COVID-19 measures in Japan

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OFFICE OF INTERNATIONAL PROGRAMS

PHARMACEUTICALS AND MEDICAL DEVICES AGENCY

Today’s topics

- Situation of COVID-19 in Japan
- Regulatory Efforts to address COVID-19
  - COVID-19 related products
  - Other products
- Global Challenges & International Collaborations

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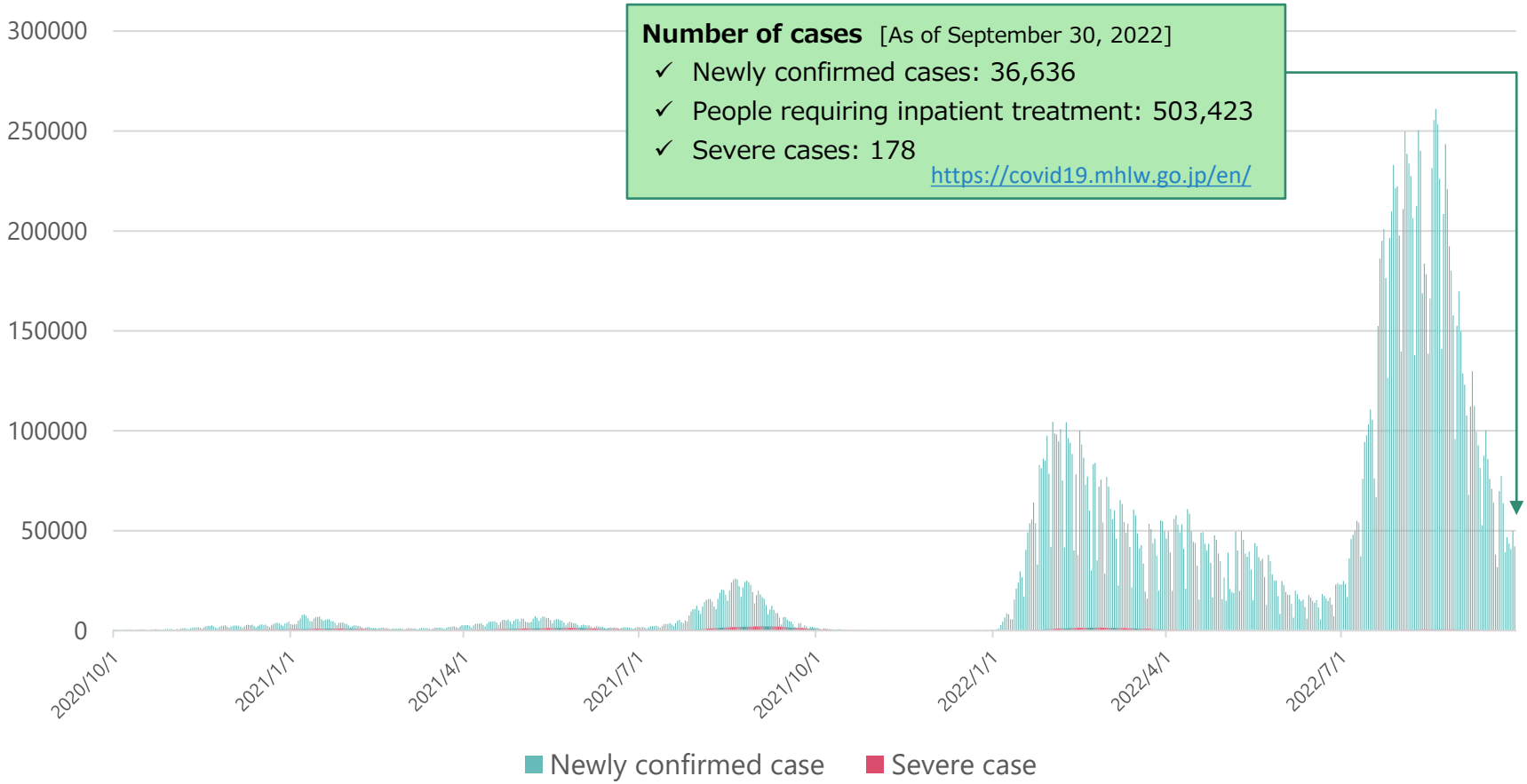
Situation of COVID-19 in Japan



Number of cases [As of September 30, 2022]

- ✓ Newly confirmed cases: 36,636
- ✓ People requiring inpatient treatment: 503,423
- ✓ Severe cases: 178

https://covid19.mhlw.go.jp/en/

Preventing COVID-19 and stopping its spread

-What should I do in my everyday life? –

https://www.c19.mhlw.go.jp/covid-19-en.html

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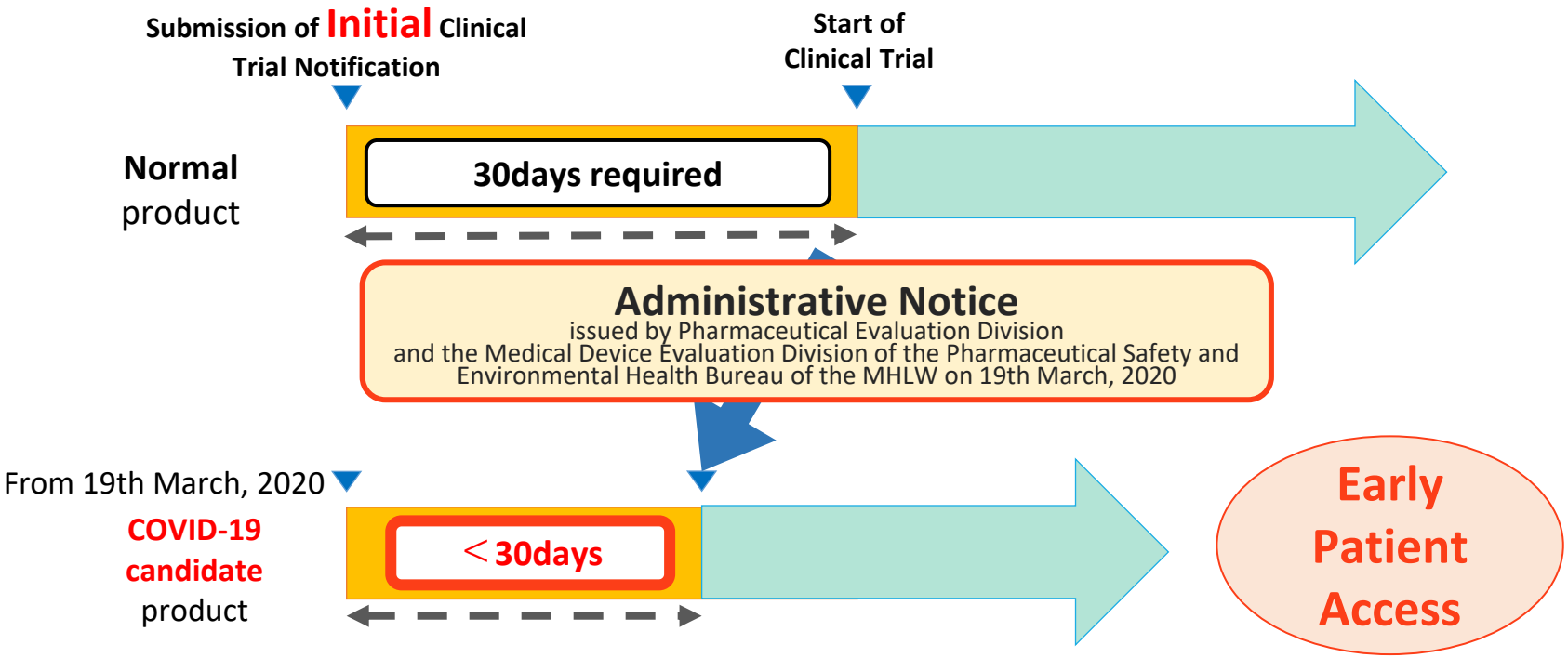
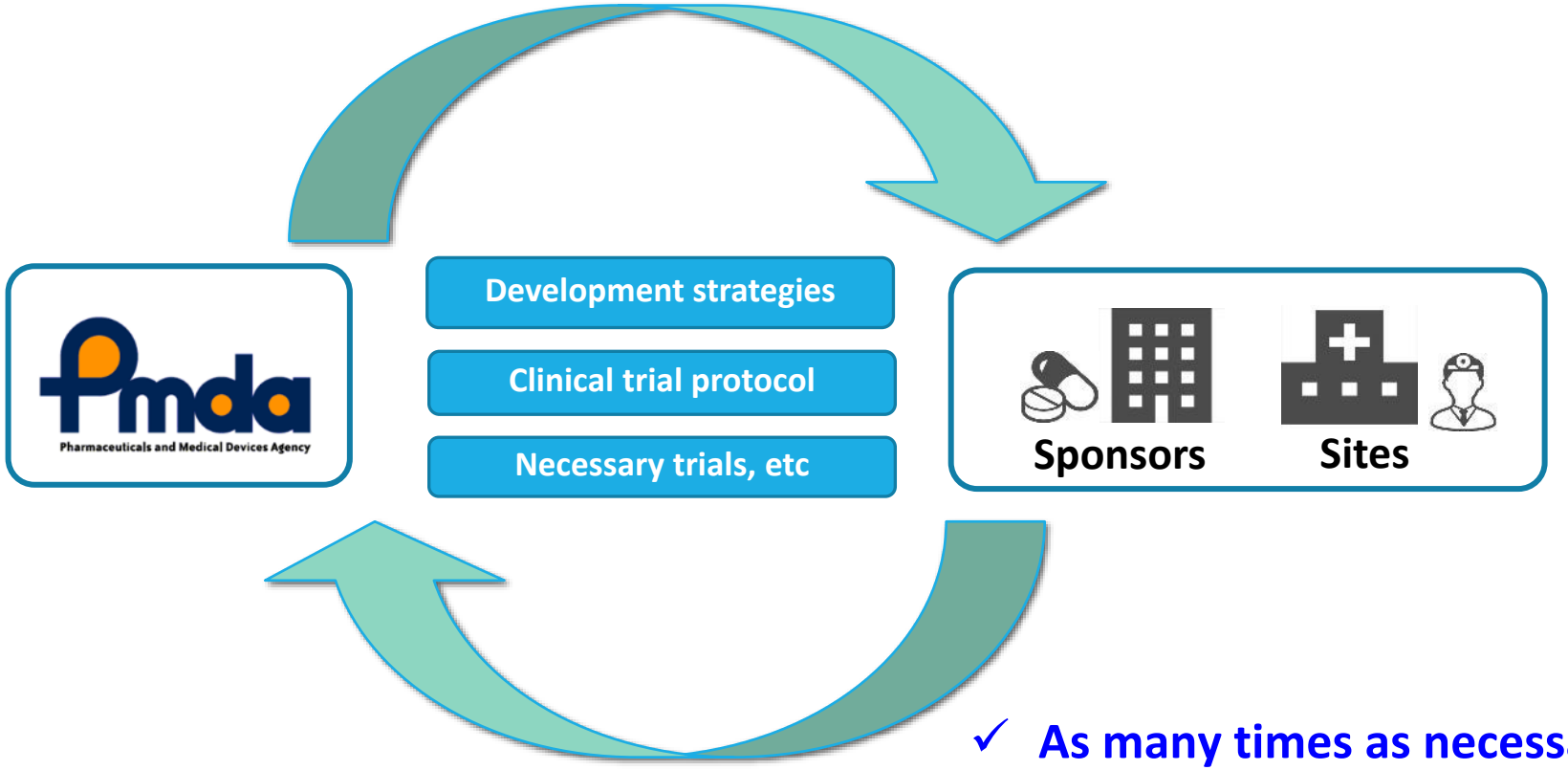
Accelerating product development



https://www.pmda.go.jp/english/int-activities/0001.pdf
https://www.pmda.go.jp/files/000235010.pdf (JP)

Free Scientific Advice for COVID-19 vaccine development



- ✓ **As many times as necessary**
- ✓ **No waiting time**
- ✓ **Free of charge**

https://www.pmda.go.jp/review-services/f2f-pre/strategies/0010.html (JP)

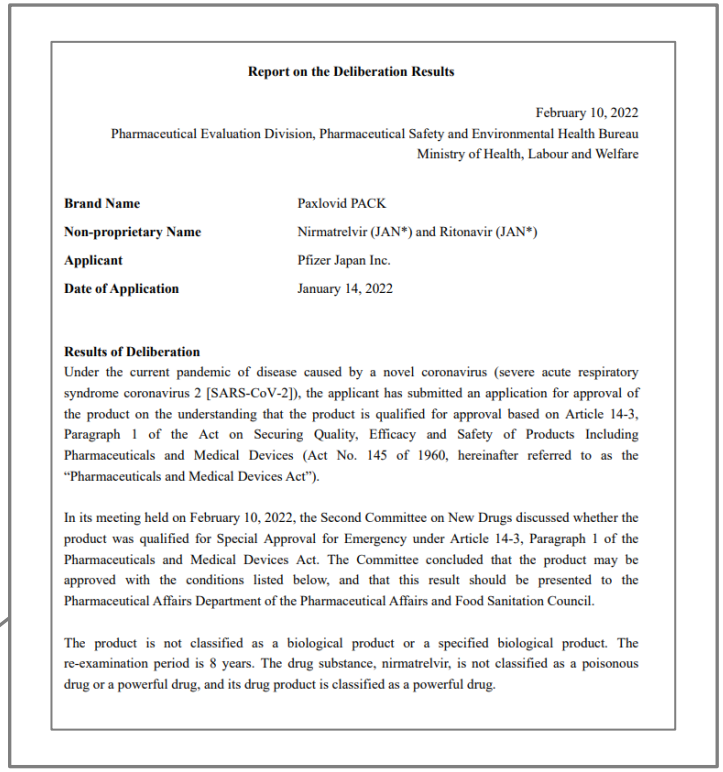
https://www.pmda.go.jp/english/int-activities/0002.pdf

Approved Medical Products for COVID-19

- Since March 2022

Products	Number of Approvals
Drugs	8
Vaccines	5
Medical Devices	27
In Vitro Diagnostics	117

*As of September 30, 2022



Report on the Deliberation Results

February 10, 2022
Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau
Ministry of Health, Labour and Welfare

Brand Name	Paxlovid PACK
Non-proprietary Name	Nirmatrelvir (JAN*) and Ritonavir (JAN*)
Applicant	Pfizer Japan Inc.
Date of Application	January 14, 2022

Results of Deliberation

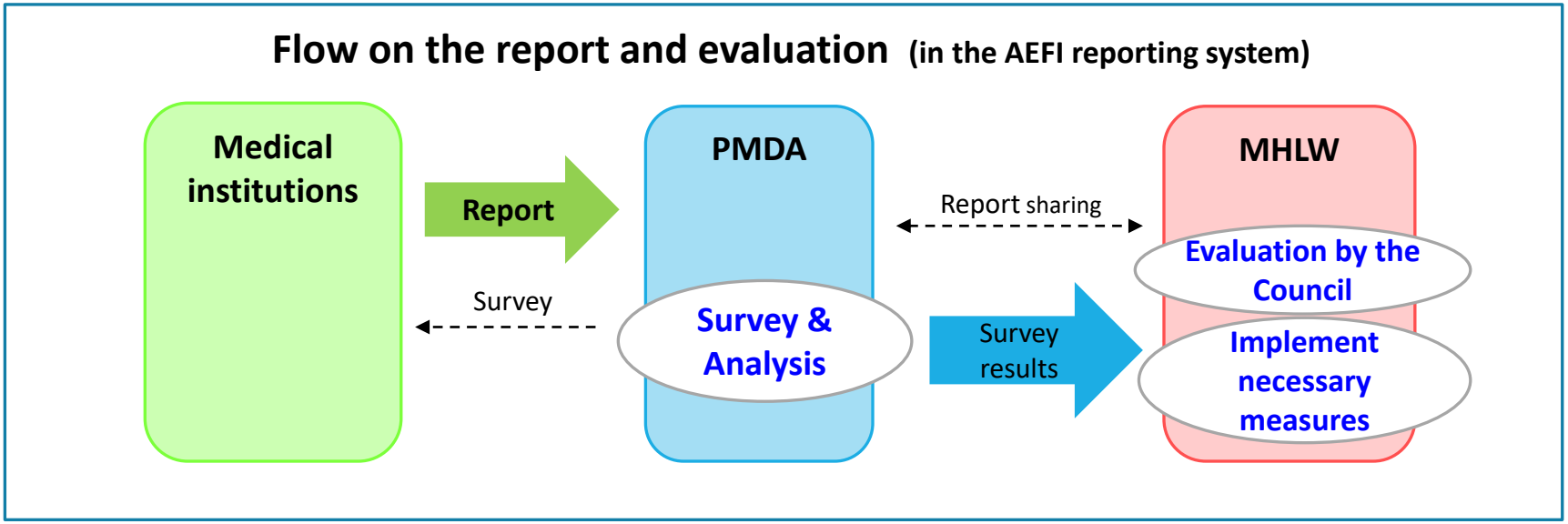
Under the current pandemic of disease caused by a novel coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), the applicant has submitted an application for approval of the product on the understanding that the product is qualified for approval based on Article 14-3, Paragraph 1 of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 145 of 1960, hereinafter referred to as the "Pharmaceuticals and Medical Devices Act").

In its meeting held on February 10, 2022, the Second Committee on New Drugs discussed whether the product was qualified for Special Approval for Emergency under Article 14-3, Paragraph 1 of the Pharmaceuticals and Medical Devices Act. The Committee concluded that the product may be approved with the conditions listed below, and that this result should be presented to the Pharmaceutical Affairs Department of the Pharmaceutical Affairs and Food Sanitation Council.

The product is not classified as a biological product or a specified biological product. The re-examination period is 8 years. The drug substance, nirmatrelvir, is not classified as a poisonous drug or a powerful drug, and its drug product is classified as a powerful drug.

English review reports available at:
https://www.pmda.go.jp/english/about-pmda/0002.html

Post-marketing Surveillance and safety evaluation of COVID-19 vaccines



- Expert Advisory Council (in MHLW)
  - Monitoring the number of reports, evaluation of individual cases and considerations of necessary measures
- MHLW, NIID, PMDA
  - Real time monitoring of safety information reported
  - Conducting field surveys on individual cases for details, if necessary

Transparency on Vaccine Safety

Health Sciences Council Assessment

回数	開催日	議題等	議事録／議事要旨	資料等	開催案内
第78回	2022年4月13日（令和4年4月13日）	（1）新型コロナワクチンの接種及び副反応疑い報告の状況並びに接種後の健康状況に係る	－	▸ 資料 NEW 4月13日 ▸ 遵守事	▸ 開催案内 NEW 4月11日
第77回	2022年3月18日（令和4年3月18日）				

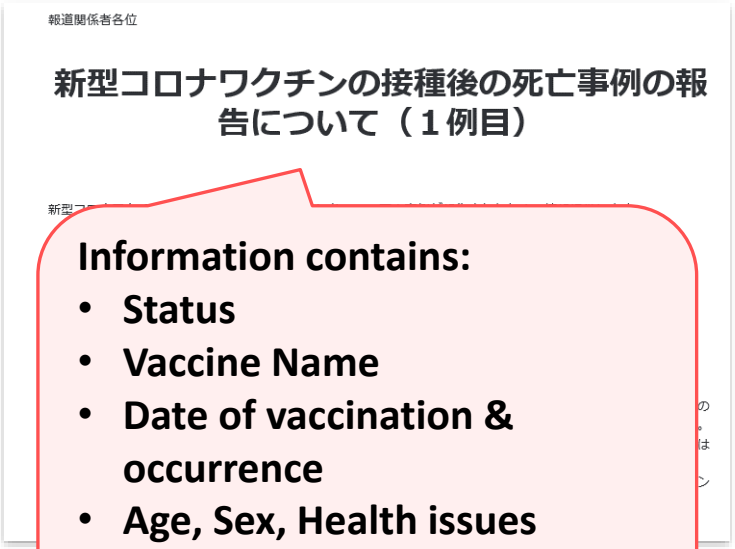
13th Apr. 2022

18th Mar. 2022

Side Effect Subcommittee of the Immunization and Vaccine Section Meeting in the Health Science Council has been held frequently to provide an overview of the status of instances of suspected adverse reactions to COVID-19 vaccines.

https://www.mhlw.go.jp/stf/shingi/shingi-yakuji_127869.html (JP)

MHLW Press Release: Report of suspected death after receiving the COVID-19 vaccine


報道関係者各位

新型コロナワクチンの接種後の死亡事例の報告について（１例目）

Information contains:

- **Status**
- **Vaccine Name**
- **Date of vaccination & occurrence**
- **Age, Sex, Health issues**
- **Evaluation**

https://www.mhlw.go.jp/stf/newpage_17104.htm (JP)l

Safety Information of COVID-19 related products

https://www.pmda.go.jp/about-pmda/news-release/0012.html#3 (JP)

“Principles for the Evaluation of Vaccines Against the Novel Coronavirus SARS-COV-2”

Background

- To ensure the efficacy and safety of vaccines used in Japan and accelerate vaccine development, the first edition of a guidance summarizing principles for evaluation on non-clinical and clinical study data required for initiation of a clinical study and application for approval was issued on September 2, 2020.
- To date, Appendices 1, 2, and 3 have been issued to supplement the first version in view of the current social circumstance and findings from development of vaccines against SARS-CoV-2 .

Guidelines

- **2 Sep., 2020 1st Edition**
- **5 Apr., 2021 Appendix 1 Evaluation of vaccines against variants**
- **11 Jun., 2021 Appendix 2 Ethical Considerations for Subjects in Placebo-Controlled studies**
- **22 Oct., 2021 Appendix 3 Evaluation of the vaccines based on immunogenicity**
- **15 Jul., 2022 Appendix 4 Evaluation of adapted versions of vaccines already in use to contain variants and new booster vaccines based on immunogenicity**

Special Approval for Emergency (SAE)

Under article 14-3 of the PMD Act, a certain medical product may be approved when

1. an emergency situation requires an unapproved medical product to be used to prevent damage to the public health caused by the spread of diseases

2. such emergency situation cannot be managed appropriately by any means other than the use of the unapproved product, and

3. such product is legally available in a country with a regulatory system for medical products that is equivalent to Japan

Amendment of the Pharmaceuticals and Medical Devices Act (PMD Act)

1. Marketing Approval in Emergencies

New mechanisms to enable early marketing approval in emergencies.

(1) Eligibility of pharmaceutical, etc. to which the early approval is applicable

A pharmaceutical, etc. that needs to be used urgently in order to prevent the spread of a disease or other health hazard that could seriously affect the lives and health of people is eligible for early approval if there is no alternative existing treatment.

(2) Application standards

Assuming that safety has been confirmed, approval may be granted if the efficacy of the pharmaceutical, etc. has been estimated.

(3) Conditions and term of approval

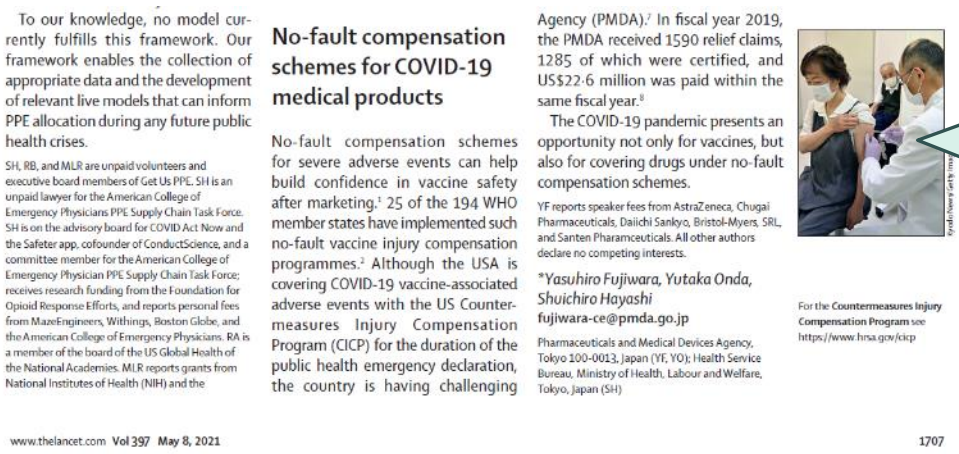
As approval is granted at the early stage where efficacy has been estimated, conditions are provided to ensure the proper use of the pharmaceutical, etc. and restrictions are set in place that limit the duration of the approval to a short term.

(4) Special measures to expedite review process

Special measures are introduced for GMP inspections, national verifications as well as regulations on containers and packaging of the pharmaceutical, etc., in order to expedite review process for approval.

2. Creation of a mechanism for electronic prescriptions

Relief service for COVID-19 vaccine/ therapeutics in Japan



To our knowledge, no model currently fulfills this framework. Our framework enables the collection of appropriate data and the development of relevant live models that can inform PPE allocation during any future public health crises.

SH, RB, and MLR are unpaid volunteers and executive board members of Get Us PPE. SH is an unpaid lawyer for the American College of Emergency Physicians PPE Supply Chain Task Force. SH is on the advisory board for COVID Act Now and the Safeter app, cofounder of ConductScience, and a committee member for the American College of Emergency Physician PPE Supply Chain Task Force; receives research funding from the Foundation for Opioid Response Efforts, and reports personal fees from MazeEngineers, Withings, Boston Globe, and the American College of Emergency Physicians. RA is a member of the board of the US Global Health of the National Academies. MLR reports grants from National Institutes of Health (NIH) and the

No-fault compensation schemes for COVID-19 medical products

No-fault compensation schemes for severe adverse events can help build confidence in vaccine safety after marketing.[1] 25 of the 194 WHO member states have implemented such no-fault vaccine injury compensation programmes.[2] Although the USA is covering COVID-19 vaccine-associated adverse events with the US Countermeasures Injury Compensation Program (CICP) for the duration of the public health emergency declaration, the country is having challenging

Agency (PMDA).[7] In fiscal year 2019, the PMDA received 1590 relief claims, 1285 of which were certified, and US$22·6 million was paid within the same fiscal year.[8]

The COVID-19 pandemic presents an opportunity not only for vaccines, but also for covering drugs under no-fault compensation schemes.

YF reports speaker fees from AstraZeneca, Chugai Pharmaceuticals, Daiichi Sankyo, Bristol-Myers, SRL, and Santen Pharmceuticals. All other authors declare no competing interests.

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For the **Countermeasures Injury Compensation Program** see https://www.hrsa.gov/cicp

Few countries have relief service in COVID-pandemic

Lancet. May 08, 2021. DOI:https://doi.org/10.1016/S0140-6736(21)00784-4

Vaccines	Relief System for Injury to Health with Vaccination (MHLW) (Funded by government subsidy and contribution from MAH)
Therapeutics	Relief Services for Adverse Health Effects (PMDA) (Funded by government, prefecture and Municipalities)

The services are applied to all vaccines/therapeutics including COVID-19 products approved as Special Approval for Emergency

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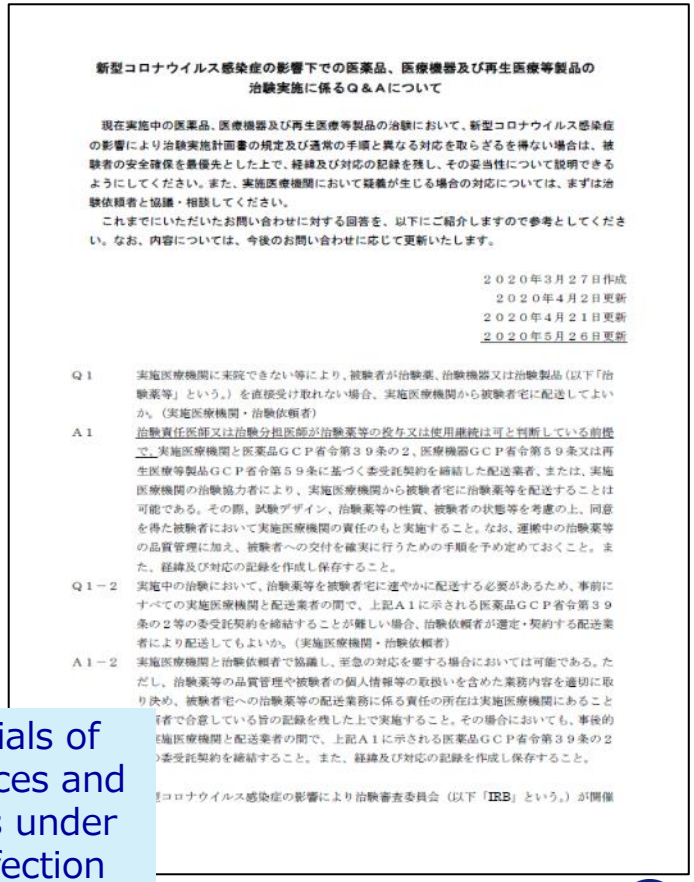
Flexibility in regulation

- Difficulty in conducting drug development under emergency conditions the same way as in normal circumstances
- Measures that differ from the provisions of the study protocol and normal procedures



新型コロナウイルス感染症の影響下での医薬品、医療機器及び再生医療等製品の治験実施に係るＱ＆Ａについて

現在実施中の医薬品、医療機器及び再生医療等製品の治験において、新型コロナウイルス感染症の影響により治験実施計画書の規定及び通常の手順と異なる対応を取らざるを得ない場合は、被験者の安全確保を最優先とした上で、経緯及び対応の記録を残し、その妥当性について説明できるようにしてください。また、実施医療機関において疑義が生じる場合の対応については、まずは治験依頼者と協議・相談してください。

これまでにいただいたお問い合わせに対する回答を、以下にご紹介しますので参考としてください。なお、内容については、今後のお問い合わせに応じて更新いたします。

２０２０年３月２７日作成
２０２０年４月２日更新
２０２０年４月２１日更新
２０２０年５月２６日更新

Ｑ１　実施医療機関に来院できない等により、被験者が治験薬、治験機器又は治験製品（以下「治験薬等」という。）を直接受け取れない場合、実施医療機関から被験者宅に配送してよいか。（実施医療機関・治験依頼者）

Ａ１　治験責任医師又は治験分担医師が治験薬等の投与又は使用継続は可と判断している前提で、実施医療機関と医薬品ＧＣＰ省令第３９条の２、医療機器ＧＣＰ省令第５９条又は再生医療等製品ＧＣＰ省令第５９条に基づく委受託契約を締結した配送業者、または、実施医療機関の治験協力者により、実施医療機関から被験者宅に治験薬等を配送することは可能である。その際、試験デザイン、治験薬等の性質、被験者の状態等を考慮の上、同意を得た被験者において実施医療機関の責任のもと実施すること。なお、運搬中の治験薬等の品質管理に加え、被験者への交付を確実に行うための手順を予め定めておくこと。また、経緯及び対応の記録を作成し保存すること。

Ｑ１－２　実施中の治験において、治験薬等を被験者宅に速やかに配送する必要があるため、事前にすべての実施医療機関と配送業者の間で、上記Ａ１に示される医薬品ＧＣＰ省令第３９条の２等の委受託契約を締結することが難しい場合、治験依頼者が選定・契約する配送業者により配送してもよいか。（実施医療機関・治験依頼者）

Ａ１－２　実施医療機関と治験依頼者で協議し、至急の対応を要する場合においては可能である。ただし、治験薬等の品質管理や被験者の個人情報等の取扱いを含めた業務内容を適切に取り決め、被験者宅への治験薬等の配送業務に係る責任の所在は実施医療機関にあること[illegible]者で合意している旨の記録を残した上で実施すること。その場合においても、事後的[illegible]施医療機関と配送業者の間で、上記Ａ１に示される医薬品ＧＣＰ省令第３９条の２[illegible]委受託契約を締結すること。また、経緯及び対応の記録を作成し保存すること。

[illegible]型コロナウイルス感染症の影響により治験審査委員会（以下「IRB」という。）が開催

Q&A on conducting clinical trials of pharmaceuticals, medical devices and regenerative medical products under the influence of COVID-19 infection

https://www.pmda.go.jp/files/000235164.pdf (JP)

Remote GCP Inspections

- Remote GCP inspections have started from May 2020.
- Notification documenting the method of remote GCP inspections was published on Nov. 16, 2020.
- Documents can be submitted through “Gateway” system from Jul. 1, 2022

https://www.pmda.go.jp/files/000237602.pdf (JP)

https://esg.pmda.go.jp/Ssk/comn001p01.init (JP)

Remote GMP Inspections

- **Since 2020 - Traveling overseas has been strictly limited due to the COVID-19 pandemic.**
- On-site inspections at foreign manufacturing sites have not been conducted.
- It is difficult to predict the future international situation. There is a concern that on-site inspections at foreign manufacturing sites may not be conducted for an extended period of time.

PMDA mainly conducts (advanced) desktop inspections or postponed on-site inspections. Since it is difficult to understand the actual situation of the manufacturing sites only by desktop inspections, a new method of inspection needs to be developed to thoroughly examine the manufacturing sites with higher risks.

As a more effective means of inspection compared to the conventional desktop inspections, **PMDA started the examination and operation of "Remote Inspection with ICT Tool."**

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Communication with global regulatory authorities

APEC
Asia-Pacific Economic Cooperation

OECD /GLP
BETTER POLICIES FOR BETTER LIVES

IMDRF

ICMRA
International Coalition of Medicines Regulatory Authorities

PIC/S

IPRP
International Pharmaceutical Regulators Programme

ICH
harmonisation for better health

Summary

- Regulatory Agilities/Efforts to;
  - Encourage COVID-19 products development
  - Accelerate COVID-19 products review
  - Ensure COVID-19 products safety
  - Conduct the regular service to protect efficacy, safety and quality of medical products
- Promoting Global Cooperation

Thank you for listening.

謝謝.