General principles on planning/designing Multi-Regional Clinical Trials E17

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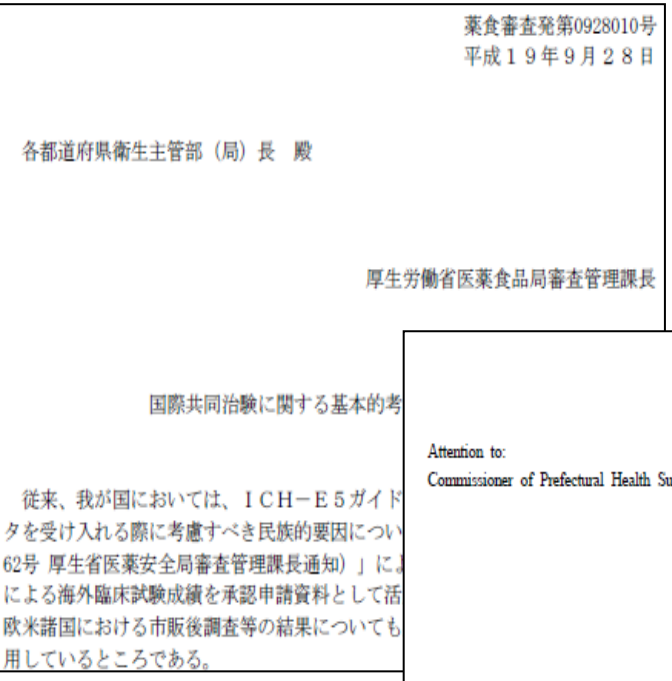
Pharmaceuticals and Medical Devices Agency (PMDA)

日本での国際共同治験に関するガイドライン

2007 年



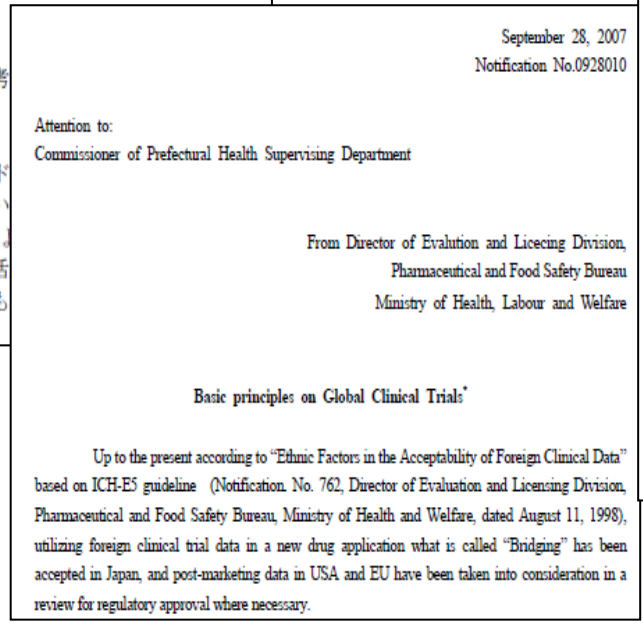
薬食審査発第0928010号
平成１９年９月２８日

各都道府県衛生主管部（局）長　殿

厚生労働省医薬食品局審査管理課長

国際共同治験に関する基本的考

従来、我が国においては、ＩＣＨ－Ｅ５ガイド
タを受け入れる際に考慮すべき民族的要因につい
62号 厚生省医薬安全局審査管理課長通知）」に
による海外臨床試験成績を承認申請資料として活
欧米諸国における市販後調査等の結果についても
用しているところである。



September 28, 2007
Notification No.0928010

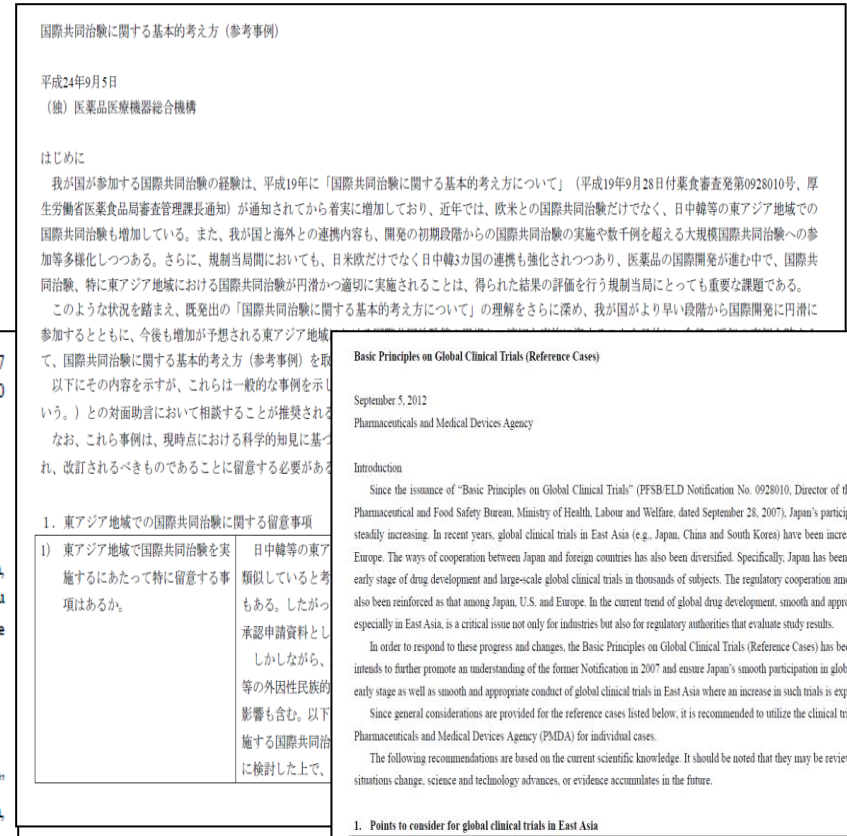
Attention to:
Commissioner of Prefectural Health Supervising Department

From Director of Evalution and Licecing Division,
Pharmaceutical and Food Safety Bureau
Ministry of Health, Labour and Welfare

Basic principles on Global Clinical Trials*

Up to the present according to "Ethnic Factors in the Acceptability of Foreign Clinical Data" based on ICH-E5 guideline (Notification No. 762, Director of Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health and Welfare, dated August 11, 1998), utilizing foreign clinical trial data in a new drug application what is called "Bridging" has been accepted in Japan, and post-marketing data in USA and EU have been taken into consideration in a review for regulatory approval where necessary.

2012 年



国際共同治験に関する基本的考え方（参考事例）

平成24年9月5日
（独）医薬品医療機器総合機構

はじめに

我が国が参加する国際共同治験の経験は、平成19年に「国際共同治験に関する基本的考え方について」（平成19年9月28日付薬食審査発第0928010号、厚生労働省医薬食品局審査管理課長通知）が通知されてから着実に増加しており、近年では、欧米との国際共同治験だけでなく、日中韓等の東アジア地域での国際共同治験も増加している。また、我が国と海外との連携内容も、開発の初期段階からの国際共同治験の実施や数千例を超える大規模国際共同治験への参加等多様化しつつある。さらに、規制当局間においても、日米欧だけでなく日中韓3カ国の連携も強化されつつあり、医薬品の国際開発が進む中で、国際共同治験、特に東アジア地域における国際共同治験が円滑かつ適切に実施されることは、得られた結果の評価を行う規制当局にとっても重要な課題である。

このような状況を踏まえ、既発出の「国際共同治験に関する基本的考え方について」の理解をさらに深め、我が国がより早い段階から国際開発に円滑に参加するとともに、今後も増加が予想される東アジア地域

て、国際共同治験に関する基本的考え方（参考事例）を取

以下にその内容を示すが、これらは一般的な事例を示し
いう。）との対面助言において相談することが推奨され

なお、これら事例は、現時点における科学的知見に基づ
れ、改訂されるべきものであることに留意する必要があ

1．東アジア地域での国際共同治験に関する留意事項

1) 東アジア地域で国際共同治験を実施するにあたって特に留意する事項はあるか。	日中韓等の東ア 類似していると考 もある。したがっ 承認申請資料とし しかしながら、 等の外因性民族的 影響も含む。以下 施する国際共同治 に検討した上で、

Basic Principles on Global Clinical Trials (Reference Cases)

September 5, 2012
Pharmaceuticals and Medical Devices Agency

Introduction

Since the issuance of "Basic Principles on Global Clinical Trials" (PFSB/ELD Notification No. 0928010, Director of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated September 28, 2007), Japan's participation in global clinical trials has been steadily increasing. In recent years, global clinical trials in East Asia (e.g., Japan, China and South Korea) have been increasing as well as those in the U.S. and Europe. The ways of cooperation between Japan and foreign countries has also been diversified. Specifically, Japan has been involved in global clinical trials at an early stage of drug development and large-scale global clinical trials in thousands of subjects. The regulatory cooperation among Japan, China and South Korea has also been reinforced as that among Japan, U.S. and Europe. In the current trend of global drug development, smooth and appropriate conduct of global clinical trials, especially in East Asia, is a critical issue not only for industries but also for regulatory authorities that evaluate study results.

In order to respond to these progress and changes, the Basic Principles on Global Clinical Trials (Reference Cases) has been developed. Based on recent cases, it intends to further promote an understanding of the former Notification in 2007 and ensure Japan's smooth participation in global drug development activities from an early stage as well as smooth and appropriate conduct of global clinical trials in East Asia where an increase in such trials is expected.

Since general considerations are provided for the reference cases listed below, it is recommended to utilize the clinical trial consultation with the Pharmaceuticals and Medical Devices Agency (PMDA) for individual cases.

The following recommendations are based on the current scientific knowledge. It should be noted that they may be reviewed and revised as needed, if situations change, science and technology advances, or evidence accumulates in the future.

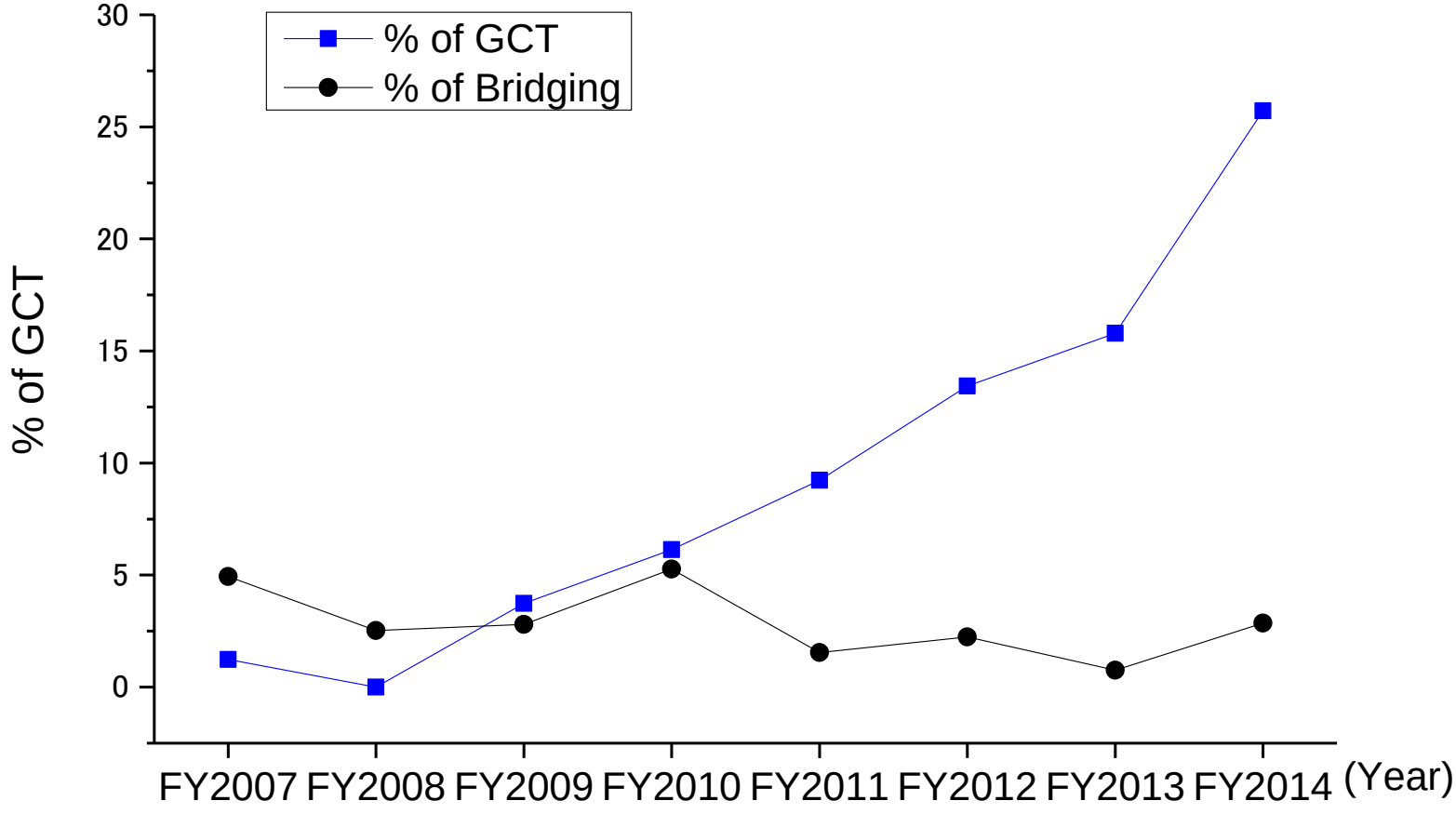
1. Points to consider for global clinical trials in East Asia

(1) What are the special points to consider when conducting a global clinical trial in East Asia?	The types and frequency of metabolic enzyme polymorphisms and gene profiles are thought to be similar among East Asian ethnicities in Japan, China and Korea. Some drugs have recently been approved mainly based on the data from pivotal global clinical trials conducted in East Asia. Data from well-designed and conducted global clinical trials in East Asia is acceptable for documents of new drug application in Japan. However, the difference in ethnic factors (intrinsic factors as well as extrinsic factors such as local clinical practice and socioeconomic condition) may affect the efficacy and safety of drugs (effects not only on the data themselves but also on

Japanese：http://www.pmda.go.jp/operations/notice/2007/file/0928010.pdf
English：http://www.pmda.go.jp/operations/notice/2007/file/0928010-e.pdf

Japanese：http://www.pmda.go.jp/regulatory/file/guideline/new_drug/GCT_jirei.pdf
English：http://www.pmda.go.jp/regulatory/file/english_guideline/new_drug/GCT-jirei_en.pdf

Development strategies for drug approval in Japan



Total	81	79	107	114	130	134	133	35
MRCT	1	0	4	7	12	18	21	9
Bridging	4	2	3	6	2	3	1	1

As of July

2014年　新たな事務連絡発出

国際共同治験開始前の日本人での第Ⅰ相試験の実施に関する基本的考え方について

事　務　連　絡
平成 26 年 10 月 27 日

各都道府県衛生主管部（局）　御中

厚生労働省医薬食品局審査管理課

国際共同治験開始前の日本人での第Ⅰ相試験の実施に関する
基本的考え方について

新しい医薬品をより早く患者のもとに届けるための対策の１つとして、国際共同治験への日本の積極的な参加を推進する観点から、これまで、「国際共同治験に関する基本的考え方について」（平成19年９月28日付け薬食審査発第0928010号厚生労働省医薬食品局審査管理課長通知）及び「「国際共同治験に関する基本的考え方（参考事例）」について」（平成24年９月５日付け厚生労働省医薬食品局審査管理課事務連絡）を発出したところです。

今般、これまでに集積された知見を踏まえ、「国際共同治験開始前の日本人での第Ⅰ相試験の実施に関する基本的考え方」を、別添のとおりとりまとめましたので、業務に活用頂くとともに、貴管下関係業者に対し、周知方ご協力お願いします。

Administrative Notice
October 27, 2014

To: Prefectural Health Department (Bureau)

Evaluation and Licensing Division,
Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare

Basic Principles for Conducting Phase I Trials in the Japanese Population
Prior to Global Clinical Trials

As one of the key factors toward timely patient access to new drugs, the "Basic principles on Global Clinical Trials" (PFSB/ELD Notification No. 0928010, Director of Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated September 28, 2007) and the "Basic Principles on Global Clinical Trials (Reference Cases)" (Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated September 5, 2012) have been issued from the perspective of promoting Japan's active participation in global clinical trials.

Based on the accumulated knowledge up to now, the "Basic Principles for Conducting Phase I Trials in the Japanese Population Prior to Global Clinical Trials" has been compiled as attached. We ask you to inform manufacturers and sellers placed under your administration to utilize this for their business operations.

ICH E17ガイドラインの目的

Final Concept Paper of E17

(dated 21 May 2014 Endorsed by the ICH Steering Committee on 5 June 2014)

Statement of the Perceived Problem

- Drug development has rapidly been globalized recently and MRCT for regulatory submission has widely been conducted in non-ICH regions as well as ICH regions. Regulatory agencies currently face challenges in evaluating data from MRCTs for drug approval. However, there is currently no harmonised ICH Guideline on MRCTs, especially focusing on scientific issues in planning/designing MRCTs, although Q&A of ICH E5 Guideline partly covers issue relating to MRCTs. An international guideline will be needed to promote conducting MRCT appropriately. A lack of harmonisation on this topic may cause additional burden for sponsor and difficult situation for conducting MRCTs.

Issues to be Resolved

- The new guideline will describe practical issues in planning/designing MRCT. Issues on data interpretation may be discussed in a process of discussion for establishing this guideline, but are out of scope in this guideline. Main objective of this guideline is to provide common points to consider in planning/desingning MRCTs and minimize conflicting opinions from regulatory bodies.

リスボン会合前の活動

- The 1st web-based conference was held on October 1st (Preparation for the Lisbon meeting)
  - Sharing a concept of E17 guideline based on the final concept paper approved by SC
  - Brief discussion about items to be discussed in Lisbon

- Discussion by e-mail after the web-conference
  - Collected comments from all parties about points to be included in E17
  - Prepared the draft document for discussion in Lisbon

ICHリスボン会合

リスボン会合での活動

Date	Task / Activity
Day 1	➢ Introduction (first F2F meeting) ➢ Short presentation from each region ➢ Discuss about a draft table of contents
Day 2-3	Continued discussion and preparation for the report to SC
Day 4	Confirm a process for discussion after the meeting and future work plan

リスボン会合の成果

- Sharing regional perspectives as to what topics should be covered in this guideline.
- Reaching a consensus on a table of contents of E17 guideline
- Initiating to draft concrete sentences of some sections in the guideline
- Confirmed that E17 guideline is really important to improve current situation of global drug developemnt and promote simultaneous regulatory submission in multiple countries/regions

Current table of contents (E17)

Current table of contents (E17)

2. General recommendations in planning/designing MRCT
   - 2.2 Clinical trial design and protocol-related points
     - 2.2.1 Pre-consideration of regional variability on efficacy/safety
     - 2.2.2 Subject selection
     - 2.2.3 Selection of doses in MRCTs
     - 2.2.4 Choice of endpoint/index
     - 2.2.5 Estimation of a sample size and a proportion of each regional subjects in an MRCT
     - 2.2.6 Collecting and handling efficacy/safety information in MRCTs
     - 2.2.7 Statistical analysis plans that specifically address the features of MRCTs
     - 2.2.8 Selection of comparator (where applicable)
     - 2.2.9 Handling concomitant medications or therapies in a MRCT
3. GLOSSARY

今後の予定

- 各項の詳細化
  - by e-mail and the web-based conference
  - The web-based conference will be held early next year (at least two meeting; probably in February and April)

- 次回対面会合を、次のICH会合に合わせて実施する方向でSteering Committeeに要望中

現在のスケジュール

- First face-to-face EWG Meeting in November 2014 in Lisbon
- Discussion by e-mail and web-based conference:

  4Q 2014 - 1Q 2015
- Second F2F EWG Meeting in 2Q 2015 for coordinating opinions of all parties and delivering Step 1 document
- Third F2F EWG meeting in 4Q 2015 for adaption of *Step 2* document
- Public consultation: 4Q 2015 - 2Q 2016
- Revision of the guideline based on comments: 2Q 2016 - 4Q 2016 (depending on contents of comments recieved)
- Fourth face-to-face EWG Meeting for adaption of *Step 4* document in 4Q 2016 or 2Q 2017

Thank You!

International Conference on Harmonisation of
Technical Requirements
for Registration of Pharmaceuticals for Human Use