

**Korea Good Manufacturing Practice and Quality Standards (Attachment 4,
Enforcement Regulations of the Korean Pharmaceutical Affairs Law)**

Article 1 (Definitions)

Definitions given below apply to the terms as used in these standards.

- “Production”** means all operations involved in the process for a finished product, including packaging labeling.

- “Subdivision”** means such operations, not undergoing a change in the quality of dosage form of the finished product, as dividing, filling and sealing each defined quality in a container or a pack which is contacted directly with drugs.

- “Batch”** or **“Lot”** means a defined quantity of the drug manufactured in the same process so that it is expected to be homogeneous.

- “Batch number”** or **“Lot number”** means the number, letter or its combination given per the batch or the lot so as to identify all the complete history of the production control and the shipment.

- “Raw material”** means any substances used for the production including those that might not be present in the finished product (intermediate products and packaging materials are excluded from this category).

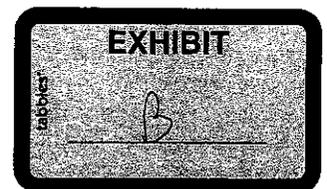
- “Packaging material”** means any materials used for packing and labeling, including container.

- “Intermediate product”** means a product in the processes, which must undergo further the necessary process before it becomes a finished product.

- “Finished product”** means any products which have undergone all the processes.

- “Finished drug product”** means any drugs in a certain dosage form which have undergone all the processes to finally administer them into the human body.

- “Pharmaceutical bulk product”** means any substances which are manufactured via



synthesis, fermentation, extraction or its combination process and become the raw materials of the finished product.

Article 2 (Premises Maintenance)

A manufacturer should make the corresponding manufactory suitable to the standards ordained by the Facility Standard Decree, and maintain the manufactory properly by regular checks so as to ensure no hindrance in the production and quality control.

Article 3 (Premises Maintenance)

A manufacturer should maintain the proper operation environment in the corresponding manufactory in accordance with the provisions of the following items so as to prevent the contamination in the process.

1. The operation environment control area should be established, and the appropriate cleanliness standards should be sustained in accordance with the kinds, the production methods and the production facilities of drugs.

2. The air-handling unit should be checked periodically.

Article 4 (Kinds of Standards)

For ensuring proper performance of the production control and the quality control, the manufacturer should prepare and maintain Master Formula, Production Control Standards, Production Hygiene Control Standards and Quality Control Standards.

Article 5 (Master Formula)

The Master Formula should be prepared as per product, including:

1. The name, the dosage form and the description of a product.
2. The date of regulatory approval and of writing.
3. The dosage & administration, effect & indication, and precaution in use.
4. Components and amounts.
5. Methods of production and in-process tests.
6. Theoretical yield per step of the processes.
7. Precaution during the operation.
8. Specification and testing methods of raw material, intermediate and finished product.
9. Specification and testing methods of packaging materials, if necessary.

10. Facilities and equipment required for production and quality control.
11. The shelf life or expiration date.
12. Storage conditions.

Article 6 (Production Control Standards)

The Production Control Standards should include each of the following items:

1. Matters related to the in-process control

- a) The production records should include:
 - (1) The name, the dosage form (limited to a finished product) and the description of a product.
 - (2) Lot number and production date.
 - (3) Lot size.
 - (4) Components and amounts.
 - (5) Lot number or test number of the raw materials used.
 - (6) The comparison of the actual yield vs. the theoretical yield per step of the processes.
 - (7) Measures taken in the processes.
 - (8) The results of in-process check and the measures taken to correct any deviation, if occurred.
 - (9) Signatures of workers in charge and the date of operation.
 - (10) Precautions or specifically observed matters.
- b) Any restriction to the production area.
- c) Methods of the in-process check, particularly double checking of weighing and sterilizing operations.
- d) Established specification for proper weighing instruments used of the weight or volume.
- e) Methods of confirming the appropriateness of raw materials to be used.
- f) Training for employees, particularly for newly recruited employees.

2. Matters related to the maintenance of the facilities and equipment:

- a) Methods of checking cleanliness and inspecting periodically.
- b) Methods of identifying the equipment and instruments in the operation.
- c) Measures taken when an accident, such as malfunctioning, occurs.

3. Matters related to the control of raw materials:

- a) The name and quantity when purchased, the conditions of the container and the method for handling any broken container.

- b) The place and method of storage.
- c) Procedures for handling any rejected materials.
- d) Measures for preventing cross-contamination in handling.

4. Matters related to the control of packaging raw materials:

- a) Methods of checking the quantity and specification when purchased.
- b) The place and method of storage.
- c) Procedures for handling any rejected materials.
- d) Methods of checking the quantity of any returned labeling materials unused.
- e) Measures taken in changing the description of labels.
- f) Measures for preventing confusion.

5. Matters related to the control of finished product:

- a) Methods of checking the approval on the entry and shipment.
- b) The place and method of storage.

6. Matters related to the production control of any toll-manufacturing product:

- a) Methods of delivery and storage for intermediate product.
- b) Method of evaluating the production records of assignee.

Article 7 (Production Hygiene Control Standards)

The Production Hygiene Control Standards should include each of the following items:

1. Areas and intervals of cleaning.
2. Methods of cleaning, chemical products and tools for cleaning.
3. Methods of evaluating cleanliness.
4. Specification for working garments and instructions for their use.
5. Methods of checking the health condition of employees.
6. Method of washing employees' hands and disinfecting, when necessary.
7. Precautions on the hygiene in the operation.

Article 8 (Quality Control Standards)

The Quality Control Standards should include each of the following items:

1. Test records including:

- a) Name and lot number.

- b) Test number.
 - c) Date of receipt, test and evaluation.
 - d) Testing items, specification and results of the tests.
 - e) Evaluation of the test results.
 - f) Signatures of analysts and a person responsible for approval.
2. The quantity, place and method of sampling.
 3. Methods of informing the test results to related departments.
 4. Calibration of equipment and instruments for the tests.
 5. Stability test and control of the reference samples.
 6. Methods of maintaining and handling of the standard samples and reagents for test.
 7. Method of dispatching the samples and evaluating the test results in the commissioned test.
 8. In the case of the toll manufacturing, methods of evaluating the test records of raw materials, packaging materials and intermediate products which are used by the assignee.

Article 9 (Organization)

- A manufacturer should establish the department of production control and of quality control independently each other, and appoint the chief managers of production department and of quality department differently, provided that in the case a toll manufacturer or subdivider that engage in the production of all products, a same person may be appointed.
- The managers of the foregoing departments should be appointed pharmacists of the corresponding manufactory, with full knowledge and experience in the practice under these standards.
- The manufacturer should deploy sufficient number of employees so as to ensure the operation without difficulties.

Article 10 (Manger of Production Control Department)

The manager of production control department, who is responsible for the affairs involved in

the in-process control, production hygiene control and storage control, should perform each of the following duties:

1. To ensure the proper operation of the production control, the manager should prepare the master formula, production control standards and production hygiene control standards.

2. The manager should prepare the production instructions including the following details and make a diligent effort to ensure whether the processes are carried out as specified:

a) The name, the dosage form (limited to a finished product) and the description of a product.

b) Lot number and production date.

c) Components and amounts.

d) Lot size

e) Theoretical yield per step of the process.

f) Precautions during the operations.

3. The manager should make a diligent effort to ensure whether the production hygiene and storage controls are performed in accordance with the specification.

4. The manager should designate a person involved in the storage control of raw materials, packaging materials and finished products.

Article 11 (Manger of Quality Control Department)

The manager of quality control department , who is responsible for the affairs involved in the quality control of raw materials, intermediate and finished products, should perform each of the following duties:

1. To ensure the quality control, the manager should prepare the master formula and quality control standards.

2. The manager should prepare the test instructions including the following details and make a diligent effort to ensure whether the tests are carried out as specified:

a) Testing items.

b) The sampling time and place thereof.

- c) The sampling quantity and method thereof.
- d) The sampling collector and analyst

3. The manager should evaluate the test results and inform them to related department in writing.

Article 12 (In-Process Control)

The in-process control should be done as follows:

1. The admission to the production area should be restricted to relevant personnel only.
2. Prior to operation, the cleanliness of the equipment and instruments to be used should be checked.
3. On the equipment and instruments in operation, the name and lot number of the product should be marked.
4. To ensure the homogeneity of finished products, proper checks should be made in the necessary process.
5. The adequacy for labeling and packaging should be checked.
6. Any labels remaining after the labeling and packaging process should be counted, and then either returned or destroyed.
7. The production records which conform to the Production Control Standards should be prepared per lot number.
8. When other operations are performed in the same or adjacent area, the persons in charge should make a diligent effort to ensure that any confusion between different packaging materials and cross-contamination between different drugs may be prevented.
9. When the aseptic operation is required, special precautions should be exercised to prevent microbial contamination, and the microbe number in the air of the area should be monitored periodically.
10. When the sterilization operation is required, it is necessary to prevent any confusion

between pre-sterilization and post-sterilization intermediate products.

11. Intermediate products should be kept separately and processed as soon as possible to avoid the deterioration of quality.

Article 13 (Production Hygiene Control)

The production hygiene control should be done as follows:

1. The facilities and equipment in the production area should be kept clean at all times.
2. A person suffering from any disease which may affect drugs should not join the operation.
3. The personnel should be instructed and trained for the production hygiene control.

Article 14 (Storage Control)

The storage control should be done as follows:

1. Raw materials and packaging materials should be separately stored as per kinds, showing the pre- or post-test items expressly.
2. Rejected raw materials and packaging materials should be isolated from other ones and handled as soon as possible.
3. Raw materials and packaging materials to be required for test, which should meet the quality standards, could be transferred to the production area.
4. Raw materials and packaging materials should be stored under the conditions not to affect their quality.
5. Each name and lot number of finished products should be recorded depending upon clients, when shipped, if necessary.
6. Returned goods should be stored separately.

Article 15 (Quality Control)

The quality control should be done as follows:

1. Tests should be performed on raw materials, intermediate products, finished products, returned goods, packaging materials and other test-requiring materials, and the test records should be prepared according to Quality Control Standards.
2. The test samples should be collected in a manner to prevent any contamination or deterioration.
3. The storage conditions of drugs should be evaluated.
4. The stability tests should be made on drugs whose quality might be affected by the lapse of time and in this case, the expiry date should be also established.
5. Tests should be made using sufficient quantities of finished products and these test samples should be also kept for 1 year after the expiry date.
6. The changes in the labels should be checked in accordance with the specification, and their samples should be also kept for reference.
7. The packaging materials to be contacted directly with drugs should be checked to ensure that they may deteriorate the quality of drug or confirm whether they may be hazardous to the human body.

Article 16 (Complaints)

Whenever complaints on the quality of drugs are received, it is necessary to find the causes of such complaints to take appropriate measures as soon as possible. The records should be kept.

Article 17 (Records)

All records, unless otherwise stipulated by other regulations, should be kept for 1 year after expiry date.

Article 18 (Training)

The manufacture should perform regular training programs of the production and quality control and other matters for employees so that they may perform their assigned tasks effective and better quality of drug may be assured.

Article 19 (Regulatory Filing)

□ A manufacturer who intends to receive the appraisal of finished products and pharmaceutical bulk products in line with their performance of the Korea Good Manufacturing Practice and Quality Standards shall submit Application Forms (No. 76 and No. 77, respectively) to the Commissioner of the Korea Food and Drug Administration.

□ Under the preceding paragraph, the manufacturer who intends to receive such appraisal is required to have the past records thereto; more than three lots per dosage form of finished products and more than three lots per manufacturing method of pharmaceutical bulk products.

Article 20 (Judgment)

□ When the Commissioner of the Korea Food and Drug Administration receives the application in accordance with Article 19, he/she may request the chairman of the Korea Pharmaceutical Manufacturers Association to review the application forms thereto.

□ Under the preceding paragraph, the Commissioner of the Korea Food and Drug Administration shall determine the applicant's compliance on the Standards based on the following review: a) production site and dosage form of finished products, b) production site and manufacturing method of pharmaceutical bulk product.

Article 21 (Inspector)

□ Under the preceding paragraph of Article 20, the Commissioner of the Korea Food and Drug Administration shall appoint an eligible inspectors to be selected from those pharmaceutical inspectors as designated under the provisions of Paragraph 1, Article 70 of the Korean Pharmaceutical Affairs Law.

□ These inspectors designated by the Commissioner of the Korea Food and Drug Administration shall be well-qualified and experienced persons who are capable of supervising the whole course of the inspection.

Article 22 (Guidance and Training)

□ The Commissioner of the Korea Food and Drug Administration shall define the detailed matters related to the performance of the Korea Good Manufacturing Practice and Quality Standards.

□ The Commissioner of the Korea Food and Drug Administration may request the chairman of

the Korea Pharmaceutical Manufacturers Association to provide the applicant with proper guidance and training of the performance of the Korea Good Manufacturing Practice and Quality Standards.

Article 23 (Others)

A manufacture who has engaged in the manufacture of biological preparations shall observe other Standards (Attachment No. 4-4) in addition to the Korea Good Manufacturing Practice and Quality Standards.