

Impact of MRCT after ICH E17 fully implement -Regulatory perspective-

5th Joint Conference of Taiwan and Japan
on Medical Products Regulation

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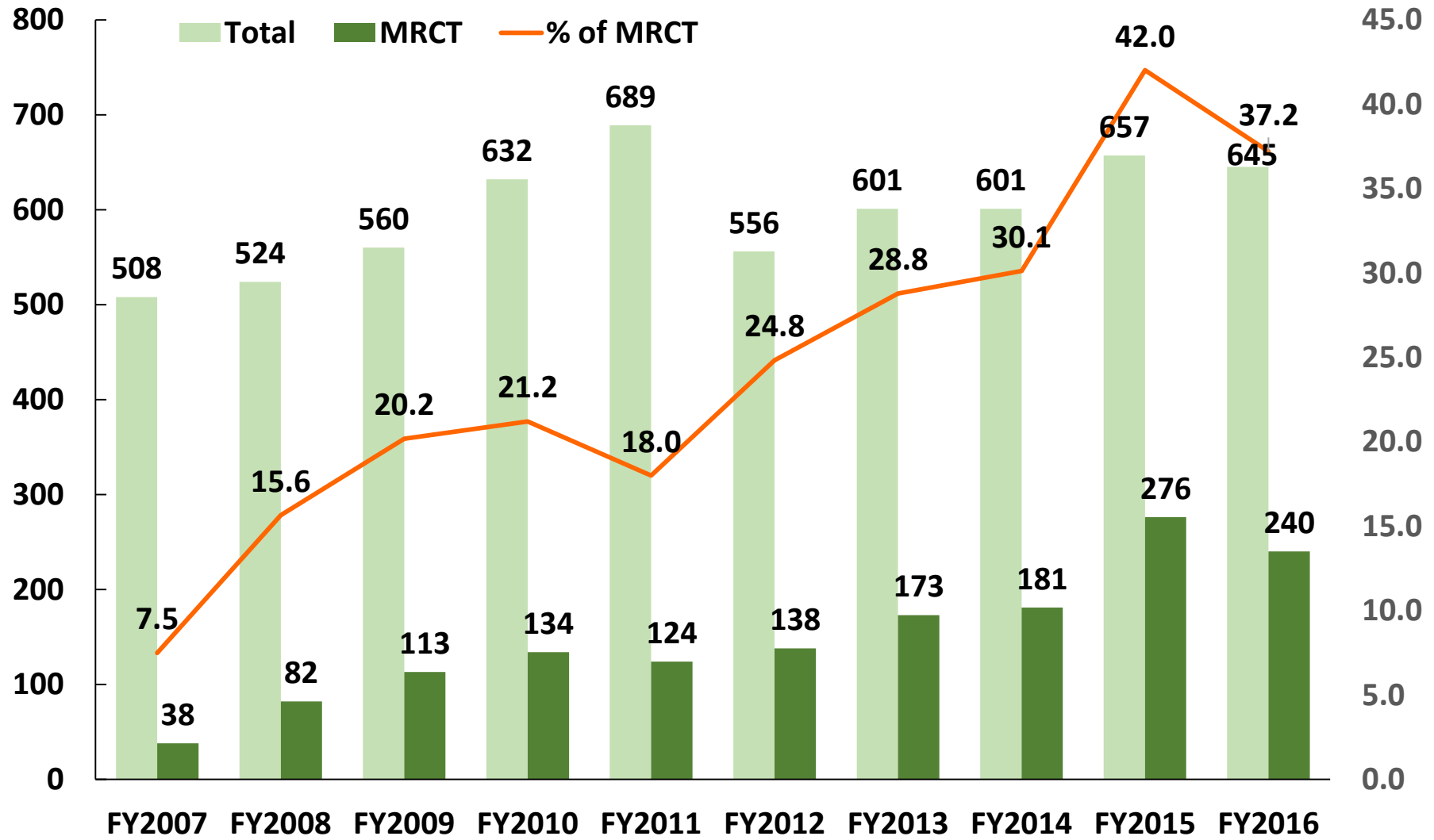
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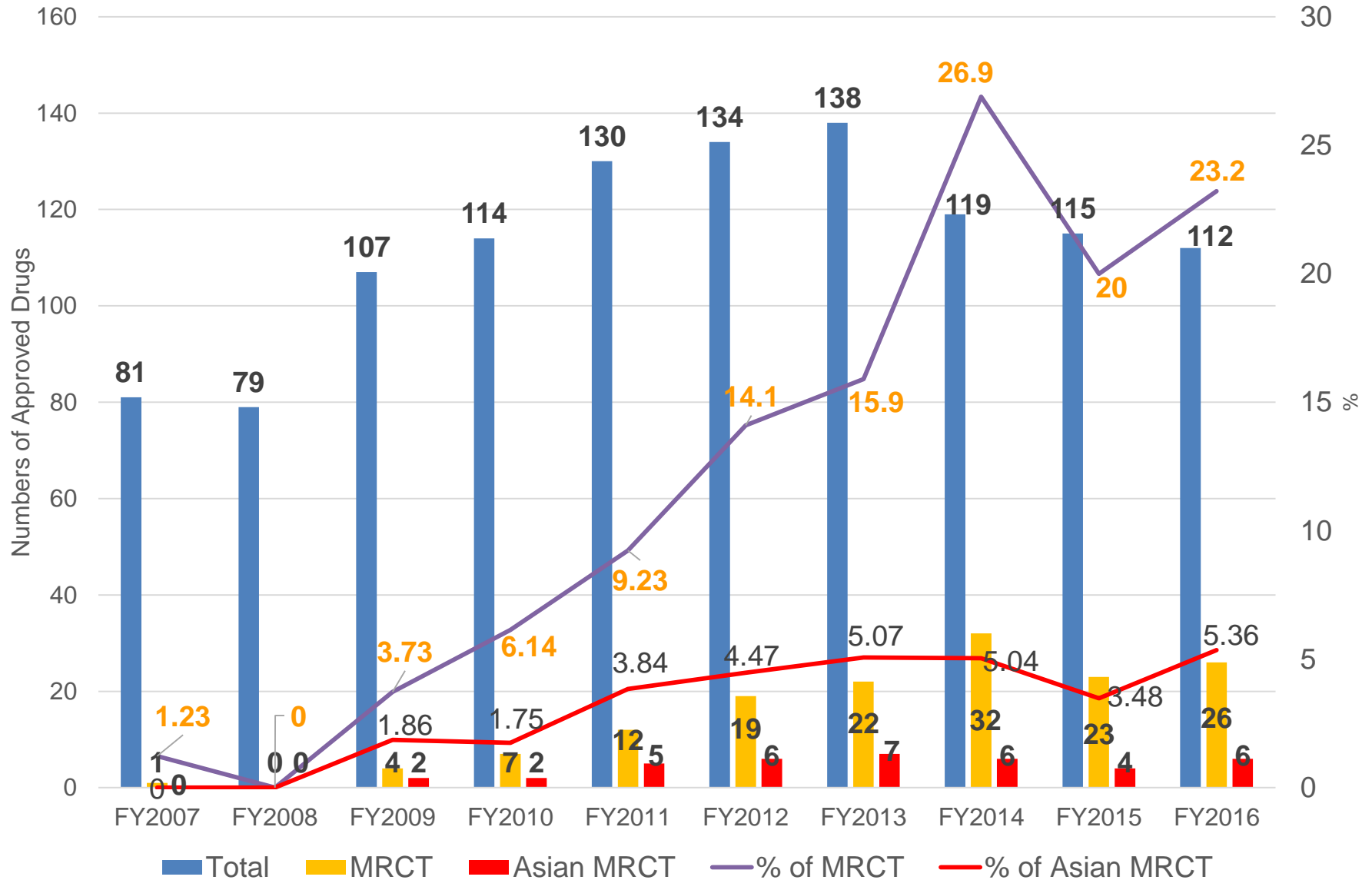
The views expressed in this presentation are those of the presenter and do not necessarily reflect the official views of Pharmaceuticals and Medical Devices Agency (PMDA).

Guideline	Issued year	Contents
Basic principles on Global Clinical Trials	2007	<ul style="list-style-type: none">➤ Basic requirements to conduct a MRCT➤ Basic points to consider in designing a MRCT
Basic principles on Global Clinical Trials (Reference Cases)	2012	<ul style="list-style-type: none">➤ Points to consider for MRCTs in East Asia➤ General points to consider for MRCTs
Basic principles for Conducting Phase1 Trials in the Japanese Population Prior to Global Clinical Trials	2014	<ul style="list-style-type: none">➤ Reference cases regarding the necessity of conducting a phase1 trial in the Japanese population

Trends of MRCT-related Clinical Trial Notifications in Japan



Trends of new drug application based on MRCTs in Japan



The state of E17 guideline



- First face-to-face EWG Meeting in November 2014 in Lisbon
- Second F2F EWG Meeting in June 2015 in Fukuoka
- Third F2F EWG Meeting in December 2015 in Jacksonville
- Step1 sign off by the experts in May-June 2016
- Reaching step2 a/b at the ICH Lisbon meeting in June 2016
- Public consultation
- Fourth F2F EWG Meeting in November 2016 in Osaka
- Fifth F2F EWG Meeting in June 2017 in Montreal
- Reaching step3/4 at sixth F2F EWG Meeting in November 2017 in Geneva !

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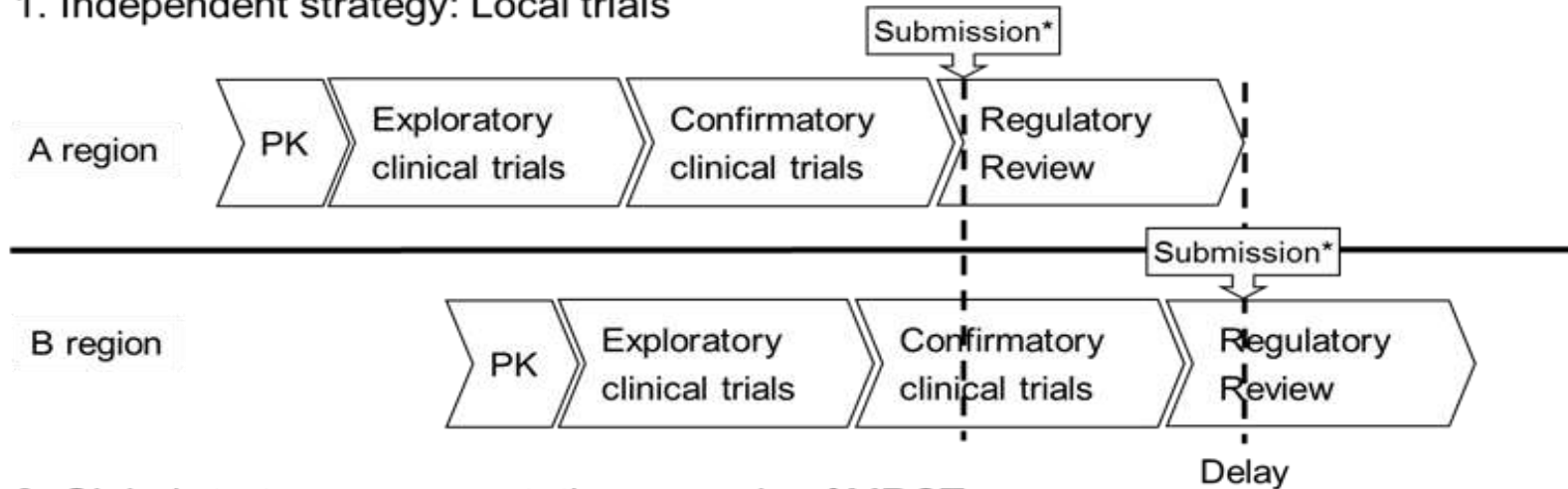
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- The purpose of this guideline is to describe general principles for the planning and design of MRCTs **with the aim of increasing the acceptability of MRCTs in global regulatory submissions.**
- The primary focus of this guideline is on MRCTs designed to provide data that will **be submitted to multiple regulatory authorities** for drug approval (including approval of additional indications, new formulations and new dosing regimens) and for studies conducted to satisfy post-marketing requirements.

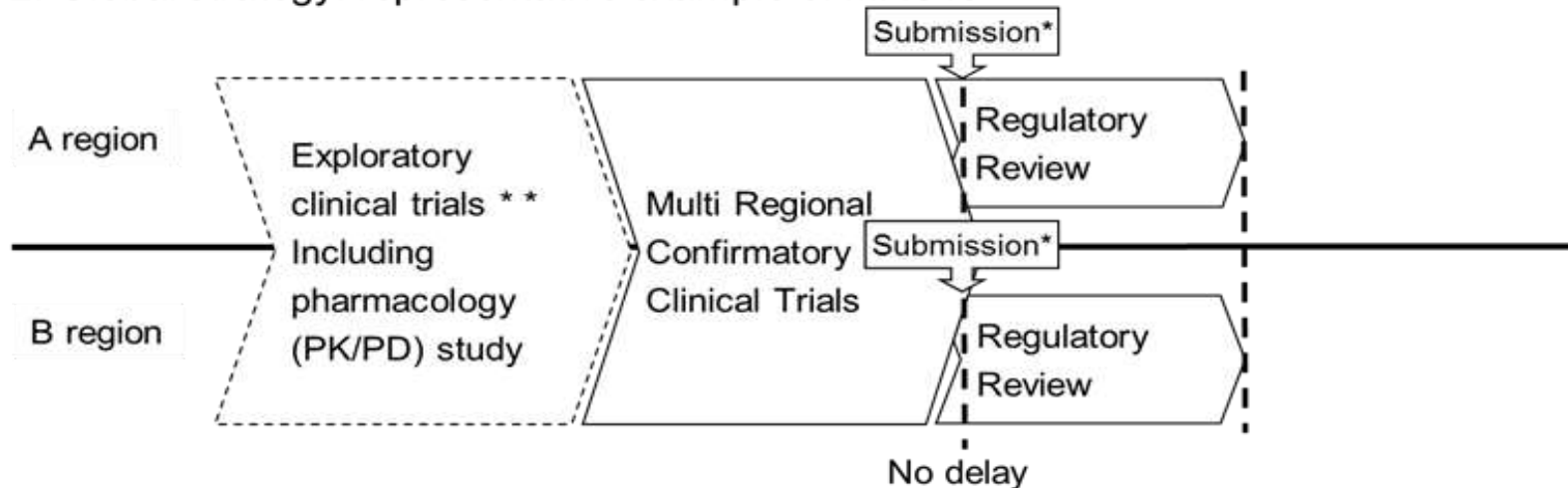
Encouraging simultaneous global drug development



1. Independent strategy: Local trials



2. Global strategy: representative example of MRCTs



*: Marketing Authorization Application/New Drug Application

** : Could be parallel single region trials or MRCTs

1. **Strategic use of MRCTs** in drug development programmes, properly designed and executed according to this guideline, can increase efficiency of drug development. MRCTs may enable simultaneous submission of marketing authorisation applications and support regulatory decision-making in multiple regions, allowing earlier access to new drugs worldwide. Although MRCTs may generally become the preferred option for investigating a new drug for which regulatory submission is planned in multiple regions, the potential for regional differences to impact the interpretability of study results should be carefully considered.

2. The **intrinsic and extrinsic factors** important to the drug development programme, should be identified early. The potential impact of these factors could be examined in the exploratory phases before the design of confirmatory MRCTs. Information about them should also be collected during the confirmatory trial for evaluation of their impact on treatment effects.
3. MRCTs are planned under the assumption that **the treatment effect applies to the entire target population**, particularly to the regions included in the trial. Strategic allocation of the sample size to regions allows an evaluation of the extent to which this assumption holds.

4. **Pre-specified pooling of regions or subpopulations**, based on established knowledge about similarities, may help provide flexibility in sample size allocation to regions, facilitate the assessment of consistency in treatment effects across regions, and support regulatory decision-making.

5. **A single primary analysis approach** for hypothesis testing and estimation of the overall treatment effect should be planned so that it will be acceptable to all concerned regulatory authorities. **A structured exploration** to examine the consistency of treatment effects across regions and subpopulations should be planned.

6. In light of diverse regional practices, **ensuring high quality of study design and conduct** in accordance with ICH E6 in all regions is of paramount importance to ensure the study results are interpretable. Careful attention to quality during trial planning, investigator training, and trial monitoring will help achieve consistently high trial quality required for a successful MRCT.

7. **Efficient communication among sponsors and regulatory authorities** is encouraged at the planning stage of MRCTs, with the goal of obtaining acceptance of a global approach to study design across the different regulatory regions.

- ▶ **Earlier access to innovative therapies**
 - Provide an innovative drug earlier to patients by synchronizing the timing of clinical drug development across different regions
- ▶ **Avoid duplication**
 - Reduce the need to conduct standalone regional or national studies.
- ▶ **Promote international harmonization**
 - A globally harmonized approach to drug development should be considered first.
- ▶ **Provide better evidences for drug approval in each region**
 - Encourage better planning and design of MRCTs based on the latest scientific knowledge and experiences
- ▶ **Longitudinal build-up of capability and infrastructure for global drug development**
 - Planning and conducting high quality MRCTs throughout drug development will build up trial infrastructure and capability

Thank You!