Points to Note in Relation to Pharmaceutical Regulatory Procedures in Japan

Japan Pharmaceutical Traders' Association
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Today's agenda

1. What is necessary in exporting APIs to Japan

2. Procedures for continuing API exports

3. What is necessary to prevent issues from occurring

1. What is necessary in exporting APIs to Japan

(1) Obtain a business number

(2) Obtain accreditation as an “Accredited Foreign Manufacturer “

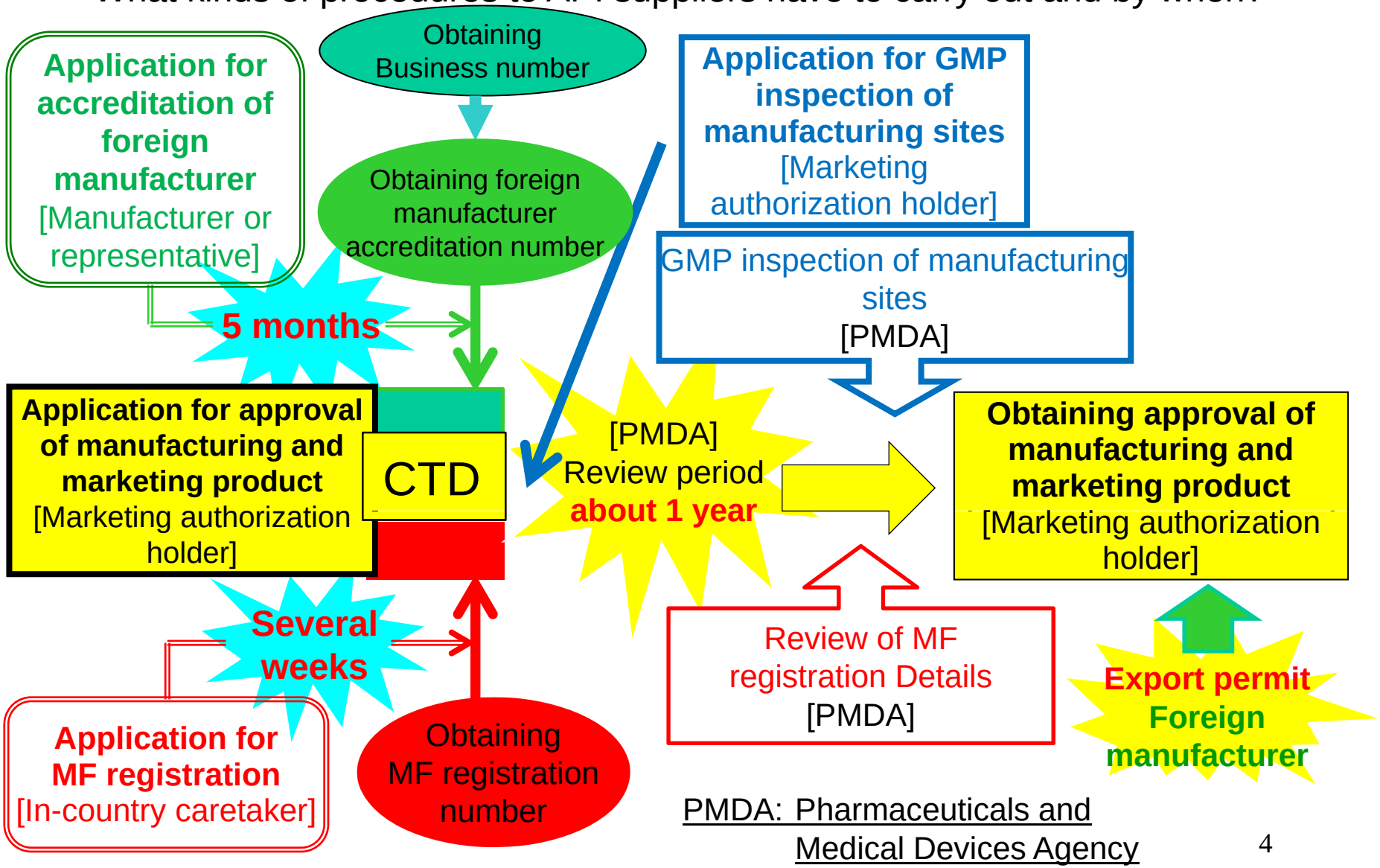
(3) MF registration (optional)

(4) Results of GMP compliance inspections by the PMDA

(5) Signing a GQP agreement with the marketing authorization holder (end user)

Schedule for procedures required for exporting APIs to Japan for the first time

- What kinds of procedures to API suppliers have to carry out and by when? -



PMDA: Pharmaceuticals and Medical Devices Agency

1. What is necessary in exporting APIs to Japan

(1) Obtain a business number

- Firstly, you need to obtain business number for each manufacturing site.

- Business numbers are different from accreditation numbers. You cannot progress onto other procedures without obtaining a business number.

1. What is necessary in exporting APIs to Japan

(2) Obtain foreign manufacturer accreditation

- If directly applying to the PDMA, create application forms and documents for review in Japanese, and pay the application fee.

- Alternatively, you may request a marketing authorization holder or an eligible representative domiciled in Japan to carry out application procedures for you. There is no accreditation for representative.

Points to note at the accreditation of foreign manufacturers

- Foreign manufacturers can make direct applications, however since applications use software issued by the Ministry of Health Labour and Welfare, attachments and documents for review must be translated into Japanese.

- The payment methods and procedures for the application fee are complicated, and responses to questions from the PMDA must be made in Japanese, therefore, in many cases, most foreign manufacturers request a marketing authorization holder, an importer, or another party domiciled in Japan with deep knowledge of the Pharmaceutical Affairs Law to carry out the application tasks.

- Accreditation must be obtained for each category.
  The review period is approximately 5 months.
  *Accreditation category
  (1) General pharmaceutical products (2) Radiopharmaceuticals
  (3) Sterile drugs (4) Biological products
  (5) Packaging, labeling, and storage

- Anyone domiciled in Japan can be an representative; however, procedures must be carried out every time changes are made to executives and manufacturing facilities, and renewal of the accreditation must be conducted every 5 years. Therefore, it is necessary to pay attention to the capabilities of the person and their knowledge in relation to the Pharmaceutical Affairs Law when selecting your representative.

1. What needs to be prepared for exporting APIs to Japan

(3) MF registration (optional)

- Prepare a CTD (modules 2 & 3) in relation to API manufacturing methods.
- Carry out registration procedures through an in-country caretaker of MF domiciled in Japan who carries out registration and subsequent management operations in Japanese.
- You may disclose all information through module 3 instead of carrying out MF registration.

- Persons responsible from the PMDA will talk about points to note in further detail, including case studies on operations and capabilities required for an in-country caretaker, in relation to post-MF registration review and subsequent maintenance management.

1. What needs to be prepared for exporting APIs to Japan

(4) Results of GMP compliance inspections by the PMDA

- The PMDA will carry out an inspection as per the GMP Ministerial Ordinance when reviewing the details of approval for a product for which the relevant API is used. Also, inspection will also be carried out when renewing the accreditation of the foreign manufacturer.
- Since marketing authorization holders will make applications for inspection (application fee), foreign manufacturers will not be required to directly pay the inspection fee.

- Thereafter, persons responsible (from the PMDA) will talk about points to note in further detail in relation to GMP compliance inspections.

1. What needs to be prepared for exporting APIs to Japan

(5) Signing a GQP agreement with the marketing authorization holder (end user)

- Quality control of APIs to be exported is to be required to be determined with the marketing authorization holders.
- What needs to be determined is stipulated in the GQP regulations.
- Change control is particularly important.

➢ Contents of agreement

- The scope of manufacturing behaviors and assurance standards, procedures for the manufacturing control, quality control, and distribution
- Manufacturing methods and test/inspection methods
- Periodic check (audit) by marketing authorization holders
- Methods of quality control at the time of transport and delivery
- Methods of prior notification on changes to manufacturing methods and testing methods (if there is an impact on quality), and the responsible person
- Methods of rapid notification and the responsible person for information on measures such as discontinuation of manufacturing, export, or sale; or recall or disposal, to prevent the occurrence or exacerbation of public health damage; and information on quality
- Information on quality and others

2. Procedures for continuing API exports

- Renewals are required every 5 years after foreign manufacturer accreditation.
  - Applications for renewal procedures must be commenced by 5 months prior to expiry.
- Change procedures must be carried out immediately if changes are made to the MF/accreditation details.
- Since GMP compliance inspections will be carried out on manufactured APIs at the time of changes to manufacturing methods and at the time of foreign manufacturer accreditation renewals, which are carried out every 5 years, inspection documents (such as those related to validation) required by the PMDA must be prepared.

3. What is necessary to prevent issues from occurring

- The majority of issues which arise in Japan are due to a lack of communication on changes, regardless of whether they are stipulated in the GQP regulations.
- Always reporting any changes to manufacturing methods, facilities, and other items to Japan beforehand to request a decision will prevent issues.
- In order to prevent communication lapses, in communicating, do not leave everything to the importer counterparty, but keep track of all end users (marketing authorization holders) who signed a final GQP agreement.

3. What is necessary to prevent issues from occurring

Communication on specific changes

- Changes related to CMC such as the manufacturing method
  → In-country caretakers of MF and marketing authorization holder
- Changes to the company name, facilities, executives and others
  → Representative for application for accreditation and marketing authorization holder

☆ If conflicts arise between the details on the approval document for the product and the actual situation due to lapses in communication on changes, in the worst case scenario, distribution of the API will be stopped and the product will be recalled.

Thank you for your attention

We wish your company every success in the Japanese market

Japan Pharmaceutical Traders' Association
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