# Regulatory Renaissance in Japan

## *Leading the Way for Pharmaceutical Pioneers!*

*The recent evolution of drug regulations is expediting new drug / clinical development & product launch in Japan. Don't miss this opportunity!*

**Phase 1 study in Japanese prior to MRCT is not required**
if overseas clinical development has been preceded
MRCT:Multi Regional Clinical Trials

**Biosimilar**
Clinical studies in Japanese for regulatory approval are not required

**Ultra-orphan drugs**
Clinical studies in Japanese for regulatory approval are not required

**Orphan & pediatric drugs**
Improvement of regulatory system

**New PMDA offices in the US**
PMDA:Pharmaceuticals and Medical Devices Agency

**PMDA/MHLW consultation is recommended to apply these regulatory changes. IQVIA Japan regulatory consulting experts will assist clients with the consultation to promote the most effective clinical development plan**
MHLW: Ministry of Health, Labour and Welfare

## 1.1 Phase 1 in Japanese Requirements prior to Multi Regional Clinical Trial (MRCT)

Previously, Phase 1 in Japanese was required prior to MRCT

- Phase 1 and/or 2 (without Japan)
- **Phase 1 in Japanese**
- Phase 3 (MRCT with Japan)

The new MHLW notice

Phase 1 in Japanese is not required when below criteria in the decision tree are met

- Phase 1 and/or 2 (without Japan)
- Phase 3 (MRCT with Japan)

### *Decision Tree:* *The decision-tree was originally created by IQVIA Japan based on the new guidance issued by MHLW for the reference*

**STEP 1**
☐ Early clinical development is **preceding outside Japan**
☐ **Safety and tolerability risks** in Japanese subjects can be tolerated and controlled
→ NO → **Careful assessment is essential** whether Japanese Phase 1 study is required or not

*Both Yes* ↓

**STEP 2**
☐ High unmet medical needs
→ NO → **STEP 3**
☐ Pharmacokinetics(PK) and safety are less affected by **ethnic factors**
☐ **Time limitation** to conduct Japanese Phase 1 study prior to MRCT
→ NO → **Careful assessment is essential** whether Japanese Phase 1 study is required or not

*Yes* ↓ *Both Yes* ↓

**Phase 1 not required***

**Note: although Phase 1 study could be skipped in general, PMDA may request sponsor to acquire Japanese PK (/Pharmacodynamics (PD)) data; and depending on the outcomes of the study at the time, they may demand for measures to ensure safety of Japanese patients in Phase III study*

## 1.2 Biosimilar

Previously, Japanese clinical study such as
Phase 1 study (PK/PD) **or** Phase 3 study (Efficacy and safety)
**was required** to assess consistency with overall population

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**Japanese clinical study data are not required** for regulatory approval if it can be explained that ethnic differences do not affect clinical assessments

## 1.3 Ultra-Orphan Drug

The drug may be approved without Japanese clinical data if:

‡ The drug is for treatment of a very serious disease and is **already approved overseas**
‡ The expected number of Japanese patients is **less than 1,000**

Clinical Studies (not Japan) → Clinical Studies (Japan) → J-NDA Filing & Review → Approval

The newMHLW notice

Approved sooner than ever

Clinical Studies (not Japan) → J-NDA Filing & Review → Approval → Submission of Japanese Clinical Data

## 2.1 Improvement of Orphan Drug Designation (ODD) System

New guidance to allow ODD at an early stage of study development and to broaden the scope of designation

Review system for ODD (No updates in the new MHLW notice)

MAA: Marketing Authorization Application
MA: Marketing Authorization

| Orphan Disease : No. of Pts < 50,000 | Clinical Trial (Exploratory) | Clinical Trial (Confirmatory) | MAA | Review 9 Month | MA | Re-examination Period: (Exclusivity Period) 10 years |
|---|---|---|---|---|---|---|

Timing of ODD grant may be at an earlier stage of study development

| Phase 1 study | Phase 2 study | Phase 3 study |
|---|---|---|

**ODD grant** at an earlier stage

The new MHLW notice

**ODD grant** at the timepoint of when efficacy evaluation for Japanese patients are available

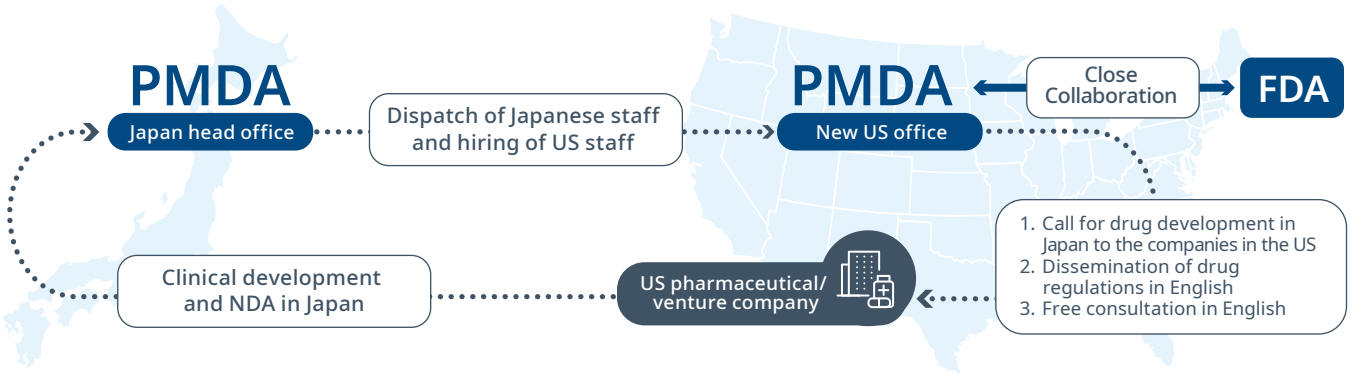
## 2.2 Promoting Pediatric Drug Development

Building a development plan for pediatric use at the time of adult drug development is now desirable for new drugs

- Dissemination of existing incentives
  - Extension of reassessment period by 2 years (maximum 10 years) for pediatric drug development
  - Addition to drug price
- Establishment of new incentives

## 3 Start-up of PMDA US Office

MHLW/PMDA intends to actively promote drug development in Japan by building relationship with the companies in the US




# IQVIA Japan Regulatory consists of expertise that lead successful pathway for your products!

*We propose an efficient regulatory strategy for drug development plan / J-NDA submission according to the new guidance*

### Regulatory Consultation Experience in IQVIA Japan

**>80** PMDA Consultation

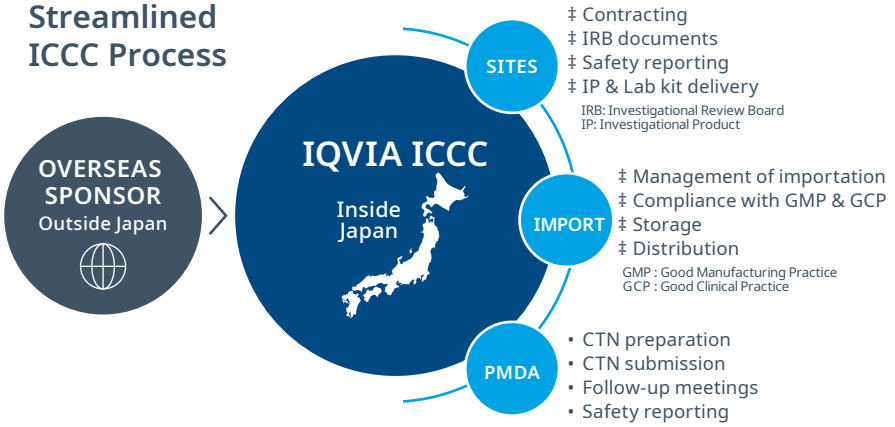
**>70** *Including Gap Analysis, NDA related activities, Orphan Drug Designation, KOL management, etc.

Study Development **>20**

ICCC Experience **>140** protocols

IQVIA Japan successfully passed all inspections and contributed to getting Sponsor products approved for marketing

### Streamlined ICCC Process




The In-Country Clinical Caretaker (ICCC) is the representative of the company who sponsors the clinical study and ensures that procedures are followed as per regulations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