Manufacturing and Marketing Control Rules for Biologics, Etc.
(Abbreviated: Biologics Rule)

[Enforced from Jan. 17, 2022]
[Ordinance of the Prime Minister No. 1717, Jul. 16, 2021, Partial Amendment]

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Article 1 (Purpose) The purpose of this Rule is to prescribe compliance that is not stipulated in Articles 43, 48, 60, and 62 of the “Regulation on Safety of Pharmaceuticals, Etc.,“ in terms of the manufacturing management and sales process of biologics, etc., by Articles 37 (1), 38 (1), and 47 (1) of the “Pharmaceutical Affairs Act.“ <Amended on Mar. 23, 2013>

Article 2 (Definitions) The terms used in this Rule have the following definitions <Amended on Mar. 3, 2008; Mar. 19, 2010; Mar. 23, 2013; Dec. 29, 2017>

1."Biologics" means medicinal product containing substances derived from living organisms or substances produced by using living organisms, such as vaccines, plasma derivatives, and antitoxins, whose potency and safety cannot be evaluated by physical and chemical tests alone.
2."Biologics, etc." mean medical products, genetically engineered drugs, cell culture drugs, cell therapies, gene therapies, and similar products.
3. "Seller of biologics, etc. (hereinafter "seller")" means a manufacturer, importer, drug wholesaler, or pharmacy operator of biologics, etc..

Article 3 (Manufacturing Manager's Compliance) ① According to Article 37, Paragraph 1 of the “Pharmaceutical Affairs Act“ (hereinafter the "Act"), when a manufacturing manager intends to manage the manufacture of biologics, etc., they must comply with the following. <Amended on Mar. 3, 2008; Mar. 19, 2010; Mar. 23, 2013; Dec. 29, 2017; Sep 10, 2021>

1. Prohibit the entry of persons other than those engaged in the manufacture of the biologics, etc. to the manufacturing site, and ensure that the biologics, etc. is not contaminated in the manufacturing process.
2. Ensure that instruments and materials handling polioviruses, bacilli, or tuberculosis bacilli are used only for the biologics, etc. in question and are labeled to prevent them from being used for other purposes.
3. Disinfect or sterilize necessary instruments and materials before manufacturing biologics, etc.
4. Prohibit persons who are infected or suspected of being infected with a contagious disease from engaging in the manufacture of biologics, etc.
5. Incinerate or dispose the items used in the manufacture or testing of biologics, etc. that are contaminated or suspected of being contaminated with pathogenic microorganisms and animal carcasses generated during the manufacturing or testing process within the manufacturing facility. However, items that have been disinfected or otherwise prevented from causing harm to health and hygiene need not be incinerated or disposed of, and items or animal carcasses that are difficult to incinerate or dispose of within the manufacturing facility may be entrusted to a waste disposal company licensed under Article 25, Paragraph 3 of the “Wastes Control Act“ to be incinerated or disposed of at a location other than the manufacturing facility.
6. Keep animals used in the manufacture or test of biologics, etc. under close observation for their health status at all times, and do not use animals infected or suspected of being infected with contagious diseases in the manufacture or testing of biologics, etc.
7. Comply with the standards prescribed by the Minister of Food and Drug Safety under the provisions of Article 52, Paragraph 1 of the Act.

② The manufacturing manager should keep a book on pathogenic microorganisms used in the manufacture or testing of biologics, etc. and preserve it for 5 years, stating the following subparagraphs. <Amended on Dec. 29, 2017>

1. Names, symbols, and usage
2. The date of acquisition or transfer, name of the acquirer and transferer (in the case of a legal entity, the name of the legal entity and the name of the representative should also be stated), and address
3. Test results for biological nature and condition (including pathogenicity) and the date of the test
4. Retention and passage status and their quantities
5. The origin of the strain used
6. Storage method of used strains

③ The manufacturing manager should keep a book on biologics, etc., record the following subparagraphs, and preserve it for 5 years. <Amended on Dec. 29, 2017>

1. Name and lot number
2. Name of the person responsible for manufacturing
3. Production start date and production end date
4. The name and symbol of the species of microorganisms used in the manufacture
5. Manufacturing process
6. Obtained stock solution amount
7. Total amount of medication before subdivisions
8. The number of containers based on their contents after subdivisions
9. Findings regarding the necropsy of animals used in manufacturing or testing
10. The date of the self-test and its results
11. The date of submission to the testing agency, date of completion, and results of the test
12. Expiration date

④ The manufacturing manager should comply with the matters prescribed and notified by the Minister of Food and Drug Safety to ensure safety in the manufacturing and quality control of biologics, etc. manufactured using genetic modification technology. <Amended on Mar 3, 2008; Mar 19, 2010; Mar 23, 2013>

⑤ When filling or packaging biologics, etc., containers or packaging materials in direct contact with the biologics, etc. should be cooled to the same temperature as the biologics, etc. through a refrigeration facility before filling or packaging. However, this shall not apply to containers or packaging materials in direct contact with the biologics, etc. that do not affect quality control.

Article 4 (Manufacturer's Compliance) ① According to the provisions of Article 38, Paragraph 1 of the Act, when a manufacturer of pharmaceutical products intends to manufacture biologics, etc., they should comply with each paragraph of Article 3. <Amended on Mar. 23, 2013>

②According to the provisions of Article 38, Paragraph 1 of the Act, when a manufacturer of pharmaceutical products, etc., selects an animal breeding establishment or intends to breed and manage animals brought in from an animal breeding establishment to manufacture or test biologics, etc, they should comply with the following subparagraphs. <Amended on Mar. 23, 2013>

1. Select an appropriate animal breeder by considering the breeding facilities and qualifications of the breeder.
2. Establish a training plan for animal husbandry, and conduct training sessions according to said plan.
3. Keep records of the animals before and after they are brought into the facility.
4. Complete and maintain the animal husbandry management guidelines.
5. Do not engage in animal cruelty.

③ The Minister of Food and Drug Safety may establish and notify the details of each subparagraph in Paragraph 2. <Amended on Mar 3, 2008; Mar 19, 2010; Mar 23, 2013>

Article 5 (Storage Compliance) ① The seller should comply with the following subparagraphs when storing biologics, etc. following Article 47, Paragraph 1, Subparagraph 4, Item A of the Act. However, in the case of a pharmacy operator, Subparagraphs 3, 7, and 8 shall be excluded.

1. Store the biologics, etc. separately from other medicinal product in a refrigerator or freezer equipped with an automatic temperature recording device (hereinafter "storage facility"). However, in the case of a pharmacy operator, an automatic temperature recording device need not be installed.
2. Maintain the temperature of the storage facility at the temperature indicated on the container or package of the biologics, etc. (hereinafter "storage temperature").
3. Designate a custodian, and ensure that the custodian checks the temperature of the storage facility at least twice daily.
4. Transfer biologics, etc. to a storage facility immediately upon receipt.
5. Ensure that biologics, etc. does not come into direct contact with the floor of the storage facility.
6. Do not leave doors to storage facilities unlocked.
7. Periodically test and calibrate the automatic temperature recording device installed in the storage facility as prescribed by the Minister of Food and Drug Safety.
8. Keep records of the verification following Subparagraph 3 and the verification and calibration following Subparagraph 7 for 2 years.

② In addition to the matters stipulated in Paragraph 1, necessary details regarding the storage methods and procedures of biologics, etc. shall be prescribed and notified by the Minister of Food and Drug Safety.

[Wholly Amended on July 16, 2021]

Article 6 (Transportation Compliance) ① The seller should comply with the following subparagraphs when transporting biologics, etc. following Article 47, Paragraph 1, Subparagraph 4, Item A of the Act.

1. Use a transport container or vehicle (hereinafter "transport facility") that meets all of the following requirements.
   a. Has a thermostat installed
   b. Equipped with a thermometer that allows you to observe temperature changes inside from the outside
   c. Have structures and devices to minimize physical impact as prescribed and notified by the Minister of Food and Drug Safety
   d. Verify as prescribed and notified by the Minister of Food and Drug Safety, taking into account transportation distance, transportation time, seasonal fluctuation factors, and product characteristics
2. Transport biologics, etc. at their storage temperature.
3. Do not turn off the thermostat during transportation
4. Do not tamper with the thermostat's temperature recordings.
5. Conduct periodic inspection and calibration of automatic temperature recording devices installed in transportation facilities as prescribed by the Minister of Food and Drug Safety.
6. Comply with the following items regarding the lot release certificate (including a certificate in electronic form, as follows) of shipment for biologics, etc. in the attached form. However, except in cases where the Minister of Food and Drug Safety recognizes that urgent supply is necessary to cope with emergency situations, such as a pandemic of bioterrorism or other infectious diseases according to the “Infectious Disease Control and Prevention Act.“
   a. Ensure that the person transporting the biologics, etc. carries the lot release certificate of the biologics, etc. in a separate form and transports the biologics, etc.
   b. Record the temperature of the transportation facility at the time of delivery of the biologics, etc. to the other seller on the lot release certificate of the biologics, etc. in the attached form and obtain the recipient's signature or seal. In this case, the recipient may request a copy.
   c. Retain the lot release certificate of biologics, etc. in the attached forms for 2 years.

7. Record the temperature measured by the thermostat and the test and calibration according to Subparagraph 5, and keep it for 2 years.

② The seller should indicate the following subparagraphs on the transportation facilities for biologics, etc.

1. Product name and quantity
2. Holding temperature and time
3. Transportation destination and time
4. The name of the shipper and recipient
5. The name and address of the business the shipper and recipient are affiliated with

③ In addition to the matters stipulated in Paragraphs 1 and 2, the necessary details regarding the transportation methods and procedures of biologics, etc. should be prescribed and notified by the Minister of Food and Drug Safety.

[Wholly Amended on July. 16, 2021]

Article 7 (Sales Restrictions) The seller should not sell biologics, etc. or store or transport them for sales purposes if they do not have storage facilities according to Article 5, Paragraph 1 and transportation facilities according to Article 6, Paragraph 1. <Amended on Jul 16, 2021>

[Wholly Amended on Dec. 29, 2017]

Supplementary Decree <No. 1731, Sept. 10, 2021> (Ordinance of the Prime Minister on the Partial Amendment of 11 Laws, including the “Enforcement Rules of the Health Functional Foods Act” to correct difficult legal terms)

This Rule shall enter into force on the date of their promulgation.

[Form 1] Lot Release Certificate for Biologics, Etc.

[Form 1] <Amended on July. 16, 2021>

Lot Release Certificate for Biologics, Etc.

The recipient must fill in the boxes marked with "※"

① Product Name			② Quantity	
③ Specification			④ Storage Method	
Manufacturer (Importer)	⑤ Business Name			
	⑥ Address			
	⑦ Lot No.		⑧ Expiration Date	
Seller (Shipper)	⑨ Business Name			
	⑩ Address			
	⑪ Package Type		⑫ Shipping Date	
Recipient	⑬ Business Name			
	⑭ Address			
	⑮ Product Temperature Upon Receipt	※	⑯ Receipt Date	※

We certify that we have shipped the above according to Article 47, Paragraph 1 of the "Pharmaceutical Affairs Act" and Article 6, Paragraph 1, Item 6 of the "Manufacturing and Marketing Control Rules for Biologics, Etc."

Date

Seller (Shipper) (Signature or seal)

Recipient (Signature or seal)

210mm×297mm

(Plain paper 60g/㎡)

Note: MFDS offers the English version as a service to an international audience. Any discrepancies or differences created in the translation are not binding and have no legal effect for compliance or enforcement purposes. The official version of this document is the Korean version.