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Newsletter (August 2020) | LAW

PUBLICATION OF AMENDED PHARMACEUTICALS AND MEDICAL DEVICES ACT – DRAFT GUIDELINES REGARDING LEGAL COMPLIANCE BY MAH AND MANUFACTURERS

I. Introduction

On December 4, 2019, the "Act on Securing the Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (the "**Act**")" was amended ("**Amended Act**") to introduce restrictions on a company's legal compliance system relating to pharmaceutical affairs (the "**Pharmaceutical Compliance System**") conducted by the license holders ("**License Holders**") who market, manufacture or sell pharmaceuticals, medical devices, regenerative medicine products, quasi-pharmaceutical products and cosmetics (collectively, the "**Healthcare Products**").[1] On August 11, 2020, draft guidelines ("**Draft Guidelines**") to the Amended Act were published and focused on restrictions regarding the legal compliance by marketing approval holders and licensed manufacturers of the Healthcare Products (collectively, the "**MAH/Manufacturers**"). The Draft Guidelines were open for a public comment period which ended on September 9, 2020.[2]

The Draft Guidelines do not cover the restrictions on the Pharmaceutical Compliance System for all of the License Holders. Specifically, the Draft Guidelines cover the restrictions only for the MAH/Manufacturers and do not cover the restrictions for: (i) pharmacies; (ii) store retailers, non-store retailers, and wholesale sellers of the Healthcare Products; (iii) blood drawing business operators; and (iv) sellers, lease operators and repairers of specially-controlled medical devices (although (i) to (iv) are also subject to the Amended Act).

Since the Draft Guidelines will be an important road map for the MAH/Manufacturers to establish their Pharmaceutical Compliance System in compliance with the Amended Act, we set out below the key items of the Draft Guidelines in the form of a Q&A.

[1] For the outline of the Amended Act, please refer to our newsletter entitled "Draft Amendment to Pharmaceuticals and Medical Devices Law 2019 and Its Influence to Companies" (https://se1910.com/ja/newsletters-ja/newsletter-november-2019-law-practice-2/)

[2] https://search.e-gov.go.jp/servlet/Public?CLASSNAME=PCMMSTDETAIL&id=495200176&Mode=0

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II. Contents of Draft Guidelines

Q1 When are the Guidelines expected to be formulated?

A1 The Guidelines are currently expected to be formulated in January 2021.[3] Since the restrictions on the Pharmaceutical Compliance System under the Amended Act will be enforced on August 1, 2021, it is anticipated that the Guidelines will apply at the same time.

Q2 Should all MAH/Manufacturers make the same effort to establish the Pharmaceutical Compliance System?

A2 The Draft Guidelines expressly state that the concrete measures to establish the Pharmaceutical Compliance System are expected to be taken depending upon the category and scale of operations of each MAH/Manufacturer. Therefore, each MAH/Manufacturer should determine their Pharmaceutical Compliance System based on the category and scale of its operations while referring to the Draft Guidelines.

Q3 What are the "pharmaceutical affairs-related laws and regulations" that MAH/Manufacturers should comply with?

A3 The Draft Guidelines provide that the following laws and regulations are considered the "pharmaceutical affairs-related laws and regulations" ("**Laws and Regulations**") that the MAH/Manufacturers should comply with:

Pharmaceutical Affairs-related Laws and Regulations
● **Pharmaceuticals and Medical Devices Law**
● **Narcotics and Psychotropics Control Act**
● **Poisonous and Deleterious Substances Control Act**
● **Cannabis Control Act**
● **Stimulants Control Act**
● **Opium Act**
● **Act on Securing of Stable Supply of Safe Blood Derivatives**
● **Pharmacists Act**
● **Act on Control of Household Products Containing Harmful Substances**
● **Act on the Regulation of Manufacture and Evaluation of Chemical Substances**
● **Act on Special Exceptions of Narcotics and Psychotropics Control Act to Prevent Act to Facilitate Fraudulent Act regarding Restricted Drugs under International Cooperation**
● **Pharmaceuticals and Medical Devices Agency Act**
● **Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms**
● **Act on Securing of Safety of Regenerative Medicines**
● **Clinical Research Act**

Q4 What kind of penalties will be imposed for the failure of establishing the Pharmaceutical Compliance System?

A4 Although the Amended Act does not provide any penalties against the violation of the provisions regarding the Pharmaceutical Compliance System, the Draft Guidelines provide

[3] https://search.e-gov.go.jp/servlet/PcmFileDownload?seqNo=0000205324

that "if the measures for establishment of the Pharmaceutical Compliance System are considered to be insufficient, an order for improvement (under Article 72-2-2 of the Amended Act) shall apply". If such order applies, the MAH/Manufacturer would need to respond to the Ministry of Health, Labour and Welfare's (MHLW) regarding compliance with such order, and there would also be a material impact on the MAH/Manufacturer's reputation as such order is published on MHLW's website.

Q5 What are the system requirements to ensure that the performance of MAH/Manufacturer's operations complies with the Laws and Regulations?

A5 The Draft Guidelines provide the following three items to ensure the compliance with the Act.

(i) Establishment of rules that should be complied with by the officers and employees

The Draft Guidelines provide that MAH/Manufacturer's internal rules should expressly provide the measures that their officers and employees should comply with and further offered the following examples as measures that should be provided in the internal rules:

＜Measures that should be provided in the internal rules＞

Measures that should be provided in the internal rules	Items that should be clarified (Examples)
Measures regarding decision-making to duly perform the operations	● Person who is authorized to make decisions ● Scope of the above authority ● Judging criteria necessary for the decision-making ● Internal procedures regarding the decision-making
Measures for each officer and employee to duly perform the operations in accordance with the decision made	● Person who is authorized to give instructions and orders ● Scope of the above authority ● Method of instructions and orders ● Procedures for operations

It is also provided that the MAH/Manufacturers should review their measures from time to time in accordance with the results of their supervision of operations and amendment to the Laws and Regulations.

(ii) Education, Training and Evaluation of Officers and Employees

The Draft Guidelines provide that the MAH/Manufacturers should inform their officers and employees of, and make sure that they comply with, the Laws and Regulations and their internal rules (together, the "**Rules**") and confirm the following points:

- Whether the officers and employees take training that is conducted in a calculated and continuous manner;
- Whether the officers and employees take training that is conducted as a result of the company's supervision of their operations or an amendment to the Laws and Regulations;

- Whether any division or contact point is established where the officers and employees may consult with in relation to the contents or application of the Rules; and
- Whether the MAH/Manufacturers evaluate their officers and employees on their compliance and understanding of the Rules to ensure that they are motivated to comply with the Rules.

(iii) Preparation, Management and Storage of Operational Records

The Draft Guidelines provide that the MAH/Manufacturers should establish a system where the contents of decision-making and performance of operations by the officers and employees are (a) reported appropriately within the company and (b) timely and accurately recorded so that the appropriateness of such decision-making and performance of operations may be later confirmed. In particular, the following points should be confirmed:

- Whether internal rules are provided in relation to document management such as the preparation, management, and storage of operational records;
- Whether the above internal rules are appropriately implemented; and
- Whether the appropriate informational security measures are taken such that the system does not allow for after-the-fact alteration of records.

Q6 What is required for the system to supervise the operations of MAH/Manufacturer's officers and employees?

A6 The Draft Guidelines provide that the MAH/Manufacturers should establish and operate a supervising system which enables them to confirm whether the decision-making and operations by the officers and employees are in compliance with the Rules and to take improvement measures where appropriate. For that purpose, the following points would be important for such system:

- Whether the internal audit division that is independent from the operations division (a) conducts the internal audit according to the internal audit plan that is made in consideration of the legal compliance risk and (b) reports to the responsible officer;
- Whether an effective whistle-blowing system is established by clarifying the whistle-blowing procedures and the protection of the whistle-blower;
- Whether information is collected by statutory auditors sufficiently and the audit's effectiveness is ensured; and
- Whether the supervision of operations and addressing of opinions are appropriately conducted by the marketing director ("**Marketing Director**"), manufacturing controller, and responsible engineer who may most effectively know the issues from the viewpoint of legal compliance regarding the manufacturing control, quality control, and post-marketing safety control (together, the "**Marketing Director/Controller**").

Q7 What other actions are required to ensure the MAH/Manufacturer's appropriate operations other than A6?

A7 The Draft Guidelines further require the MAH/Manufacturers to consider the following actions:

- Appoint a responsible officer (Chief Compliance Officer) who will be in charge of compliance with the Laws and Regulations of the entire operation of MAH/Manufacturers;

- Deploy a person at the departmental level who will play a central role in ensuring compliance with the Laws and Regulations based on the unique characteristics of each division;
- If the scale of the MAH/Manufacturers require company-wide efforts for legal compliance, establish a compliance supervision division which would lead the company-wide legal compliance under the supervision of the Chief Compliance Officer; and
- If an external director is appointed,
  - Encourage the external director to understand the Pharmaceutical Compliance System; and
  - Establish a system where the employees and each division reports to the external director regarding legal compliance issues.

Q8 What is required to clarify the Marketing Director/Controller's authority?

A8 The Amended Act requires clarification of the Marketing Director/Controller's authority. In particular, the Draft Guidelines provide that the MAH should clarify the scope of the following authority of the Marketing Director and share its contents within the company.

- Authority regarding the instructions and supervision of the operations for: (i) quality; (ii) domestic quality operations; and (iii) safety control and any other person engaged in other manufacturing control, quality control and post-marketing safety control (collectively, the "**Manufacturing/Quality/Safety Control**");
- Authority regarding the decisions and implementation of the: (i) abandonment, collection and suspension of sale of Healthcare Products; (ii) revision of attached documents; (iii) provision of information to medical professionals; (iv) reports to MHLW; and (v) other measures regarding quality control and post-marketing safety control;
- Authority regarding the management and supervision of manufacturers in order to secure the appropriate and smooth implementation of manufacturing and quality control of the Healthcare Products; and
- Other authority regarding the Manufacturing/Quality/Safety Control.

Similarly, Manufacturers are required to clarify the scope of authority of the person in charge of manufacturing control or the responsible engineer and to share its contents within the company.

Q9 What measures are required in order to comply with the GQP Ministerial Ordinance?

A9 The Amended Act requires that MAH/Manufacturers (i) grant the authority required for the implementation of quality control and post-marketing safety control to, and (ii) supervise the operation of, the Marketing Director/Controller. The Draft Guidelines further provide as follows:

(i) Grant of Necessary Authority to the Marketing Director/Controller

The GQP ministerial ordinance, GVP ministerial ordinance, QMS ministerial ordinance, GMP ministerial ordinance and GCTP ministerial ordinance (collectively, the "**GQP Ministerial Ordinances**") provide the details regarding the operations that the Marketing Director/Controller and other responsible persons should perform. MAH/Manufacturers need to confirm the following points so that these operations are performed appropriately.

- Whether the authority that is necessary for the Marketing Director/Controller and other responsible persons to perform the relevant operations is granted and whether the scope of such authority is expressly shared within the company; and
- Whether consideration has been given as to what kind of authority needs to be granted to each responsible person in order to avoid the situation where the authority granted to the Marketing Director/Controller and other responsible persons is insufficient, and therefore, the Manufacturing/Quality/Safety Control has been compromised and a violation of law or regulation occurs.

(ii) Supervision of Operations by the Marketing Director/Controller

The following actions must be taken by the MAH/Manufacturers so that they can supervise the Marketing Director/Controller's operations:

- Confirm whether the Marketing Director/Controller has duly exercised their authority and performed the operations appropriately regarding Manufacturing/Quality/Safety Control; and
- Take any improvement measures where necessary.

Q10 What is required as "other necessary measures for the proper performance of the MAH/Manufacturer's operations"?

A10 The Amended Act requires a company to take measures necessary for the appropriate performance of the MAH/Manufacturer's operations. In addition to the foregoing, the Draft Guidelines provide that it is important to take the following measures:

1. **Measures to avoid the marketing of Healthcare Products inconsistent with their approvals**
   - To monitor the discrepancy between the Healthcare Product's approval and the actual state of manufacturing and other operations in relation to the method of manufacturing and examination of the Healthcare Products and other matters that could affect the quality of the Healthcare Products;
   - In the case of any discrepancies, to adjust the manufacturing and operations in line with the Healthcare Product's approval; and
   - To take the necessary measures, including obtaining any necessary approvals of the Healthcare Products.
2. **Measures to duly report any side effects**
   - To collect, consider, and report safety control information in accordance with the GVP Ministerial Ordinance by:
     - Ensuring sufficient personnel,
     - Arranging for the appropriate system,
     - Supervising operations, and
     - Implementing other necessary measures.
3. **Measures to duly provide information regarding the Healthcare Products**
   - Supervision of operations to ensure that accurate information regarding the Healthcare Products is provided based on scientific and objective grounds and that no advertisement violates the advertisement restrictions under the Act; and
   - Other measures.

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Q11 Please explain the responsible officer's responsibility.

A11 Under the Amended Act, the "officer who is responsible for the operations regarding pharmaceutical affairs" is regarded as the responsible officer under the Act. The responsible officer is obliged to act proactively to ensure that MAH/Manufacturers comply with the Laws and Regulations, which includes the establishment and operation of the Pharmaceutical Compliance System. If an MAH/Manufacturer violates the Laws or Regulations due to a failure by the responsible officer, such responsible officer will be responsible for such violation.

Q12 Please explain who would be considered a "responsible officer".

A12 In the Draft Guidelines, a responsible officer is provided as below. An executive officer would not be considered a responsible officer under the Act.

Category of Company	Responsible Officer
Joint Stock Company (except for the company with nomination committee, etc.)	● Director representing the company; and ● Director in charge of operations on the Laws and Regulations[4]
Joint Stock Company (company with nomination committee, etc.)	● Representative Executive Officer; and ● Executive Officer in charge of operations on the Laws and Regulations
Membership Company	● Member representing the company; and ● Member in charge of operations on the Laws and Regulations
Other Corporations	Person similar to the foregoing

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Q13 Please explain the appointment of the Marketing Director/Controller.

A13 The Amended Act provides that the Marketing Director/Controller must have the capability and experience that are necessary to comply with the Laws and Regulations.

The Guidelines provide that the Marketing Director/Controller should be appointed in consideration of the following matters:

- Upon appointment, the following steps should be implemented: (a) consider what kind of authority should be given to the Marketing Director/Controller based on the matters that the Marketing Director/Controller should comply with and the matters that should be conducted by the Marketing Director/Controller under the Act and GQP Ministerial Ordinance; (b) clarify the scope of such authority; and (c) make an objective judgement

[4] The operations on the Laws and Regulations in the table above means the: (i) operations regarding matters that are subject to restriction under the Act such as applications for approval, marketing, Manufacturing/Quality/Safety Control, and advertisement of Healthcare Products; and (ii) operations regarding matters that are subject to restriction under other Laws and Regulations. It must also include the operations regarding the compliance with the Laws and Regulations. Operations also includes the operations on advertisements and compliance with the Laws and Regulations other than the Act. In addition, an officer of an MAH/Manufacturer who is not in charge of the operations on the Laws and Regulations would not be considered a responsible officer under the Act.

as to whether a candidate has **(i) knowledge, (ii) experience, (iii) comprehension ability and (iv) judgment ability** to perform the operations regarding such authority;
- Whether a candidate has the **leadership** to give effective instructions to and supervise the responsible person and person in charge of the relevant division in close coordination with each division regarding Manufacturing/Quality/Safety Control; and
- Whether a candidate's position within the company enables him/her to state his/her opinion without hesitation to the responsible officer.

Q14 Please explain the Marketing Director/Controller's obligations to express their opinion.

A14 The Amended Act provides that if it is necessary for the Marketing Director/Controller to fairly and duly conduct Manufacturing/Quality/Safety Control, they are obliged to express their opinions in writing to the MAH/Manufacturers. In response to this, the Draft Guidelines require the Marketing Director/Controller to perform the following actions:
- To make endeavors to determine the legal compliance issues proactively and positively;
- To try to have close coordination with the related divisions and the responsible person and person in charge at such division so that the legal compliance issues may be determined on a broad basis in relation to Manufacturing/Quality/Safety Control;
- Expressly indicate their opinion to MAH/Manufacturers; and
- Express opinions in writing so that the fact that the opinion was expressed may be recorded.

For your information, the report on urgent matters may primarily be made orally and not in writing.

Q15 Please explain an MAH/Manufacturer's obligation to respect the opinions of the Marketing Director/Controller and to take measures accordingly.

A15 The Amended Act provides that MAH/Manufacturers must respect the opinions of the Marketing Director/Controller and consider whether it is necessary to take any measures for legal compliance, and if necessary, take the relevant measures. Also, MAH/Manufacturers must retain records of the contents of the measures taken and store such records. If the opinion was addressed by the Marketing Director/Controller, but no measures were taken, the MAH/Manufacturers must retain the records of the fact that no measures were taken, the reasons why no measures were taken, and store such records.

In response to such provision, the Draft Guidelines provide that it is necessary for MAH/Manufacturers to expressly establish the following system/methods:
- A system which respects the opinions of the Marketing Director/Controller and allows the responsible officers and committee to receive such opinions and consider whether it is necessary to take any measures based on such opinions;
- Express indication of the responsible officers that take relevant measures;
- Methods of expressing the opinions by the Marketing Director/Controller; and
- System in which the necessary measures are taken by MAH/Manufacturers.

III. Conclusion

The Draft Guidelines are an important road map for the Pharmaceutical Compliance System that is required by the Amended Act, therefore, it would be useful to closely examine the Draft

Guidelines and begin determining if there are any deficiencies in your company's own Pharmaceutical Compliance System. Many companies would need to implement or consider actions in order to comply with the Amended Act, which would include changing the organization, establishment of and/or amendment to their internal rules. As such, in anticipation of the establishment of the Guidelines, it would be important to organize an internal team and provide input to the management. It would also be necessary to continue to follow and address the issues brought forth in the public comments and responses to such public comments.

（12 August 2020）

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Sonderhoff & Einsel Law and Patent Office regularly provide the advice regarding healthcare-related restrictions including the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices and related legal advice such as dealing with public comments, dealing with compliance, preparation of, negotiations on and amendment to, contracts, training, dealing with authorities and dispute litigation.

The information provided herein is provided for general purposes and is not designed to provide concrete, professional advice. For detailed advice, please contact **Ms. Ayuko Nemoto**（a-nemoto@se1910.com）, our responsible partner, who will deal with the case individually.

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