-face Meetings

a. Before a face-to-face meeting the ICH Coordinators should:
   - Notify the ICH Secretariat about items/issues/topics for inclusion in the MC or Assembly Agenda, at least one month prior to the meeting whenever possible.
   - Distribute meeting announcements to representatives of their respective Member.
   - Verify, discuss, and distribute the meeting schedules to all representatives concerned, and comment on the draft schedule as appropriate.
   - Provide the name(s) of nominated representatives for their Member (Topic Leader, Deputy Topic Leader, experts, etc.) for each topic under discussion
   - Check the preliminary draft agendas (MC meeting, Assembly, Coordinators meeting, ICG or Regulators meeting as appropriate).

b. During a face-to-face meeting the ICH Coordinators should:
   - Ensure that relevant information is conveyed to the expert of their region.
   - Help the ICH Secretariat in the preparation of the draft provisional minutes of the meeting as needed (i.e., by providing notes, suggestions, comments and specific wording, in a continuous way during the meeting).
   - Confirm the list of actions endorsed on each topic and subject.

c. After a face-to-face meeting the ICH Coordinators should:
   - Ensure appropriate follow-up on every subject according to the list of actions endorsed.
   - Review the provisional report of the meeting distributed by the ICH Secretariat after the meeting, and coordinate comments from their Member (collect and consolidate comments from their respective representatives as appropriate) respecting the designated deadline.

IV. ICH Technical Coordinators

An ICH Technical Coordinator may be designated by an ICH Founding Regulatory Member as they are required to appoint experts in all WGs. ICH Technical Coordinators support their Assembly/MC representative and Coordinator in Guideline harmonisation activities, mainly by applying their scientific knowledge.

Examples of the types of functions a technical coordinator would perform include the following:

- Facilitating identification of new topic proposals from their respective organisation.
- Assisting in identification of appropriate expert representatives from their Member for a WG.
- Liaising with experts during the MC and Assembly meetings and communicating as necessary to the MC representative of his or her Member organisation.
- Ensuring that draft Guidelines are reviewed for compliance with their regional regulations prior to endorsement in the Assembly.
- Ensuring experts reflect the views and policies of the Member they represent.
- Reviewing the Guidelines and comments during discussion in ICH and before publication.

V. ICH Observer

An ICH Observer may submit a request to appoint an Observer expert to a Working Group (WG) using the template provided in Annex 12 for approval of the MC. The ICH Secretariat will provide the MC with any applications received. In the request, the Observer should include an explanation of their interest, information about their available expertise, and how they expect to contribute to the work of the WG. An Observer would need to submit a separate request for each WG that it is requesting to nominate an expert. The ability for an Observer to participate in a WG is based on the favorable decision of the MC.

If the MC agrees that an Observer may appoint an Observer expert to a WG, the Observer may appoint only one Observer expert to actively participate in the WG; however, an alternate Observer expert may also be named. The alternate Observer expert may be copied on emails and may listen during teleconferences of the WG but would not participate in the discussion. In the event that the Observer expert cannot participate in the WG, the alternate Observer expert would replace the Observer expert. The Observer should provide the contact information of any experts who will be participating in a WG to the ICH Secretariat. This information will be provided to the Regulatory Chair and Rapporteur of the relevant ICH WG. For the purposes of continuity, the same nominated expert should participate for the duration of the WG. If their participation cannot be sustained and the Observer needs to replace the originally appointed expert, it is the responsibility of the departing Observer expert to fully brief the new Observer expert on the status of the WG and progress to date.

Observer experts participating in WGs retain Observer status and thus do not opine on WG decisions. Observer experts would be expected to attend the WG meetings and participate in the discussion when they are able to contribute new information on scientific technical content. While thus contributing to the technical discussion of the WG however, the Observer expert's views are not considered for the consensus (e.g. they cannot preclude consensus) when decisions are made. Based on the understanding that the Observer expert is joining the WG with technical expertise in the Guideline topic it is further expected that the expert would not request the WG to explain concepts under discussion or to revisit issues that have been previously decided on. With that said, the Observer expert may seek clarification outside of the WG meetings if necessary. Observer experts participating in the WG will be invited to sign off the *Step 1* Technical Document and as regards Observer experts representing a regulator also the *Step 3* ICH draft Guideline. This sign-off will be on a voluntary basis; because Observers do not vote on key decisions the absence of a signature from an Observer will not lead to the suspension of a Guideline. Furthermore, the absence of an Observer from a WG meeting would not prevent a quorum from being established and would not prevent a WG meeting from taking place.

Annex 2: Ground Rules for Good Practices of ICH Working Groups

I. Conduct of Meetings

1) Materials to be presented at a meeting should be distributed a minimum of 24 hours prior to the meeting, if feasible and appropriate.

2) Meetings should be conducted in the most efficient manner possible. All participants will act in a respectful and professional manner. Excessive posturing by any Member should be avoided.

3) All positions taken during meetings should be based on facts, to the extent possible, and justifications either for or against provisions will be as fact-based as possible, recognizing that reasonable hypothetical solutions may be considered.

4) Although not required, it is considered a good practice to develop meeting minutes that summarize key topics of discussion, including substantive proposals, as well as any significant controversies or differences of opinion, and their resolution. These minutes should be shared with all Members of the Working Group (WG) following the meeting.

5) At the end of each meeting, the WG should develop a plan for next steps.

6) The ICH Secretariat will conduct the initial call for nomination of WG experts; however, the Rapporteur should track attendance of experts for each meeting of the WG.

7) The Rapporteur may wish to obtain support from a Rapporteur Supporter. The Rapporteur Supporter would not contribute subject matter expertise to the discussion but would function to assist in organisation of the EWG/IWG (coordination of meetings, agenda development, capture agreements and outcomes of EWG/IWG discussions, etc.) under the direction of the Rapporteur.

8) The Regulatory Chair should ensure that the opinions of all Members are expressed and that the discussion remains in scope of the approved Concept Paper and in line with the Business Plan.

II. Participation

9) The presence of at least one expert representative from each Founding Regulatory Member and if nominated, one expert from each Founding Industry Member and, if nominated, one expert from each Standing Regulatory Member is required to constitute a quorum for a WG meeting (section 4.4 of the Rules of Procedures of the Assembly).

10) All Regulatory and Industry Members as well as Observers who have appointed experts to a WG are expected to actively participate in and contribute to the work of the WG on a continuous and regular basis until the work is completed to ensure continuity. If the appointed expert is absent from two consecutive meetings and is unable to resume participation in WG meetings, the Member/Observer should appoint another qualified expert to replace the original member. Experts should be replaced only in exceptional circumstances and should be minimized to the extent possible.

11) In the event that an expert is replaced, the original member has the responsibility to provide all relevant background information to the new expert to orient the new expert to the WG's work to date. This includes history on discussions and agreements of the EWG/IWG. The new expert should have the expertise needed to actively contribute to the EWG/IWG.

12) If an expert of an EWG/IWG has been absent for a significant number (e.g. two or more) of the Working Group meetings either face-to-face or via teleconference, the Regulatory Chair or Rapporteur should inform the ICH secretariat. The ICH secretariat should then inform the Coordinator of the respective region. The ICH Coordinator should work with their respective

Assembly and/or MC Member representatives as appropriate to identify a solution (e.g., naming an alternate or replacement for their originally appointed expert(s)). In the event that a solution cannot be provided, the Regulatory Chair and Rapporteur should provide a report to the MC. The MC should seek an explanation from the Member/Observer whose representative has been absent and discuss a plan for addressing the gap.

13) A new member/expert to an EWG/IWG already in progress should not ask or expect the EWG/IWG to reconsider previous decisions made by the EWG/IWG prior to that expert's membership.

14) Actions or behaviors which seriously impair the proper functioning of the ICH WGs should be avoided. For example, engaging in political, nationalist, propagandist, private profit-oriented or other behavior which is extraneous and detrimental to the technical scientific scope and mission of ICH. This may also include intimidating behavior and other uncivil or disrespectful treatment of the ICH Secretariat or ICH Members, Observers, and their staff and expert representatives. It can also include seeking to exert pressure and undue influence on the ICH Secretariat, ICH Members or Observers by pursuing financial, political, diplomatic, or other channels outside of ICH.

Annex 3: Procedure for the Organisation of Working Group Interim Meetings

This procedure applies to exceptional Working Group (WG) interim face-to-face meetings outside of the regularly occurring biannual ICH meetings. In exceptional circumstances, a WG's interim meeting may be necessary for a WG to achieve its assigned work objectives or to facilitate efficiency of the harmonisation process. The arrangement of any WG interim face-to-face meeting will be subject to approval by the ICH MC.

1) Request to organise an interim meeting

If a WG is interested in holding an interim meeting, it can provide a request to the MC either during or between biannual face-to-face meetings. The request should include the reason for the meeting (including why a teleconference or web conference option would not serve the purpose and why there is a need to meet before the next biannual meeting), the anticipated accomplishments, a Business Plan, a proposed location, and a tentative date. If a WG proposes to hold a WG interim meeting, this must be discussed and agreed by the MC. The decision to hold an interim meeting is contingent on the ability to obtain a quorum to the meeting. A quorum consists of at least one expert representative from each Founding Regulatory Member and if nominated, one expert from each Founding Industry Member and, if nominated, one expert from each Standing Regulatory Member (section 4.4 of the Rules of Procedures of the Assembly). The Coordinators of a quorum should confirm the ability for their agency to attend the interim meeting within two weeks following the request to hold an interim meeting by the WG. Once the Coordinators confirm the ability for their agency to attend the interim meeting, the ICH Secretariat should solicit endorsement by the MC.

2) Meeting Organisation

The Rapporteur and Regulatory Chair, or MC/Assembly Member representative of the host region, and their respective Coordinator will work with the ICH Secretariat to organize the interim meeting. Once the MC endorses a WG's interim meeting, the Rapporteur, Regulatory Chair, and Coordinator of the hosting agency will identify a date by contacting all WG representatives and choosing a date in accordance with each participant's availability.

The location of the meeting will be arranged with the ICH Coordinators of the hosting region and the ICH Secretariat. The meeting venue is to be financed or hosted by either an ICH Industry or Regulatory Member of the host region. The financing Member should be directly involved in any planning/logistical decisions associated with the meeting that would have meeting cost implications. Each Member or expert will be responsible for funding the costs of travel, food, and accommodation for their individual experts.

Once a date and location have been determined, the ICH Secretariat will send out a request for nominations of experts to attend the interim meeting to each Member and Observer of the Working Group. Once the experts have been confirmed, a meeting confirmation will be sent to the WG experts with the meeting location and date.

3) Meeting Attendance

For meetings of a WG, a quorum is required at minimum in order for the interim meeting to occur. The same rules for meetings of the WGs, as outlined in section 4.4 of the Rules of Procedures of the Assembly, apply to WG interim meetings

4) Follow-up after the meeting

After the meeting, the WG will prepare a report that summarises the progress made, the achievements and conclusions reached, and the list of actions with clear deadlines and responsible individuals. Draft reports shall be circulated to all experts who attended the meeting for discussion and adoption. Approved reports should be sent by the Rapporteur of the WG, to the ICH Secretariat for circulation to the MC and Coordinators of the MC Members.

Annex 4: Maintenance Procedure for Q3C, Q3D, and M7

This Maintenance Procedure applies to revision of the Q3C Guideline for Residual Solvents, Q3D Guideline for Elemental Impurities, and M7 Addendum for the Assessment and Control of DNA Reactive (mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk. The procedure explains the process for revising the existing Guidelines as new solvents, metals or impurities are accepted or as new data becomes available. These changes include the following revisions for each Guideline:

- Q3C – Incorporation of Permitted Daily Exposure (PDE) for new solvents and revising the PDE for solvents already listed in Q3C as new toxicological data for solvents becomes available.
- Q3D - Incorporation of Permitted Daily Exposure (PDE) for new elemental impurities/routes of administration and revising the PDE for elemental impurities already listed in Q3D as new toxicological data for elemental impurities becomes available.
- M7 Addendum– Incorporation of acceptable limits (Acceptable Intakes (AIs) or PDEs) for new DNA reactive (mutagenic) impurities and revising acceptable limits for impurities already listed in the Addendum as new data becomes available.

Data and/or proposals pertaining to the revision of the Q3C, Q3D, or M7 Guidelines with supporting information can be submitted directly to the ICH Secretariat from either an ICH Member or Observer or other interested ICH stakeholders.

Information provided within a proposal should be based on significant toxicity data from studies such as repeat-dose studies, reproductive toxicity studies, genotoxicity studies, and carcinogenicity studies and/or other relevant studies. Single-dose toxicity data alone are not sufficient. The toxicity data should be of sufficient quality to calculate a PDE or AI. Genotoxicity and carcinogenicity data are of primary importance for revisions to the M7 Guideline.

An Expert Working Group (EWG) will evaluate any proposals received. The membership of an EWG will generally not change however, the same procedure applies for establishment of an EWG/IWG as outlined in section 1.5.1 – EWG/IWG Membership of this SOP. As appropriate, an ICH Observer may submit a request to the Assembly to nominate an Observer expert to the EWG.

The Rapporteur should be a Founding Regulatory Member and will serve a two-year term. The role of the Rapporteur for each working group will rotate every two years to a new Founding Regulatory Member. The ICH Assembly will be notified following each rotation of the Rapporteur. Proposals will be evaluated once every 2 years following rotation of the Rapporteur. The ICH Secretariat will share any proposals received with the new Rapporteur and ICH Coordinators. The Rapporteur will facilitate the review of any proposals received by the EWG and the EWG will make a recommendation on whether the proposal should be supported by the Management Committee (MC).

If a proposal for maintenance is supported by an EWG, the EWG should submit a revised work plan to the MC to outline this work. The MC will then provide a recommendation to the Assembly for approval on whether the EWG should be tasked with making the revision.

A revision will be considered only on presentation of new data or previously un-recognised toxicity data sufficient to result in a significant change, or because of convincing evidence that the existing data used to calculate a PDE are invalid. Minor changes in a PDE will not be considered. The Regulatory

Chair (or in the absence of a Regulatory Chair, the Rapporteur) with the consensus of the EWG members, will assign data reviews to the EWG and request subsequent recommendations.

The Rapporteur will ordinarily rely on correspondence or teleconferencing to avoid unnecessary travel. Based on the discussion, with requests for further information to the proposing group and/or individual as appropriate, the Rapporteur will prepare an assessment report based on the EWG's approval with a recommendation to accept, with or without modifications, or reject any proposed revisions.

After endorsement by the Assembly, either at the next formal meeting or by electronic endorsement, the recommendation of the EWG will be published in each region for public comment (*Step 3* of the ICH process). In addition, the proposal will be provided to each pharmacopoeia for their publication.

After closure of the public comment period, the Regulatory Chair (or in the absence of a Regulatory Chair, the Rapporteur) may convene a meeting of the EWG or will rely on correspondence or teleconferencing to consider the comments and finalise the proposal for the revised Guideline. The final recommendation for the Guideline and implementation is then forwarded to the Assembly for adoption in consultation with the MC. Implementation will follow regional practices. With approval of the ICH Assembly, the change will be provided to the pharmacopoeias at regional/national level for publication.

When a new or revised PDE or AI is recommended by the EWG, approval by the ICH MC is required. Once approval occurs, the information should be disseminated as quickly as possible to all ICH participants and other members of the chemical and pharmaceutical communities. It is recommended that the following actions should be taken by the MC to ensure rapid transmission of the new information:

- Publish relevant information on the ICH website;
- Request publication of revisions by the pharmacopoeias of the ICH regions in their Forums or websites;
- Request that each member publish the new or revised PDE or AI information on its respective websites.

Annex 5: Q4B Maintenance Procedure

1 - Background Information:

The ICH Q4B Guideline Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions reached *Step 5* in November 2007. Subsequently, the individual topic-specific Annexes reached *Step 5* in accordance with the dates listed on the ICH website. Because the inputs to the Q4B process were from the Pharmacopoeial Discussion Group (PDG) harmonisation process, it is recognised that the pharmacopoeial texts could be updated as technology and requirements change, or for other reasons. Because changes to the pharmacopoeial texts could have an impact on the interchangeability assessment contained in the Annexes, it is necessary to have a maintenance procedure for updating the Annexes when needed.

In November 2018, ICH and the PDG agreed to collaborate in the maintenance of the current ICH Q4B Annexes, following the maintenance procedure described below.

2 - Maintenance Procedure:

The need to revise an ICH Q4B Annex is triggered by the PDG's sign-off of a revised text which is the subject of an existing Q4B Annex. Potentially non-harmonised and/or local requirements are highlighted in the sign-off coversheet.

The Formal Step Process outlined in section 2.1 of this SOP and highlighted below applies to the maintenance of the Q4B Annexes. However, further to *Step 2a*, based on the level of change made to the revised Q4B Annex, the document should either proceed to *Step 2b* and then be published for comments, or it should directly be submitted to the Regulatory Members of the Assembly for adoption at *Step 4* and published as final. The latter may be deemed appropriate for example in the case of revisions limited to an update on the pharmacopoeial reference texts (i.e. updated versions of the pharmacopoeia).

- ***Step 1:***

The PDG compares the corresponding current ICH Q4B Annex, the PDG sign-off text as well as the corresponding Ph. Eur., JP and USP chapters as published in the respective Pharmacopoeias. All other pharmacopoeias are informed by the PDG of the ongoing review via the contact list of the International meeting of World Pharmacopoeias (IMWP).

Based on this review, the PDG prepares a revised Q4B Annex, which is submitted to the ICH Secretariat.

- ***Steps 2 a/b*:**

Further to receiving from the PDG a revised Q4B Annex, the ICH Secretariat initiates *Step 2a* at the level of the ICH Assembly as per section 2.1.2.

ICH will determine whether the revised Q4B Annex should proceed to *Step 2b* and *Step 3* according to the level of change made to the Annex.

- ***Step 3*:**

Further to the successful completion of *Step 2b,* the revised Q4B Annex becomes the subject of a regulatory consultation, following similar rules described in section 2.1.5.

The regulatory consultation and discussion should focus on the Q4B outcome in the Q4B Annex, i.e. regulatory interchangeability, comments on the harmonised pharmacopoeial text itself are not expected. Comments will be evaluated by the PDG and the Q4B Annex is revised by the PDG where necessary.

- ***Step 4*:**

Further to successful completion of *Step 3*, the PDG submits the revised Q4B Annex to the ICH Secretariat for adoption by the Regulatory Members of the Assembly, in line with section 2.1.6.

- ***Step 5*:**

Once *Step 4* is finalised, the revised Q4B Annex moves to the final step of the process. The revised Q4B Annex is published on the ICH website and is implemented by each of the Regulatory Members in their respective regions, as described in section 2.1.7.

The corresponding PDG Chapter moves to the PDG stage 5 (inter-regional acceptance). All other pharmacopoeias are informed by the PDG via the contact list of the International meeting of World Pharmacopoeias (IMWP).

Annex 6: MedDRA Points to Consider (PtC) Working Group

The MedDRA Points-to-Consider (PtC) Working Group (WG) was established with the scope of developing a PtC document on Good MedDRA Selection Practices and advising on standards for data output. The PtC WG develops and maintains the *MedDRA Term Selection: Points to Consider* and the *MedDRA Data Retrieval and Presentation: Points to Consider* documents synchronized with MedDRA version updates; its remit was later extended to enable the WG to provide guidance on ICH MedDRA initiatives on an as-needed basis.

The MedDRA Management Committee provides oversight of the MedDRA PtC WG for matters that relate to the improved operation and use of MedDRA *(i.e. PtC documents, Acronyms & Abbreviations, etc.).* However, the ICH Management Committee oversees any activities that relate to Guideline development *(Guideline, Q&As, Addendum, etc.)*. When proposing any new work activities, the PtC WG will be asked to develop a Concept Paper with detailed information on the scope, need, benefits, deliverables, cost, timeframe, and membership, for the support of either the MedDRA Management Committee or the ICH Management Committee, depending on the type of work to be completed. For work activities related to Guideline development, the Assembly will be asked to approve a Concept Paper outline and the ICH MC should approve the final Concept Paper. For work activities not related to Guideline development, the MedDRA MC will be asked to approve a Concept Paper. Additionally, the Assembly should be notified of all ongoing work activities of the MedDRA PtC WG and the WG should provide a report at each face-to-face meeting of the Assembly.

I. Endorsement of PtC documents

The PtC documents are not subject to regional implementation, but provide a best practice approach. Generally, the PtC WG releases a new version of the PtC documents for every version of MedDRA. PtC documents with major changes (i.e., significant new documents, new concepts in existing documents) will be signed off by the ICH Members of the PtC WG and endorsed by the MedDRA MC and the ICH Assembly will be informed of the changes. PtC documents with minor changes (e.g., simple revisions) will be agreed between the Rapporteur/Co-Rapporteur and Regulatory Chair for publication if there is consensus in the PtC WG.

Once signed-off, the PtC documents are available for public consultation. Any comments are forwarded to the PtC WG and will be taken into consideration for the release of the next version of the documents.

II. Membership

The PtC WG is established in line with the procedure outlined in section 1.5 Establishment of EWG/IWG of this SOP. Additionally, the MedDRA PtC WG usually also includes a representative from both MSSO and JMO.

III. Working Procedures

The PtC WG has an on-going mandate to work by tele/web conference and e-mail. The group is asked to report at MedDRA Management Committee tele/web conferences when there is a need for a face-to-face meeting. Justification will need to be provided for all face-to-face meetings, for ICH Management Committee approval.

The PtC WG usually meets every 18 months during the week of the ICH face-to-face meeting; however, the WG may need to meet every 12 months, as the necessity for holding meetings depends on the feedback received from users and the time of release of MedDRA (March and September). The usual maintenance of both PtC documents on term selection and on data retrieval & presentation does not require frequent face-to-face meetings. A large part of the work is done by correspondence, and major and only complex changes to MedDRA are discussed during face-to-face meetings. The Rapporteur with support of the Regulatory Chair is asked to report on progress and issues to both the MedDRA MC and ICH Assembly on a regular basis. Unresolved issues will be brought to the attention of the MedDRA MC as appropriate.

IV. Designation of the Rapporteur / Co-Rapporteur and Regulatory Chair

The nomination of a Rapporteur/Co-Rapporteur and a Regulatory Chair proceeds in line with section 1.5.2 of this SOP. The PtC WG should also be consulted and invited to discuss their leadership. Additionally, the MedDRA MC will be asked to support the nomination(s) prior to the official designation of the Rapporteur/Co-Rapporteur by the Assembly and the Regulatory Chair by the MC.

The MedDRA MC will reassess the term of the Rapporteur and Regulatory Chair, as needed and consult with the ICH MC regarding any need to rotate the Rapporteur or Regulatory Chair.

Annex 7: Streamlined Procedure

The purpose of the streamlined procedure is to develop a Guideline in an accelerated timeframe in response to an emerging health care problem.

When it is critical for ICH Members to develop a Guideline that other ICH Members share an interest in, then the task could be undertaken under the auspices of ICH. Under such circumstances the ICH Assembly in close consultation with the Management Committee (MC) would grant the use of the streamlined procedure in order to make the process as short and efficient as possible.

In addition to time constraints, the following conditions are required to make a document eligible for the streamlined procedure:

1) The presence of an emerging health issue, such as:
    a. A health problem that affects many persons
    b. A significant change in state of art of science.
2) A draft or final document should already exist in one of the ICH regions (including an Observer) that would provide a strong foundation for the development of the ICH Guideline.

There should be consensus from the ICH Members that the draft document would be the starting point in the development of the ICH Guideline, no Concept Paper would be necessary and the country(s)/region(s) originating the document would lead the EWG responsible in developing the Guideline. However, a Business Plan is still necessary.

ICH Industry Members are not required to participate in the development of the Guideline.

The Assembly in close consultation with the MC will consider proposals for the streamlined procedure on a case-by-case basis.

I. Process for streamlined procedure

Upon approval of a streamlined process by the Assembly, the objectives and expected outcome of the harmonisation action is confirmed. Additionally, a timetable and Business Plan with an accelerated timeline will be developed.

The composition of the Expert Working Group (EWG) is confirmed, which can include outside experts if invited as an *ad hoc* Observer. The ICH Members designate a Topic Leader, as in the normal process and the region originating the documents nominates a Rapporteur, and one of the ICH Regulatory MC Members nominates a Regulatory Chair.

The Step Process for the streamlined procedure is the same as the normal ICH process with the exception of the absence of a Concept Paper. The form of communication to be used for the sign-off will be electronically or by postal mail.

II. Streamlined procedure Step Process

In principle, the agreement of the ICH Members is necessary for initiating any ICH harmonisation activities. However, in exceptional cases when ICH Member consensus cannot be achieved, the Assembly will proceed to voting where a majority decision will make a determination.

a. *Step 1*: Consensus building between the experts - The Rapporteur circulates the existing document to the EWG for comments and discussion. As the document has been agreed to in principle, the comments are unlikely to be major. The experts reach consensus on the document and sign-off at *Step 1*.
b. *Steps 2a* and *2b*: The Assembly and the ICH Regulatory Members, endorse the Technical Document and Draft Guideline, respectively, through an electronic approval process organised by the ICH Secretariat.
c. *Step 3*: Regulatory consultation: The draft Guideline is published for comments in each of the ICH regions (the comment period may be shortened to accommodate regulatory needs and timetables). After addressing all regulatory consultation results, the EWG regulatory experts reach consensus on the *Step 3* Experts Draft Guideline and sign-off on it.
d. *Step 4*: Adoption of a harmonised Guideline: The Assembly endorses the final harmonised Guideline through an electronic approval process or at a face-to-face meeting.

III. Safeguard Clause

In case of unexpected delays in the procedure that would jeopardize reaching consensus and finalising the ICH Guideline on time, the country/ region from which the document originated may withdraw the document from the ICH process in order to meet its own deadlines at any time during the process in consultation with the other Members

Annex 8: ICH Topic Proposal Template

1. Topic Title
2. ICH Topic Description
Type of Harmonisation Action: New Guideline ☐ Revision of existing Guideline ☐ Category of Harmonized Procedure: Quality ☐ Safety ☐ Efficacy ☐ Multidisciplinary ☐
Brief statement of perceived problem (caused by lack of harmonisation):
Main technical and scientific issues to be addressed (which require harmonisation):
Objective and expected outcome of proposed harmonisation work:
3. Strategic Importance of Topic
Why is this important for international harmonisation? *1. How does the proposal potentially conserve regulatory/industry resources? Which specific areas are likely to benefit more (e.g. generics, NCEs, biologics)?* *2. How does the proposal potentially improve the timing of access of new drugs to patients?* *3. Given the new construct, which industries and which regulators are likely to most benefit?*
4. Feasibility
Would the proposal be in alignment with current laws and regulations in the ICH regions? (If not, identify regions in which incompatibilities or obstacles could be expected) *1. Level of effort required to complete the Guideline* *2. Time to complete the Guideline* *3. When benefits of the completed Guideline would be realized* *4. How does the proposed topic relate or potentially complement or conflict with existing Guidelines* *5. How would the proposed topic potentially compete for ICH resourcing within and across categories (Q, S, E, M)* *6. Do any of the ICH regions already have a domestic Guideline relating to the new topic? (If so, please identify those regions and related respective Guidelines)*

5. Source of Proposed Topic
Topic proposed by: ORGANISATION:_____ CONTACT NAME:_____

Annex 9: ICH Concept Paper Template

Final Concept Paper

[Title]

Endorsed by the Management Committee on [day/Month/Year]

Type of Harmonisation Action Proposed

[Is a new harmonised Guideline being recommended, or a revision of an existing Guideline? What category of procedure would this fall into?]

Statement of the Perceived Problem:

[Provide a brief description with an indication of the magnitude of the problems currently caused by a lack of harmonisation, or - in the case of new scientific developments - anticipated if harmonisation action is not taken.]

Issues to be Resolved:

[A summary of the main technical and scientific issues, which require harmonisation. Include whether the issue is relevant to any pediatric or other special subpopulation.]

Background to the Proposal:

[Further relevant information, e.g., the origin of the proposal, references to publications, and discussions in other fora.]

Type of Expert Working Group Recommended:

[Recommendation on whether the EWG (if needed) should be an extended EWG - for topics with implications beyond new drug research. Indicate what type of expertise will be needed for this working group e.g. clinicians, toxicologist, chemists.]

[If the issue is relevant to any pediatric population, provide a recommendation on whether the EWG should include representation of a pediatric expert(s)]

Indicate if the scope of activities of the Working Group would warrant expertise from any of the following fields:

- □ Advanced Therapy Medicinal Products
- □ Bioequivalence Studies
- □ Biostatistics and clinical trial methodology
- □ Biotechnology-derived products
- □ Electronic standards or technical considerations
- □ Generics
- □ Good Manufacturing Practices
- □ Non-clinical safety
- □ Novel dosage forms

- □ Pharmacogenomics
- □ Pharmacovigilance
- □ Pediatrics
- □ Post-marketing clinical trials
- □ Pre-marketing clinical trials
- □ Small Molecules/New chemical entities
- □ Therapeutic area-specific Safety/Efficacy (please specify): _____
- □ Vaccines
- □ Other (please specify): _____

Timing:

[When should the topic under consideration begin harmonisation? How long is it anticipated to take to develop a harmonized Guideline/revise existing Guideline?]

Annex 10: Business Plan Template

Final Business Plan

Title

date

Endorsed by the Management Committee on day/Month/Year

1. **<u>The issue and its costs</u>**

- *What problem/issue is the proposal expected to tackle?*
- *What are the costs (social/health and financial) to our stakeholders associated with the current situation or associated with "non-action"?*

2. **<u>Planning</u>**

- *What are the main deliverables?*
- *What resources (financial and human) would be required?*
- *What is the time frame of the project?*
- *What will be the key milestones?*
- *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?*

3. **<u>The impacts of the project</u>**

- *What are the likely benefits (social, health and financial) to our key stakeholders of the fulfilment of the objective?*
- *What are the regulatory implications of the proposed work – is the topic feasible (implementable) from a regulatory standpoint?*
- *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?*

4. **<u>Post-hoc evaluation</u>**

- *How and when will the results of the work be evaluated?*

Annex 11: Work Plan Template

ICH XXX EWG/IWG Work Plan

Day Month, Year

Topic Adoption date: Month Year

Rapporteur: Name of Rapporteur / Co-Rapporteur, Member

Regulatory Chair: Name of Regulatory Chair, Member

Last Face-to-Face Meeting: City, country, Month Year

Please note that Sections 1 and 2 of this Work Plan will be made publicly available on the ICH public website.

1. Key milestones

1.a. Current status of key milestones

*Please provide in the table below for context the **relevant past achieved key milestones**, such as: Concept Paper endorsement, Business Plan endorsement, Step 1 or Step 2a/b, stakeholder engagement, training, etc., (recommended 1 – 6 milestones).*

Past completion date	Milestone
Month Year	*Short title of the deliverable such as: Concept Paper endorsement, Business Plan endorsement, Step 1 or Step 2a/b on document (recommended 5 – 20 words)*
Month Year	*Short title of the deliverable such as: Concept Paper endorsement, Business Plan endorsement, Step 1 or Step 2a/b on document (recommended 5 – 20 words)*
Month Year	*Short title of the deliverable such as: Concept Paper endorsement, Business Plan endorsement, Step 1 or Step 2a/b on document (recommended 5 – 20 words)*

1.b. Future anticipated key milestones

*Please provide in the table below the **main deliverable(s)to be achieved in the next year(**s): Step 1 sign-off, Step 2a/b endorsement, Step 3 sign-off, Step 4 adoption, or any other relevant high-level deliverables (finalised documents, public consultation period, special actions to advance the topic through ICH, e.g. stakeholder engagement or training, etc.) (recommended 3 – 6 milestones).*

Expected future completion date	Milestone
Month Year	*Short title of the deliverable such as: Step 4 adoption, public consultation period, etc… (recommended 5 – 20 words)*
Month Year	*Short title of the deliverable such as: Step 4 adoption, public consultation period, etc… (recommended 5 – 20 words)*

Month Year	*Short title of the deliverable such as: Step 4 adoption, public consultation period, etc… (recommended 5 – 20 words)*
Month Year	*Short title of the deliverable such as: Step 4 adoption, public consultation period, etc… (recommended 5 – 20 words)*
Month Year	*Short title of the deliverable such as: Step 4 adoption, public consultation period, etc… (recommended 5 – 20 words)*
Month Year	*Short title of the deliverable such as: Step 4 adoption, public consultation period, etc… (recommended 5 – 20 words)*

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
Month Year	Month Year	*Task/Activity such as: internal consultation, teleconference, review, stakeholder engagement, training, etc… (5-10 words)*	*Brief summary of task/activity objectives and targeted outcome (recommended 10 - 20 words).*
Month Year	Month Year	*Task/Activity such as: internal consultation, teleconference, review, stakeholder engagement, training, etc… (5-10 words)*	*Brief summary of task/activity objectives and targeted outcome (recommended 10 - 20 words).*
Month Year	Month Year	*Task/Activity such as: internal consultation, teleconference, review, stakeholder engagement, training, etc… (5-10 words)*	*Brief summary of task/activity objectives and targeted outcome (recommended 10 - 20 words).*
Month Year	Month Year	*Task/Activity such as: internal consultation, teleconference, review, stakeholder engagement, training, etc… (5-10 words)*	*Brief summary of task/activity objectives and targeted outcome (recommended 10 - 20 words).*
Month Year	Month Year	*Task/Activity such as: internal consultation, teleconference, review, stakeholder engagement, training, etc… (5-10 words)*	*Brief summary of task/activity objectives and targeted outcome (recommended 10 - 20 words).*
Month Year	Month Year	*Task/Activity such as: internal consultation, teleconference, review, stakeholder engagement,*	*Brief summary of task/activity objectives and targeted outcome (recommended 10 - 20 words).*

		training, etc… (5-10 words)	
Month Year	Month Year	*Task/Activity such as: internal consultation, teleconference, review, stakeholder engagement, training, etc… (5-10 words)*	*Brief summary of task/activity objectives and targeted outcome (recommended 10 - 20 words).*
Month Year	Month Year	*Task/Activity such as: internal consultation, teleconference, review, stakeholder engagement, training, etc… (5-10 words)*	*Brief summary of task/activity objectives and targeted outcome (recommended 10 - 20 words).*
Month Year	Month Year	*Task/Activity such as: internal consultation, teleconference, review, stakeholder engagement, training, etc… (5-10 words)*	*Brief summary of task/activity objectives and targeted outcome (recommended 10 - 20 words).*

3. Summary of any current issues

Does the Working Group currently encounter any issues?

☐ Yes ☐ No

If you answered yes, please provide here a summary of any current challenging points which should be raised for the information of the ICH Management Committee, or on which ICH Management Committee guidance is needed.

4. Necessity of face-to-face meeting at the next ICH meeting

Does the Working Group wish to meet face-to-face at the next ICH meeting?

☐ Yes ☐ No ☐ Not yet determined

If you answered yes, please present here the justification of the consensus view of the EWG/IWG on the necessity for the group to meet face-to-face at the time of the next ICH meeting, in line with the work plan presented above.

Expected work progress at the next ICH meeting

Please also provide in the table below a detailed description of the work that would be undertaken during the ICH meeting.

Note: Consideration will be given to the timing the work plan is completed and whether details around the work that would be undertaken during the ICH meeting can already be available.

Date	Task / Activity	Details
Day 1	*Task/Activity (5-10 words)*	*Brief summary of task/activity objectives and targeted deliverable / outcome (recommended 10 - 20 words)*
Day 2	*Task/Activity (5-10 words)*	*Brief summary of task/activity objectives and targeted deliverable / outcome (recommended 10 - 20 words)*
Day 3	*Task/Activity (5-10 words)*	*Brief summary of task/activity objectives and targeted deliverable / outcome (recommended 10 - 20 words)*
Day 4	*Task/Activity (5-10 words)*	*Brief summary of task/activity objectives and targeted deliverable / outcome (recommended 10 - 20 words)*

Annex 12: Template for ICH Observer Request to Appoint an Expert to a Working Group

ICH OBSERVER

Request to Appoint an Expert to a Working Group

1. Date of request:

2. Name of ICH Observer:

3. Name of the Working Group the Observer is requesting to appoint an Observer expert:

4. Describe the Observer's primary interest in participating in the Working Group:

5. Briefly describe the expertise of the individual being nominated and the expected contribution to the work of the Working Group:

6. (If available) Contact details of nominated expert:

First name:
Last name:
Title:
Job title:
Email:
Phone:

Annex 13: Template for Industry Member Request to Appoint an Expert to a Working Group

ICH INDUSTRY MEMBER

Request to Appoint an Expert to a Working Group

1. Date of request:

2. Name of ICH Industry Member:

3. Name of the Working Group the Industry Member is requesting to appoint an expert to:

4. Describe the Industry Member's primary interest in participating in the Working Group:

5. Briefly describe the expertise of the individual being nominated and the expected contribution to the work of the Working Group:

6. Describe how the Industry Member or its affiliate members will be affected or regulated by the guideline in question:

7. (If available) Contact details of nominated expert:

First name:
Last name:
Title:
Job title:
Email:
Phone:

Annex 14: *Step 1* Experts Sign-Off

Topic Reference: ***STEP 1 – EXPERTS***

CODE: GUIDELINE TITLE

Consensus on a Technical Document to be submitted to the ICH Assembly under *Step 1* of the ICH Process

***Step 1* Technical Document signed-off by the**

DESIGNATED EXPERTS FROM THE ICH EXPERT WORKING GROUP

The official ICH procedure specifies that a *Step 1* Technical Document can be submitted to the Assembly for endorsement when the designated experts of the ICH Members reach consensus and sign the *Step 1* sign-off sheet.

Document Reference: **----------**

Document Date: **----------**

	Signature	*Name*	*Date (DD-MM-YY)*
Rapporteur	.....	.....	.....
Regulatory Chair	.....	.....	.....
Experts of Founding Regulatory& Industry Members			
EC, Europe	.....	.....	.....
FDA, United States	.....	.....	.....
	.....		
MHLW/PMDA, Japan	.....	.....	.....
EFPIA	.....	.....	.....
PhRMA	.....	.....	.....
JPMA	.....	.....	.....
Experts of Standing Regulatory Members			
Health Canada, Canada	.....	.....	.....
Swissmedic, Switzerland	.....	.....	.....

Topic Reference: ***STEP 1 – EXPERTS***

CODE: GUIDELINE TITLE

Document Reference: ----------

Document Date: ----------

Signature	*Name*	*Date (DD-MM-YY)*

Experts of Regulatory Members

(To be filled based on WG participants)

.....	.....	.....

Experts of Industry Members

(To be filled based on WG participants)

.....	.....	.....

Observer experts who participate in the Working Group are invited to sign-off the *Step 1* Technical Document in recognition of their contribution to the discussion.

Experts of Standing Observers

(To be filled based on WG participants)

.....	.....	.....

Experts of Observers

(To be filled based on WG participants)

.....	.....	.....

Plenary Working Party experts are invited to sign the *Step 1* Experts Draft Guideline in recognition of their contribution to the discussion.[7]

Experts of Plenary Working Party

(To be filled based on PWP participants)

[7] Only applicable to WGs with associated PWPs.

Annex 15: *Step 3* Regulatory Experts Sign-Off

Topic Reference: ***STEP 3 – REGULATORY EXPERTS***

CODE: GUIDELINE TITLE

Conclusion of *Step 3* of the ICH Process[8]

Step 3 experts draft Guideline signed-off by the

DESIGNATED REGULATORY EXPERTS FROM THE ICH EXPERT WORKING GROUP

The official ICH procedure specifies that a *Step 3* experts draft Guideline can be submitted to the Regulatory Members of the Assembly for adoption as an ICH Harmonised Guideline when the designated experts of the ICH Regulatory Members reach consensus and sign the *Step 3*.

Document Reference: **----------**

Document Date: **----------**

	Signature	*Name*	*Date (DD-MM-YY)*
Rapporteur	**.....**	**.....**	**.....**
Regulatory Chair	**.....**	**.....**	**.....**
Experts of Founding Regulatory Members			
EC, Europe	**.....**	**.....**	**.....**
FDA, United States	**.....**	**.....**	**.....**
MHLW/PMDA, Japan	**.....**	**.....**	**.....**
Experts of Standing Regulatory Members			
Health Canada, Canada	**.....**	**.....**	**.....**
Swissmedic, Switzerland	**.....**	**.....**	**.....**

[8] The comments received by the ICH Regulatory Members on the regional consultation on the *Step 2b* Guideline have been considered for the preparation of a *Step 3* experts draft Guideline which, once signed-off by the experts designated by the Regulatory Members, will be submitted to the Regulatory Members of the Assembly for adoption as a harmonised Guideline (*Step 4* of the Process).

Topic Reference: ***STEP 3 – REGULATORY EXPERTS***

CODE: GUIDELINE TITLE

Document Reference: ----------

Document Date: ----------

Signature *Name* *Date (DD-MM-YY)*

Experts of Regulatory Members
(To be filled based on WG participants)

....

Regulatory Observer experts who participate in the Working Group are invited to sign the *Step 3* Experts Draft Guideline in recognition of their contribution to the discussion.

Signature *Name* *Date (*DD-MM-YY*)*

Experts of Regulatory Observers
(To be filled based on WG participants)

....

Plenary Working Party experts of Regulatory Members are invited to sign the *Step 3* Experts Draft Guideline in recognition of their contribution to the discussion.[9]

Regulatory Experts of Plenary Working Party
(To be filled based on PWP participants)

....

[9] Only applicable to WGs with associated PWPs.

Annex 16: *Step 3* Regulatory Experts Sign-Off without Public Consultation

Topic Reference: ***STEP 3 – REGULATORY EXPERTS***

CODE: GUIDELINE TITLE

Step 3 of the ICH Process[10] without public consultation

Step 3 Experts Document signed-off by the

DESIGNATED REGULATORY EXPERTS FROM THE ICH EXPERT WORKING GROUP

The official ICH procedure specifies that a *Step 3* Document can be submitted to the Assembly for adoption as an ICH Harmonised Guideline when the Designated Experts of the ICH Regulatory Members reach consensus and sign the *Step 3*.

Document Reference: **----------**

Document Date: **----------**

	Signature	*Name*	*Date (DD-MM-YY)*
Rapporteur	**.....**	**.....**	**.....**
Regulatory Chair	**.....**	**.....**	**.....**
Experts of Founding Regulatory Members			
EC, Europe	**.....**	**.....**	**.....**
FDA, United States	**.....**	**.....**	**.....**
	.....		
MHLW/PMDA, Japan	**.....**	**.....**	**.....**
Experts of Standing Regulatory Members			
Health Canada, Canada	**.....**	**.....**	**.....**
Swissmedic, Switzerland			

[10]Once signed-off by the experts designated by the Regulatory Members, this document will be submitted to the Assembly for adoption as a harmonised Guideline (*Step 4*) without public consultation.

Topic Reference: ***STEP 3 – REGULATORY EXPERTS***

CODE: GUIDELINE TITLE

Step 3 **of the ICH Process** **without public consultation**

Document Reference: **----------**

Document Date: **----------**

Signature *Name* *Date (DD-MM-YY)*

Experts of Regulatory Members
(To be filled based on WG participants)

....

Regulatory Observer experts who participate in the Working Group are invited to sign the *Step 3* Experts Draft Guideline in recognition of their contribution to the discussion.

Experts of Regulatory Observers
(To be filled based on WG participants)

....

Plenary Working Party experts of Regulatory Members are invited to sign the *Step 3* Experts Draft Guideline in recognition of their contribution to the discussion.[11]

Regulatory Experts of Plenary Working Party
(To be filled based on PWP participants)

....

[11] Only applicable to WGs with associated PWPs.