

Japan Update

IMDRF Mar. 2019 Moscow



- Regulatory Authorities in Japan -

MHLW

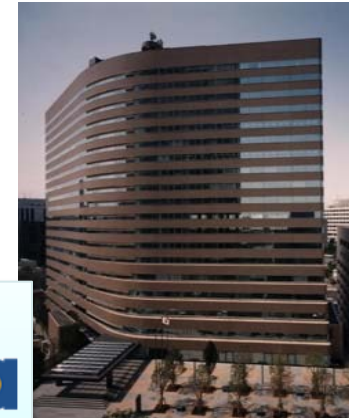
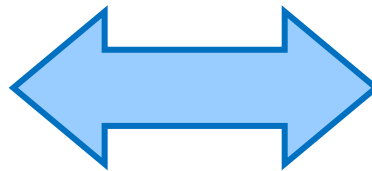
Ministry of Health, Labor and Welfare

- Final Authorization of applications
- Publishing Guidelines
- Advisory committee
- Supervising PMDA Activities

PMDA

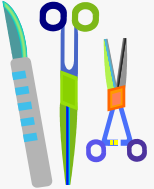



Pharmaceuticals and Medical Devices Agency

- Scientific Review for Drugs & MD
- GCP, GMP Inspection
- Consultation on Clinical Trials etc.





Medical Device Regulations in Japan

Classification	Class I	Class II	Class III	Class IV
Category	General MDs	Controlled MDs	Specially controlled MDs	
Premarket regulation	Self-declaration	Third party certification	MHLW approval (PMDA review)	
Example				
Post market safety (vigilance/surveillance)	PMDA and MHLW			



IMDRF

International Medical
Device Regulators Forum

Agenda

- Revision of PMD Act
- PMDA's Organization Reform
- Asian Training Centre
- Other

Review of previous amendment & consideration

Following the supplementary provisions at the time of the amendment of FY2013 Law, the prospects for 5 years after enforcement has been stipulated. We will consider the PMD Act based on the perspectives of prospects for the future including changes in the population structure and the effects of technological innovation in addition to the implementation situation after the revision law enforcement.

Based on the fact that pharmaceutical administration is being influenced from the viewpoint of research and development and practical use of drugs and medical devices, provision of products and information to citizens, and quality assurance, we mainly focus on the following three themes for proceeding with consideration.

Theme ① **Establishment of rapid access for innovative drugs and medical devices and enhancement of safety measures.**

Theme ② Enhancement of a system for ensuring appropriate manufacture, distribution and sale of drugs and medical devices

Theme ③ Ideal pharmacies and pharmacists and safety ways for obtaining drugs

Note: Additionally, we will consider the necessary of amendment of the law related to safety blood products for ensuring stable supply at a committee for blood business, and the consideration result will be reported at the subcommittee this autumn.

Theme ①

Establishment of Rapid access for Innovative drugs and medical devices and Enhancement of safety measures.

(Problem consciousness)

The international collaboration development has been extended while creation of breakthrough drugs and medical devices by personalized medicines with AI, nucleic acid medicines, genomic drug discovery, cancer genome, development of big data utilization, and we move into the era of selecting countries and regions for development and approval applications based on regulatory environments by a development main body. To provide a necessary medical product to a patient in one country, the regulatory implementation might be an issue corresponding to technical innovation flexibly and efficiently.

We need to further review and **clarify the system to reduce the burden of companies and ensure the international consistency** in terms of assurance about quality and safety, in addition to **improvement of predictability of approval reviews.**

(Viewpoints of consideration (examples))

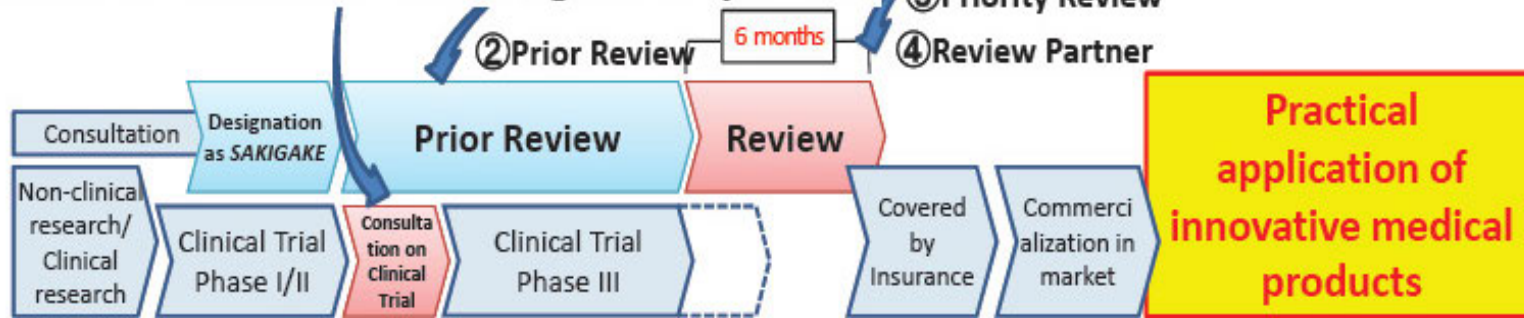
- **Clarification of an approval system for rapid practical use of drugs and medical devices** which are especially highly required for healthcare and expected breakthrough property in development stages based on the premise of ensuring safety
- Clarification of a system for smoothly utilizing electronic medical information including patient registry for approval application of new drugs and post-marketing safety measurements
- Introduction of an effective quality control method considering international regulatory consistency and efficiency
- Introduction of a procedure for changing a systematic manufacturing process with high prevision

SAKIGAKE Designation System

【Ordinal Review】



【Review under SAKIGAKE Designation System】



※Accept the data of Phase III after the application depending on conditions

⑤Strengthening post-marketing safety measures (re-evaluation period)

(Reference) Implementation of Strategy of Sakigake

An *innovative MD/IVD for patients in urgent need of innovative therapy* may be designated as a Sakigake Product if;

- 1) its premarket application will be filed in the first in the world AND
- 2) prominent effectiveness can be expected.

Once an MD/IVD is designated, its developer can enjoy such benefits as:

A) Prioritized Consultation by PMDA

C) Prioritized Review

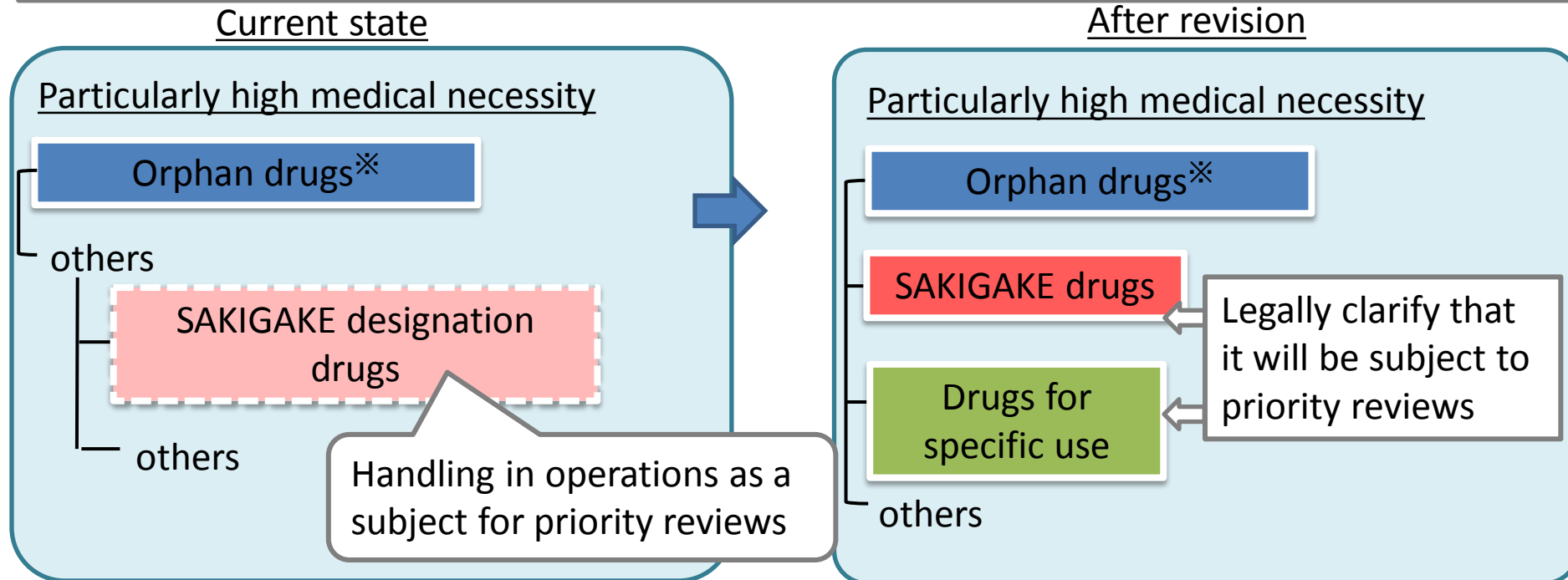
(12 months → 6 months [MD])

B) Pre-application substantive review

D) Review Concierge assigned by PMDA

Legislation of “SAKIGAKE designation system”

- Legislation of SAKIGAKE designation system
- Legislation of Prioritisation of Specific Drugs, such as pediatric drug *etc.*.
- The law provides for securing necessary funds and taking tax measures to promote study and research.



(※) The number of patients who may use the drug should be less than 50,000 in Japan, or the drugs should be indicated for difficult-to-treat diseases.

Appropriate approval systems for medical devices

Characteristics of medical devices

- Various types
- Continuous update/ improvement
- Large effect of operators

Current state and issues

- irrational limitation (specific disease areas) on “approved intended use” ?
- Change of approval system is not fit for continuous improvement and refinement ?

[main opinion]

- need for examination on how regulations are tailored to the characteristics of medical devices, including approvals by classification based on characteristics and functions of their own, not based on individual diseases and organs.

Direction of consideration

- Rapid application for other organs and body parts (medical devices having cauterization and irradiation functions *etc.*)
- Approval reviews capable of continuous improvement and refinement by confirmation of the improvement and refinement plan in the review process and recognition of partial change of rapid approvals in the area

Organization Reform in PMDA (from 1st January, 2019)

1. Strengthening of Management planning function

- Reorganize the planning and coordinating department in a developmental manner and set up a new management planning department to strengthen the functions that support management decisions of the executive management including the president and to further advance the risk management

2. Strengthening of collaboration of medical device divisions and streamline organization

- Establish a department specializing in medical devices, while strengthened collaboration and coordination among each division of the medical device field and established a system to efficiently carry out tasks in order to carry out more highly specialized tasks based on the characteristics of medical devices

Medical Device Unit

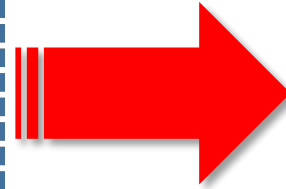
3. Enhancement of organization of pharmaceutical safety department

- Strengthen the structure of the drug safety department in order to respond to specialization and advancement of drug safety measures

Medical Device Unit ①

Review offices of medical devices

- Office of Medical Device I
- Office of Medical Device II
- Office of Medical Device III



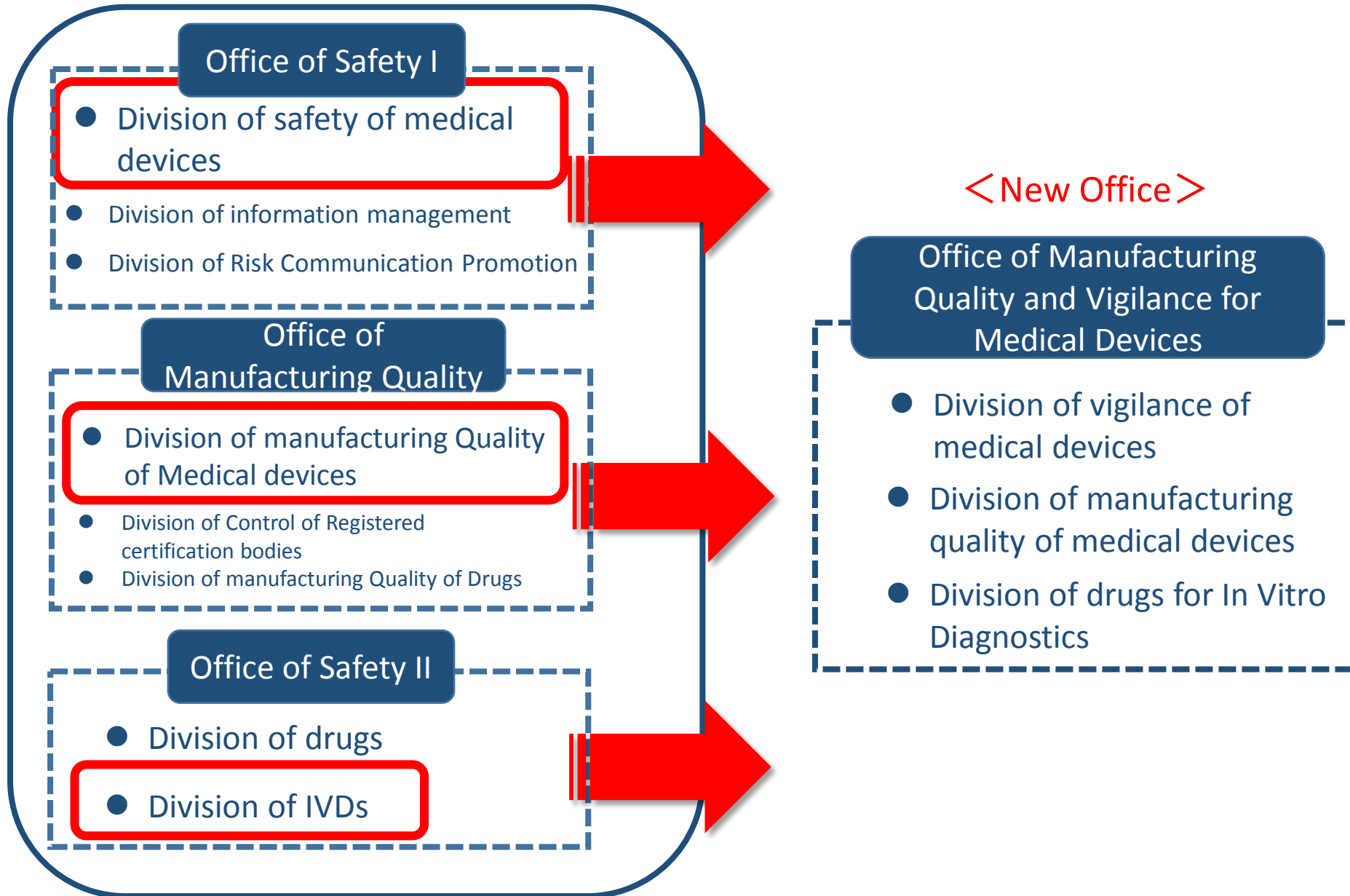
- Office of Medical Device I
- Office of Medical Device II

The following teams are set as cross-sectional teams of each office.

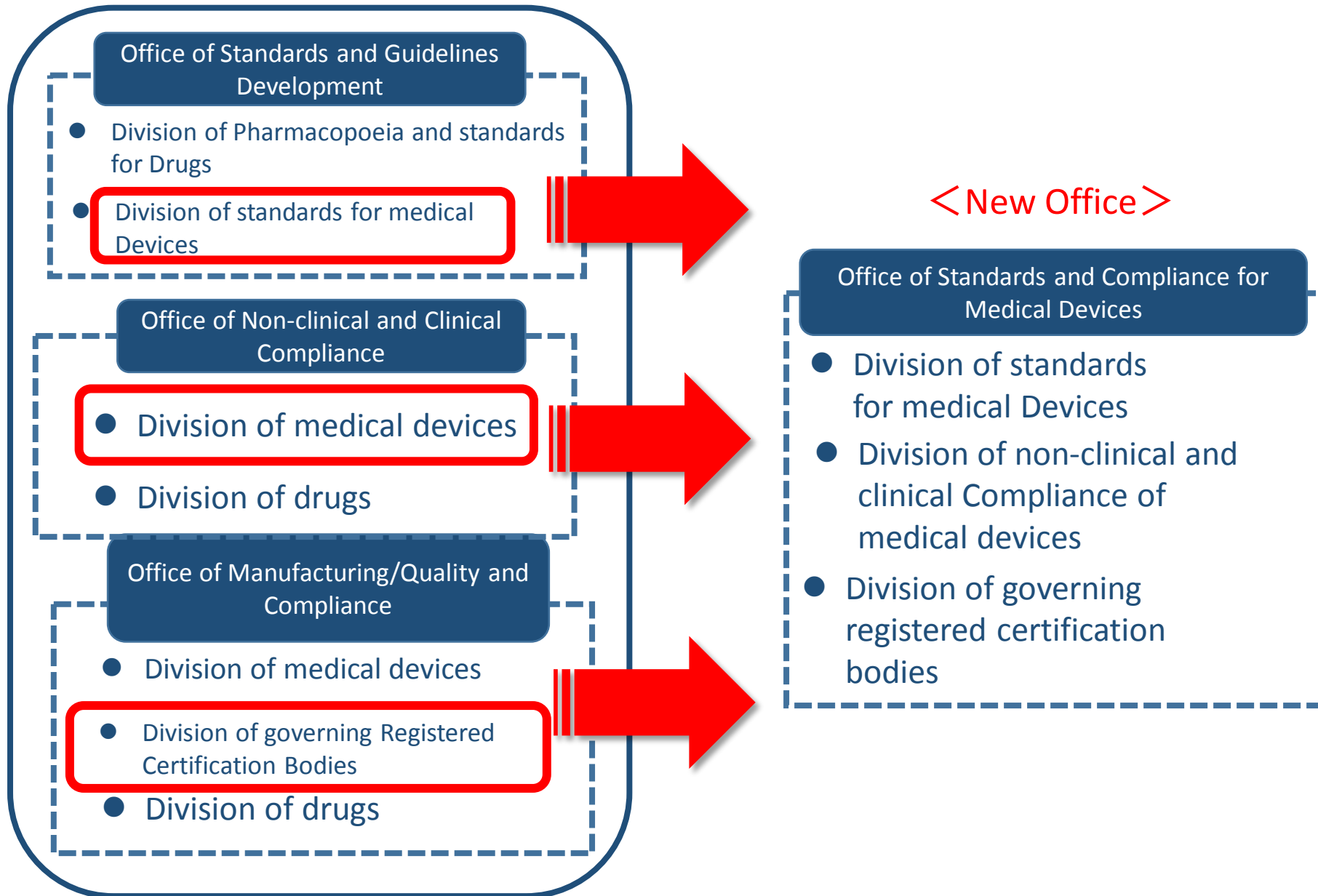
- ① Clinical evaluation team
- ② Biological safety team
- ③ Electrical safety (including laser) team
- ④ AI and software team (including cyber security measures)
- ⑤ Generic device team (including the clarification of substantial equivalence)
- ⑥ International support team (including IMDRF)
- ⑦ Regulatory science team
- ⑧ Regenerative medical product review division, biological device team (viral safety evaluation of biological products)
- ⑨ Remanufacturing SUD team

Note: the underlined part added

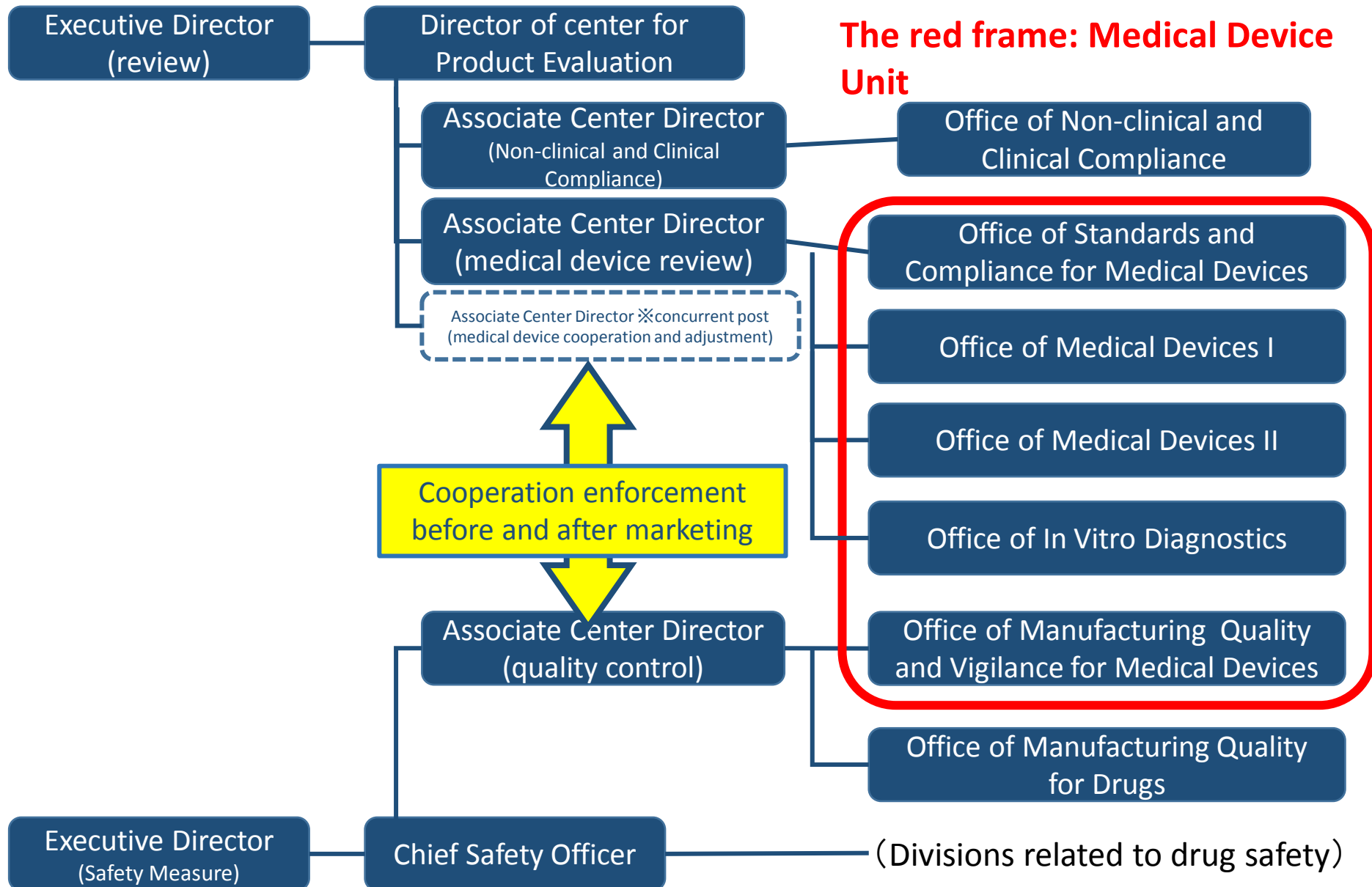
Medical Device Unit ②



Medical Device Unit ③



Medical Device Unit ④



Current situation of review time based on collaboration plan

Category	Target value (80 th percentile)	Result (FY2014)	Result (FY2015)	Result (FY2016)	(preliminary) Result (FY2017)
New medical devices (priority)	9.0	8.1	8.2	8.0	5.5
New medical devices (normal)	12.0	9.7	8.7	11.9	11.9
Improvement (clinical)	9.0	9.0	11.6	8.8	8.9
Improvement (non- clinical)	7.0	8.1	6.7	6.0	5.9
Generic (new)	5.0	6.4	6.1	4.4	4.4
Generic (partial change)	4.0	4.7	4.1	3.9	4.0

(month)

※ 80th percentile values are the target values for FY 2018.

※ Review results at the end of September, the following year of application.

※ Excluding expedited review products and products changed for application category

※ The day of receiving application is the starting date for the tabulation.

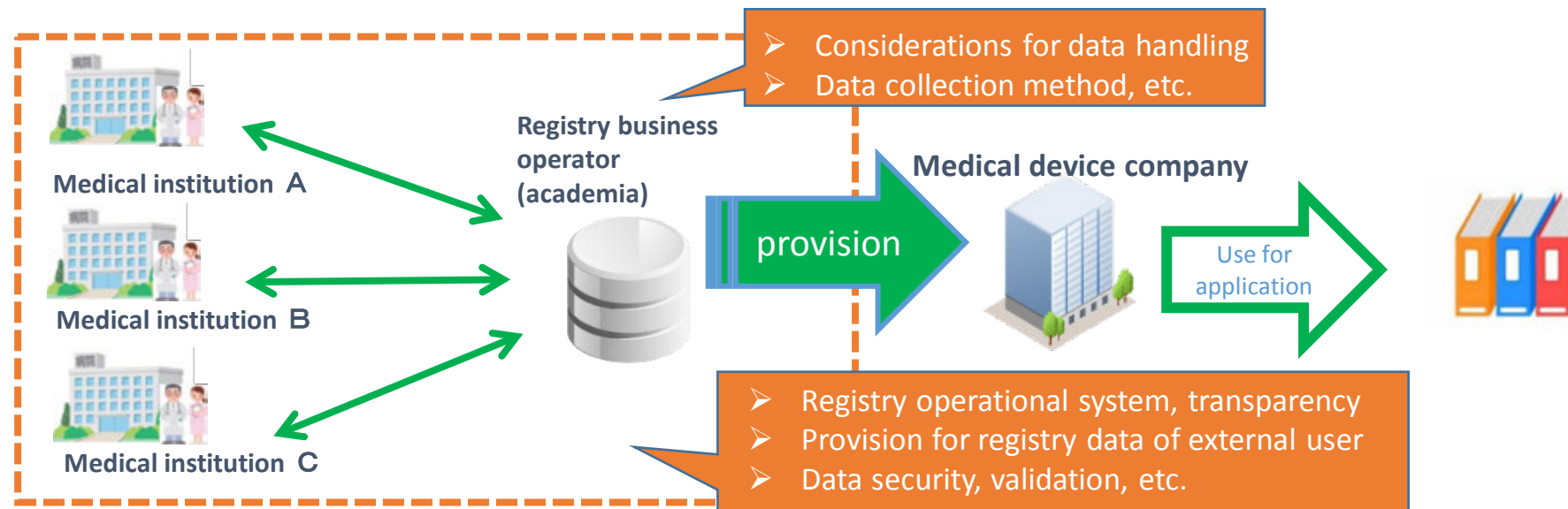
New consultations for registry (draft)

Registry utilization consultation (tentative name)

- Client: Registry business operators (mainly academia) . Companies can sit with them.
- Consultation content: advice for how to think about the plan based on the premise that it is utilized for approval application or re-examination and use-results evaluation application, and general principles on improvement of registry quality and reliability assurance
- The number of consultations is 3 cases per month as a target.

Registry reliability consultation (medical devices) (tentative name)

- Client: Medical device companies. Consultation together with registry business operators.
- Consultation purpose: Confirmation and advice on the registry reliability before application or launch of use-results survey for individual products which are planned for approval application or use-results evaluation application by using the registry.



ATC Seminar scheduled to be held in FY2019 (draft)

	Contents	Date	Location	Remarks
1	Pediatric Review	July 8-11, 2019	Tokyo (PMDA)	Co-hosted by U.S.FDA
2	Review and safety measures for drugs	July 22-26, 2019	Tokyo (PMDA)	Co-hosted by WHO
3	Appropriate application and review procedures for drugs (GRM)	September, 2019	Taipei	
4	GMP (Good Manufacturing Practice)	November 12-15, 2019	Toyama	Co-hosted by PIC/S
5	Review and safety measures for medical devices	November 25-29, 2019	Tokyo (PMDA)	APEC-LSIF-RHSC pilot CoE Workshop
6	Quality control (Herbal Medicine)	December, 2019	Toyama	
7	Multi-regional Clinical Trials for Drugs	January 21-24, 2020	Tokyo (PMDA)	APEC-LSIF-RHSC CoE Workshop
8	Pharmacovigilance	February 3-6, 2020	Tokyo (PMDA)	APEC-LSIF-RHSC CoE Workshop

※ We are planning and scheduling the others including seminars held abroad. They will be published upon decision.

APEC Training Centre of Excellence for regulatory Science in Medical Device @APEC LSIF RHSC

- APEC LSIF (Life Science Innovation Forum) RHSC (Regulatory Harmonisation Steering Committee) has started activities in Medical Device area
- PMDA ※ is designated as APEC Training Centers of Excellence for Regulatory Science (CoE) in Medical Device area in Pilot
- PMDA will conduct pilot CoE training in November, and try to have formal designation of CoE.

※ Other than PMDA, Taiwan FDA, University of Southern California and Northeastern University are also designated.

Evaluation points for Next generation medical device

- MHLW Expert Consultative group reports consideration of evaluation points for device for BNCT* (Boron Neutron Capture Therapy)

* BNCT: One of innovative cancer therapy. Administering Boron 10, then irradiating low-energy neutrons. Boron accumulates tumor cells, and after capturing neutron, yields lethal alpha particles which destroy tumor cells. On the other hand, normal cells stay safe as neutrons do not affect normal cells and alpha particles are effective only within 10 micron.

Thank you for your attention!
Any Question?

