

**Provisional Translation (as of January 2021)\***

PMDA/CPE Notification No. 1116002

November 16, 2020

To: (applicable stakeholders)

Director of Center for Product Evaluation  
Pharmaceuticals and Medical Devices Agency

Procedure for Remote Inspection as a part of compliance inspection on drugs and  
regenerative medical products

Pharmaceuticals and Medical Devices Agency (hereinafter referred to as “PMDA”) conducts the following compliance inspections (hereinafter collectively referred to as “compliance inspection”) under commission from the Minister of Health, Labour and Welfare.

- Document-based inspection and GCP on-site inspection for approval of drugs and regenerative medical products
- Document-based inspection and GPSP on-site inspection for interim evaluation, reexamination, and reevaluation of drugs
- Document-based inspection and GPSP on-site inspection for approval review after conditional and time-limited authorization, reexamination, and reevaluation of regenerative medical products

Procedures for compliance inspection are specified in the following notifications (hereinafter collectively referred to as “Notifications on procedure”).

- “Procedure for document-based inspection and GCP on-site inspection on application data/documents for approval of drugs as well as that for document-based inspection and GPSP on-site inspection on application data/documents for interim evaluation, reexamination, and reevaluation of drugs” (PMDA Notification No. 0831001 by Chief Executive of Pharmaceuticals and Medical Devices Agency dated August 31, 2020)
- “Procedure for document-based inspection and GCP on-site inspection on application data/documents for approval of regenerative medical products as well as that for document-based inspection and GPSP on-site inspection on application

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\* This English version of the Japanese Notification is provided for reference purposes only. In the event of any inconsistency between the Japanese original and the English translation, the former shall prevail.

data/documents for approval review after conditional and time-limited authorization, reexamination, and reevaluation of regenerative medical products” (PMDA Notification No. 0914001 by Chief Executive of Pharmaceuticals and Medical Devices Agency dated September 14, 2020)

As described in Notifications on procedure, PMDA’s inspectors may examine records/documents which form the basis of the inspected trials and studies from PMDA office remotely through the cloud system and video conferencing system (hereinafter referred to “Remote Inspection”). Details of the procedures for Remote Inspection are provided in the Annex.

This notification is effective on November 16, 2020. Please inform all of the members of your association about this notification.

## Procedure for Remote Inspection as a part of compliance inspection on drugs and regenerative medical products

Pharmaceuticals and Medical Devices Agency (hereinafter referred to as “PMDA”) conducts the following compliance inspections (hereinafter collectively referred to as “compliance inspection”) under commission from the Minister of Health, Labour and Welfare.

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As described in Notifications on procedure, PMDA’s inspectors (hereinafter referred to as “inspectors”) may examine records/documents which form the basis of the inspected trials and studies (hereinafter referred to as “documentation”) from PMDA office remotely through the cloud system or video conferencing system (hereinafter referred to as “Remote Inspection”). Details of the procedures for Remote Inspection are provided in the Annex.

## 1. Policy of Remote Inspection

A compliance inspection is usually conducted by examining documentation presented by an applicant, marketing authorization holder (MAH), sponsor, sponsor-investigator, medical institution, and/or their contract vendors (hereinafter referred to as “applicant, etc.”) and interviewing them about inspected trials and studies according to the date and place of the inspection previously notified by PMDA (hereinafter referred to as “usual compliance inspection”).

In a Remote Inspection, on the other hand, the applicant, etc. present documentation in advance, and then inspectors examine the documentation and interview the applicant, etc. in 2 steps of pre-inspection and main-inspection. In some cases, however, neither the prior presentation of documentation nor pre-inspection is conducted, but only the main-inspection is conducted by examining all documentation and interviewing the applicant, etc.

## 2. Procedure for Remote Inspection

### (1) Prior communication about Remote Inspection

- [1] PMDA shall inform the applicant, etc. of their intent to conduct compliance inspection as Remote Inspection by e-mail or telephone at the time of scheduling as specified in the Notifications on procedure, in principle. In addition, inspectors may have a pre-meeting about the Remote Inspection with the applicant, etc. where necessary.
- [2] PMDA shall confirm the schedule of pre-inspection and the method of presenting documentation with the applicant, etc. by e-mail preferably 1 to 2 months before the main-inspection.
- [3] The applicant, etc. shall reply either (a) or (b) as their method of presenting documentation to the inspectors.
  - (a) Uploading documentation through the cloud system
  - (b) Storing documentation in CD or DVD and sending them to PMDAIf it is difficult to present by neither the above (a) nor (b) for some reason, the applicant, etc. should consult the inspectors whether paper documentation is acceptable. If it is accepted, the applicant, etc. should submit these as specified in 3. (4) [2].
- [4] If the applicant, etc. present documentation by the above method (a), inspectors shall provide information necessary for setting the cloud system to the applicant, etc. by e-mail as soon as possible.
- [5] If the applicant, etc. present the documentation by the method in [3] (a), they shall issue an account to each inspector to access the cloud system and also provide a user manual of the cloud system specified in 4. (2) [3] as appropriate.

(2) Presentation of documentation

[1] In usual compliance inspection, inspectors inform the applicant, etc. of the sampling condition/scope (such as subject ID, clinical site, period, etc.) of documentation on the day of or one day before the inspection. In Remote Inspection, inspectors shall inform the applicant, etc. of them preferably by 10:00 am, 13 business days before the main-inspection.

If any concern is found at the prior check, etc., inspectors may change the sampling condition/scope and request the applicant, etc. to submit additional documentation where necessary.

[2] The applicant, etc. shall present documentation to the inspectors by a method in either (a) or (b) in 2. (1) [3] by 10 business days before the main-inspection. If it is inevitably difficult to submit these by the deadline, the applicant, etc. shall consult the inspectors.

(3) Pre-inspection

[1] Usually, inspectors shall conduct a pre-inspection within 10 business days. During this period, inspectors shall examine the documentation presented by the applicant, etc. and identify concerns.

If any concern is found, inspectors shall send inquiries to the applicant, etc. by e-mail or other means as appropriate.

[2] If requested by inspectors, the applicant, etc. shall present the appropriate documentation and respond to inquiries promptly.

[3] Inspectors shall inform the applicant, etc. of concerns to be examined at the main-inspection by e-mail by noon, 1 business day before the main-inspection (for inspection on a clinical study not involving Japan, 2 business days before the main-inspection). This, however, shall not apply to cases where additional concerns are found after the above communication.

(4) Main-inspection

[1] Inspectors shall examine documentation not presented at the pre-inspection through the video conferencing system and interview the applicant, etc. about the concerns identified during the pre-inspection.

[2] If requested by inspectors, the applicant, etc. shall present the appropriate documentation and respond to inquiries promptly.

(5) Post-inspection

The applicant, etc. shall take actions on the unresolved concerns at the main-inspection according to direction by inspectors as soon as possible. In such a case, the applicant, etc. can explain the concerns through the video conferencing system.

### 3. Points to be considered for preparation of documentation

#### (1) General matters

The applicant, etc. shall present not all documentation the applicant, etc. have but those to be presented to the inspectors at a usual compliance inspection. The applicant, etc. shall present documentation with and without sampling condition/scope specified. If the applicant, etc. have limited experience with compliance inspections or Remote Inspection, they should consult inspectors about documentation to be presented in advance.

#### (2) Points to be considered for presentation of documentation (electronic records)

[1] The applicant, etc. should present all the required documentation at a pre-inspection in principle. If the applicant, etc. want to present documentation through the video conferencing system at main-inspection, they should communicate this matter with the inspectors and do so. In addition, if there are documentation that have been submitted as documents of Annex 2 or 6 specified in the Notifications on procedure, the applicant, etc. should communicate this matter with the inspectors. If these have to be additionally presented as documentation, the inspectors shall direct the applicant, etc. to do so.

[2] The applicant, etc. should show the folder structure, etc. in the cloud system so that the inspectors can readily access the target documentation. In addition, the applicant, etc. should present supplementary documents necessary for the inspectors to access the documentation.

#### (3) Points to be considered for conversion of documentation from paper into electronic records

[1] The applicant, etc. shall establish a procedure for scanning paper documentation and follow it. The applicant, etc. should confirm the following points about the electronic documentation obtained by scanning.

- They are clear with adequate contrast.
- They are consistent with the paper documentation in terms of the number of pages.
- Both sides of each paper have been scanned if applicable.

[2] Inspectors may request the applicant, etc. to present original paper documentation where necessary.

[3] The applicant, etc. should consult inspectors how to handle documentation for which scanning is difficult.

#### (4) Points to be considered for mail delivery of documentation

[1] If the documentation is submitted in a form of CD or DVD, the applicant, etc.

should send documentation in CD or DVD to the Office of Non-clinical and Clinical Compliance, PMDA by 10 business days before the main-inspection. PMDA shall destroy the submitted CD or DVD upon notification of the inspection result in principle, but not return them.

- [2] If the paper documentation is submitted, the applicant, etc. should send paper documentation to the Office of Non-clinical and Clinical Compliance, PMDA by mail if applicable. In addition, the following points should be noted as well.
- The due date of submission shall be determined through communication with the inspectors irrespective of the pre-inspection period.
  - The number of days (desirably) from receipt of the documentation to return will be 5 business days. If there is any issue, the applicant, etc. should consult the inspectors.
  - If any concern is found, the inspectors shall send inquiries to the applicant, etc. by e-mail, or telephone as appropriate. If the applicant, etc. cannot respond to the inquiries without the documentation, they should respond after the documentation are returned.
  - The applicant, etc. should bear the expenses for mail delivery (submission and return of documentation).

#### 4. Points to be considered for the cloud system and video conferencing system

##### (1) Common points

- [1] The applicant, etc. should conclude a contract with a service provider of the system and bear the expenses for use of the system (except for the expenses for PMDA's access to the system).
- [2] The applicant, etc. should ensure security of the system. If any unauthorized access occurs because of a security vulnerability and communication interception by fault of the service provider, the applicant, etc. should take appropriate actions including stopping use of the system. If there is any point to be considered in PMDA to ensure the security, the applicant, etc. should inform the inspectors in advance.
- [3] The applicant, etc. should take appropriate preventive actions for sound leakage and unauthorized access by communication interception on devices and lines used for connections.
- [4] The applicant, etc. should perform enough connectivity test of the system to be used for the first time. For the system which has been used multiple times, the connectivity test may be omitted.
- [5] If any critical security problem occurs in the system, the applicant, etc. should

promptly communicate this incident with PMDA. The applicant, etc. and PMDA should decide to suspend or postpone the Remote Inspection. The timing of re-start and the method should be determined through consultation.

(2) Points to be considered for the cloud system

[1] The applicant, etc. should issue to each inspector an account to connect and operate the cloud system. In principle, Read-only access authority is sufficient. If the applicant, etc. issue any other authority for some reason, it should be accepted by the inspectors in advance, and the applicant, etc. should communicate the points to be considered. In addition, if any change or addition of an inspector is made, an additional account should be issued as required. The same account should not be issued to more than one inspector.

[2] The applicant, etc. should retain the documentation in the cloud system and accounts of the inspectors until notification of the inspection result.

[3] When the applicant, etc. use the system for Remote Inspection for the first time, they should provide the inspectors with a user manual of the Cloud system. The user manual includes the following contents and is available for any kind of compliance inspection.

- Operation method
- Account issuance method
- No-operation timeout time
- Log-in method/authentication method (use or non-use of one-time password)
- Other requirements (recommended browser, etc.)

If the user manual is updated, the applicant, etc. should provide the revised version at the next Remote Inspection.

[4] The applicant, etc. should consider the following points as well.

- The inspectors without their account will not access or operate the cloud system but may look at the screen that an inspector with his or her account operates.
- The inspectors access the cloud system through PMDA's network system. If a connection through PMDA's network system is not available, the applicant, etc. should change the presentation method of documentation (electronic records).
- The applicant, etc. should confirm the file formats accessible through the cloud system (for example, PDF, Word, Excel) before upload of documentation.
- Any system which takes a long time to access may not be able to be used



for Remote Inspection in the future.

(3) Points to be considered for the video conferencing system

- [1] The applicant, etc. should make appropriate arrangements as sending the inspectors a meeting invitation for the pre-meeting and main-inspection.
- [2] The applicant, etc. should inform the inspectors of the name and department of participants in the pre-meeting and main-inspection in advance by e-mail. At the pre-meeting and main-inspection, the applicant, etc. should verify identities of the participants. If an additional person participates in the pre-meeting and main-inspection, applicant, etc. should inform the inspectors about his or her name and department in advance.
- [3] The applicant, etc. should make communication lines (usually 1 or 2 lines) available for the main-inspection as required. At the timing specified in 2. (3) [3], the applicant, etc. should ask the inspectors about the number of communication lines required.
- [4] If the applicant, etc. record video or audio of the pre-meeting and main-inspection to make internal records, they should obtain permission in advance. The recorded video and audio data should be used only internally for compliance inspection and must not be leaked out through external use (presentation at a conference, etc.) or the Internet. In addition, upon notification of the inspection result, the applicant, etc. should delete such data immediately. If inspectors record video or audio in PMDA, they shall do the same action.
- [5] The applicant, etc. should consider the following points as well.
  - Any video camera function should be turned off unless required. Any microphone should be muted unless required.
  - If the participants have an internal meeting, the applicant, etc. should ask the inspectors in advance.
  - If unknown participant is found during the pre-meeting and main-inspection, the applicant, etc. should force unknown participant out, if applicable.
  - If the inspection takes a long time or involves an interpreter, the break time should be arranged by mutual agreement.

5. Others

- [1] PMDA shall post information necessary for efficient and effective implementation of Remote Inspection at the PMDA's website and modify the content where necessary.

- [2] PMDA may change a period of pre-inspection, etc. taking account of circumstances of the product.
- [3] PMDA shall take a survey, etc. of Remote Inspection and, based on the results, revise this notification where necessary.
- [4] If conduct of a compliance inspection as Remote Inspection becomes necessary instead of scheduled usual compliance inspection, PMDA shall inform the applicant, etc. of this matter and consult them about the inspection schedule.