

# Regulatory Efforts to Combat COVID-19 in Japan

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Health Authority Forum: Japan, September 13<sup>th</sup>

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# Situation of COVID-19 in Japan as of August 29<sup>th</sup>, 2021

Cumulative number of confirmed cases is **1,450,487** cases

Cumulative number of deaths is **15,939** cases

<https://covid19.mhlw.go.jp/extensions/public/en/index.html>

**The 4th State of emergency** was declared in

**Okinawa, Tokyo, Saitama, Chiba, Kanagawa, Osaka, Ibaraki, Tochigi, Gunma, Shizuoka, Kyoto, Hyogo, Fukuoka, Hokkaido, Miyagi, Gifu, Aichi, Mie, Shiga, Okayama, and Hiroshima.**

- Other 12 areas are under the Priority Preventative Measures

[https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000164708\\_00079.html](https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000164708_00079.html)

**Vaccination** started on Feb. 17<sup>th</sup> from healthcare professionals, and April 12<sup>th</sup> for elderly aged 65 or older.

- **Total number of vaccine doses administered**  
**127,420,574 (1st: 70,699,480 2nd: 56,721,094)**

<https://japan.kantei.go.jp/ongoingtopics/vaccine.html>

# Statements by the Chief Executive Dr. FUJIWARA

## 9 statements issued:

As of 13 July, 2021

### PMDA to Offer Free Scientific Advice for COVID-19 Vaccines Development

### Special Approval for Emergency on Remdesivir for COVID-19

8th May, 2020

### Special Approval for Emergency on First COVID-19 Vaccine in Japan

16th February, 2021

On 14<sup>th</sup> February, the first COVID-19 vaccine applied by Pfizer Japan Inc. was granted Special Approval for Emergency in Japan. With this Special Approval for Emergency, Japanese citizens can now start vaccination with prioritization to protect themselves against SARS-CoV-2.

- Special Approval for Emergency on First COVID-19 Vaccine in Japan (16 February, 2021)
- PMDA Reveals Principles on Evaluation of COVID-19 Vaccines (12 October, 2020)
- PMDA to Offer Free Scientific Advice for COVID-19 Vaccines Development (6 October, 2020)
- For Your Access to Japanese Clinical Trial/Clinical Research Information (4 June, 2020)
- First Approval of Antigen Test for COVID-19 (13 May, 2020)
- Special Approval for Emergency on Remdesivir for COVID-19 (8 May, 2020)
- Four IVDs Approvals for COVID-19 and Response to the Increased Ventilator Demand (21 April, 2020)
- PMDA Takes Further Steps to Speed up Clinical Development of COVID-19 Products (10 April, 2020)
- PMDA pledge to tackle COVID-19 Pandemic (31 March, 2020)

# Discussion in ICMRA

Active discussions on product development in workshops.

- Global regulatory workshop on COVID-19 Real-World Evidence and Observational studies #1-4
- Global regulatory workshop on COVID-19 therapeutic development #1-2
- Global regulatory workshop on COVID-19 vaccine development #1-2
- ICMRA Vaccine Safety Collaboration Workshop #1
- ICMRA Pregnancy and Lactation Workshop #1
- ICMRA COVID-19 Virus Variants workshop #1
- ICMRA workshop on enabling manufacturing capacity in the COVID-19 pandemic #1

## Global regulatory workshop on COVID-19 vaccine development



A virtual meeting, held under the umbrella of the International Coalition of Medicines Regulatory Authorities (ICMRA), convening experts from medicines regulatory authorities, the World Health Organization (WHO) and the European Commission

18 March 2020

The SARS-CoV-2 pandemic that has infected to date more than 1,000,000 people worldwide presents an extraordinary challenge to global health. Commercial vaccine development timelines for SARS-CoV-2 vaccine candidates using different DNA, protein and viral vectored vaccines. The rapid spread of the virus requires prompt development for therapeutic candidates to enter clinical trials; additionally, the need of developing pre-exposure prophylaxis (PrEP) and post-exposure

## Global regulatory workshop on COVID-19 therapeutic development



A virtual meeting, held under the umbrella of the International Coalition of Medicines Regulatory Authorities (ICMRA), convening experts from medicines regulatory authorities, the World Health Organization (WHO) and the European Commission

2 April 2020

The COVID-19 pandemic that has infected to date around 1,000,000 people worldwide presents an extraordinary challenge to global health. SARS-CoV-2 therapeutic candidates, including (repurposed) direct acting antivirals and immunomodulating agents are being considered and investigated.

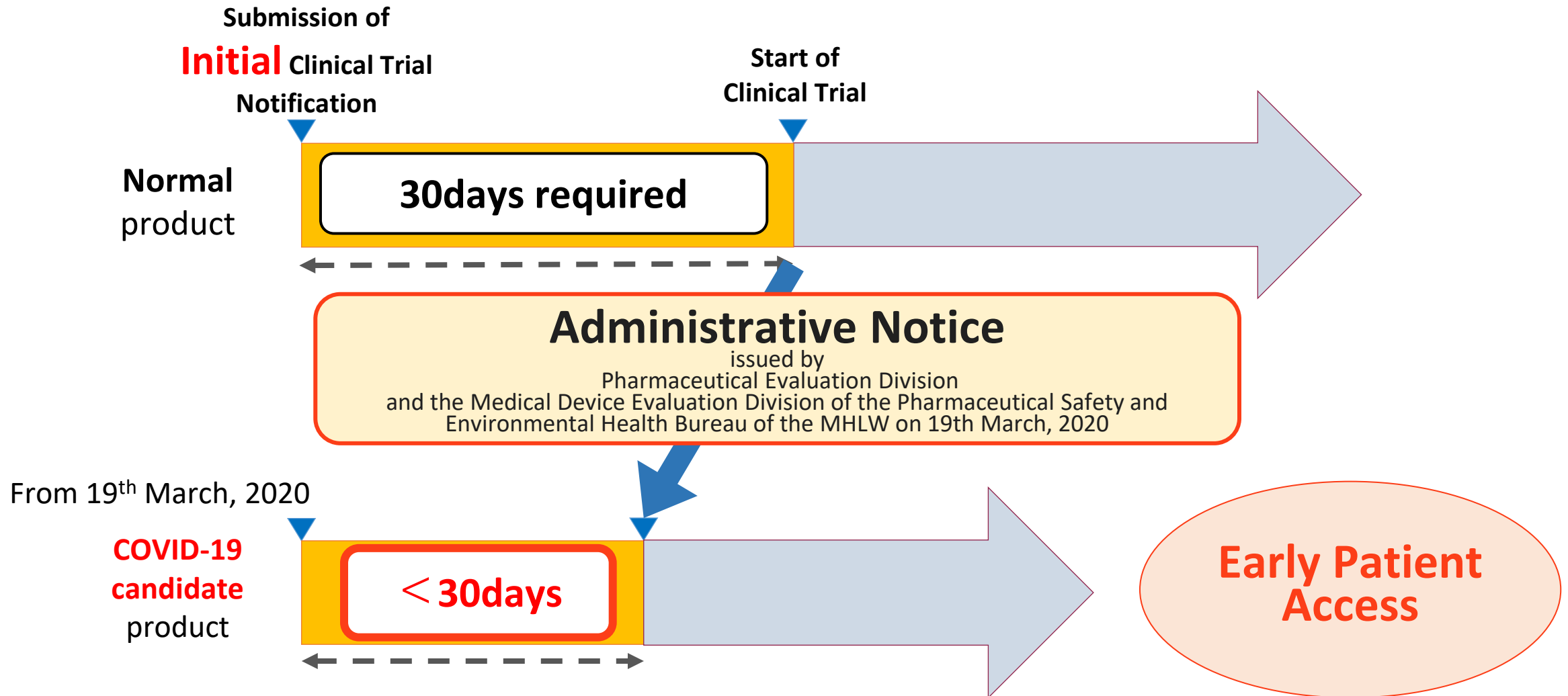
The rapid spread of SARS-CoV-2 requires prompt development for therapeutic candidates to enter clinical trials; additionally, the need of developing pre-exposure prophylaxis (PrEP) and post-exposure

# Regulatory Flexibilities/Agilities during COVID-19

## Clinical Trial, GCP

Document Title (Links are only in Japanese)	Summary of Flexibilities/Agilities
Handling on clinical trial notifications of COVID-19 (Administrative Notice dated March 19, 2020) <a href="https://www.pmda.go.jp/files/000234901.pdf">https://www.pmda.go.jp/files/000234901.pdf</a>	Clinical trials on COVID-19 <b>can be started without waiting 30 days after the submission of clinical trial notification</b> if investigation by PMDA is completed.
Handling on review of COVID-19 clinical trials by Institutional Review Board (IRB) (Administrative Notice dated April 1, 2020) <a href="https://www.pmda.go.jp/files/000234902.pdf">https://www.pmda.go.jp/files/000234902.pdf</a>	The IRB meeting of each medical institution <b>can be held by e-mail and online basis</b> other than face-to-face. It can be applied <b>only when the review is urgently needed</b> . The details of meeting must be recorded and stored.
Handling on the storage of informed consent forms during clinical trials (Administrative Notice dated April 7, 2020) <a href="https://www.pmda.go.jp/files/000234903.pdf">https://www.pmda.go.jp/files/000234903.pdf</a>	The following documents <b>can be regard as original documents if it is difficult to store the signed informed consent</b> . 1. <b>Copies</b> – when they are making the signed informed consent in writing, the copies certified as having made based on the process that is established to guarantee the identity with the original. 2. <b>Electric signature</b> – Only when the documents with the sign can be stored based on the prepared procedure manual with keeping their readability, and in case it is possible to deliver its copy to the subject.

# Allowing Quick Start of Clinical Trials



# Regulatory Flexibilities/Agilities during COVID-19

## Clinical Trial, GCP (continued)

Document Title (Links are only in Japanese)	Summary of Flexibilities/Agilities
Handling of implementation guidelines for document-based conformity inspection and GCP on-site inspection for the time being associated with COVID-19 (Administrative Notice dated May 12, 2020) <a href="https://www.pmda.go.jp/files/000235011.pdf">https://www.pmda.go.jp/files/000235011.pdf</a>	<ol style="list-style-type: none"><li>1. Considering the infection risk, GLP/GCP document-based conformity inspection and GCP on-site inspection <b>can be postponed</b>.</li><li>2. The Authority <b>can conduct remote inspections</b> to Sponsors.</li><li>3. <b>Confirmation of management on clinical trial sites by sponsor can be done without GCP on-site inspection</b>. However, when there are any serious concern, sponsor should undergo on-site inspection after the pandemic is settled.</li><li>4. <b>Sealing on documents is not needed</b>.</li></ol>
Q&A on clinical trial of drugs, medical devices, and regenerative medical products under the influence of COVID-19 (Administrative Notice dated March 27, 2020) <a href="https://www.pmda.go.jp/files/000235164.pdf">https://www.pmda.go.jp/files/000235164.pdf</a>	<p><b><i>Will be updated occasionally</i></b></p> <ol style="list-style-type: none"><li>1. Delivery of the investigational medicinal products</li><li>2. IRB</li><li>3. On-site monitoring</li><li>4. protocol deviations</li><li>5. Examinations specified in the clinical trial protocol</li></ol> <p>etc.</p>



# Regulatory Flexibilities/Agilities during COVID-19

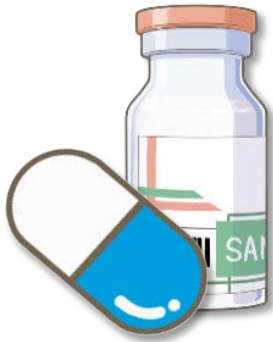
## Marketing Approval

Document Title (Links are only in Japanese)	Summary of Flexibilities/Agilities
Handling on regulatory reviews of drugs, medical devices, IVDs, and regenerative medical products for the time being associated with COVID-19 (Administrative Notice dated April 13, 2020) <a href="https://www.pmda.go.jp/files/000234904.pdf">https://www.pmda.go.jp/files/000234904.pdf</a>	<ol style="list-style-type: none"><li>1. <b>Prioritize</b> examination, investigation and inspection of <b>Covid-19 medicines</b></li><li>2. <b>Promote IT means</b> for exchange of information, communication and documentation with applicants and manufacturers due to Covid-19 pandemic</li><li>3. Promote the IT measures for all medicines under evaluation</li></ol>
Handling on review processes for COVID-19 related medical devices such as ventilators, etc. (Administrative Notice dated April 13, 2020) <a href="https://www.pmda.go.jp/files/000234905.pdf">https://www.pmda.go.jp/files/000234905.pdf</a>	<ol style="list-style-type: none"><li>1. In addition to responding to consultations on ventilators, etc., <b>flexible response</b> to enable prompt regulatory procedures based on the actual access timing.</li><li>2. <b>Clarified points to consider</b> in regulatory procedures when supplying parts such as ventilators.</li><li>3. <b>Prioritize and promptly process partial changes</b> in approval items related to manufacturing registration and addition of manufacturing site.</li></ol>
Handling on regulatory reviews of disinfectant as newly designated quasi-drugs for the time being associated with COVID-19 (Administrative Notice dated April 24, 2020) <a href="https://www.pmda.go.jp/files/000234940.pdf">https://www.pmda.go.jp/files/000234940.pdf</a>	In order <b>to expedite the regulatory reviews on disinfectant</b> , the sponsor which request for the expedited regulatory process must inform MHLW when they apply for an approval. Also, they must respond to query from PMDA as soon as possible.
Handling on regulatory reviews of medical products against COVID-19 (PSEHB/PED Notification No. 0512-4, PSEHB/MDED Notification No.0512-1 May 12, 2020) Updated on June 17 <sup>th</sup> , 2021 <a href="https://www.pmda.go.jp/files/000235010.pdf">https://www.pmda.go.jp/files/000235010.pdf</a> <a href="https://www.pmda.go.jp/files/000241284.pdf">https://www.pmda.go.jp/files/000241284.pdf</a>	The notice describes <b>priority review and flexibility on review process and dossiers of clinical data for medical products against COVID-19</b> . MA applicants can submit, instead of the clinical trial data conducted in compliance with the related law, <b>the clinical study data funded by public sector such as MHLW</b> ,

# Speedy Approvals of COVID-19 Products

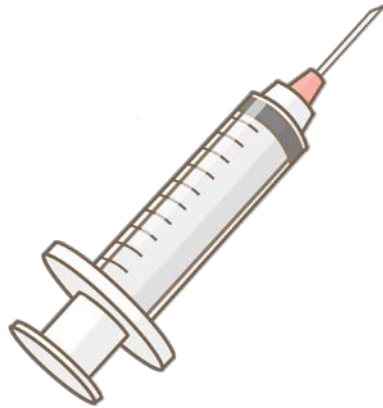
The number of approved products (As of August 29th, 2021)

Drugs



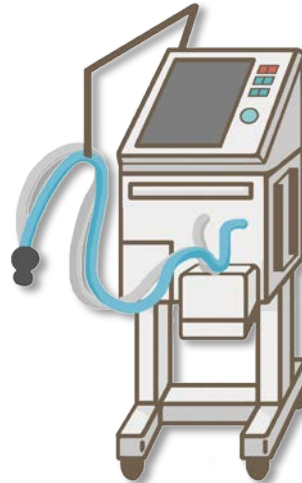
**3** product

Vaccines



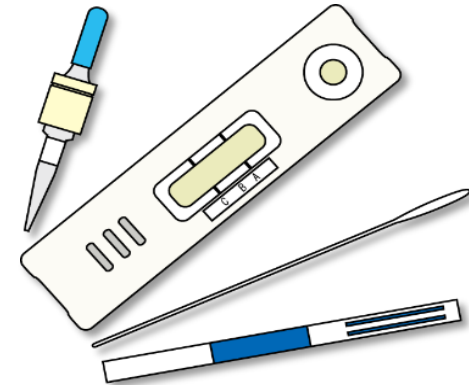
**3** product

Medical Devices



**23** products

IVDs



**72** products

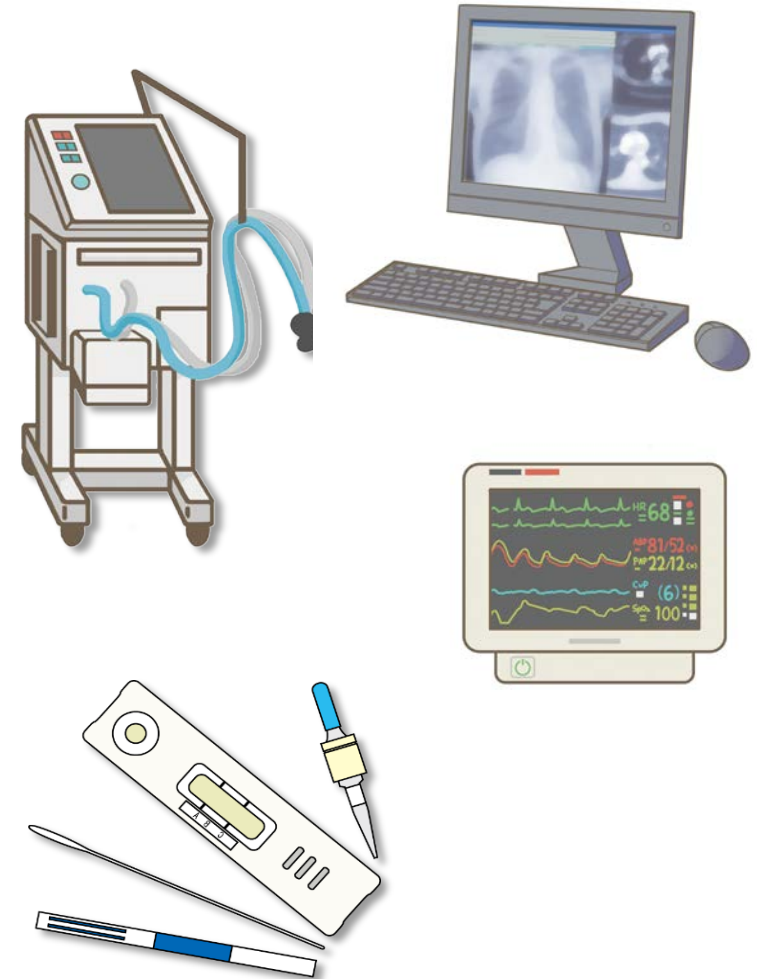
# Approved Medical Devices and IVDs for COVID-19

## Medical devices

- Ventilators
- Heart-lung bypass systems
- Software for diagnostic imaging system workstation
- Software for central monitor and program
- Syringes with needle, etc.

## IVDs

- SARS-CoV-2 nucleic acid kits
- SARS-CoV-2 antigen kits, etc.



# Safety Measures (ventilators and tracheal tubes)

For healthcare professionals

For patients and families of home medical care

Notification for Self-inspection

Medical Safety Information  
Pharmaceuticals and Medical Devices Agency  
https://www.pmda.go.jp/english/safety/info-services/safety-information/0001.html

Extra issue No. 2 April 2020

Medical Safety Information  
Pharmaceuticals and Medical Devices Agency  
https://www.pmda.go.jp/english/safety/info-services/safety-information/0001.html

Extra issue No. 1 April 2020

**Reminder Series No. 1  
(Precautions in Ventilator Use, etc.)**

In response to the spread of COVID-19, use of ventilators is increasingly required in clinical settings. Key points for safe handling and use of ventilators in past issues of PMDA Medical Information have been extracted and organized as a reminder.

(Case 1) A ventilator was unintentionally switched to battery operation. After an empty battery alarm was activated, ventilation stopped. It was found that the AC adapter was disconnected.

**1 Precautions for power source during use**

- When using a ventilator, always check indicators and/or messages to make sure that AC power is being supplied.

Continuing to use the unit operating on battery power unaware of alarm activation is extremely dangerous. The battery will eventually run out and ventilation will stop.

PMDA Alert for Proper Use of Medical Devices  
Pharmaceuticals and Medical Devices Agency

No.1 July 2020

**PMDA July 2020**

**For patients who use a ventilator, etc. at home and their families or other caregivers**

- A study conducted by the Ministry of Internal Affairs and Communications (MIC) revealed that radio waves (not including from Wi-Fi) emitted by mobile phones, etc. (including smartphones and tablet-type devices) can affect the operation of ventilators, etc. (including ventilators for adults and bilevel positive airway pressure units)
- In particular, patients and their families or other caregivers need to be careful when a ventilator, etc. is used at home.
- Please pay attention to the following to reduce the impact of radio waves. This is not aimed to limit the use of mobile phones, etc. by patients and their families or other caregivers.

Smartphones

Tablets

Mobile phones

Keep mobile phones, etc. at a greater distance from the medical device than recommended by the medical device manufacturer.

Ask medical staff for the proper distances.

Consult with medical staff if you find any unusual behavior of the ventilator, etc. during use.

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Pharmaceuticals and Medical Devices Agency

**Pmda**

This English version is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

PSEHB/MDED Notification No. 1221-1  
PSEHB/PSD Notification No. 1221-1  
December 21, 2020

To: Commissioners of Prefectural Health Departments (Bureaus)

Director of Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare  
(Official seal omitted)

Director of Pharmaceutical Safety Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare  
(Official seal omitted)

Self-inspection, etc. of Ventilators concerning Products Used in Combination with Them

Precautions for proper use of ventilators have been in place by the MSB Notification No. 248 Preventive Measures for Medical Accidents Associated with a Ventilator, which is a Life-supporting Device, dated March 27, 2001 as well as the package inserts and instruction manuals prepared by the marketing authorization holders (MAHs).

Recently, when a closed bronchial suction catheter was connected between the circuit of the ventilator and the cannula to aspirate sputum in intubated patients, there was a case in which an alarm to notify the disconnection was not triggered when a leak occurred due to the disconnection between the bronchial suction catheter and the cannula. In this case, the bronchial suction catheter, which was not designated by the MAH of the ventilator as a medical device to be used in combination with the ventilator, was used. There may be situations in which a medical device not designated for specific uses has to be used due to lack of alternatives in clinical practice.

If the alarm is not triggered, medical personnel may not be able to detect the disconnection of the breathing circuit at an early stage, which may cause a serious health hazard to the patient due to dyspnea, etc.

Commissioners of prefectural health departments or bureaus are requested to instruct the MAHs of ventilators under their jurisdiction to conduct a self-inspection, etc. of their products as shown below.

Of note, this notification has been informed to the professional organizations, the Pharmaceuticals and Medical Devices Agency (PMDA), and MAHs of ventilators.

1. Scope of this Notification  
Ventilators and bilevel positive airway pressure units (hereinafter referred to as

Pharmaceuticals and Medical Devices Agency  
3-3-3 Kasumigaoka, Chiyoda-ku, Tokyo 100-0013 Japan  
E-mail: safety\_info@pmda.go.jp

# Summary

- Situation of COVID-19 in Japan is still serious, but vaccination has been started and related pharmaceutical products are approved promptly with regulatory flexibility and agility.
- The most of our efforts are published in English on PMDA Website for transparency.
- Working with world to combat COVID-19 through ICMRA activities, etc.
- Post marketing safety measures of related products have been taken promptly and accurately such as PMDA Safety Information etc. for ventilators and tracheal tubes.

# Thank you!