Assurance System of Quality, Performance, and Safety of Veterinary Medical Devices
Based on the Law for Ensuring the Quality, Efficacy, and Safety of Drugs and Medical Devices

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Contents

1. Administrative Organizations and Affairs under Jurisdiction for Veterinary Medical Devices .................................. 2

2. Outline of the Assurance System of Quality, Performance, and Safety of Veterinary Medical Devices

          Based on the Law for Ensuring the Quality, Efficacy, and Safety of Drugs and Medical Devices ........................................... 2

3. Licensing System for the Manufacturing/Marketing Business ................................................................. 3

4. Registration System of Manufacturers ............................................................................................................ 5

5. Registration System of Foreign Manufacturers .................................................................................................. 6

6. Approval System for Manufacturing/Marketing .................................................................................................. 6

7. Notification System for Manufacturing/Marketing .................................................................................................. 8

8. Licensing System for the Repairing Business ..................................................................................................... 8

9. Distribution Management System .................................................................................................................. 9

10. Device Use Evaluation .......................................................................................................................................... 9

Revised in February 2017
1. Administrative Organizations and Affairs under Jurisdiction for Veterinary Medical Devices

The Ministry of Agriculture, Forestry and Fisheries (MAFF) holds jurisdiction over affairs concerning veterinary Medical Devices used only for animals based on the Law for Ensuring the Quality, Efficacy, and Safety of Drugs and Medical Devices (Law No. 145, 1960). The Ministry of Health, Labor and Welfare (MHLW) holds jurisdiction over affairs concerning medical devices for humans.

National government organizations under jurisdiction concerning veterinary Medical Devices are as follows:

(1) Animal Products Safety Division (APSD) of the Food Safety and Consumer Affairs Bureau (FSCAB), MAFF (supervising section on laws and regulations of animal pharmaceutical affairs)
- Planning of regulation and operation concerning risk management of veterinary Medical Devices
- Control of manufacturing/marketing approval of veterinary Medical Devices
- Licensing of the manufacturing/marketing business and repairing business, registration of the manufacturing business for veterinary Medical Devices
- Registration of foreign manufacturers of veterinary Medical Devices
- Pharmaceutical supervision, guidance

(2) National Veterinary Assay Laboratory (NVAL), MAFF (an organization responsible for the technical response for animal pharmaceutical affairs)
- Approval review, confirmation of notification and evaluation of usage results of veterinary Medical Devices
- GMP (Good Manufacturing Practice) compliance review of veterinary Medical Devices
- GLP (Good Laboratory Practice)/GCP (Good Clinical Practice) compliance review of veterinary Medical Devices
- Quality assay
- Technical guidance

(3) PASC, PAFSC: Council for VMPs (a council on veterinary pharmaceutical affairs)
- Investigation/discussion on important considerations concerning veterinary pharmaceutical affairs
  Agenda: Approval and evaluation of the usage results of new veterinary Medical Devices

2. Outline of the Assurance System of Quality, Performance, and Safety of Veterinary Medical Devices Based on the Law for Ensuring the Quality, Efficacy, and Safety of Drugs and Medical Devices

For the purpose of ensuring quality, performance, and safety of veterinary Medical Devices, various systems have been established based on applicable laws and regulations including the Law for Ensuring the Quality, Efficacy, and Safety of Drugs and Medical Devices, Enforcement Ordinance of the Law for Ensuring the Quality, Efficacy, and Safety of Drugs and Medical Devices (Cabinet Order No. 11, Series of 1961), and Control Regulations of Veterinary Medical Products (Control Regulations, Ministerial Ordinance No. 107, Series of 2004).

The outline of the Law for Ensuring the Quality, Efficacy, and Safety of Drugs and Medical Devices concerning veterinary Medical Devices is as follows:

(1) Substitution rules for veterinary Medical Devices
  ✔ For medical devices intended for use only in the animals in the law, the “Minister of Health, Labor and Welfare” and “MHLW Ordinance” are substituted with the “Minister of Agriculture, Forestry and Fisheries” and “MAFF Ordinance”, respectively. (Article 83)

(2) Purpose
To improve health/hygiene by implementing the necessary regulations to ensure the quality, efficacy, and safety of drugs, quasi drugs, medical devices and devices used for regenerative medicine. (Article 1)

(3) License for the manufacturing/marketing business
- A person who intends to manufacture/market medical devices shall obtain a license for the manufacturing/marketing business. The Minister of Agriculture, Forestry and Fisheries (the Minister) may provide a license for manufacturing/marketing veterinary Medical Devices by type of medical devices (specially-controlled medical devices, controlled medical devices or general medical devices). (Article 23-2)
- A person who intends to manufacture/market medical devices as a business should obtain registry from the Minister by factory. (Article 23-2-3)
- Foreign manufacturers of medical devices may obtain registry from the Minister by factory. (Article 23-2-4)
- A person who intends to manufacture/market specially-controlled medical devices or controlled medical devices should obtain approval for manufacturing/marketing by each product. The Minister shall provide approval for manufacturing/marketing veterinary Medical Devices. (Article 23-2-5)
- Marketing authorization holders (MAHs) of veterinary Medical Devices who have been designated by the Minister based on input from the Pharmaceutical Affairs and Food Sanitation Council (PAFSC) should undergo evaluation on the usage results by the Minister. (Article 23-2-9)

(4) Licensing of the marketing business of medical devices
- A person who intends to run a marketing business or leasing business of specially-controlled medical devices or specially designated maintenance required medical devices should obtain the license from the governor of the prefecture where the business office is located. (Article 39)
- A person who intends to run a repairing business of medical devices should obtain the license for the repairing business. The Minister shall grant this license by specified type of device. (Article 40-2)

(5) Distribution, advertisement and supervision
- Marketing and leasing of adulterated medical devices, mislabeling medical devices and unapproved medical devices are banned. (Article 55 and Article 65)
- False or exaggerated reporting for medical devices should not be advertised. (Article 66)
- Name, manufacturing method, efficacy, effect or performance for unapproved medical devices should not be advertised. (Article 68)
- National or prefectural pharmaceutical inspectors shall conduct on-site inspection for ensuring appropriate provision of medical devices. (Article 69)

(6) Clinical studies
- This law system regulates the compliances required for persons who intend to request a clinical study of medical devices. (Article 80-2)

3. Licensing System for the Manufacturing/Marketing Business
(1) Types of medical devices
Veterinary Medical Devices are classified into the following (i)-(iii) depending on the degree of risk, and the licensing system of the manufacturing/marketing business is established according to each category.
(i) Specially-controlled medical devices (intermediate/high/extremely high degree of risk)
Medical devices requiring appropriate management because the occurrence of adverse reactions or impaired function (only if a device is used appropriately for the appropriate usage) may have a significant adverse effect on the life and health of animals. (e.g. closed circulating anesthesia system, closed circulating incubator)

(ii) Controlled medical devices (low-intermediate degree of risk)
Medical devices other than the specially-controlled medical devices requiring appropriate management because the occurrence of adverse reactions or impaired function may have a significant adverse effect on the life and health of animals. (e.g. anesthesia apparatus, respiratory equipment, visceral function substitute device)

(iii) General medical devices (extremely low-low degree of risk)
Medical devices other than the specially-controlled medical devices and controlled medical devices for which the occurrence of adverse reactions or impaired function may have little chance of a significant adverse effect on the life and health of animals. (e.g. sterilizer for medical use, stethoscope, clinical thermometer)

The Minister shall designate the medical devices specified in the “Specially-controlled medical devices, controlled medical devices and general medical devices designated by the Minister based on the provisions of Paragraphs 5-7 of Article 2 in the Law for Ensuring the Quality, Efficacy, and Safety of Drugs and Medical Devices” (Ministerial notice, No. 2217, Series of 2004) as specially-controlled medical devices, controlled medical devices or general medical devices based on input from PAFSC. Besides, the Minister shall designate the medical devices which may have a significant adverse effect on diagnosis, treatment or prevention of diseases without appropriate management because they require specialized knowledge and a technique for the maintenance inspection, repairing and other management (not limited to specially-controlled medical devices) as “specially designated maintenance required medical devices”. However, no medical device for animals has been designated up until now.

For reference: A device for humans was designated as a specially designated maintenance required medical device in the Ministry of HLWM Notification No. 297, Series of 2004.

(2) Types of licenses and licensing procedures

The license of veterinary Medical Devices manufacturing/marketing business should be obtained for managing responsibly and manufacturing/marketing manufactured/imported medical devices as a business. Applicants should submit the license application of the manufacturing/marketing business corresponding to the medical device types they would handle provided in Table 1 to the Minister through the governor of the prefecture where the office with the major function is located.

<table>
<thead>
<tr>
<th>Types of medical devices</th>
<th>Types of licenses</th>
</tr>
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<tbody>
<tr>
<td>Specially-controlled medical devices</td>
<td>First type medical device manufacturing/marketing business</td>
</tr>
<tr>
<td>Controlled medical devices</td>
<td>Second type medical device manufacturing/marketing business</td>
</tr>
<tr>
<td>General medical devices</td>
<td>Third type medical device manufacturing/marketing business</td>
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</table>

After reviewing the license application of the manufacturing/marketing business at APSD of
FSCAB, MAFF based on the submitted documents from the applicant, the license of the manufacturing/marketing business is granted. (A person who is granted a license of the first type of medical device manufacturing/marketing business is assumed to be granted the licenses of the second type of medical device manufacturing/marketing business and the third type of medical device manufacturing/marketing business. A person who is granted the license of the second type of medical device manufacturing/marketing business is assumed to be granted the third type of medical device manufacturing/marketing business.)

The process of the licensing procedure usually takes 6 months. However, this does not include the period required to prepare a response to instructions on the correction of defects in the application and attached documents.

This license becomes invalid without updating every 5 years. The process for updating the license usually takes 3 months.

MAHs for medical devices should assign a General Marketing Supervisor meeting the eligibility requirements corresponding to the types of medical devices (completion of a specialized course for physics or chemistry at colleges and universities, experience with medical device manufacturing) to conduct quality control and post-marketing safety control of the medical devices they should handle.

(3) License requirements for the manufacturing/marketing business

In order to obtain the license for the manufacturing/marketing business of medical devices, the business system concerning manufacturing control and quality control of the medical devices they should handle should conform to the standards specified in the “Ordinance of Business System Standards concerning Manufacturing Control and Quality Control for Veterinary Medical Devices and In-vitro Veterinary Diagnostic Reagents” (Ordinance of Manufacturing Control System, Ministerial ordinance No. 59, Series of 2014) and the method for post-marketing safety control of the medical devices they should handle should conform to the standards specified in GVP (GVP Ordinance, Ministerial ordinance No. 20, Series of 2005).

4. Registration System of Manufacturers

(1) Registry classification and procedures of the manufacturing business

A person who manufactures medical devices as a business should obtain registry for the manufacturing business by factory. Applicants should submit the application for registry to the Minister through the governor of the prefecture where the factory is located.

After reviewing the registry application of the manufacturing/marketing business at APSD of FSCAB, MAFF based on the submitted documents from the applicant, the manufacturing/marketing business is registered.

The process of the registering procedure usually takes 3 months. However, this does not include the period required to prepare a response to instructions on the correction of defects in the application and attached documents.

This registry becomes invalid without updating every 5 years. The process for updating the registry for the manufacturing business usually takes 3 months.

A Responsible Engineering Supervisor should be assigned meeting the eligibility requirements corresponding to the types of medical devices they should manufacture (completion of a specialized course for physics or chemistry, experience with medical device manufacturing) in the factory.
5. Registration System of Foreign Manufacturers

A person who intends to manufacture veterinary medical devices in foreign countries which are to be imported to Japan (foreign manufacturer) can obtain registry from the Minister. The application for the registry should be submitted to the Minister (not through the prefectural governor).

After reviewing the registry application of foreign manufacturers at APSD of FSCAB, MAFF, the foreign manufacturers are registered. The process of the registering procedure usually takes 3 months.

This registry becomes invalid without updating every 5 years. The process for updating the registry for foreign manufacturers usually takes 3 months.

6. Approval System for Manufacturing/Marketing

(1) Approval procedures

A person who intends to manufacture and market specially-controlled medical devices or controlled medical devices should obtain approval for manufacturing/marketing from the Minister by product.

The approval review of a medical device to be manufactured/marketed is implemented for (i) product (name), (ii) shape, structure and size, (iii) raw materials and materials, (iv) method for using, (v) performance and effect, (vi) method for manufacturing, (vii) assay method, (viii) storage method, and (ix) shelf life based on documents submitted by the applicant. Approval of medical devices guarantees the quality, performance and safety of those devices.

MAHs submit the approval application for manufacturing/marketing addressed to the Minister to NVAL, MAFF.

The approval application for manufacturing/marketing medical devices is reviewed at NVAL. The Minister provides approval for manufacturing/marketing on the assumption that a medical device is manufactured at a registered factory for the manufacturing business or foreign manufacturing business.

Review of new medical devices for animals (new veterinary Medical Devices ) is firstly implemented through investigation and discussion by the concerned Advisory Committee of PASC, PAFSC: Council for VMPs. After completion of the review in the Advisory Committee, the Council for VMPs starts its review. Then, the result is discussed or reported at the Pharmaceutical Affairs Subcommittee.

After a final decision is made that the approval is acceptable following the completion of all these reviews/assessments, the specified procedures are performed and the application is approved.

The process of the approval procedure usually takes 12 months for new veterinary Medical Devices and 6 months for generic devices. However, this does not include the period required to prepare a response to instructions on the correction of defects in the application and attached documents or instructions by PAFSC.

(2) Documents required for approval application

Approval review for medical devices is implemented based on the documents submitted by an applicant. Documents required for the application differ depending on whether the device is new or the device has the same identity as an existing approved device.

The scope of data which should be submitted at the time of the application for veterinary Medical Devices is provided in Table 2.

(3) GMP compliance inspection

In order to obtain the approval of medical devices, the procedures for manufacturing control and quality control of the product at a factory should conform to the “Ministerial Ordinance for
Manufacturing Control and Quality Control for Veterinary Medical Devices and Veterinary In-vitro Diagnostic Reagent” (GMP Ordinance, Ministerial ordinance No. 40, Series of 1995). After the application for approval, the compliance of these medical devices to GMP is reviewed by NVAL staffs and is confirmed by documents and an on-site inspection based on the application of compliance inspection submitted at the time of the application for approval. GMP compliance of the approved device is verified every 5 years. The Minister shall issue a standard conforming certificate if the result of the inspection of GMP compliance for medical devices is acceptable. Medical devices are divided by product group category. When a medical device on approval is to be manufactured at factories for which a standard conforming certificate of the same product group category as the one on approval has been issued (sterilization, storage of the final product in Japan), it is not necessarily subject to the GMP compliance inspection.

For reference: Medical devices manufactured for humans are required to conform to the QMS (Quality Management System) Ordinance (Ministerial Ordinance on Standards for Manufacturing Control and Quality Control for Medical Devices and In-vitro Diagnostic Reagent, MHLW Ordinance No. 169, 2004) but not to the GMP Ordinance. MHLW has established the QMS Ordinance based on ISO 13485:2003 in place of the previous GMP Ordinance for medical devices for international harmonization with regards to regulations of medical devices for humans. The QMS Ordinance covers not only the inspection of manufacturing but also quality control standards over the total product life cycle and management.

(4) Compliance inspection on standards for reliability of application data (GLP and GCP)

Data of nonclinical studies on the safety of specially-controlled medical devices should be collected and prepared in accordance with the “Ordinance on Standards for Implementation of Nonclinical Studies on the Safety of Veterinary Medical Devices” (GLP Ordinance, Ministerial ordinance No. 31, Series of 2005) based on OECD’s Principle of Good Laboratory Practice (GLP principle).

A person who intends to perform a clinical study of veterinary Medical Devices should follow the “Ordinance on Standards for Implementation of Clinical Studies on Veterinary Medical Devices” (GCP Ordinance, Ministerial ordinance No. 32, Series of 2005).

Besides, a person who intends to request a clinical study for new mechanical devices should submit notification of the clinical study addressed to the Minister beforehand.

Table 2 Scope of data which should be attached at the time of the application for veterinary Medical Devices

<table>
<thead>
<tr>
<th>Type of data</th>
<th>Application category*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>(1)</td>
</tr>
<tr>
<td>A. Origin or development history, usage situation in foreign countries</td>
<td>○</td>
</tr>
<tr>
<td>B. Physical-chemical test data (e.g. physical-chemical property, specifications and assay procedures)</td>
<td>△</td>
</tr>
<tr>
<td>C. Data on manufacturing procedures</td>
<td>○</td>
</tr>
<tr>
<td>D. Study reports on setting of the specification</td>
<td>○</td>
</tr>
<tr>
<td>E. Study data on safety (e.g. data on changes over time)</td>
<td>△</td>
</tr>
<tr>
<td>F. Data on safety studies</td>
<td>○</td>
</tr>
<tr>
<td>G. Study data on performance</td>
<td>○</td>
</tr>
<tr>
<td>H. Data on performance</td>
<td>○</td>
</tr>
<tr>
<td>I. Data on clinical studies</td>
<td>○</td>
</tr>
</tbody>
</table>

** Table 2 Scope of data which should be attached at the time of the application for veterinary Medical Devices.**
* Application category (1) Completely new device for veterinary use (except for devices approved or
certified for human use and small steel tools)
(2) A device approved or certified for human use but new for veterinary use (except for
small steel tools)
(3) A device which is the same as the approved one for veterinary use in efficacy and effect
but different from the approved one in shape or structure (except for small steel tools)
(4) A device which is the same as the approved one for veterinary use in shape and
structure but different from the approved one in efficacy and effect (except for small
steel tools)
(5) A device for which an identity of approved veterinary medicinal device is found and
small steel tools
○ and ●: Data requiring attachment
▲ and ▲: Data for which requirement for attachment shall be determined depending on the changed
content
×: Data not requiring attachment
● and ▲: If the attached data of the application for approval or certification for human use can be used,
the data can be attached.
** In category (5), data on G is required for a needleless syringe.

7. Notification System for Manufacturing/Marketing
General medical devices require no approval and can be marketed by self-certification of MAHs. In
this case, MAHs should submit notification for manufacturing/marketing addressed to the Minister to
NVAL by product handled beforehand. NVAL shall confirm the notification for
manufacturing/marketing of medical devices.

8. Licensing System for the Repairing Business
(1) Licensing of the medical device repairing business
A person who repairs devices as a business should obtain the license for the repairing business.
A person who performs repairing of medical devices as a business should obtain the license for the
medical device repairing business by business facility. The license for the medical device repairing
business is granted to each business facility according to the category specified by the Minister
(repairing category) depending on the target device. Therefore, the license application of this repairing
business is submitted to the Minister directly.
After reviewing the license application of the repairing business at APSD of FSCAB, MAFF, the
license of the repairing business is granted.
The process of the licensing procedure usually takes 6 months.
The license for the repairing business becomes invalid without updating every 5 years. The process
for updating the license usually takes 3 months.
(2) Repairing category of medical devices
Licensing for the medical device repairing business is categorized as follows:
(i) Repairing of specially designated maintenance required medical devices (No device is
designated as of January 2017)
(ii) Repairing of medical devices other than (i)
(3) License requirements for the medical device repairing business
In order to obtain the license for the medical device repairing business, the business facility should conform to the rules of the business facility for the medical device repairing business specified in Article 11 of the MAFF ordinance (No. 35, Series of 2005) of the structure and facilities of the factory (GMP for VMPs related to the Structure and Facilities).

The prefectural governor shall have a veterinary pharmaceutical inspector conduct an on-site inspection in the business facility at the time of the license application (license update) for the repairing business and determine whether the structure and facilities are in accordance with Article 11 of the Regulations for Buildings and Facilities, then submit the result to the Minister.

In addition, a Responsible Engineering Manager of the business facility must meet the eligibility requirements including more than 3 years of experience in the repairing business of medical devices.

9. Distribution Management System

(1) Licensing for the marketing business and leasing business of specially-controlled medical devices

A person who performs marketing, leasing or displaying of specially-controlled medical devices for those purposes as a business should obtain the license for the specially-controlled medical devices marketing business. The prefectural governor shall grant the license for the marketing business and leasing business to each business facility of each location.

The license for the marketing business and leasing business of specially-controlled medical devices becomes invalid without updating every 6 years.

(2) Notification of the marketing business and leasing business of controlled medical devices

A person who intends to perform marketing, leasing or displaying of controlled medical devices for those purposes as a business should submit a notification of matters specified in the MAFF Ordinance (outline of the structure and facilities) to the prefectural governor beforehand.

(3) Pharmaceutical supervision

About 2000 veterinary pharmaceutical inspectors including national inspectors are assigned all over Japan in order to monitor/supervise the facilities for manufacturing/marketing, manufacturing, marketing, repairing, and leasing veterinary Medical Devices as with veterinary medicinal drugs. Prefectural veterinary pharmaceutical inspectors are those staff mainly belonging to the responsible divisions of MAFF and the Livestock Division and Livestock Hygiene Service Centers.

Veterinary pharmaceutical inspectors constantly conduct on-site inspections in facilities of MAHs of medical devices, manufacturers of medical devices and distributors of medical devices for monitoring. The main tasks of the veterinary pharmaceutical inspector are as follows:

(i) On-site inspection of manufacturing control system, GVP and structure/facilities of a factory

(ii) Monitoring of unapproved/unlicensed/defective medical devices and falsely labeled products

(iii) Control of fallaciousness and excessive advertising

10. Device Use Evaluation

Since medical devices are often provided to the market after several short-cycle improvements/refinements of products, a concerned medical device may not be marketed even if reexamination or reevaluation is conducted after a certain period. On the one hand, for a product which is placed in the animal’s body, it is necessary to collect information during a certain period set depending on the product characteristics and confirm the efficacy and safety based on this information in order to ensure the efficacy and safety, whether or not the product has novelty, rather than conducting reexamination or reevaluation after a certain post-approval period. Because of these
characteristics of medical devices, device use evaluation has been introduced as an alternative system of reexamination/reevaluation. The Minister shall designate the medical devices, which are to be subjects for device use evaluation, based on input from PAFSC.

Data of the effect or performance and safety of the concerned medical device based on the device use result obtained during the research period should be attached to the application of device use evaluation.

Application documents should be collected and prepared in accordance with the “Ordinance on Good Post-marketing Study Practice (GPSP Ordinance, Ministerial ordinance No. 34, Series of 2005).