出國報告（出國類別：國際會議)

參加國際醫藥法規協和會(ICH) E6(R3)（Good Clinical Practice）藥品優良臨床試驗規範(ICH GCP)專家工作組會議出國報告

服務機關：衛生福利部食品藥物管理署

姓名職稱：陳琬瑜 技正

派赴國家：新加坡

出國期間：108 年 11 月 16 日~108 年 11 月 21 日

報告日期：109 年 1 月

摘要

國際醫藥法規協和會(International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, ICH) 係於 1990 年由美國、歐盟及日本藥政主管機關及醫藥業界代表，共同發起成立之國際法規協和組織，主要目的是協和各國藥品法規與審查標準，致力於藥品品質、安全、有效等指引之制定，以期加速新藥研發。我國食品藥物管理署(下稱本署) 經多年的耕耘與努力，於 2018 年 6 月 ICH 會議中正式成為 ICH 藥政法規單位會員，顯示我國藥品法規已獲得國際認可，也是我國參與國際醫藥技術性合作組織之重要里程碑。

ICH 每年召開兩次會議，輪流於歐、美、亞地區舉行，經 2019 年 6 月 ICH 大會同意在多學科 (Multidisciplinary)組別下，成立非正式的 E6(R3) 工作組 (Informal Working Group)。本次於 108 年 11 月 16 日至 21 日於新加坡參加 E6(R3)工作組第一次面對面會議，會議中完成概念文件(concept paper)及業務計畫(business plan) ，並對於指引草案重點與架構等議題討論，製作工作成果簡報檔提報大會，獲 ICH 管理委員會同意正式成立 E6(R3) 專家工作組，展開 ICH GCP 指引修訂活動。

關鍵字：國際醫藥法規協和會(ICH)、ICH E6、藥品優良臨床試驗(GCP, Good Clinical Practice)

目錄

壹、 背景說明及目的

國際醫藥法規協和會(International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, ICH) 係於 1990 年由美國、歐盟及日本藥政主管機關及醫藥業界代表，共同發起成立之國際法規協和組織，主要目的是協和各國藥品法規與審查標準，致力於藥品品質、安全、有效等指引之制定，以期加速新藥研發。我國食品藥物管理署(下稱本署) 經多年的耕耘與努力，於 2018 年 6 月 ICH 會議中正式成為 ICH 藥政法規單位會員，顯示我國藥品法規已獲得國際認可，也是我國參與國際醫藥技術性合作組織之重要里程碑。

ICH E6 (Guideline for Good Clinical Practice)自公布以來已超過二十餘年，規範臨床試驗的執行過程及參與者的職責，包括試驗委託者、試驗主持人、監測者及人體試驗委員會(IRB)等，確保對受試者的保護和試驗結果的可靠性。於 2016 年完成修訂第二個版本 ICH E6（R2），增訂附錄以因應電子數據來源的使用及導入風險管理(risk based approach)的概念，鼓勵試驗的設計、進行、監測、記錄及通報方面實施改進且更有效的方法。然，許多相關利益關係者表示該版本不足以因應受試者參與不同試驗類型的風險程度差異，在風險管理方面應有更多的彈性變通，認為版本內容太過侷限，不應以附錄方式呈現，須更通盤地規劃整體內容並重新修訂。

2017 年 ICH 發表修訂 GCP 的反饋意見(Reflection paper)，規劃修訂 ICH E8 及 E6(R2)，旨為提供更具彈性的管理方針，以靈活應用於日益多元化的臨床試驗及因應多樣性的數據來源。建議修訂版本保留傳統介入性的臨床試驗規範，強化管理其他新型態的臨床試驗，繼續確保臨床試驗的品質及數據可靠性。

爰此，2019 年 6 月經 ICH 大會同意展開 E6（R3）主題，將全面檢視 ICH E6(R2)架構及內容並重新修訂，以供法規主管機關、醫療或研究機構等單位於臨床試驗執行過程或決策上有更明確之參考依據。本次於 2019 年 11 月新加坡舉行的面對面 (face to face)會議(為期 4 天)，完成“概念文件(Concept paper) 和業務計劃(Business Plan)”， 成立正式 Expert Working Group (EWG)，並獲大會同意進入 step 1。

貳、 過程

一、 行程表

日期	工作摘要
11 月 16 日	啟程：桃園-新加坡 會議地點：Grand Copthorne Waterfront Hotel

11 月 17 日至 20 日	參加 ICH E6(R3) Informal WG 工作組會議並向 ICH 大會報告工作進度
11 月 21 日	返程：新加坡-桃園

二、 會議內容摘要

本次 ICH 會議聚集 16 會員機構及 32 觀察會員機構共 450 參加者，有 14 項主題進行工作組面對面會議。會議第一天早上由 ICH 秘書處舉行 ICH Briefing Session，介紹 ICH 背景、架構、運作方式及管理方針。Session 結束隨即開始為期 4-5 天的工作組會議，每天會後各國皆會自行召開 Caucus meeting，各工作組會回報當天會議結果及待討論議題，以供各國掌握工作組進度。

本次職代表出席 ICH E6(R3)專家工作組面對面會議，會議為期 4 天(2018/11/17~11/20)，本次出席 ICH E6(R3)專家工作組之專家代表共計 23 人，包括來自美國 FDA、歐盟 EC、日本 PMDA、加拿大 Health Canada、巴西 ANVISA、新加坡 HSA、臺灣 TFDA、中國 NMPA 等法規會員代表，及美國藥品研究及製造商協會 (Pharmaceutical Research and Manufacturers of America, PhRMA)、歐洲製藥工業協會聯合會(European Federal Pharnaceutical Industrial Association, EFPIA)、日本製藥工業協會 (Japan Pharmaceutical Manufacturers Association, JPMA)、及國

際藥品製造商和協會聯合會 International Federation of Pharmaceutical Manufacturers &Associations, IFPMA)等業界會員代表以及世界衛生組織(WHO)代表。會議由美國 FDA 官員擔任主導報告員(Rapporteur)，歐盟(EC)官員擔任法規主席(Regulatory Chair)，四天會議討論內容摘要如下：

(一)第 1 天會議(11 月 17 日)

1.會議討論議題：

- 成員自我介紹並分享工作經驗。
- 檢視 4 天會議的工作議程及預定工作進度。
- 討論 Concept paper 及 Business plan 內容。
- 討論 E6(R3)版本架構及草擬方向。

2.會議總結摘要：

- 本次面對面會議前，已先開過 2 次電話會議，針對已草擬出的 concept paper 及 Business plan 逐字討論，確認法規合適性及用詞、字義的一致性。
- 初步共識認為 R3 版本不要把各利益關係者(stakeholder)(如試驗委託者、試驗主持人，IRB 等)的職責散落於各章節描述，應考量臨床試驗執行過程的全面性及強化落實 GCP 的目的性。
- 規劃 R3 版本仍以 R2 內容為基礎修訂，擬建立三個部分，分別為

總體原則與目的(principle &objective)、Anex1（針對傳統interventional trial)及 Anex2(針對非傳統性 interventional trial)。

(二)第二天會議(11 月 18 日)

1.會議討論議題：

- 討論及分享各國現況遭遇問題及挑戰。
- 請曾參與 ICH E6(R2)修訂工作組的與會代表分享修訂經驗及簡要提出未來修訂重點及方向。
- 討論是否邀請外部專家作為 Ad-hoc obersever ，如具代表性的病人團體及學術研究機構，以供更多意見納入 R3 修訂參考。

2.會議總結摘要：

- 各國拋出現況問題及互相交流，包含試驗委託者與試驗主持人之責任劃分、試驗主持人授權範圍不夠明確、試驗計畫書與實務面操作不符、GCP 查核缺失的判定依據、嚴重不良反應的通報責任劃分、如何推動全面電子化病人同意書等問題。
- ICH 會員國對於 GCP 查核的判定依據是否完全遵造 ICH GCP 指引的作法不一，大部分國家仍以其國內臨床試驗相關法規為主，並參考 ICH 指引為輔。原則上，不違背 ICH 指引的規定。
- 各會員國認為儘早納入多方利益關係者的想法，有助 R3 的修訂，

至於納入哪些外部專家及如何蒐集意見(如舉辦地區性研討會或問卷調查)，將參考其他工作組的經驗及作法，並研提方案徵求 ICH 委員會認可。

(三)第三天會議(11 月 19 日)

1.會議討論議題：

- 請各國針對 Caucus meeting 提出回饋意見。
- 討論 CTTI (Clinical Trials Transformation Initiative)對 ICH E6(R2)的問卷調查結果。
- 與 M11 工作小召開聯合會議，互相交流。
- 準備隔天向 ICH 大會報告的簡報。

2.總結摘要：

- 初步同意納入病人團體及學研界代表參與修訂討論，但大部分會員國對如何納入病人團體意見的做法表達疑慮，初步共識將該構想向 ICH 大會報告，待大會同意後再討論細節及程序。
- 持續討論總體原則(principle)的內容，主要參考 R2 版本第二章，並就擬強化之處增列。
- 由於 CTTI 城市問卷調查結果，亞洲國家的樣本數太少，會上認為這樣的調查結果有偏差，故僅供各會員國參考。會上共識未來若要

進行問卷調查應該統一問卷設計版本，並納入各會員國意見。

- 確認隔天提會簡報內容及工作期程規劃，包含 R3 版本架構及納入外部專家構想等，預計 2020 年仍有舉辦工作組面對面會議的必要性，細節及內容將持續以電話會議進行討論及建立溝通機制。

(四)第四天會議(11 月 20 日)

1.會議討論議題：

- 列席向 ICH 大會報告本工作組之工作進展及規劃
- 請各國針對 Caucus meeting 提出回饋意見。
- 持續討論 R3 principle 的架構及內容。
- 會議總結及後續工作。

2.總結摘要：

- 今日主要列席向 ICH 大會報告本工作組之工作進展及規劃，由本工作組之主持人代表報告及回應問題，所有工作組成員均列席聆聽。經 ICH 大會同意正式成立 E6(R3)專家工作組，獲大會同意進入 step1。
- 持續討論 E6(R3)臨床試驗指引內容，預計花費 18-24 個月制訂總體原則、目標文件及附件 1。達 step1 目標，後續再接續啟動 Anex2。有關總體原則、目標文件及附件 1，初步共識仍是以 R2 版本內容

修訂，將重要且應遵循的基本規定及精神置於總體原則。

- 本小組將與 E8 或 M11 其他工作小組的交流經驗及密切合作，擬研議更多方的利益相關者包括學術界和病人團體參與修法。
- 因各會員國實施 ICH E6(R2)的期程規劃不一，將再討論舉辦 Regional workshop 的可行性或問卷調查的內容及收集方式。

參、 心得及建議

一、參與國際會議，拓展視野，受益良多。

本次代表我國參與本 E6(R3)工作組會議，能與各國具豐富經驗的法規單位及業界代表先進共同討論及交流，受益良多。透過實質參與 ICH 專家工作組會議，有機會了解每份具國際公認技術性指引都是透過各會員國代表分工合作，經多次反覆不斷地討論、修正、蒐集意見並經過大會各階段嚴謹的議會程序所產出，過程實屬不易，也令人佩服。本次會前 3 次的電話會議及新加坡 4 天的面對面會議，正式通過大會成立 EWG 並進入 step1，未來仍持續透過密集的電話會議及面對面會議完成各階段的里程碑，盡早修訂完成供從事臨床試驗相關人員實務操作之參考。

二、了解國際法規趨勢，精進國內法規，與國際接軌。

我國目前藥品臨床試驗法規係以 103 年修訂完成的「藥品優良臨

床試驗準則(GCP)」為主，該準則架構及內容主要參據 ICH E6 GCP。由於國際間對 2016 年修訂的 ICH E6(R2)仍有許多歧見，且各會員國實施的期程不一，故迅速成立 ICH E6(R3)專家工作組，以期解決該指引內容不足或須強化之處。我國雖曾公告採認 ICH 規範採認清單，惟目前尚未將 ICH E6(R2)增修附錄納入我國「藥品優良臨床試驗準則」。適逢參與本工作組初步了解 ICH E6(R3)的修訂方向及規劃，有助我國未來修訂 GCP 準則之參考，以期制定符合國際管理規範，且同時符合國內需求的法規。

三、 持續爭取參與國際會議，尋求機會，深化國際合作。

我國自 2017 年正式成為 ICH 會員國後，積極派員參與各專家工作組，掌握國際藥政法規之管理趨勢，進而提升我國國際競爭力與能見度。感謝過去先進在藥政法規持續地耕耘及奉獻得到國際間的認同，深感榮幸。希望未來我國能持續派員參與國際組織活動，持續不斷地厚植本署人員的法規科學能力，以強化我國於國際組織之參與度及影響力，深化國際合作關係。

肆、 附件

附件 1、會議照片及工作組成員名單

E6(R3) EWG Good Clinical Practice (GCP)

Expert list

ANVISA, Brazil Dr. Carla Abrahao Brichesi	CDSCO, India Mr. Arun Kumar Pradhan
EC, Europe Lisbeth Bregnhoj Dr. Fergus Sweeney	EFPIA Susanne Nørskov Rebecca Stanbrook
FDA, United States Dr. Ni Aye Khin Dr. Celia Witten	Health Canada, Canada Dr. Carole Legare
HSA, Singapore Ms. Sumitra Sachidanandan	IFPMA Mr. Guodong FANG
IGBA Dr. Gerald Beuerle Dr. Manjunath Krishnappa	JPMA Mr. Mitsuaki Aoyagi Mr. Eiji Kawakatsu
MHLW/PMDA, Japan Ms. Aki Kitabayashi Ms. Eriko Ymazaki	NMPA, China Ms. Zhimin YANG
PhRMA Deborah Driscoll	Swissmedic, Switzerland Dr. Stephanie Juritz
TFDA, Chinese Taipei Ms. Wan-Yu Chen	TGA, Australia Dr. Nitin Bagul
TITCK, Turkey Dr. Nihan BURUL BOZKURT	WHO Dr. Ray Corrin

Disclaimer: Expert Working Groups 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 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.

附件 2、ICH E6(R3) Final Concept Paper

Final Concept Paper
ICH E6(R3): Guideline for Good Clinical Practice
Dated 17 November 2019
Endorsed by the Management Committee on 18 November 2019

Type of Harmonisation Action Proposed

The action proposed is a full rewrite and reorganization of the ICH E6(R2) Guideline entitled *Good Clinical Practice (GCP)*. The goal of this effort will be multifaceted and will include addressing the application of GCP principles to the increasingly diverse trial types and the data sources being employed to support regulatory and healthcare related decision-making on drugs, and provide flexibility whenever appropriate to facilitate the use of technological innovations in clinical trials. The development of E6(R3) will address the complexities of clinical trials in the current global regulatory climate.

The revision will retain the concepts and guidance in E6(R2) as appropriate. The scope will not be limited to those concepts, but will expand, modify, and reorganize all appropriate sections to provide scientific and ethical guidance that enables a diversity of approaches that are relevant and adaptable to the variety of clinical trial designs and innovative technologies. The revision also aims to address identified gaps or inconsistencies in existing ICH guidances as appropriate. This work will set out principles which will be aligned with those set out in E8(R1) *Revision of General Considerations for Clinical Studies*. When complete, E6(R3) will be composed of an overarching principles and objectives document, Annex 1 (interventional clinical trials), and Annex 2 (additional considerations for non-traditional interventional clinical trials). The overaching principles and objectives document and Annex 1 will replace the current E6(R2). The development of Annex 2 will commence once the principles and objectives document and Annex 1 complete ICH step 1.

Statement of the Perceived Problem

In the two decades since ICH E6 was first drafted, clinical trials have become more complex with respect to trial design, use of technology, quantity of data collected and involvement of central testing facilities or other service providers. ICH E6(R2) was developed with multiple addenda to address the emerging use of electronic data sources and risk management processes. However, since the development of E6(R2), clinical trials have continued to evolve with new designs and technological innovations. There is also a desire that E6(R3) should be developed to provide guidance that is applicable to different clinical trial designs and to focus on key principles and objectives. E6(R2) included a focus on a proportionate, risk-based approach to the design and conduct of clinical trials. E6(R3) will be designed to further advance this concept and to encourage relevant parties to utilize this approach.

In addition, data generated initially for healthcare purposes outside of a clinical trial or captured using innovative technological tools are being explored to serve an increasingly important role in supporting regulatory and healthcare decisions on drugs. However, E6(R2) is not fully designed to address emerging technologies, innovations in trial design, the diversity of data sources, testing facilities, and service providers, or to address other emerging complexities of the current clinical trial climate. In the absence of a modernized guideline, reference may be made to the current provisions in E6, even though the requirements may not be fully adapted to these technologies, or stakeholders may fail to adopt the current requirements. The application of the current standard to new technology is clearly challenging. Consequently, the design and conduct of trials, including in particular investigator site, test facility or service provider activities and record-keeping, may fail to take full advantage of technological innovations and the full potential of the risk-based considerations related to participant protection, data integrity or other public health considerations.

Issues to be Resolved

The new guideline will retain its focus on good clinical practice and will refer to relevant critical-to-quality factors similar to those identified in the E8(R1) *Revision of General Considerations for Clinical Studies*. Importantly, the guideline will provide flexibility to, among other things, accommodate the increased role of technology and variety of data sources in clinical trials. Increased reliance on electronic systems will also necessitate updating the language in the guideline on the validity of electronic systems, documentation and signatures, among other things.

The proposed rewrite will include more specific discussions and refinement to E6 principles in the context of different trial types and data sources in the annexes as described below:

- Annex 1 - Interventional clinical trials

  This will include the use of unapproved or approved drugs in a controlled setting with prospective allocation of treatment to participants and collection of trial data. This Annex will be developed simultaneously with the principles and objectives document to ensure consistency and to provide stakeholders with a complete package that can replace E6(R2); and

- Annex 2 - Additional considerations for non-traditional interventional clinical trials

  This will include designs such as pragmatic clinical trials and decentralized clinical trials, as well as those trials that incorporate real world data sources. Before the drafting of Annex 2, its scope will be further clarified, to define the nature of trials involved, in an update to this concept paper.

The proposed E6(R3) revision work will initially involve the simultaneous development of the overarching principles and objectives document and the first annex to produce a unified package to replace ICH E6(R2). This approach will allow us to align the principles and objectives with the specific guidelines for interventional trials and enable the existing E6(R2) document to be superseded by simultaneous finalization of the principles and objectives document and Annex 1.

附件 2、ICH E6(R3) Final Concept Paper(續)

Background to the Proposal

- ICH E6(R2) Good Clinical Practice
- ICH E8(R1) General considerations for clinical studies
- FDA,United States, Guidance for Industry Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring, 2012
- EC, Europe, EMA: Reflection Paper on Risk Based Quality Management in Clinical Trials, 2013
- MHLW/PMDA, Japan, MHLW: Revision of the guidance on the Ministerial Ordinance on Good Clinical Practice for Drugs, 2019
- MHLW/PMDA, Japan, MHLW: Basic Principles of Quality Management in Clinical Trials, 2019
- MHLW/PMDA, Japan, MHLW: Basic Principles of Risk-Based Monitoring in Clinical Trials, 2019
- ICH Q9, Quality Risk Management
- Clinical Trials Transformation Initiative workshops on quality by design and quality risk management
- TransCelerate Biopharma, Inc. risk-based monitoring resources
- Sensible Guidelines for the Conduct of Clinical Trials meetings, 2007-2012
- OECD Recommendation on the Governance of Clinical Trials 2013
- Risk proportionate approaches in clinical trials Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use 25 April 2017.
- ICH Reflection on "GCP Renovation": Modernization of ICH E8 and Subsequent Renovation of ICH E6, 2017.

Type of Expert Working Group and Resources

The EWG will include experts from various disciplines including clinical, statistical, data science, clinical outcomes assessment, regulatory compliance, and potentially others. The group should have overlap of expertise with the experts of the E8(R1) EWG and work in close collaboration with them. The work of the group will involve engagements with a variety of stakeholders including academia and patient advocacy groups throughout the development process.

Timing

This work is considered time-critical and highly anticipated by the regulated community. The working group was launched in September of 2019 and the first face-to-face meeting is scheduled for November of 2019. It is anticipated that the process to create the overarching principles and objectives document and Annex 1 is expected to take 18 - 24 months to reach *Step 1*, once the concept paper and business plan are endorsed. After the priniciples and objectives document and Annex 1 complete *Step 1*, the work on Annex 2 will commence.

附件 3、ICH E6(R3) Final Business Plan

Final Business Plan
ICH E6(R3): Guideline for Good Clinical Practice
Dated 17 November 2019
Endorsed by the Management Committee on 18 November 2019

1. The issue and its costs

- *What problem/issue is the proposal expected to tackle?*

  In the two decades since ICH E6 was first drafted, clinical trials have become more complex with respect to trial design, use of technology, quantity of data collected and involvement of central testing facilities or other service providers. ICH E6(R2) was developed with multiple addenda to address the emerging use of electronic data sources and risk management processes. However, since the development of E6(R2), clinical trials have continued to evolve with new designs and technological innovations. There is also a desire that E6(R3) should be developed to provide guidance that is applicable to different clinical trial designs and to focus on key principles and objectives. E6(R2) included a focus on a proportionate, risk-based approach to the design and conduct of clinical trials. E6(R3) will be designed to further advance this concept and to encourage relevant parties to utilize this approach.

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

  E6(R2) is not fully designed to address emerging technologies, innovations in trial design, the diversity of data sources, testing facilities, and service providers, or to address other emerging complexities of the current clinical trial climate. In the absence of a modernized guideline, reference may be made to the current provisions in E6, even though the requirements may not be fully adapted to these technologies, or stakeholders may fail to adopt the current requirements. The application of the current standard to new technology is clearly challenging. Consequently, the design and conduct of trials, including in particular investigator site, test facility or service provider activities and record-keeping, may fail to take full advantage of technological innovations and the full potential of the risk-based considerations related to participant protection, data integrity or other public health considerations.

2. Planning

- *What are the main deliverables?*

  This work will set out principles which will be aligned with those set out in E8(R1) *Revision of General Considerations for Clinical Studies*. When complete, E6(R3) will be composed of an overarching principles and objectives document, Annex 1 (interventional clinical trials), and Annex 2 (additional considerations for non-traditional interventional clinical trials). The overaching principles and objectives document and Annex 1 will replace the current E6(R2).

附件 3、ICH E6(R3) Final Business Plan(續)

The development of Annex 2 will commence once the principles and objectives document and Annex 1 complete ICH *Step 1*. The revision aims to address identified gaps or inconsistencies in existing ICH guidances as appropriate.

The proposed rewrite will include more specific discussions and refinement to E6 principles in the context of different trial types and data sources in the annexes as described below:

- Annex 1 - Interventional clinical trials

  This will include the use of unapproved or approved drugs in a controlled setting with prospective allocation of treatment to participants and collection of trial data. This Annex will be developed simultaneously with the principles and objectives document to ensure consistency and to provide stakeholders with a complete package that can replace E6(R2); and

- Annex 2 - Additional considerations for non-traditional interventional clinical trials

  This will include designs such as pragmatic clinical trials and decentralized clinical trials, as well as those trials that incorporate real world data sources. Before the drafting of Annex 2, its scope will be further clarified, to define the nature of trials involved, in an update to this concept paper.

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

  The EWG will include experts from various disciplines including clinical, statistical, data science, clinical outcomes assessment, regulatory compliance, and potentially others. The group should have overlap of expertise with the experts of the E8 EWG and work in close collaboration with them. The work of the group will involve engagements with a variety of stakeholders including academia and patient advocacy groups throughout the development process.

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

  Fall 2019 through Fall of 2021.

  This work is considered time-critical and highly anticipated by the regulated community. The working group was launched in September of 2019 and the first face-to-face meeting is scheduled for November of 2019. It is anticipated that the process to create the overarching principles and objectives document and Annex 1 is expected to take 18 - 24 months to reach *Step 1*, once the concept paper and business plan are endorsed. After the priniciples and objectives document and Annex 1 complete *Step 1*, the work on Annex 2 will commence.

- *What will be the key milestones?*

  The established ICH processes and procedures should be followed. The proposed revision is expected to take approximately 18-24 months to reach Step 1.

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

  The EWG will plan and execute multiple engagements with other ICH groups (especially the group working on E8) to ensure mutual learning and consistency. The EWG is planning to engage with appropriate stakeholders, including those from academic and patient-advocacy backgrounds, to maximize the relevance and utility of E6(R3).

3. The impacts of the project

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

  The proposed revision to ICH E6 would likely primarily benefit innovators who typically conduct clinical trials, such as those in the pharmaceutical and biotech sectors. work will also inform innovators who are utilizing or exploring the use of diverse trial types and the data sources being employed to support regulatory and healthcare related decision-making on drugs, The revised E6 will highlight that achieving GCP principles and objectives can be accomplished through the use of multiple tools and methods. It will also highlight that the implementation of GCP principles should be a thoughtful, deliberative, and risk-based process as clinical trials can vary greatly and certain aspects of GCP may not be applicable to every trial. The revised E6 will take into consideration the diversity of clinical trials.

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

  We expect the revised E6 to be implementable from a regulatory perspective.

4. Post-hoc evaluation

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

  The draft revisions will be subject to review and feedback from stakeholders. The development of annexes in addition to the principles document as a part of E6(R3) is expected to add robustness and flexibility that enables future adoption whenever appropriate.