ICH E6(R3) の背景・概念

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本演題発表に関連して、開示すべきCOI関係にある企業等はありません。

発表内容

- E6改訂の背景/目的
- 現在の作業状況と今後の予定

ICH-E6: An Important Global Standard for Clinical Trial Conduct

- **E6: Good Clinical Practice (GCP) – finalized in 1996**
- **Describes the responsibilities and expectations of stakeholders in the conduct of clinical trials**
- **GCP covers aspects of monitoring, reporting, and archiving clinical trials**
- **E6 (R2) – finalized in 2016**
- **Addendum to encourage implementation of improved and more efficient GCP approaches**
- **Updated standards for electronic records**

ICH E8 & E6
Connected Development

E8 clinical trial design principles

E6 GCP clinical trial conduct principles

E6改訂の背景

- 1996年　ICH-E6 策定
- 2016年　ICH-R6(R2) Integrated addendumの追加
  - リスクベースアプローチ
  - 技術革新への対応（電子システム等の既存概念の明確化）

- 2016年 パブリックコメントにおける国際コンソーシアム等からの意見
  - 多様な試験のタイプの違いによるリスクの違いに十分に配慮されていない
  - 試験の質に関する重要な要因に、より焦点を当てるべきである
- 2017年1月: ICH Reflection Paper
  ‘GCP Renovation’（E8の近代化とそれに続くE6改訂）

E8：臨床試験の一般指針
E6：医薬品の臨床試験の実施の基準

E6改訂の目的

- 臨床試験のデザインやデータソースの多様化に対応するため、GCP Renovationの一連の作業として、ICH E8（臨床試験の一般指針）の近代化に引き続き、現行のICH E6(R2)ガイドラインを改訂するもの

＜ICH Reflection on “GCP Renovation”（January 2017）より＞

1: Revision to ICH E8

- Address broader concerns about the principles of study design and planning for an appropriate level of data quality
- Provides comprehensive cross-referencing to the family of ICH guidance documents

2: Renovation of ICH E6 GCP

- Address flexibility concerns with respect to a broader range of study types and data sources
- Retains the current focus on good clinical investigative site practices

ICH Reflection Paper on GCP Renovation
http://development.ich-public-backend.dev8.penceo.com/sites/default/files/2019-04/ICH_Reflection_paper_GCP_Renovation_Jan_2017_Final.pdf

EWG活動経緯

- 2019年6月
  - ICHアムステルダム会合にて，新規トピックとして採択
    （提案団体：FDA）
- 2019年11月17日～20日
  - シンガポールにて ICH E6(R3) Informal Working Group (IWG) 会合開催
  - Concept Paper, Business Plan承認
- 2019年11月～ EWG活動開始
  - 定期電話会議
  - 2020年5月：バンクーバー会合代替電話会議
  - 2020年11月：アテネ会合（中止）→代替となる電話会議を実施。

Concept Paper (1)

Issues to be Resolved

- Overarching Principles and Objectives
- Annex 1 - Interventional clinical trials

現行のR2を置き換えるもの

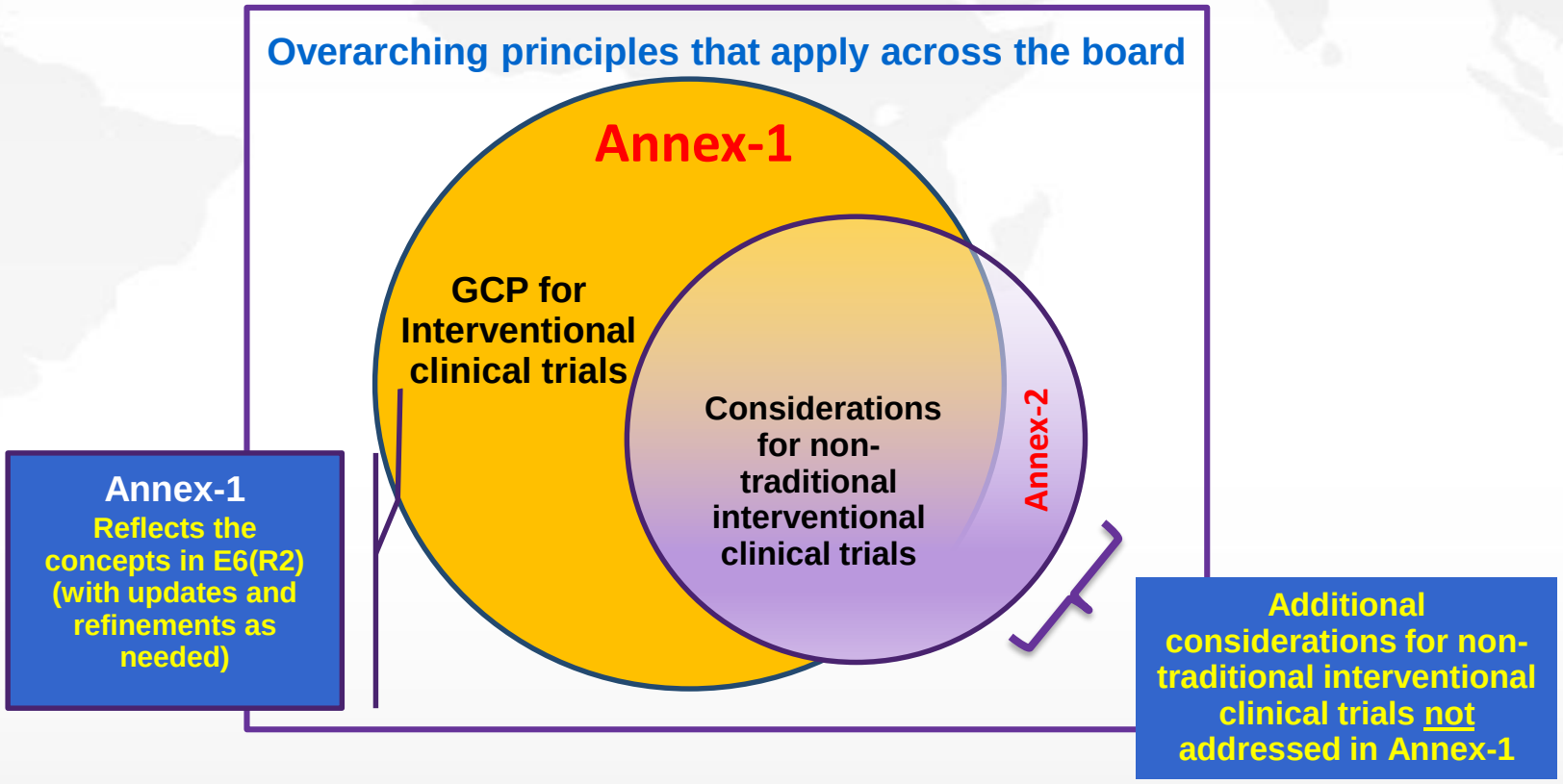
This will include the use of unapproved or approved drugs in a controlled setting with prospective allocation of treatment to participants and collection of trial data. This Annex will be developed simultaneously with the principles and objectives document to ensure consistency and to provide stakeholders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

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

追加の考慮が必要な点

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.

Conceptual Representation of the Approach to ICH E6(R3)



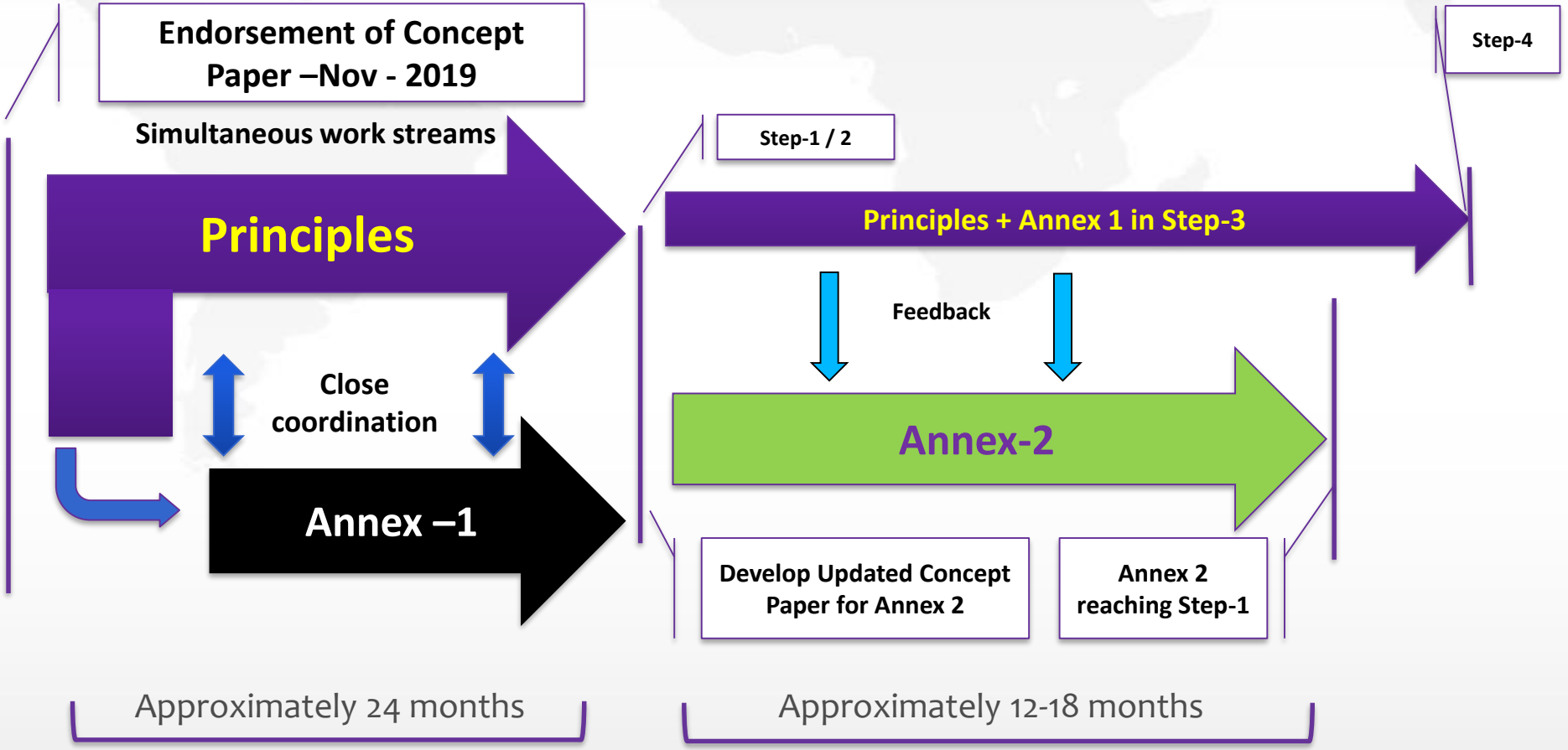
Annex 1 and Annex 2

- **Annex 1 – Interventional Clinical Trials**
  - Considers principles as they relate to the use of unapproved or approved drugs in a controlled setting with prospective allocation of treatment to participants and collection of trial data

- **Annex 2 – Additional Considerations for Non-traditional Interventional Clinical Trials**
  - Considers principles as they relate to the use of non-traditional clinical trial designs such as pragmatic clinical trials and decentralized clinical trials, as well as those trials that incorporate real world data sources

Approach to E6(R3) Development

Simultaneous work on the principles & Annex-1



Engagement

- Many stakeholders are impacted by ICH-E6 GCP guidelines
- E6 stakeholder outreach approaches are approved by ICH and are ongoing.
- The knowledge gained by learning from stakeholder experiences and viewpoints will further enrich EWG discussions

- ICH E6 Summary Engagement Plan - https://admin.ich.org/sites/default/files/2020-05/E6-R3_PublicEngagemenSummary_2020_0421.pdf

Concept Paper (2)

- **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 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.

様々なステークホルダーの意見を取り入れながら検討を進める

Stakeholder Engagement

- 各地域における意見聴取
  - アカデミア、患者団体、その他ステークホルダーからのE6改訂に関する意見聴取
  - 対象や方法は各地域に任される
  - 結果の概要をEWGに共有

- EWG会議へのステークホルダーの参加
  - アカデミアの専門家（及び今後、場合によっては他のステークホルダー）を招聘し、EWG会議（ただし内部議論とは分けて開催）に参加いただく
  - ガイドライン案作成早期に実施

https://admin.ich.org/sites/default/files/2020-05/E6-R3_PublicEngagemenSummary_2020_0421.pdf

➡日本では厚生労働科学特別研究班にて対応

ICH-E6(R3)

- Comprehensive principles that remain relevant as technology evolves and clinical trial design advances
- Risk-based approach and proportionality
- Thoughtful process throughout clinical trial conception, design, conduct and analyses

Progress

- EWG continued its work on the principles and introduction of ICH-E6(R3).
- Major principles are now outlined and explained.
- Unlike ICH-E6(R2), the draft principles for ICH-E6(R3) contain further explanations and important considerations.
- The ICH-E6(R3) principles are designed to be interdependent and should be viewed as a connected body.
- The EWG further refined the introduction of ICH-E6(R3) to serve stakeholders by providing details on how to read and utilize ICH-E6(R3).

Progress

- Principles of ICH-E6(R3) are meant to remain relevant as trial designs, methodology, and technology evolve.
- Principles address multiple key concepts including:
  - ❑ Focusing on critical to quality factors, such as the risks to participants and risks to trial results
  - ❑ Highlighting the importance of risk-based, proportional approach to determining trial processes and design elements
  - ❑ Encouraging the incorporation of innovations that are customized to fit the design and purpose of the trial
- Engagement with stakeholders

Progress

Stakeholder input

- Focus on-risk-based approach, proportionality, and fit-for-purpose. Minimize over-interpretation and avoid a “one size fits all approach.”
- Focus and clarify important aspects such as remote monitoring, quality and risk management.
- Accommodate new trial designs (e.g., decentralized trials, platform, and adaptive trials), and new data sources, such as real-world data (e.g., medical records, claims).
- Address trends in technology for trial conduct (e.g., bringing trials to participants, telehealth, e-Consent, remote training, IP shipment to participants).
- Input from investigators, academic research institutions, and trial participants is critical to inform trial design and conduct. Engage participants as partners in protocol design, trial conduct, and other aspects of clinical trials. Identify outcomes relevant to participants.
- Importance of doing adequate clinical trials, avoid wasting resources or time of participants and investigators.
- Others: scope, informed consent, GCP training, activity logs, drug accountability, data and information management, clear language-not jargon

Themes from the Principles (work-in-progress)

- **Declaration of Helsinki**
- **Rights, safety, and well-being of trial participants is paramount**
- **Consent and consent process are integral features of the ethical conduct of a trial. Should take into consideration:**
  - Relevant aspects of the trial (e.g., trials in emergency situations),
  - The potential use of technology to inform participants and obtain informed consent.
- **Independent ethics review – IRB/IEC**
- **Trials should be scientifically sound for their intended purpose**
- **Trials should be conducted by qualified individuals**
- **Clinical trial designs and processes should be proportionate to the risks inherent in the trial, including those to participants, and the importance, to the trial objectives, of the data being collected**

Themes from the Principles (work-in-progress)

- **Quality should be built into the design and conduct of the trial**
- **Clinical trials should be well-articulated in a concise and operationally viable protocol**
- **Clinical trials should be designed and conducted to generate reliable results**
- **Roles, tasks and responsibilities in clinical trials should be clear and documented appropriately**
- **Investigational products being studied in clinical trials should be:**
  - manufactured in accordance with Good Manufacturing Practice (GMP) standards and
  - stored, shipped, and handled in accordance with the product specifications and the approved protocol.

Work on Annex-1 - GCP for Interventional Clinical Trials

Gap Analysis

Gap Analysis

Stakeholder Comment Analysis

- **Academic Responses**
  - Open letter to EMA & ICH
  - Published articles
- **Responses to CTTI survey, comments, and interviews on "Informing the Renovations to the ICH E6" Project**
- **Regional Engagement Materials**
  - Americas Engagement Meeting (meeting transcripts and public comments)
  - Europe Engagement Meeting (meeting report)
  - Survey findings from Japanese academic investigators

ICH Guideline Analysis

- All Efficacy Guidelines + M11
- Peer-review publications

Purpose: to identify opportunities for improvement in E6 (R3) highlighted by external stakeholders and to provide EWG with information on where E6 (R3) modifications may be needed.

現在の作業状況

- Overarching Principles
  ー構成や追加すべき項目、内容・文案の検討を継続

- Annex 1
  ー改訂作業に向けた論点及び進め方の議論を開始

- Stakeholder Engagement
  ーアカデミア・患者団体からの意見聴取

Next Steps:

- EWG determining changes needed in R3
- EWG determining potential structure and content in R3 Annex 1
- EWG to continue to refine the draft introduction and principles
- Continue the engagement with stakeholders

今後のEWGの予定

- マイルストーン
  - 2021年 5月～6月 : ICH仁川会合
  - 2021年5月～11月:Annex 1までについて Step 1※到達
  - Annex1までStep1到達後、Annex2の検討開始

※Step1：専門家作業部会（EWG）による技術ドキュメント（ガイドライン案のベース）作成

ご清聴，ありがとうございました