European Business Council (EBC) Medical Devices and IVD Committee

Meeting of Representatives

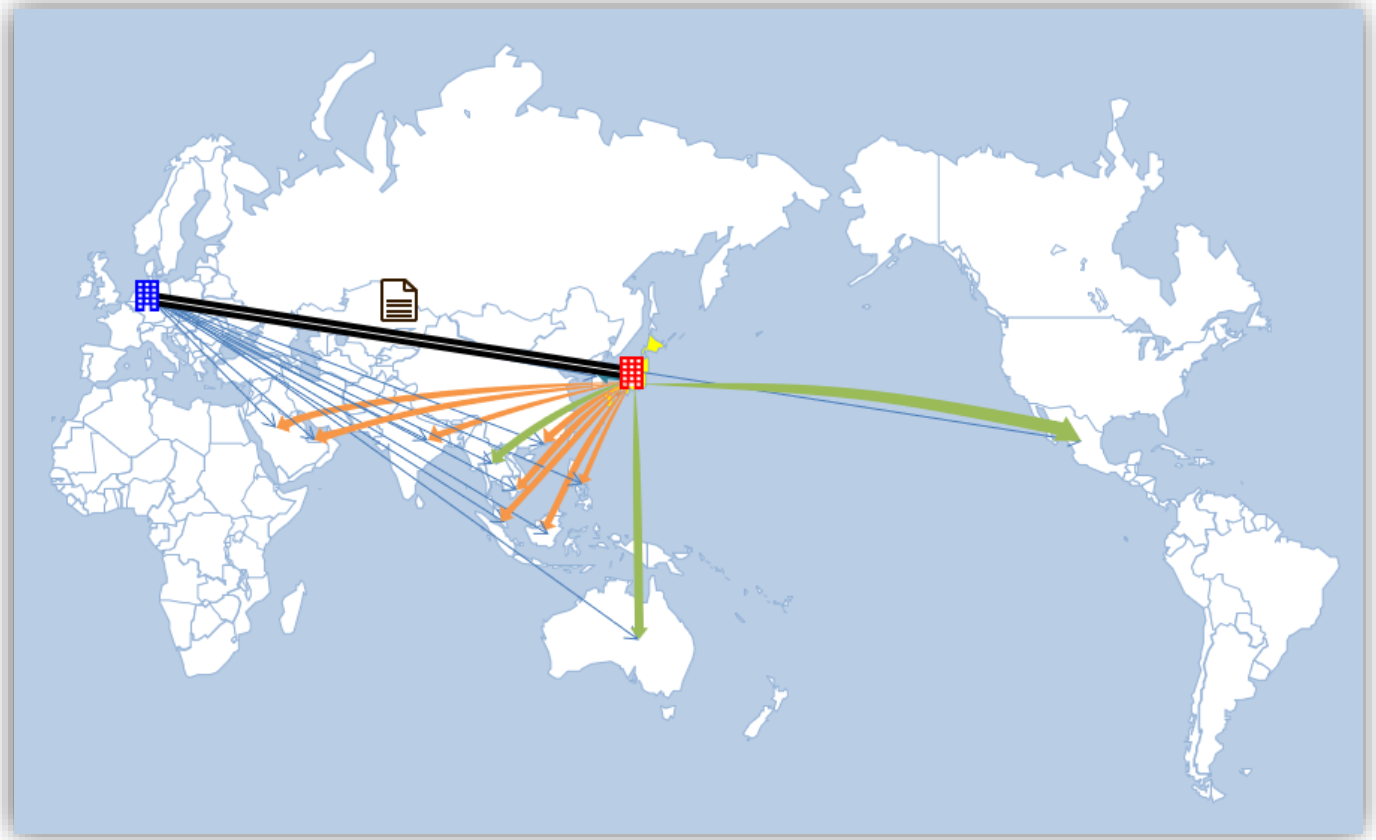
Report of the Pharmaceutical Affairs Subcommittee of PMDA

December 10, 2020

Committee Vice-Chairperson in Charge: Takeshi Fujiwara
Subcommittee Chairperson: Miyo Nishimuta

Basic Action Plan of Pharmaceutical Affairs Subcommittee

In 2020 and 2021
Through meetings with the government and pharmaceutical affairs related activities of the EBC, we propose optimization of the medical devices review and the related legal system.



Report of the Pharmaceutical Affairs Subcommittee

Agenda

- Report of the activities of the Pharmaceutical Affairs Subcommittee from January to December 2020
- Topics in 2020

Report of the activities of the Pharmaceutical Affairs Subcommittee from January to December 2020

- Legislation Committee (5 times)
  Review Related Subcommittee (6 times)
  WG to Improvement of review operations: notifications (1 time)
  WG on Interpretation of Fair Advertising Standards (3 times)
  WG on the Revision of the Law (1 time)
- WG on Medical Device Cyber Security (4 times)
- MDSAP Opinion Exchange Meeting (2 times)
- Clinical Evaluation Committee (4 times)
- WG for Consideration of New Approval System (8 times)
- QMS Committee (5 times)
- PMS Committee (5 times)
  Defect Terminology WG (12 times)
  WG to study improvement of package insert use (3 times)
- Small Bore Standards Review WG (2 times)
- Health and Labour Sciences Research: QMS (3 times)
- Health and Labour Sciences Research : Watanabe Group (1 time)

- Plan on Collaboration for Optimizing Medical Device Regulations and Review (January 22)
- Regular meetings to exchange opinions on approval reviews and safety measures for medical devices and in-vitro diagnostics (August 28)
- Public-Private Dialogue for the Creation of Innovative Pharmaceuticals, Medical Devices, and Regenerative Medicine Products (November 16)

Thank you all for taking time out of your busy schedule.

Subcommittee on Review Related Matters (Legislation Committee)

Based on the progress table of the collaboration plan, various factors in the approval review will be extracted, shared within the industry, and presented to the administration as input.

PIC Mr. Murakami [Novocure Co., Ltd.]
Ms. Makishima [B. Braun AESCULAP, Ltd.]
Ms. Nishimuta [Biotronik Japan, Inc.]

In order to implement the new approval system and realize smooth approval reviews, we will, when appropriate, cooperate with the government to address issues and promote action on each issue to be resolved.

- Improve review quality and efficiency:
  Enhancement of training, minimization of mandatory Japanese-language attachments, improvement of the operation of the certification system, response to ISO 10993-1 revisions, efficient response to changes, review of new approval systems, streamlining and computerization of procedures, assurance of data reliability and reduction of burden
- Clinical related: How best to evaluate, use of RWD, international harmonization
- QMS related: certificate of conformity, operation of MDSAP
- Safety related: Legislation on digitization of package inserts and UDI
- Utilization of international standards for medical devices

*Activity report from WG is available for items in gray

WG on Interpretation of Fair Advertising Standards (Legislation Committee)

Development of standards, clear guidelines, and Q&A for medical device advertising.
Revision of guidelines for advertising-related display of unapproved medical devices.

PIC Mr. Mizumachi [LivaNova Co., Ltd.]

Starting on 9/24, a WG meeting was held once a month (3 times by November), and the following were discussed.

(1) Consideration of Q&A for concerns regarding viewing of advertisements by public (2nd installment)

→ This will not be published as a Q&A, but will be published on the JFMDA website as an industry guideline.

(2) Revision of the Detailed Rules for Guidelines on the Display of Unapproved Medical Devices

→ The current "Detailed Rules for Guidelines on the Display of Unapproved Medical Devices" has a part referring to "Import Inspection Procedure for Drugs and Deleterious Substances" but as of August 31, 2020 it was changed to "Main points of import confirmation of drugs", so the content will be changed accordingly. This will also be published on the JFMDA site after revision.

(3) Revised Q&A on Medical Device Advertising

→ As the content of "Q&A on Medical Device Advertising" issued on January 27, 2011 has become outdated, we decided to review it together with the other matters. (now in progress)

MDSAP Opinion Exchange Meeting

Full-scale implementation of MDSAP

PIC Mr. Takeda [Radiometer K.K.]

Mainly the following activities were carried out

- The following items were examined for full-scale introduction of MDSAP.
  - MDSAP Expenses
  - Timing of full-scale implementation of MDSAP
  - Consideration of notifications that need to be revised for full implementation of MDSAP

The following results were obtained from the above activities.

- MDSAP costs 200,000 yen per facility. However, there is no need to pay this fee if MDSAP is not used. (selective system)
- The timing of full-scale implementation of MDSAP will be around April 2022. The current pilot operation will be maintained in 2021. (It will involve no expenses)
- Notifications that need to be revised include notices of extension of pilot operations and notices of inspection procedures. We will continue to review the affected notifications.

JWG4 (small bore)

Move from ISO 594-1 to ISO 80369 series

PIC Mr. Araki [Philips Japan Co., Ltd.]
Mr. Takeda [Radiometer K.K.]

Mainly the following activities were carried out

- Changes in field of neuroanesthesia (ISO 80369-6)
- Changes in field of enteral nutrition (ISO 80369-3)

The following results were obtained.

- Changes in the field of neuroanesthesia have almost been completed.
- In the field of enteral nutrition, progress on making changes has been slow. Therefore, government and academic societies are collaborating to promote change.

Clinical Evaluation Committee / Legal Compliance T1

Objective: To examine legal and regulatory issues related to clinical trials and clinical research and make proposals

PIC JFMDA Clinical Evaluation Committee
Mr. Ohta [Biotronik Japan, Inc.]
Mr. Mori [Medical U&A Co., Ltd.]

Activities:
Reviewed “clinical trial related” notifications issued pursuant to the revision of the Drugs and Medical Devices Law on 9/1 and exchanged opinions with MHLW regarding the definition and applicability of the term "devices used in clinical trials" that is to be used from this time onward.

Outcome:
It was confirmed that the purpose of the revision was to unify the reporting of adverse reactions and adverse events in order to protect trial subjects.
It was also confirmed that the transitional measures for "Clinical trial notifications and reports of defects" could be made using the same format as before for 2 years, until September 2022.
The explanation of specific cases was completed at the 2020 briefing session on clinical trials and clinical evaluations of medical devices (November 20).

In the future:
The basic line of thinking on the devices used in clinical trials (especially in combination with other devices) that are specified in the protocol will be discussed continuously and issued as a Q&A.

Clinical Evaluation Committee / Clinical Evaluation Optimization T4

Objective: To study the effective use of the "clinical evaluation report"

PIC JFMDA Clinical Evaluation Committee
Mr. Ohta [Biotronik Japan, Inc.]
Mr. Mori [Medical U&A Co., Ltd.]

Activities:
Revision of the “Guidelines for Preparation of Clinical Evaluation Reports ”: After repeated discussions with PMDA, this WG prepared revisions, which were confirmed and finalized by PMDA.
The Guidelines are intended to be used as a manual for the preparation of the “clinical evaluation report” that is prepared as material for use in consultations or for attachment to the approval application when a literature-based clinical evaluation is acceptable for an item that must go through clinical trials.

Outcome:
Completed revision of the “Manual for Preparation of Clinical Evaluation Reports and Materials for use in Consultations on Clinical Evaluation, Part 1: Preparation Procedures” (November 1)
An explanation was provided at the 2020 briefing session on clinical trials and clinical evaluations of medical devices (November 20), and the Manual has been posted on the JFMDA website.
A link will be posted on the PMDA website in the near future.

In the future, we plan to discuss the "basic line of thinking" (part 2) in relation to cases described in clinical evaluation reports and their acceptability.

WG for Consideration of New Approval System

Consider what medical devices are particularly necessary in medical care and examine the related approval processes in order to ensure quick access to innovative medical devices introduced after the revision of the PMD Act, and to enhance safety measures

PIC Ms. Makishima [B. Braun AESCULAP, Ltd.]
Mr. Toyofuku [Siemens Healthcare Co., Ltd.]
Ms. Nishimuta [Biotronik Japan, Inc.]

Examined laws, ordinances, and draft notifications, etc. with an eye to implementing mainly the following two new approval systems

1. Conditional early approval system (PHOENIX: PHysical OpEratioN of Items' eXtrapolative and inclusive approval)
This system pertains to devices whose functions have potential application to other fields. Its purpose is to expedite addition of application to other organs and parts by limiting the number of facilities and operators that can use the device and enhancing post-marketing safety measures.
⇒ Relevant major notifications have been issued

2. Procedure for expansion of indication, etc. using change plan (IDATEN: Improvement Design within Approval for Timely Evaluation and Notice)
This system pertains to medical devices that are expected to be modified or improved immediately after approval. Its purpose is to realize an approval review pathway that enables continuous improvement and refinement by confirming the change plan during the review process and accepting partial changes that are made rapidly within the planned scope.
⇒ Issues to be considered in the future

- Examine the process from the standpoint of ensuring smooth insurance coverage after final notification of change to which IDATEN applies
- Preparation of operational Q&A

QMS Committee

Collection and dissemination of opinions on QMS from industry associations and issuing requests to government

PIC Mr. Suga [Radiometer K.K.]
Mr. Hatoyama [B. Braun AESCULAP, Ltd.]
Mr. Takeda [Radiometer K.K.]

Mainly the following activities and requests were carried out

- Request for revision of the QMS Ministerial Ordinance (Consistency with ISO 13485: 2016)
- Request for expanded application of certificate of conformity (A wide range of certificates also proves a small range)

The following results were obtained.

- Publication of public comments on the revised QMS Ordinance in 2020, scheduled to take effect in March 2021
- The application of the certificate of conformity was expanded by amendment of the law last year, and the expansion was enforced as of September, 2020.

QMS Certificate of Conformity Optimization WG

Promote more rational use of QMS certificates

PIC Mr. Takeda [Radiometer K.K.]

Considered systems by which multi-sheet certificates could be converted a single page in order to facilitate the management of certificates of conformity.

- It was discovered that making certificates a single page does not necessarily make management easier.
- The opinion was expressed that we should take future amendments of the law into account when considering the ideal form for the certificate of conformity, and we intend to look into this in the future.

Revision of the Defect Reporting Handbook and change in method for submitting applications electronically

PIC Mr. Tanita [Nippon Lifeline Co., Ltd.]

1. WG for Revision of Defect Reporting Handbook
   In response to related notifications issued after the 7th edition, the handbook was revised to accommodate the new defect report form to which all reporters must switch by April 2021, with the addition of an explanation on selection of terminology for describing defects. The 8th edition of the handbook was published in October.

2. System Improvement WG
   The XML tool is being modified to comply with the 4th edition of the Glossary of Defect Terminology, which is scheduled to be published at the end of December 2020.

Defect Terminology WG (PMS Committee)

Update Glossary of Defect Terminology and Import IMDRF Glossary

PIC Mr. Tanita [Nippon Lifeline Co., Ltd.]

1. Update of defect reports collection
   The 3rd edition of the glossary was published in March, which incorporates change requests by various groups and IMDRF survey result terminology. The 4th edition of the glossary is currently being created in accordance with the updated IMDRF glossary.

2. Incorporating IMDRF Glossary
   The 4th edition that is currently being created will include a translated version of the IMDRF Glossary as a common glossary in the glossary for Japan.

WG to study improvement of package insert use

Improvement of the use of package inserts and consideration of electronic methods of use

PIC PMS Committee
Mr. Araki [Philips Japan Co., Ltd.]

Summary of Activities

In order to improve use on the basis of the provisions of Article 68-2-2, it was divided into TF 1–3 as of September 2020, and a Q&A notification was prepared.

1) The paper version is to be provided at the time of the initial delivery of pharmaceuticals, medical devices, etc., with the cooperation of wholesalers as necessary.
2) In addition, it is necessary to establish a system to display information on the outer packaging of the product that enables access to the latest package insert information, and to reliably deliver the information to medical institutions, pharmacies, etc. via paper media, etc. when the information is revised.
3) For medical devices, etc., attention should be paid to the methods of providing information as befits the characteristics of products such as programmable medical devices and specially controlled medical devices requiring expert installation.

Health and Labour Sciences Research Group (QMS)

Conduct research on international harmonization of QMS

PIC Mr. Takeda [Radiometer K.K.]

Mainly the following activities were carried out

- Preparation of QMS ministerial ordinance and detailed explanation in accordance with ISO 13485: 2016
- Preparation and dissemination of guidance on the management of electromagnetic documents and records

The following results were obtained for these activities.

- Publication of comments on the QMS Ministerial Ordinance and preparation of a draft of an article-by-article explanation (currently in final proofreading).
- Prepared guidance on the management of electromagnetic documents and records and posted it on the PMDA website.

Health and Labour Sciences Research Group (Watanabe Group)

Research on guidance on appropriate implementation of hazard prevention measures for medical devices

PIC Mr. Tanita [Nippon Lifeline Co., Ltd.]

1. Fact-finding survey on implementation of safety management practices by MAHs
   The objective is to conduct a questionnaire survey of marketing authorization holders to provide guidance on effective safety management practices and balance with QMS. We are currently reviewing the contents of the questionnaire.

2. Investigation and analysis of recall (repair) cases
   The objective is to survey and analyze occurrence by type over the past 3 years and use the data for early discovery of devices that need to be recalled. We are currently surveying and analyzing cases.

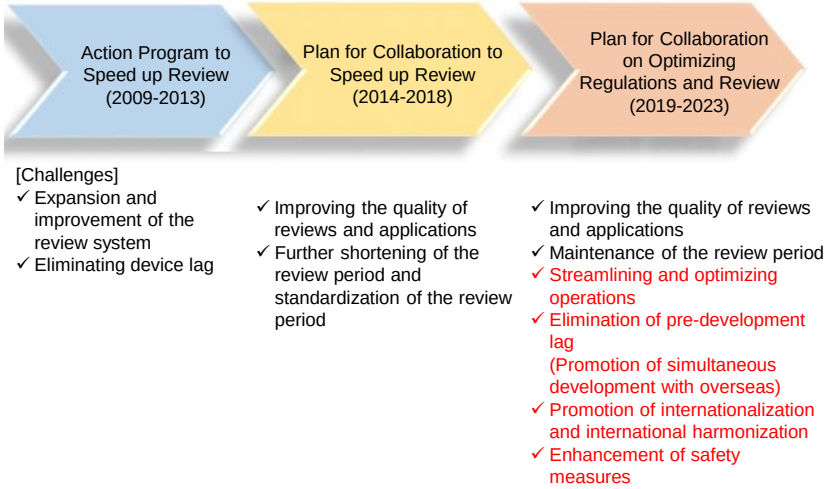
Working-Level Council on New Plan for Collaboration / Steering Meeting

Plan for Collaboration on Optimizing Medical Device Regulations and Review (5-year plan starting in FY 2019 (first fiscal year of the Reiwa era))

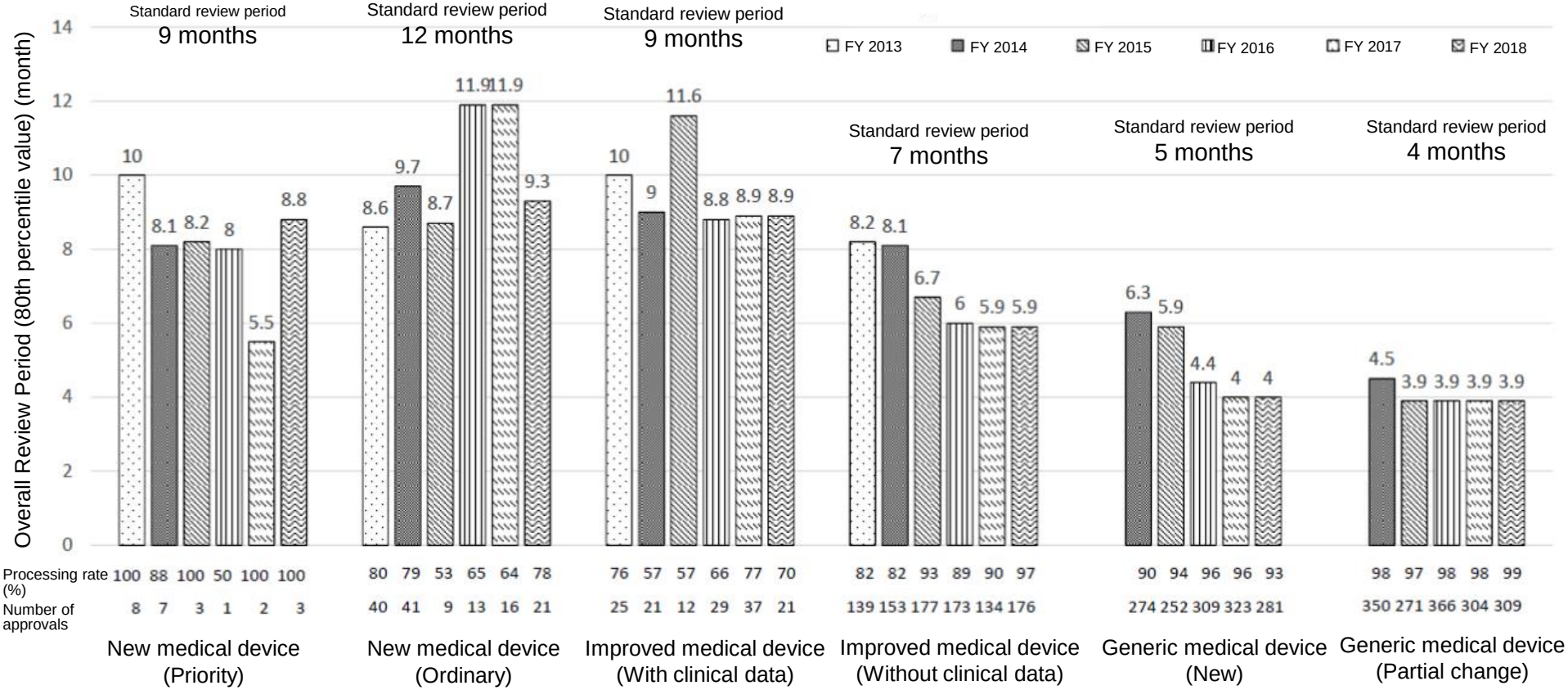
PIC Ms. Makishima [B. Braun AESCULAP, Ltd.]
Mr. Murakami [Novocure Co., Ltd.]
Ms. Nishimuta [Biotronik Japan, Inc.]

In order to optimize the medical device development process and the related regulations, the plan will promote the following: eliminating development lag to reduce the time until companies submit applications, firmly maintaining the review period at the world's fastest level, improving the quality of reviews and applications, making operations more streamlined and efficient, and international harmonization of various regulations.

1. Efforts to streamline applications and the approval process while also improving their quality
2. Efforts to enhance safety measures based on the characteristics of medical devices
3. Other efforts to improve access to medical devices, streamline and optimize application procedures, and promote international harmonization
4. Establishment of a Standard Business Processing Period
5. Continued implementation of time clock surveys (industry)

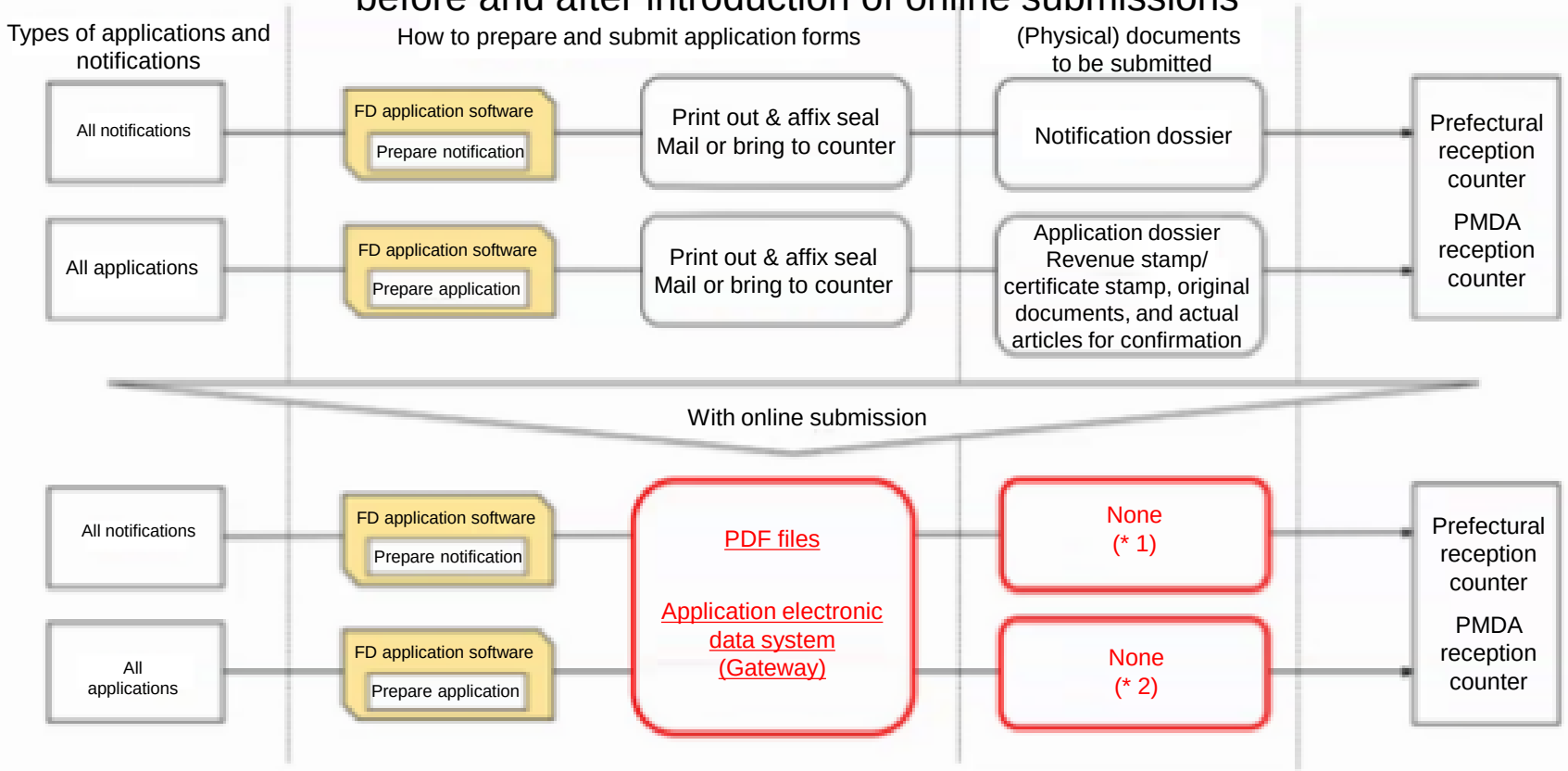


Overall Review Period for Medical Devices (application cohort) (plan for collaboration)



* Calculated in accordance with "Plan for Collaboration to Speed up Review" and Item 2 of the Agreement of Implementers For each fiscal year's application items, the overall review period for approved items as of the end of September of the following year.
* The processing rate is calculated by dividing the number of approvals by (number of approvals + number under review) × 100.
* For generic medical devices, the start date is the date on which compliance with the checklist is confirmed. There is no data for FY 2013 because that was before the checklist came into use.

■1. Change in documents to be submitted and submission methods before and after introduction of online submissions



*1 Plan to accept online submission of notifications and applications created with DWAP as well (for notification: starting in April 2022; for applications: concurrently with FD application software in FY 2022).

*2 When the application fee is paid to the national or prefectural government not by a revenue stamp or certificate stamp but by electronic payment, transfer, etc. The application fee to the government will be processed by Pay-easy. Application fees to prefectures should be paid according to the respective prefecture's payment method.

Topics in 2020

- Response to COVID-19
- Response to new types of medical devices
- Recent movement toward enforcement of the revised PMD Act

Status of approval and certification of medical devices targeting COVID-19 and related symptoms

(Last Updated: August 5, 2020)

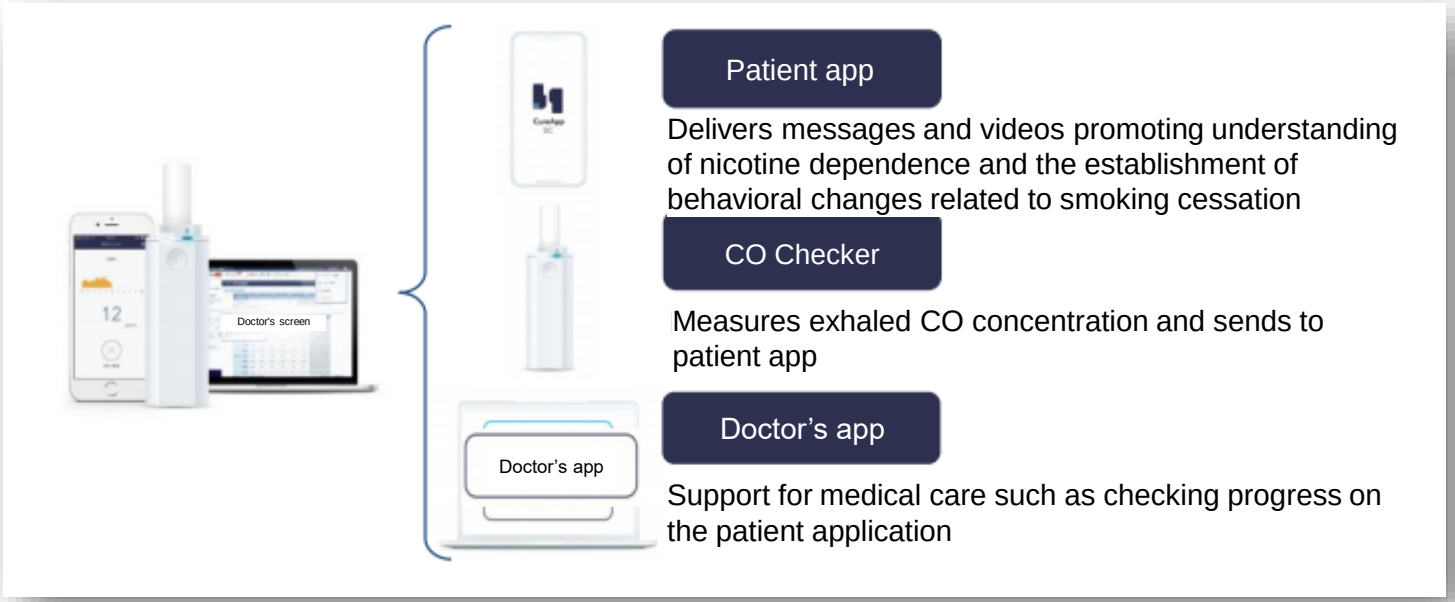
No.	Product Name	Company Name	Category	Approval Date (Certification Date)
1	NKV-550 Series Ventilator	NIPPON KODEN KOGYO CO., LTD.	Ventilator	April 24, 2020
2	E30 System	Philips Japan Co., Ltd.	Ventilator	May 1, 2020
3	Trilogy Evo Series	Philips Japan Co., Ltd.	Ventilator	May 12, 2020
4	OMRON Infrared Forehead Thermometer MC-720	Omron Healthcare Co., Ltd.	Noncontact far infrared thermometer	(May 26, 2020)
5	Pulmonary Image Analysis Program InferRead CT Pneumonia	CES Descartes Co., Ltd.	Image detection support program	June 3, 2020
6	Puritan Bennett 560	Covidien Japan Co., Ltd.	Ventilator	June 12, 2020
7	MEDIGRIP Surgical Gloves, No Powder	Toray Medical Co., Ltd.	Surgical gloves	(June 12, 2020)
8	Acoma Ventilator ART-21 EX	ACOMA Medical Industry Co., Ltd.	Ventilator	June 19, 2020
9	NSH Heparinized Cannula	Senko Medical Instrument Mfg. Co., Ltd.	Cannula for extracorporeal circulation	June 25, 2020
10	COVID-19 Pneumonia Image Analysis Support Program Ali-M3	MIC Medical Co., Ltd.	Image detection support program	June 29, 2020
11	Heart-lung machine S5	LivaNova Co., Ltd.	Heart-lung machine system	July 13, 2020
12	Biometric Monitor InteliVue MX850/750	Philips Japan Co., Ltd.	Multi-item monitor with important parameters	July 31, 2020

*Only those with approval conditions are listed.

Materials submitted to Ministry of Health, Labour and Welfare at the 18th Regular Meeting for the Exchange of Opinions on Approval Reviews and Safety Measures for Medical Devices and In-Vitro Diagnostics https://www.mhlw.go.jp/content/11124500/000681361.pdf

Medical Devices and Healthcare Project

This project uses AI and IoT technologies, measurement technologies, and robotics technologies in an integrated manner to research and develop the following: systems that use medical devices and medical device programs (treatment apps, etc.) to provide more advanced diagnosis and treatment, medical devices for which there is a great need in medical settings, and medical devices and healthcare that contribute to prevention and improvement of QOL for the elderly.



Excerpt from Chuikyo General-1-1 2.11.11https://www.mhlw.go.jp/content/12404000/000693018.pdf

Amended PMD Act

Act for Partial Revision of the Measures to Ensure Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, etc.

Promulgation Date: December 4, 2019

[Enforcement in the first year](Approval system tailored to the characteristics of innovative medical devices, medical devices with specific applications, and other medical devices, etc.)

- June 4 - July 3, 2020 Public Comment
- Cabinet Order promulgated on July 28, 2020
- Promulgation of Ministerial Ordinance at the end of August 2020 and issuance of various notices
- Enforced September 1, 2020

[Second year of implementation] (Digitization of package inserts, legal compliance system, surcharge system, etc.)

- To be enforced August 1, 2021

[Enforcement in the third year] (Bar code displays, etc.)

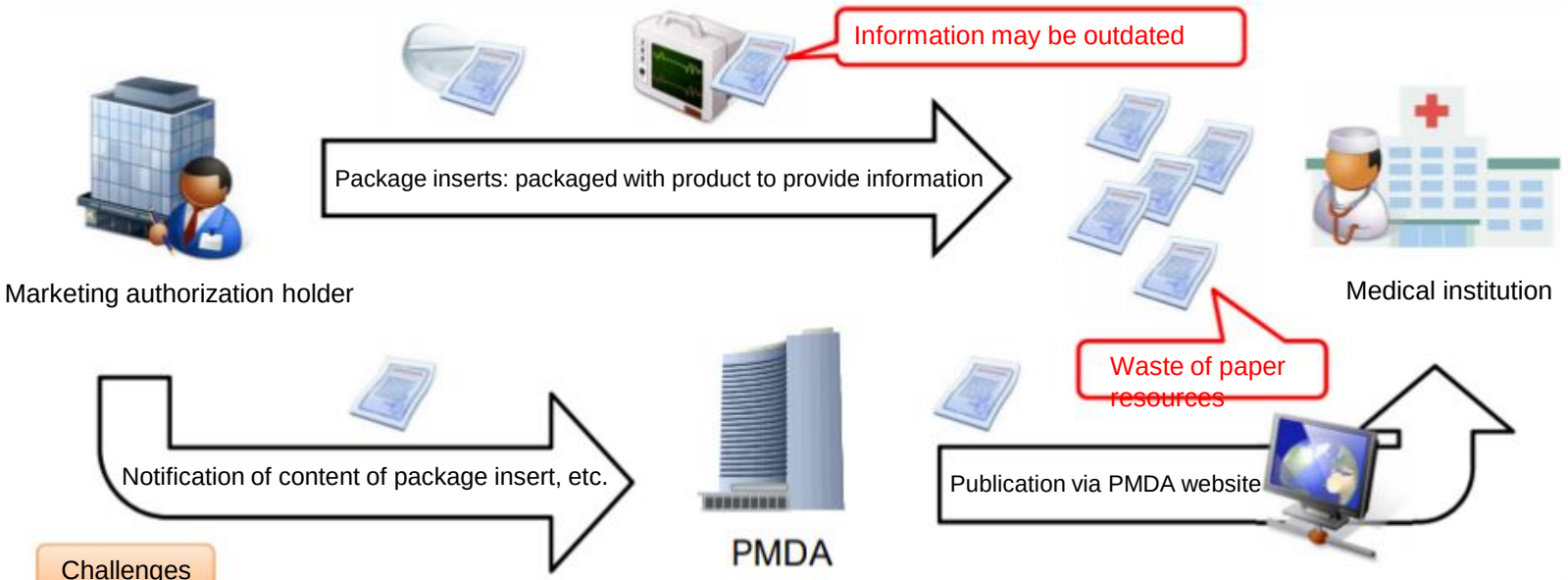
- To be enforced December 1, 2022

Current system and issues related to package inserts

Existing system

○ Presently, dosage and administration, and other precautions for use and handling of drugs, etc. are to be described in "package inserts or on containers or wrappers". (PMD Act Article 52, etc.)

○ For prescription drugs, OTC drugs requiring a pharmacy consultation, and specially controlled medical devices, notification is given on content of package insert, and the package inserts are published on the PMDA website. (PMD Act Article 52-2)



Challenges

For discussion at Council meeting (November 8, 2018; The 8th meeting of the Pharmaceutical and Medical Devices System Subcommittee of the MHLW Health Science Council)

○ Package inserts are frequently revised, and the one packaged with the product may not be up-to-date.

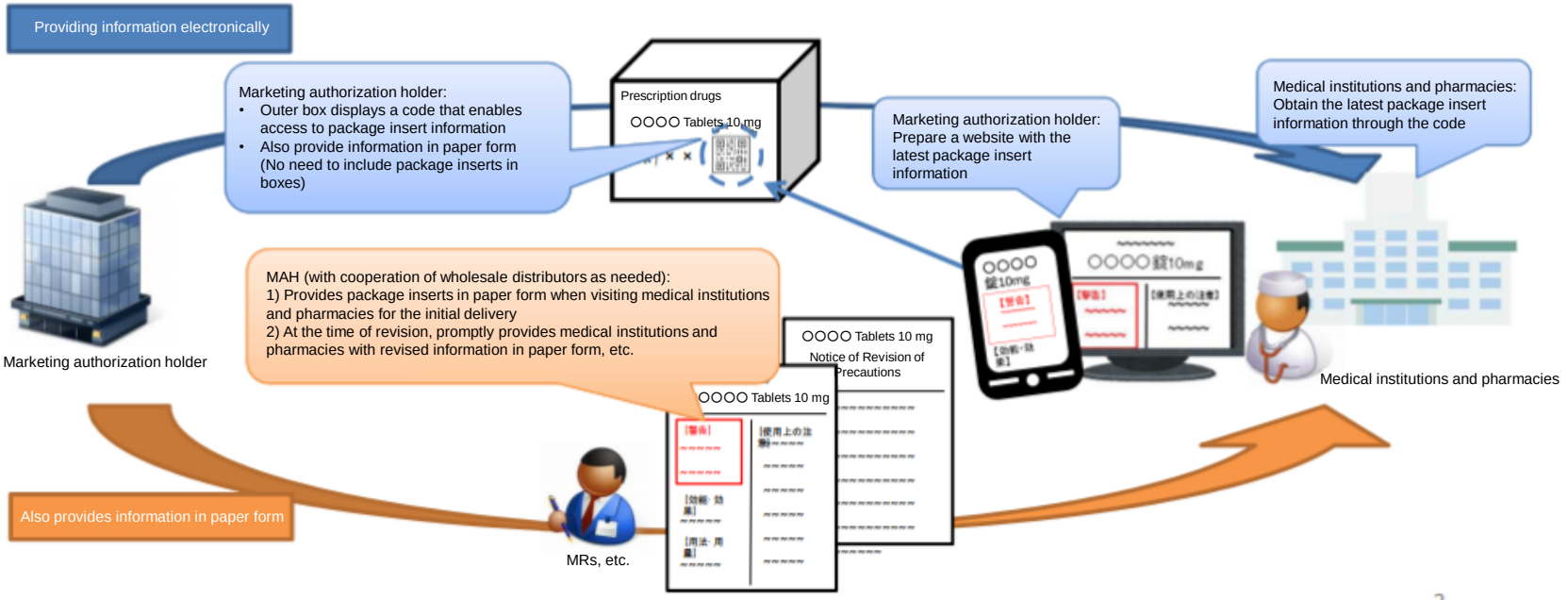
○ Each time the same drug, etc. is delivered to a medical institution or pharmacy, a large number of package inserts accumulate in one facility, leading to waste of paper resources.

https://www.mhlw.go.jp/content/11121000/000682481.pdf

Enforcement in the second year R3.8.1

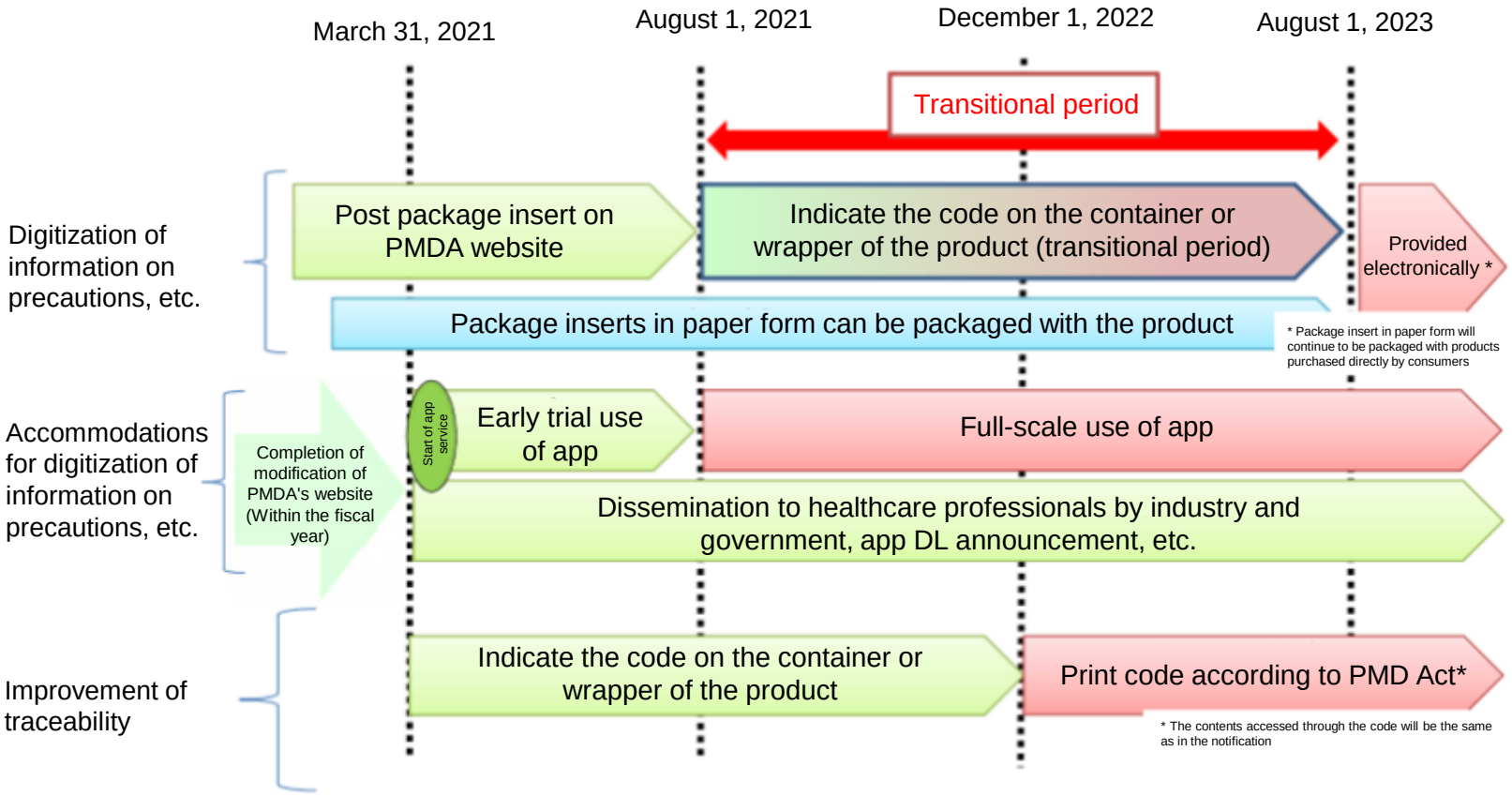
System after legal revision (Effective August 1, 2021)

- ○ Discontinue packaging of package insert with products and basically adopt provision of information electronically.
- ○ In addition to electronic methods of providing information, the information must also be provided in paper form at the time of the initial delivery of the pharmaceutical or medical device, with the cooperation of the wholesale distributor when necessary, at the responsibility of the marketing authorization holder. In addition, makers must display information on the outer packaging of the product that enables access to the latest package insert information and build a mechanism whereby information can be reliably delivered in paper form, etc. to medical institutions, pharmacies, etc. when the information is revised.
- ○ For OTC drugs and other products that are purchased directly by consumers, it is necessary to ensure that the contents of package inserts can be immediately confirmed at the time of use, so package inserts should continue to be enclosed in the package in paper form.



https://www.mhlw.go.jp/content/11121000/000682481.pdf

Schedule, etc.



○ Related systems are being developed to enable access to information on precautions, etc. published by PMDA by reading codes.
○ In order to ensure a smooth transition, information will be provided to marketing authorization holders and medical and pharmaceutical providers through seminars, etc.

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Thank you very much.