17th DIA Japan Annual Meeting 2020

- Beyond Innovation -

November 8-10, 2020 | ※ Virtual Event

Promoting the Centralized Institutional Review Board (CIRB)

R&D Head Club
Recommendations from the "Clinical Trial Environment Improvement Task Force"

Daiichi Sankyo Company, Limited

Takeshi Yamazaki

DIA

Disclaimer

- The views and opinions expressed in the following PowerPoint slides are those of the individual presenter and should not be attributed to DIA, its directors, officers, employees, volunteers, members, chapters, councils, Communities or affiliates, or any organization with which the presenter is employed or affiliated.
-

R&D Head Club

Our Vision

Japan leads the development of innovative medicines in the world.

Our Mission

Through discussions with Japanese regulators, policy makers, healthcare professionals, academia, patient groups, etc., we will make bold proposals as a development professional for pharmaceutical companies and contribute to the development of global innovative drugs.

R&D Head Club "Clinical Trial Environment Improvement Task Force" Activities (2018～)

1. Promotion of appropriate and transparent site cost

2. Clarification of ideal role for investigator, CRC and CRA

3. Promotion of central IRB

R&D Head Club member company

	Company name		Company name
1	AbbVie GK	11	Janssen Pharmaceutical K.K.
2	Amgen K.K.	12	JAPAN TOBACCO INC
3	Astellas Pharma Inc.	13	MSD K.K.
4	AstraZeneca K.K.	14	Nippon Boehringer-Ingelheim Co., Ltd.
5	Bristol-Myers Squibb K.K.	15	Novartis Pharma K.K
6	Chugai Pharmaceutical Co., Ltd.	16	Otsuka Pharmaceutical Co., Ltd.
7	Daiichi Sankyo Co., Ltd	17	Pfizer R&D Japan GK*
8	Eisai Co., Ltd.	18	Sanofi K. K.
9	Eli Lilly Japan K.K	19	Shionogi & Co., Ltd.
10	GlaxoSmithKline K.K.	20	Takeda Pharmaceutical & Co., Ltd.

*Secretariat

R&D Head Club “Clinical Trial Environment Improvement Task Force” Working Group 3

Department	Name
AbbVie GK	Masayuki Tanabe
GlaxoSmithKline K.K.	Takeo Araki
Daiichi Sankyo Co., Ltd	Takeshi Yamazaki
Chugai Pharmaceutical Co., Ltd.	Harada Ayaka
JAPAN TOBACCO INC	Motoyasu Sano
Nippon Boehringer-Ingelheim Co., Ltd.	Shizuko Kawahara
Novartis Pharma K.K	Tomohiro Uchida
Pfizer R&D Japan GK	Koji Uesugi

※ Company name in alphabetical order

DIA

Current Status of the Institutional Review Board (IRB) in Japan

- ✓ Most sites establish their individual IRBs and review only their matters
  →Few IRBs specialize in therapeutic specific areas

- ✓ Many sites work as both clinical trials office and IRB office ?
  →Most staff are not SMOs, but resources of healthcare professionals

- ✓ Increasing complexity of clinical trials and the development of new technologies (e.g. gene therapy, regenerative medical product) have led to a widespread (increasing burden) increase in knowledge required for IRB members

Current IRB challenges considered by the sponsor from the perspective of international competitiveness (1)

IRB is less frequent than overseas

– Many sites hold IRB approximately once a month (sometimes not held for more than one month due to Obon holidays, etc.)

– At sites where deliberation cases are concentrated, deliberation of new cases may be months ahead.

- The initiation of the clinical trial will be delayed and the enrollment period will be shortened. (for Competing enrollment)
- If the protocol is amended, the timing of approval of the change is different for each sites.

Current IRB challenges considered by the sponsor from the perspective of international competitiveness (2)

Efforts (costs and time) required for IRB preparation and assessment occur frequently at both sites and sponsors.

<Sponsor's Perspective>

- Support for preparation of ICF (site-specific methods available)
- Additional Interview to prepare before IRB, if any
- Prepare different IRB materials for each site,
  (Extra Printing, Filing, and Shipping cost and time)
- Need to negotiate unique clinical trial expenses
- IRB review costs are incurred at each site

Current IRB challenges considered by the sponsor from the perspective of international competitiveness (2)

Efforts (costs and time) required for IRB preparation and assessment occur frequently at both sites and sponsors.

<Site's Perspective>

- Heavy site burden due to the additional workload for IRB document preparation to notification of IRB assessment during daily medical practices.
- Additional time and effort is required, due to lack of uniformity in the information presented by the sponsor, such as the composition of the ICF, concept of clinical trial expenses, and safety information data. Time and effort are required.

Comparison of workload and costs to IRB (1)

Study	Total sites	Number of CIRB	IRB request -SIV (Day)		SIV -Site Close (month)		IRB expense (Thousands of yen/site)	
			Individual IRB	CIRB	Individual IRB	CIRB	Individual IRB	CIRB
A	12	3 (1*)	125.4	40.0 (⇩85.4)	17.6	7.9 (⇩ 9.7)	182.0	NA
B	38	3 (1)	121.3	126.0 (⇧4.7)	19.5	18.7 (⇩ 0.8)	74.0	30.9 (⇩43.1)
C	63	7 (3)	415.4	307.4 (⇩108.0)	38.6	42.3 (⇧ 3.7)	64.4	65.3 (⇧ 0.9)

＊Number of IRB cases Request-SIV period

DIA

Comparison of workload and costs to IRB (2)

	Individual IRB	CIRB
Number of sites: 31	21 (21 sites)	1 (10 sites)
First IRB file	672,000 yen 1site(Average) 2,000 yen × 16 books	93,000 yen (⇩ 57.9)
Time for consultation with sites	252 hours 8-16 hours (12 hours on average)	10 hours (⇩ 242)
ICF preparation	315 hours 10-20 hours (15 hours on average)	14 hours (⇩ 301)

DIA

Current IRB challenges considered by the sponsor from the perspective of international competitiveness (3)

Increasing complexity of clinical trials and the development of new technologies (e.g., Gene therapy, Tissue-engineered medical products) have led to a difficult judgement in terms of protection of the rights of human subjects.

- Few IRBs specialize in specific areas
- IRB Members Require Broad Knowledge
- Article 28, Paragraph 2, Guidance 3 of the GCP stipulates that the requirements for establishment of the IRB are "the majority of members," and it is difficult for the IRB to have many members.
- Decreased international competitiveness of clinical trials.

Effects of CIRB

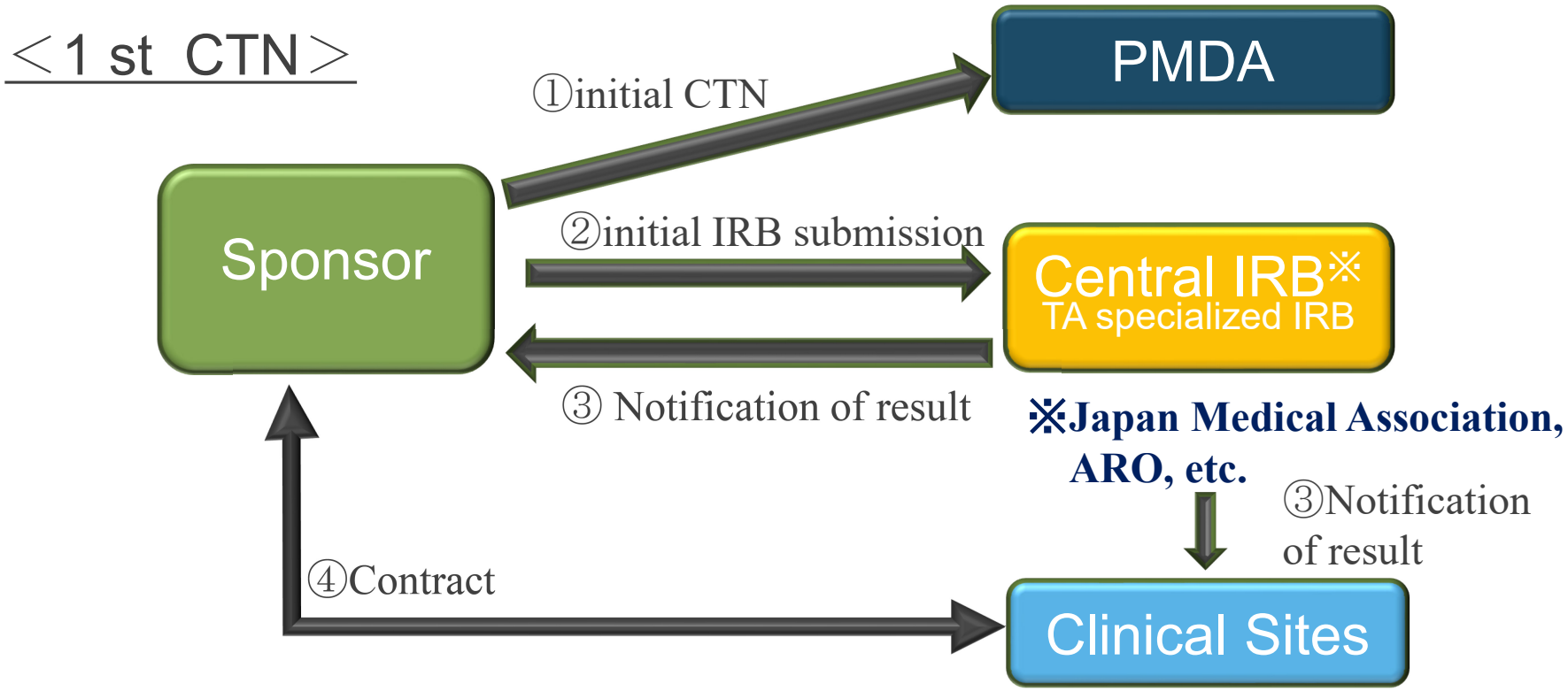
- The establishment of a CIRB allows for efficient conduct of clinical trial procedures and reviews at both sites and the sponsor.

- As for multicenter trials, it is possible to improve international competitiveness in clinical trials by actively utilizing CIRB and conducting it with one IRB review per trial in Japan.

Prospective Challenges in Promoting CIRB

- **Sites**
  - ✓ Difficulty for head of clinical site to decide whether to delegate to CIRB
  - ✓ Decrease in IRB review revenue at each site
  - ✓ Resistance to CIRB deliberation of SAEs generated at own sites
  - ✓ Separation of CIRB and own IRB Operations
- **Sponsor**
  - ✓ Strong decision to utilize CIRB (and not asking for the acceptance of each site)
  - ✓ Dual examination (CIRB ⇒ Individual IRB) would be cumbersome
  - ✓ Necessity on unified informed consent forms and clinical trial expenses across pharmaceutical companies.
- **Government Administration**
  - ✓ Change decision to select IRB from heads of the medical institutions to Principle Investigators
  - ✓ Feasibility of GCP Amendment (Change in Preparer of ICF)
  - ✓ We believe that improvements to the GCP for CIRB have been completed.

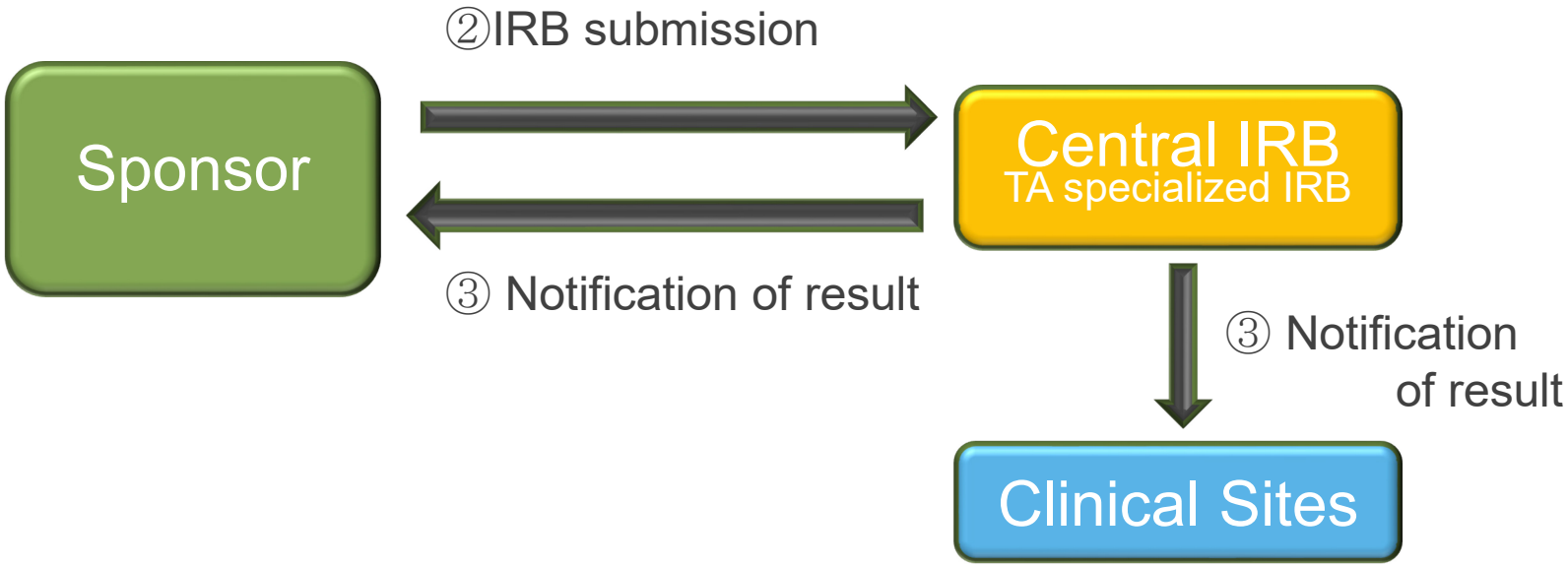
CIRB conceived by R&D Head Club Working Group III



- Use a standardized format for ICF.
- Clinical trial expenses, are the same at all sites.
- If any additional sites are to be added, report (need not be assessed) to the CIRB.

CIRB conceived by R&D Head Club Working Group III

＜IRB review During Clinical trial＞



- CIRB deliberates on amendments to protocol and ICF
- SAEs and safety information are formatted as defined by CIRB

CIRB perception

- Reviewing of the IRB per trial, as in the EU Member States, is considered to have the effect of promoting patient enrollment, reducing clinical trial costs, and enhancing IRB expertise, which may lead to an increase in international competitiveness in clinical trials.

- However, in order to realize CIRB in Japan, it is necessary to resolve a number of challenges, such as standardization of informed consent documents and clinical trial expenses and division of duties between IRB and CIRB at each site.

DIA