Regulatory progress
of Artificial Intelligence

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Disclaimer:

- Views expressed in this presentation are those of the presenter and not necessarily those of PMDA.

- No Conflict of Interests on this presentation.

Content

1. How PMDA identifies the emerging issues for further study that are not currently being addressed within the agency

2. How PMDA is preparing for review of AI-based Medical Devices

To improve review efficiency and expedite the development of novel products that can improve the lives of patients

Regulatory Science Center
(est. April 2018)

1. PMDA's command center on regulatory science

2. Actively utilize clinical trial data and electronic healthcare records

3. Approach for advanced therapies and technologies
   - Science Board
   - Horizon Scanning

Regulatory Science Center
- Collaboration with other PMDA Offices -
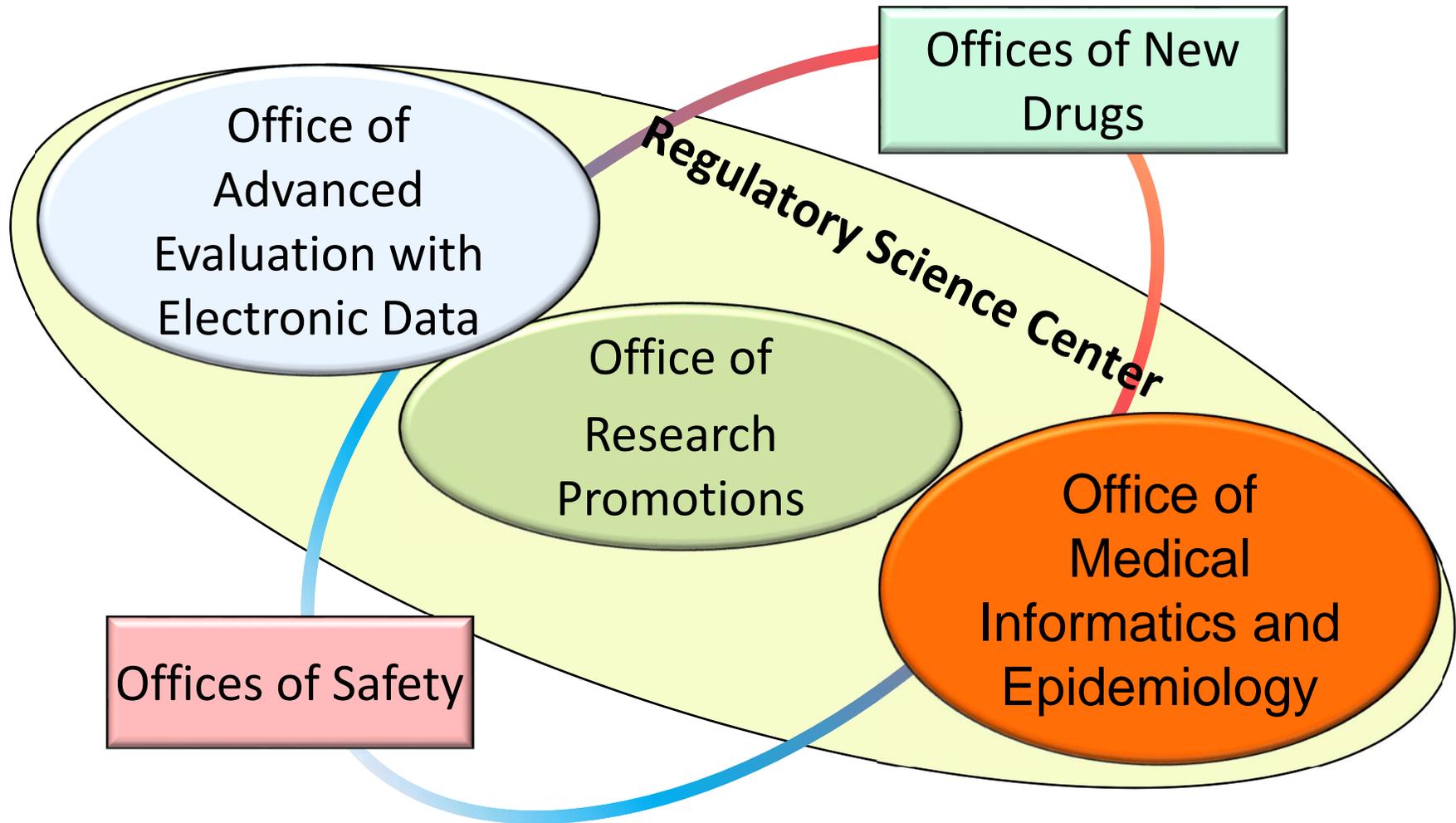
PMDA's Horizon Scanning

- Identify emerging technologies/products

- Assess their impacts on the regulation and regulatory actions (e.g. product review)

- Inform the Agency so that it can proactively address them

PMDA's Science Board

- To clarify review points for PMDA-regulated products not currently easily assessed with existing systems

- To reduce uncertainty in development

Science Board: to close the gap between scientific innovation and product review

When other PMDA Divisions have a challenging question, they come to Science Board!

Collaboration

Academia
Universities, institutes, medical institutions

Exchange opinions between top-class researchers in Japan and PMDA reviewers on assessment methods of cutting-edge technologies

Examples: Themes of Science Board

Subcommittee of Cellular and Tissue-based Products (1st term: FY2012 – 2013)

Evaluate tumorigenicity of cellular and tissue-based products derived from induced pluripotent stem cells (iPSCs)

Subcommittee of Artificial Intelligence (3rd term: FY2016 – 2017)

Overview new technologies using AI and discuss their totally new characteristics in order to facilitate the future review and consultations on the products.

Subcommittee of Genome Editing (4th term: FY2018 – 2019)

Assess the risk of genome edited products

Content

1. How PMDA identifies emerging issues for further study that are not currently being addressed within the agency

2. **How PMDA is preparing for review of AI-based Medical Devices**

Publication of reports from the Science Board on the Journal

Regulatory Science on AI-based Medical Devices and Systems

Kiyoyuki Chinzei,[1] Akinobu Shimizu,[2] Kensaku Mori,[3] Kanako Harada,[4] Hideaki Takeda,[5] Makoto Hashizume,[6] Mayumi Ishizuka,[7] Nobumasa Kato,[8] Ryuzo Kawamori,[9] Shunei Kyo,[10] Kyosuke Nagata,[11] Takashi Yamane,[12] Ichiro Sakuma,[4] Kazuhiko Ohe,[13] Mamoru Mitsuishi[14,#]

Advanced Biomedical Engineering　　Volume 7 (2018) Pages 118-123
　https://doi.org/10.14326/abe.7.118

Outcome documents of the Science Board :　PMDA Website (English)

https://www.pmda.go.jp/english/rs-sb-std/sb/outcome-docs/0001.html

Characteristics of AI Medical Systems

1. Plasticity-adaptively changing behavior through learning

   – the conformity to the marketing approval and product identity: a departure from the approval criteria may necessitate application of partial change

2. Predictability

   – the unpredictability of the AI output due to the black box nature of the deep learning algorithms

3. Quality of data

   – quality control of data as source materials

● Others: Degree of Autonomy

   – may modify relationship between doctors and patients in the future

Classification of AI devices based on the timing of learning

		Performance change after shipment or start of service	
		No	Yes
Learning after shipment or service	No	Same as conventional medical devices	N/A
	Yes	• System continuingly learns, but performance stays static • The manufacturer may update the system to implement the result of learning in upgrade • The manufacturer takes responsibility for risk management and control the dataset	• Performance changes by learning • Performance may be worsened by improper learning • Who makes AI learn with what kind of dataset? Control of learning and the dataset by the manufacturer can be tricky

AI-devices for CAD

<Scope>

- Computer-aided detection (CADe)
- Computer-aided diagnosis (CADx)

Device algorithm evolves over time based on the new evidence collected in the field after the device goes into the market (adaptive).

It should be an adjunct tool and not intended to replace a clinician's review of the radiograph or his or her clinical judgment.

Preparing for review of AI-based Medical Devices

The Report from Science Board

A Draft Guidance on Evaluation
Indices for AI-based Systems

Discussion with Academia,
MHLW, and NIHS

Inputs from stakeholders

Review Points of PMDA
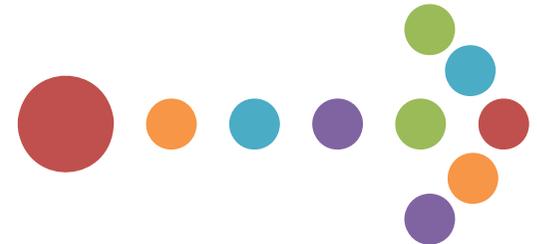
Review points of PMDA

1. Adaptive device ① changing behavior through learning

How can we ensure the change do not compromise the safety and effectiveness of the device?

- Approval within the acceptance range that does not alter the clinical relevance

→ Rationale for the acceptance range and validation of the test methods

- Justification for the post-market learning

→ Who, when, with what kind of data, how, the condition of upgrading and control strategy

Review points of PMDA

1. Adaptive device ②

• Define management system

→ Not only data management but also management excluding off-label use

→ Scope of IEC62304 that defines the life cycle requirements for medical device software

→ consecutive performance testing

→ countermeasure against the deviation from its clinically required specification

2. the black box nature due to the deep learning algorithms

- Describe the network structure and algorithm design and function
- Evaluate output performance with a range of inputs
- A provision to meet the unexpected behavior
→ Premise is that the dataset is valid and reliable

3. Quality of data
   (pre/post-market learning, performance testing)

- High quality data (teacher data)
- Explain that the training/test set is appropriate

$\rightarrow$ At least meet the clinical relevance

$\rightarrow$ Generalizability

$\rightarrow$ Avoid overtraining (the algorithm may become tuned to the test data if the same test set is used multiple times)

- Control strategy for the post-market learning

Review points of PMDA

Provision of information

- help clinicians use the AI-device in an appropriate manner
- provide provide understandable and practicable information to the users
- the expected device effectiveness and safety
- concept of design (network structure, how AI learned and will learn, data quantity and quality)
- the range of performance tested
- device limitations

Summary

- PMDA has set up a framework to better keep pace with the emerging scientific issues important to PMDA.

- PMDA is preparing review points for the novel technology on how those products will be evaluated.

→ PMDA offers consultations to give guidance and advice on medical devices as well as drugs and biologics from the early phases of development

Thank you for your kind attention!