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Attachment

Questions and Answers (Qs and As) regarding "Provision of Information on Precautions for Drugs, etc."

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(Printing of Codes, etc. on Containers or Wrappings)

Q1. What is the specific unit of product requiring the printing of the codes specified in Article 52, Paragraph 1; Article 63-2, Paragraph 1; and Article 65-3, Paragraph 1 of the Act (hereinafter referred to as "code")?

A1. Containers or wrappings (hereinafter referred to as "containers, etc.") requiring the printing of codes necessary to obtain information on precautions, etc. are the sales packaging unit (minimum packaging unit usually sold from wholesalers, etc. to medical institutions, pharmacies, etc. [hereinafter referred to as "medical institutions, etc."]).

Q2. It is stated that for a container, etc. of a product that has too small an area on which a code is printed, it is unnecessary to print a code on the container as long as a code is indicated on a "document to be attached" to the product. What is specifically a "document to be attached"?

A2. It refers to paper on which a code is printed. A code shall be printed on paper in a size and clarity that can be read properly by healthcare professionals. In addition, it is desirable to explain that a code is used to electronically obtain information on precautions, etc. provided by a MAH（herein after referred to as "MAH"）.

Q3. What is the "document containing information on precautions, etc." specified in "I. Information on precautions, etc." of the Director's Notification?

A3. It refers to a printout of a document containing information on precautions, etc. (electronic package insert) that is required to be disclosed on the website of the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as the PMDA"). In addition to information on precautions, etc., if there is any information necessary to promote the proper use of drugs, etc., such

information shall be added to the document in accordance with the instructions.

In addition to the document containing information on precautions, etc., materials to provide information, such as an instruction manual containing information on precautions, etc., may be prepared and issued separately, as done before.

Q4. What are assumed to be “medical gases or other similar drugs for which it is not appropriate to print a code on their containers, etc. because of their usage”?

A4. Medical gases that are installed in places where it is difficult to approach are assumed. More specifically, liquid oxygen and liquid nitrogen delivered to ultra-low temperature storage tanks are assumed.

Q5. What are assumed to be medical devices that cannot be packed in containers, etc. due to their structure and properties?

A5. Large medical devices, such as installation-controlled medical devices specified in Article 114-55, Paragraph 1 of the Enforcement Regulation of the Act, are assumed.

Q6. It is likely that codes cannot be utilized at medical institutions, etc. if a medical device is supplied with no “outer box” because it cannot be packaged in a container, etc. due to its structure or properties or if the outer box of a medical device is disposed of after delivery. In such cases, is it acceptable to provide a code by using other easier methods for a medical institution, instead of printing it on a container, etc.?

A6. For a product supplied with no container, etc., a document containing a code shall be issued separately as an exceptional case stipulated in Article 224, Paragraph 4 of the Enforcement Regulation of the Act. For a product whose container, etc. may be disposed of by healthcare professionals, it is acceptable to print a code on the container, etc. and then provide a document containing the code separately. A document containing a code does not need to be any dedicated document to provide the code, and the code may be added to any existing document such as an instruction manual.

Q7. For a drug, etc. to be stored at ultra-low temperatures whose code printed on its container, etc. cannot be read (or is difficult to read) because

it is stored in a storage/transportation container until immediately before administration or because it is frosted, is it acceptable to separately provide a document containing the code to access the information on precautions, etc. disclosed on the PMDA's website on a voluntary basis?

A7. It is acceptable to do so.

Q8. Is it necessary to change the term "package insert" as a document, which is included in phrases, such as "For details, see the package insert," indicated on the container, various materials, etc. of a product, when a document containing information on precautions, etc. is no longer attached to the product?

A8. Even when a document containing information on precautions, etc. is no longer attached to a product, no responses, such as changing the term, are necessary for a product already released to the market. When a package insert is no longer included in a product, it is desirable to change the term "package insert" indicated on a container, various materials, etc. to "electronic package insert." However, if it takes time for the change, it is desirable to take an appropriate action while communicating with healthcare professionals to avoid confusion among them.

Q9. In the sales packaging unit, is it necessary to include fixed phrases to urge users to check the latest information on precautions, etc. via a code, for example, "Be sure to check the latest information on precautions, etc. prior to use," or to place an indication such as "To check the information on precautions, etc." near the code?

A9. It is acceptable to include such phrases for such purposes, although it is not required to include fixed phrases. In particular, when a similar barcode for manufacturing control, etc. is already placed on a container, etc., the code shall be indicated clearly to prevent healthcare professionals from being confused.

Q10. If a QR code for manufacturing control is printed on the main body of a product, is it acceptable to continue using the QR code as long as this fact is indicated on the container, etc. or the instruction manual?

A10. It is acceptable to use a QR code, etc. for manufacturing control in addition to a code as long as an appropriate annotation about the meaning of the QR code, etc. is placed to prevent healthcare professionals from being confused.

Q11. Is it acceptable to continuously enclose paper-based information on precautions, etc. (a printout of an electronic package insert) in a product even after the termination of the transitional measures?

A11. Except for the products exceptionally specified in the Enforcement Regulation of the Act, enclosure of conventional paper-based package inserts shall be avoided for the purpose of promptly providing safety information, etc. As shown in II, 3, (3) of the Director's Notification, however, for a medical device, other than medical devices provided primary for the ordinary use of general consumers, if it is assumed that consumers will purchase such a medical device directly instead of through a medical institution, a document containing information on precautions, etc. shall be attached to the medical device, in principle, in addition to the printing of a code.

Q12. Is it necessary to print a code on a container, etc. of a product (product in stock) manufactured and marketed before the termination of the transitional measures?

A12. It is unnecessary to print a code on a container, etc. of a product manufactured and marketed before the termination of the transitional measures.

Q13. Is it acceptable to print a QR code, etc. to access the company's website on a container, etc. in addition to a code?

A13. It is acceptable to do so as long as an instruction that information on precautions, etc. must be checked via the code or an appropriate explanation about the purpose of using the QR code, etc. is provided to prevent healthcare professionals from being confused.

(Disclosure of Information on Precautions, etc.)

Q14. In the case of combination drugs, etc., a package insert and an instruction manual may be included in the respective individual packaging boxes. In and after August 2021, is it acceptable to include information on precautions, etc. in an instruction manual, post the instruction manual on the PMDA's website, and then make it accessible via a code?

A14. Information that is accessible via a code shall be only information on precautions, etc. in the format disclosed on the PMDA's website. (Any instruction manual in the arbitrary format of each company is not acceptable.)

Q15-1. Regarding III, 4, (1) of the Director's Notification, in cases where a drug requires a change to its information on precautions, etc. from the viewpoint of proper use in response to any change in its composition, product description, shelf life, etc. and its product before the change is still available in the medical settings, how should such cases be handled if it is necessary to continuously disclose the information on precautions, etc. before the change?

A15-1. It is possible to post the electronic package inserts before and after the change on the PMDA's website. Refer to the PMDA's site for companies for more specific information.

Q15-2. Regarding III, 4, (1) of the Director's Notification, some medical devices, etc. that are not the latest version may be still available in the medical settings. How should such cases be handled as it is necessary to continuously disclose the information on precautions, etc. before the change even after a change has been made to information on precautions, etc.?

A15-2. The function to post electronic package inserts of different versions or electronic package inserts of previous versions on the PMDA's website shall be used. Refer to the PMDA's sites for companies for more specific information.

(System to Provide Information on Precautions, etc.)

Q16. Is it acceptable to provide information on precautions, etc. to a healthcare professional who first purchases a product before delivery of the product?

A16. If there is a common understanding with the healthcare professional, it is acceptable to provide the information on precautions, etc. before delivery of the product.

Q17. What kind of documents containing information on precautions, etc. to be provided to first purchasers, etc. are assumed specifically?

A17. Printouts, etc. of electronic package inserts required to be disclosed on the PMDA's website are assumed.

Q18. Is it acceptable to provide an instruction manual, etc. for a medical device, etc. as a means of providing paper-based information on precautions, etc. to first purchasers?

A18. It is acceptable to do so. However, the latest information on precautions, etc. must be included in the instruction manual, etc. In addition, the information on precautions, etc. to be included in the instruction manual, etc. shall quote verbatim the information in the electronic package insert to prevent healthcare professionals from being confused.

Q19. Regarding the provision of information on precautions, etc. to first purchasers, etc., is it acceptable to omit the provision of a printout of an electronic package insert if there is a common understanding with a healthcare professional?

A19. It is acceptable to do so if there is a common understanding with the healthcare professional. When any change is made to information on precautions, etc., however, it is necessary to establish a system to provide necessary information to the healthcare professional for whom the provision of a printout of an electronic package insert was considered unnecessary at the time of the first purchase.

Q20. A medical institution to which any product has been delivered before enforcement of the Act does not correspond to a "first purchaser, etc." even if a product is delivered to the medical institution for the first time after enforcement of the Act. Therefore, is it acceptable to consider it unnecessary to provide a printout of an electronic package insert?

A20. It is acceptable to consider it unnecessary to provide such information to a medical institution which does not correspond to a "first purchaser, etc.," regardless of the timing of enforcement of the Act. It is, however, necessary to provide such information for a healthcare professional at a medical institution, if it is likely that a healthcare professional is not informed of the latest information on precautions, etc. in cases such as a substantially long period having passed since the latest delivery.

Q21. For a series of multiple products, etc. using an electronic package insert, when information on precautions, etc. for one of the products has already been provided to a healthcare professional, and when another product using the same electronic package insert is delivered to the healthcare professional, is it unnecessary to provide the information on precautions, etc. again?

A21. It is acceptable to do so if there is a common understanding with the healthcare professional, but the information on precautions, etc. shall be provided upon request.

Q22. Is it acceptable to post information on precautions, etc. for a product on the company's website, thereby providing users with information by accessing the website when the product is first purchased by healthcare professionals and when a change is made to the information on precautions, etc.?

A22. It is acceptable if there is a common understanding with the healthcare professional. It is, however, necessary to disclose the latest information on precautions, etc. on the PMDA's website and make the information on precautions, etc. on the website accessible via a code.

Q23. How should any change in information on precautions, etc. be provided? Is it acceptable to use mail or fax as a "method of providing a document containing information on precautions, etc."?

A23. Possible methods include, for example, provision by a person who has an opportunity to be in contact with healthcare professionals on a daily basis such as an MR (medical representative), provision of a document containing information on precautions, etc. (a printout of an electronic package insert), sending electronic data to healthcare professionals, sending by fax, etc. It is desirable to use a method of provision that allows healthcare professionals to easily check any change in information on precautions, etc. for the convenience of each healthcare professional.

Q24. When a change has been made to information on precautions, etc., is it possible to package an announcement document containing information about the change with a product as a notification of change to healthcare professionals?

A24. It is acceptable to simply inform of the change in the information on precautions, etc.

Q25. Is it acceptable to think that any description modification without substantial change in the information does not correspond to “a change in information on precautions, etc.”?

A25. It is acceptable. In such cases, however, the information on precautions, etc. shall be provided upon request.

Q26. Is it acceptable for MAHs to appropriately determine the necessity of information provision to healthcare professionals and the range of information to be provided when a change has been made to information on precautions, etc., according to the importance in safety management, as was before?

A26. It is acceptable to do so. It is, however, necessary to take appropriate measures so that necessary up-to-date information is provided.

Q27. Is it acceptable to outsource the provision of the latest information on precautions, etc. for drugs, etc. for healthcare professionals to a licensed distributor or wholesale distributor?

A27. It is acceptable to do so as long as a system by which information can be reliably provided has been established with an outsourcing contract, etc. between an MAH and a licensed distributor or wholesale distributor. Even in such cases, however, it should be noted that the MAH, who is responsible for providing information on precautions, etc., needs to establish a system to manage the outsourcer appropriately.

Q28. Is the system necessary to provide information on precautions, etc. positioned as part of the system based on the GVP Ministerial Ordinance (for the implementation of safety assurance measures)?

A28. The system necessary to provide information on precautions, etc. is required based on Article 68-2-2 of the Act and is not positioned as part of the system based on the GVP Ministerial Ordinance. However, when changing information on precautions, etc., etc. and providing the information to healthcare professionals as a part of safety assurance measures, it is necessary to implement it in accordance with the procedures prepared prescribed pursuant to the GVP Ministerial Ordinance. Therefore, if the

requirements for the system necessary for providing information on precautions, etc. shown in the Enforcement Regulation of the Act and the Director's Notification are met, it is acceptable to establish a system necessary to provide information on precautions, etc. as part of the system prescribed pursuant to the current GVP Ministerial Ordinance.

Q29. Is there any requirement that the marketing supervisor-general, etc. must serve as the person responsible for establishing a system and providing such information under the system and as the approver of the operating procedures for providing information on precautions, etc.?

A29. There are no specific requirements for the person responsible for these duties. It is acceptable to appoint an appropriate person and grant necessary authority to the person on the responsibility of each company.

Q30. What is the specific intention of the statement in IV, 3, (2) of the Director's Notification, "procedures to properly and smoothly conduct the operations related to the provision of information on precautions, etc."?

A30. Any procedure necessary to properly and smoothly conduct the operations as the MAH shall be established, in addition to the "procedure for providing information on precautions, etc." and the "procedure for mutual cooperation when information on precautions, etc. is provided in cooperation with a licensed distributor or a wholesale distributor." For example, possible procedures may include a procedure for handling any improper description of information on precautions, etc., a procedure for handling complaints from healthcare professionals, etc. It is, however, acceptable to consider such procedures depending on the operations of the MAH.

Q31. Is it necessary to establish a system to provide information for generic drugs and long-listed drugs as well?

A31. It is necessary to establish a system to provide necessary information for all drugs, etc. including generic drugs and long-term listed drugs so that healthcare professionals can obtain information on precautions, etc. appropriately at the time they need it. If it could not be provided before prescription or dispensing due to unavoidable circumstances, necessary information should be provided promptly to healthcare professionals.

(Questions and Answers Specific to Medical Devices)

Q32. For a product for which the approval cancellation procedure has not been conducted but which is not marketed by its MAH, is it necessary to disclose its electronic package insert on the PMDA's website?

A32. Products requiring the disclosure of their electronic package inserts on the PMDA's website are marketed products. Therefore, for any product for which the procedure for cancellation of marketing approval, etc. (hereinafter referred to as "approval cancellation procedure") has not been conducted, it is necessary to disclose its electronic package insert on the PMDA's website.

For medical devices, however, any product which will not be marketed by the MAH on and after the date of enforcement of the Act (August 1, 2021) does not require the disclosure of its electronic package insert on the PMDA's website even if the approval cancellation procedure has not been conducted as of the date of enforcement of the Act.

For any product for which the approval cancellation procedure has been conducted, it is desirable to continue the disclosure of its electronic package insert on the PMDA's website, if it is currently used by healthcare professionals or patients.

For any product which will not be marketed in the future, it is desirable to take the approval cancellation procedure, taking into account the actual use status in the market, except when only the components are marketed that are specified in the Questions and Answers (Q & A) on Approval Applications, etc. of Medical Devices and in Vitro Diagnostics (Notification No. 1125-22 of, Counselor, Minister's secretariat, Ministry of Health, Labour and Welfare dated of November 25, 2014).

In addition, refer to Q43 and A43 for used medical devices.

Q33. When changes are made to the Instructions for Package Inserts in the future, is it necessary to revise the electronic package insert of a product, for which the approval cancellation procedure has been conducted, posted on the PMDA's website in order to respond to the new instructions?

A33. If it can be judged that information has been appropriately provided to healthcare professionals on the responsibility of each company and that it is possible to provide sufficient information by electronic package inserts prepared according to the Instructions for Package Inserts before a change,

for example, it is not necessary to revise all the electronic package inserts posted on the PMDA's website according to the new instructions.

Q34. In the cases that medical devices such as implantable medical devices or active medical devices for which the approval cancellation procedure has been conducted or for which the approval cancellation procedure has not been conducted but which will not be marketed are being used continuously by healthcare professionals or patients, is it acceptable for their MAHs to decide the period for posting the information on precautions, etc. on the PMDA's website at their discretion?

A34. It is acceptable to do so as long as the MAH can show a high probability that the use of the medical device has been terminated. Even for a product for which the approval cancellation procedure has been conducted or for which the approval cancellation procedure has not been conducted but which will not be marketed, the MAH should be ready to provide the printout of the latest information on precautions, etc. if requested by healthcare professionals while the information on precautions, etc. is posted on the PMDA's website.

Q35. In the cases that the approval cancellation procedure of a medical device has been conducted or the approval cancellation procedure has not been conducted but the medical device will not be marketed, and information on precautions, etc. of the medical device is continuously posted on the PMDA's website, is it acceptable to revise the information and post the latest information on precautions, etc., if it is judged necessary to revise the information on precautions, etc.?

A35. Even for a product for which the approval cancellation procedure has been conducted or for which the approval cancellation procedure has not been conducted but which will not be marketed, if it is judged necessary to revise the safety information including the information on precautions, etc. in its electronic package insert, the MAH should revise the information and be ready to provide the printout of the latest information on precautions, etc.

Q36. Based on Article 68-2 of the Act, is the timing of disclosure of information on precautions, etc. for Class I to III medical devices similar to that of disclosure for product items requiring package insert submission (Class IV medical devices)?

A36. Similar to product items requiring package insert submission, the MAH shall respond as described below:

(1) For a product item which is newly marketed after obtaining approval, etc., its information on precautions, etc. shall be disclosed before the start of marketing. However, if the provision of the information on precautions, etc. to medical institutions, etc. is started before the start of marketing, it is desirable to disclose the information on precautions, etc. before that.

(2) When changing the information on precautions, etc., the MAH shall disclose the information on precautions, etc. after the change by the day on which the MAH starts to provide the information on precautions, etc. after the change or the day on which the marketing of the product for which the information on precautions, etc. after the change is included in its package insert, etc., whichever comes first.

Q37. For a set of medical devices in different combinations in each case that is lent to a medical institution by a distributor/leaser, obligatory printing of a code may be inefficient on the contrary. In such a case, is it acceptable to provide a paper-based package insert, as was before, instead of printing a code?

A37. It is necessary to print a code on the container, etc.

Q38. For a single component common to multiple medical devices that links to various information on precautions, etc., multiple different package inserts are attached to one package (container). In such a case, how should codes be indicated?

A38. Multiple codes shall be indicated. In addition, the codes shall be indicated clearly by showing which code corresponds to which product to prevent healthcare professionals from being confused.

Q39. For a medical device that can display the latest information on precautions, etc. disclosed on the PMDA's website by connecting to the network through its built-in operating system or via online help, etc., it is possible to always access the latest information on precautions without indicating a code. For such a product, is it acceptable to omit the indication of a code on its container, etc.?

A39. It is necessary to print a code on the container, etc.

Q40. For a medical device set such as an orthopedic device set that is lent to a medical institution upon its request, is it acceptable to indicate a code on documents to be delivered with the products, such as a list of rental orthopedic devices and a delivery notice?

A40. It is acceptable to do so.

Q41. For combination medical devices, is it acceptable to provide a code based on the approval of the combination medical devices, as was before?

A41. It is acceptable to do so.

Q42. Regarding the provision of information on precautions for a medical device program provided via an electronic communication line, it is stated, "...provides information on precautions, etc. before providing the medical device program" or "...method that allows a user of the medical device program to see it easily." What are the specific options actually?

A42. For a medical device program, information shall be provided using an appropriate method selected from among the following options, for examples.

(1) To display the URL disclosing the electronic package insert on the screen to be downloaded inside or outside the program. Refer to the PMDA's site for companies for the URL to be posted.

(2) To place the PDF version of the latest electronic package insert on the same screen to download the program.

(3) To make the latest electronic package insert in the program.

Q43. If a distributor resells a medical device manufactured and distributed between August 1, 2021 and July 31, 2023, the end of the transitional measure period, as a used medical device on and after August 1, 2023, how should the distributor deal with the used medical device without a code?

A43. The distributor shall obtain information on precautions, etc. corresponding to the used medical device from the MAH and provide it to the healthcare professional, or shall provide a document containing the code to the healthcare professional separately.

(Questions and Answers Specific to In Vitro Diagnostics)

Q44. Is it necessary to disclose information on precautions, etc. on the PMDA's website also for common reagents distributed as components of in vitro diagnostics?

A44. If information on precautions, etc. for individual products including common reagents is disclosed on the PMDA's website, it is not necessary to separately disclose information on precautions, etc. for common reagents distributed as components on the PMDA's website. For any common reagent alone, in the case that approval or accreditation has been obtained, or notification has been submitted separately, it should be noted that disclosure of information on precautions, etc. for the common reagent on the PMDA's website is necessary.

Q45. Regarding the method of providing information on precautions, etc. when a healthcare professional first purchases a reagent dedicated to a diagnostic device (in vitro diagnostic) or when a change is made to information on precautions, etc., if a diagnostic device is capable of reading a barcode containing the lot information about the dedicated reagent, displaying the information on precautions, etc. for the reagent on the device monitor via a testing system, etc., and showing/printing it, is it acceptable to provide information using the function?

A45. It is acceptable to do so as long as there is a common understanding with the healthcare professional and the latest information on precautions, etc. is reliably provided to the healthcare professional before the use of the in vitro diagnostic.

Q46. For a product for which the approval cancellation procedure has not been conducted but which is not marketed by its MAH, is it necessary to disclose its electronic package insert on the PMDA's website?

A46. Products requiring the disclosure of their electronic package inserts on the PMDA's website are marketed products. Therefore, for any product for which the procedure for cancellation of marketing approval, etc. has not been conducted, it is necessary to disclose its electronic package insert on the PMDA's website.

For in vitro diagnostics, however, any product which will not be marketed by the MAH on and after the date of enforcement of the Act (August 1, 2021) does not require the disclosure of its electronic package insert on the PMDA's

website even if the approval cancellation procedure has not been conducted as of the date of enforcement of the Act.

For any product which will not be marketed in the future, it is desirable to conduct the approval cancellation procedure, taking into account the actual use status in the market.