MINISTRY OF HEALTH

THE SOCIALIST REPUBLIC OF VIETNAM
Independence - Freedom - Happiness

No. 03/2018/TT-BYT

Hanoi, February 09, 2018

CIRCULAR

GOOD DISTRIBUTION PRACTICES FOR PHARMACEUTICAL PRODUCTS AND PHARMACEUTICAL STARTING MATERIALS

Pursuant to the Law on Pharmacy No. 105/2016/QH13 dated April 06, 2016;

Pursuant to the Government's Decree No. 54/2017/ND-CP dated May 08, 2017 on guidelines for implementation of the Law on Pharmacy;

Pursuant to the Government's Decree No. 75/2017/ND-CP dated June 20, 2017 defining functions, tasks, entitlements and organizational structure of the Ministry of Health;

At the request of Director General of Drug Administration of Vietnam,

The Minister of Health hereby promulgates a Circular on Good Distribution Practices for pharmaceutical products and pharmaceutical starting materials.

Chapter I

GENERAL PROVISIONS

Article 1. Scope

This Circular provides for application and inspection of compliance with principles of Good Distribution Practices for pharmaceutical products and pharmaceutical starting materials.

Article 2. Definitions

For the purposes of this Circular, the terms below shall be construed as follows:

1. *"distribution of pharmaceutical products"* means the division, movement and storage of pharmaceutical products from the warehouse of the manufacturer/importer of such products or from a distributor to the end user thereof or to a distribution point or between distribution points by means of various transport methods.

2. *"distribution of pharmaceutical starting materials"* means the division, movement and storage of pharmaceutical starting materials from the warehouse of the manufacturer/importer of such products to a manufacturer of finished pharmaceutical products or to a distribution/storage point of the distributor or between distribution points by means of various transport methods.

3. *"Good Distribution Practices for Pharmaceutical Products and Pharmaceutical Starting Materials"* mean a set of principles and standards for distribution of pharmaceutical products and pharmaceutical starting materials, ensuring that the quality of a pharmaceutical product is maintained by means of adequate control of the numerous activities which occur during the distribution process as well as providing a tool to secure the distribution system from unapproved pharmaceutical products and pharmaceutical starting materials.

4. *"distributors"* include a facility that is responsible for distributing pharmaceutical products and pharmaceutical starting materials, pharmaceutical product and pharmaceutical starting material wholesalers, distributors of vaccines that are part of the National Expanded Program on Immunization of provinces or districts and other facilities that distribute pharmaceutical products and pharmaceutical starting materials for non-commercial purposes.

5. *"deficiency"* means a deviation from principles and standards of Good Distribution Practices or other applicable regulations on pharmacy management.

6. *"WHO"* stands for World Health Organization.

7. *"GDP"* stands for Good Distribution Practices.

Chapter II

APPLICATION OF PRINCIPLES OF GOOD DISTRIBUTION PRACTICES FOR PHARMACEUTICAL PRODUCTS AND PHARMACEUTICAL STARTING MATERIALS

Article 3. Principles of GDP for pharmaceutical products and pharmaceutical starting materials

1. WHO principles of GDP for pharmaceutical products shall be applied according to the Appendix I hereof and updated document specified in Clause 3 of this Article.

2. WHO principles of GDP for pharmaceutical starting materials shall be applied according to the Appendix II hereof and updated document specified in Clause 3 of this Article.

3. In the cases where any of the principles of WHO principles of GDP for pharmaceutical products and pharmaceutical starting materials provided in the Appendix I and Appendix

II hereof is amended, the Drug Administration of Vietnam shall translate and publish the amended contents on its website and the web portal of the Ministry of Health.

Article 4. Regulated entities

1. Pharmaceutical product distributors shall apply and comply with GDP principles in the Appendix I hereof and updated documents published on the web portal of the Ministry of Health and website of the Drug Administration of Vietnam.

2. Pharmaceutical starting material distributors shall apply GDP principles in the Appendix II hereof and updated documents published on the web portal of the Ministry of Health and website of the Drug Administration of Vietnam.

3. Distributors of vaccines that are part of the National Expanded Program on Immunization of provinces or districts shall apply GDP principles in the Appendix I hereof (except for Points 5.3, 5.5, 5.6, 5.9, 6.3, 6.4, 7.5, 7.6, 8.1, 8.2, 8.3, 8.4, 8.5, 8.8, 8.12, 9.6, 9.11, 10.3, 12.1, 13.8, 13.9, 15.1, 15.2, 15.3, 15.4, 20.1, 20.2, 20.3, 20.4, 20.5, 20.6, 20.7 and 20.8) and updated documents published on the web portal of the Ministry of Health and website of the Drug Administration of Vietnam. Distributors are not required to apply for inspection of compliance with GDP principles as prescribed in Chapters III and IV of this Circular.

4. Distributors shall apply updated GDP document within 12 months in the case of change of storage facility or equipment for distribution of pharmaceutical products and pharmaceutical starting materials or within 06 months in the case of other updates, from the date on which the updated document is published on the web portal of the Ministry of Health or website of the Drug Administration of Vietnam.

Chapter III

INPSECTION OF COMPLIANCE WITH PRINCIPLES OF GDP FOR PHARMACEUTICAL PRODUCTS AND PHARMACEUTICAL STARTING MATERIALS

Article 5. Documents used as basis for inspection of compliance with principles of GDP for pharmaceutical products and pharmaceutical starting materials

1. Documents used as basis for inspection of compliance with GDP principles by a pharmacy business establishment are those included in its application for certificate of eligibility for pharmacy business (the distributor is not required to submit these documents because they have been submitted when it applies for the certificate of eligibility for pharmacy business) prescribed in Article 38 of the Law on Pharmacy and Article 32 of the Government's Decree No. 54/2017/ND-CP dated May 08, 2017 on guidelines for the implementation of the Law on Pharmacy (hereinafter referred to as "the Decree No. 54/2017/ND-CP"). In the case of a distributor of controlled pharmaceutical

products, the documents prescribed in Article 38 of the Law on Pharmacy and Article 49 of the Decree No. 54/2017/ND-CP are required to be submitted.

The technical documents about distributors shall be prepared in accordance with guidelines for the site master file provided in the Appendix III hereof or the site master file that is updated in the case of change of scope of operation.

2. Documents used as basis for inspection of compliance of a non-commercial distributor with principles of GDP include:

a) An application form (Form No. 02 in the Appendix IV hereof);

b) The technical documents about the distributor that are prepared in accordance with guidelines for the site master file provided in the Form No. 05 in the Appendix IV hereof.

3. The distributor that wishes to apply for issuance of the certificate of GDP compliance together with the certificate of eligibility for pharmacy business shall specify this in the application form for issuance of the certificate of eligibility for pharmacy business.

Article 6. Procedures for inspection of compliance with principles of GDP for pharmaceutical products and pharmaceutical starting materials

1. Receipt of application:

The distributor shall submit 01 application prescribed in Article 5 of this Circular and pay assessment fees according to regulations of the Minister of Finance on fees for assessment of GDP for pharmaceutical products and pharmaceutical starting materials to the Department of Health.

2. Procedures for receiving and inspecting an application are specified in:

a) Clauses 2, 3, 4, 5 and 6 Article 50 of the Decree No. 54/2017/ND-CP, applicable to the distributor that trades in combined pharmaceutical products that contain narcotic active ingredients, psychotropic active ingredients or precursors;

a) Clauses 2, 3, 4 and 5 Article 51 of the Decree No. 54/2017/ND-CP, applicable to the distributor that trades in toxic pharmaceutical products, toxic pharmaceutical starting materials, pharmaceutical products and active ingredients on the list of banned substances in certain fields;

c) Clauses 2, 4 and 5 Article 33 of the Decree No. 54/2017/ND-CP, applicable to the pharmacy business establishment that trades in pharmaceutical products other than those mentioned in Points a and b of this Clause.

3. Within 05 days from the date on which the satisfactory application is received, the Department of Health shall establish an inspectorate, notify the distributor of the

inspectorate and expected date of carrying out an on-site inspection at the distributor. Within 15 days from the date of notification, the inspectorate shall carry out an on-site inspection at the distributor.

Article 7. Procedures for inspection and classification of compliance with principles of GDP for pharmaceutical products and pharmaceutical starting materials

1. Inspection procedures:

a) Step 1. The inspectorate shall declare the Decision on establishment of inspectorate, purposes and contents and plan for the site inspection at the distributor;

b) Step 2. The distributor shall make a brief introduction of organization, personnel, application of GDP principles or specific contents in conformity with the inspected contents;

c) Step 3. The inspectorate shall inspect and assess the application of GDP principles at the distributor;

d) Step 4. The inspectorate shall hold a meeting with the distributor to inform deficiencies identified during the inspection (if any); assess the degree of each deficiency; discuss with the distributor about its dissenting opinions about the assessment of each deficiency; assess the degree of compliance of the distributor with GDP principles;

dd) Step 5. An inspection record is prepared and signed:

The inspectorate shall prepare a record on inspection of compliance with GDP principles using the Form No. 03 in the Appendix IV hereof. The record shall classify the degree of compliance of the distributor with GDP principles as prescribed in Clauses 2 and 3 of this Article, list and analyze the deficiencies (if any) that need to be corrected by the distributor, and include assenting and dissenting opinions of the inspectorate and the distributor.

The inspection record shall be signed by head of the distributor and head of the inspectorate. The record shall specify members of the inspectorate, location, date and scope of the inspection and be made into 03 copies, among which one is kept by the distributor and the others are kept by Department of Health.

2. Inspection of the degree of compliance with GDP principles:

The degree of compliance of a distributor with GDP principles shall be assessed as prescribed in the Appendix IV hereof and includes:

a) GDP degree 1 distributor;

b) GDP degree 2 distributor;

c) GDP degree 3 distributor.

Article 8. Processing results of inspection of compliance with principles of GDP for pharmaceutical products and pharmaceutical starting materials

1. In case the GDP inspection record concludes that the distributor is in GDP degree 1 according to Point a Clause 2 Article 7 of this Circular:

Within 10 days from the end of the on-site inspection at the distributor and the date of signing the inspection record, the Department of Health shall issue the certificate of eligibility for pharmacy business or issue the certificate of GDP compliance according to the Form No. 06 in the Appendix IV hereof.

In the case of a distributor of controlled pharmaceutical products, within 20 days from the end of the on-site inspection at the distributor and the date of signing the inspection record, the Department of Health shall issue the certificate of eligibility for pharmacy business or the certificate of GDP compliance according to the Form No. 06 in the Appendix IV hereof.

2. In case the GDP inspection record concludes that the distributor is in GDP degree 2 according to Point b Clause 2 Article 7 of this Circular:

a) Within 05 days from the end of the on-site inspection at the distributor and the date of signing the inspection record, the Department of Health shall request the distributor in writing to correct the deficiencies specified in the inspection record.

In the case of a distributor of controlled pharmaceutical products, within 15 days from the end of the on-site inspection at the distributor and the date of signing the inspection record, the Department of Health shall request the distributor in writing to correct the deficiencies specified in the inspection record.

b) After corrective actions are taken, the distributor shall send a notification and evidences (documents, images, videos or certificates) proving that the deficiencies specified in the inspection record are corrected;

c) Within 20 days from the date on which the notification of corrective actions taken is received, the Department of Health shall assess the correction result and conclude GDP compliance status of the distributor.

- In case results of corrective actions make the distributor comply with GDP principles, the Department of Health shall issue the certificate of eligibility for pharmacy business or the certificate of GDP compliance according to Form No. 06 in the Appendix IV hereof;

- In case results of corrective actions show that the distributor still fails to comply with GDP principles, the Department of Health shall provide explanation for rejecting the application in writing.

d) Within 06 months from the date on which additional documents are requested in writing by the Department of Health, the distributor shall submit additional documents as requested. If the distributor fails to satisfy such request by the aforementioned deadline or the application is not satisfactory within 12 months from the first time it is submitted, the application will be rejected.

3. In case the GDP inspection record concludes that the distributor is in GDP degree 3 according to Point c Clause 2 Article 7 of this Circular:

Within 05 days from the end of the on-site inspection at the distributor and the date of signing the inspection record, the Department of Health shall send notify the distributor in writing of its failure to comply with with GDP principles and refusal to issue the certificate.

4. Within 05 days from the date of issuing the certificate of eligibility for pharmacy business or the certificate of GDP compliance, the Department of Health shall publish the following information on the website of the Department of Health:

a) Name and address of the distributor;

b) Full name of the pharmacist, pharmacy practice certificate number;

c) Number of the certificate of eligibility for pharmacy business and certificate of GDP compliance (if any);

d) Expiry date of the inspection of compliance with GDP principles;

dd) Distributor's scope of operation.

Chapter IV

INSPECTION OF MAINTENANCE OF COMPLIANCE WITH PRINCIPLES OF GDP FOR PHARMACEUTICAL PRODUCTS AND PHARMACEUTICAL STARTING MATERIALS

Article 9. Periodic inspections of maintenance of compliance with principles of GDP for pharmaceutical products and pharmaceutical starting materials

1. A periodic inspection of maintenance of compliance with GDP principles at a distributor (including non-commercial distributor and distributor of controlled pharmaceutical products) shall be carried out every 03 years from the end of the previous inspection (excluding unscheduled inspections and audits by the Ministry of Health or Department of Health).

2. In November, the Department of Health shall publish the plan for periodic inspections of maintenance of compliance of the distributor with GDP principles in the succeeding year on its website.

3. According to the periodic inspection plan published by the Department of Health, the distributor shall submit an application for the periodic inspection prescribed in Clause 7 of this Article to the Department of Health at least 30 days before the date of carrying out the inspection according to the published plan.

Example: The expected date of carrying out a periodic inspection at distributor A is on August 18, 2018, such distributor shall submit an application for the periodic inspection to the Department of Health before July 18, 2018.

4. In case the distributor fails to submit the application for the periodic inspection by the aforementioned deadline, within 10 days from the deadline for submission of the application prescribed in Clause 3 of this Article, the Department of Health shall request the distributor in writing to provide explanation for failure to submit the application for the periodic inspection.

5. Within 30 days from the date on which the Department of Health requests the distributor in writing to provide explanation for failure to submit the application for the periodic inspection, if the distributor fails to submit the application as prescribed, the Department of Health shall revoke the distributor's certificate of eligibility for pharmacy business as prescribed in Clause 2 Article 40 of the Law on Pharmacy or submit a written request for suspension of the non-commercial distributor.

6. After submitting the application within the time limit, the distributor shall continue its distribution activities within the scope specified in the certificate of eligibility for pharmacy business or the certificate of GDP compliance in the case of a non-commercial distributor from the date on which the application is submitted to the date on which the periodic inspection results are obtained.

7. An application for the periodic inspection of maintenance of compliance with GDP principles includes:

a) An application form (Form No. 01 in the Appendix IV hereof);

b) Updated technical documents about infrastructure, technology and personnel of the distributor (in case of change);

c) A brief report on the distribution of pharmaceutical products and pharmaceutical starting materials over the last 03 years from the date of the previous inspection (excluding unscheduled inspections and audits by the Ministry of Health or Department of Health) to the date on which the periodic inspection is requested.

8. Procedures for inspecting and classifying results of inspection of compliance with GDP principles are specified in Articles 6 and 7 of this Circular.

Article 10. Processing results of periodic inspection of compliance with principles of GDP for pharmaceutical products and pharmaceutical starting materials

1. In case the GDP inspection record concludes that the distributor is in GDP degree 2 according to Point a Clause 2 Article 7 of this Circular:

Within 10 days from the end of the on-site inspection at the distributor and the date of signing the inspection record, the Department of Health shall issue the certificate of GDP compliance according to Form No. 06 in the Appendix IV hereof.

2. In case the GDP inspection record concludes that the distributor is in GDP degree 1 according to Point b Clause 2 Article 7 of this Circular:

a) Within 05 days from the end of the on-site inspection at the distributor and the date of signing the inspection record, the Department of Health shall request the distributor in writing to correct the deficiencies and submit a notification of corrective actions taken to the Department of Health;

b) Within 45 days from the date on which the Department of Health requests in writing, the distributor shall take corrective actions and send a notification enclosed with evidences (documents, images, videos or certificates) proving that the deficiencies specified in the inspection record are corrected;

c) Within 20 days from the date on which the notification of corrective actions taken and evidences are received, the Department of Health shall assess the correction result and conclude GDP compliance status of the distributor as follows:

- In case results of corrective actions make the distributor comply with GDP principles, the Department of Health shall issue the certificate of GDP compliance;

- In case results of corrective actions show that the distributor still fails to comply with GDP principles, the Department of Health shall request the distributor in writing to keep taking corrective actions and send an additional notification. The time limit for keeping taking corrective actions and sending the additional notification is 45 days from the date of receiving the request.

d) Within 90 days from the end of the on-site inspection, if the distributor fails to send a notification of corrective actions taken or the corrective actions still fail to comply with GDP principles after they are taken as prescribed in Point c of this Clause, the Department of Health shall send a notification of non-compliance with GDP principles and shall, according to the nature and severity of the violation, take one or several actions specified in Points a and b Clause 3 of this Article.

3. In case the GDP inspection record concludes that the distributor is in GDP degree 3 according to Point c Clause 2 Article 7 of this Circular:

Within 05 days from the end of the on-site inspection at the distributor and the date of signing the inspection record, the Department of Health shall, according to the assessment of risk of deficiencies in pharmaceutical product quality and safety, send a notification of non-compliance with GDP principles and shall, according to the nature and severity of the violation, take one or several following actions:

a) Impose penalties against administrative violations in accordance with the law on penalties for administrative violations;

b) Revoke the issued certificate of eligibility for pharmacy business and the certificate of GDP compliance (if any) as prescribed in Article 40 of the Law on Pharmacy.

In case the distributor is ineligible for one or several business activities specified in the issued certificate of eligibility for pharmacy business, the Department of Health shall revoke the issued certificate of eligibility for pharmacy business in order to remove the business activity for which the distributor is ineligible and revoke the certificate of GDP compliance (if any) as prescribed in Article 40 of the Law on Pharmacy and issue the certificate of eligibility for pharmacy business which is conformable with the business activity for which the distributor is eligible.

4. Within 05 days from the date of concluding that the distributor maintains its compliance with GDP principles or issuing the decision on revocation of the issued certificate of eligibility for pharmacy business because the distributor fails to maintain its compliance with GDP principles, the Department of Health shall publish the GDP compliance status according to Clause 4 Article 8 of this Circular in the case of compliance with GDP principles or information concerning the revocation of the issued certificate of eligibility for pharmacy or the issued certificate of GDP compliance (if any) in the case of failure to maintain compliance with GDP principles on its website.

Article 11. Change control

1. During the interval between periodic inspections, the distributor shall apply for issuance of the certificate of eligibility for pharmacy business as prescribed in Point b Clause 1 Article 36 of the Law on Pharmacy or send a notification of change made using the Form No. 06 in the Appendix IV hereof in one of the following cases:

a) Change of one of the contents specified in Point b Clause 1 Article 39 of the Law on Pharmacy;

b) Change of the location of the storage facility at the same business location;

c) Addition of a storage facility at a new location at the same business location;

c) Expansion of the existing storage facility;

dd) Change in the structure and layout of the storage facility;

e) Change of the auxiliary system or change of principles of design and operation of the utility system which affects the storage conditions.

2. The distributor that makes the change specified in Point a Clause 1 of this Article shall submit an application for issuance of the certificate of eligibility for pharmacy business prescribed in Clauses 2 and 4 Article 38 of the Law on Pharmacy or the documents prescribed in Clause 2 Article 5 of this Circular in the case of a non-commercial distributor.

Procedures for inspecting, classifying and processing the result of inspection of compliance with GDP principles are specified in Articles 6, 7 and 8 of this Circular.

3. The distributor that makes the change specified in Points b and c Clause 1 of this Article shall submit a notification of change enclosed with technical documents corresponding to the change to the Department of Health.

a) The Department of Health shall carry out an on-site inspection at the distributor. In case the distributor complies with GDP principles, the Department of Health shall give a written consent to the change by the distributor.

b) Procedures for inspecting, classifying and processing the result of inspection of the distributor that makes the change mentioned in Point b Clause 1 of this Article are specified in Articles 6, 7 and 10 of this Circular;

c) Procedures for inspecting, classifying and processing the result of inspection of the distributor that makes the change mentioned in Point c Clause 1 of this Article are specified in Articles 6, 7 and 8 of this Circular;

4. The distributor that makes the change specified in Points d, dd and e Clause 1 of this Article shall submit a notification of change enclosed with technical documents corresponding to the change to the Department of Health. The Department of Health shall assess the notification of change sent by the distributor:

a) Within 10 days from the date on which the notification is received, the Department of Health shall send a written consent to the change in case the change complies with GDP principles;

b) Within 10 days from the date on which the notification is received, the Department of Health shall send a notification of corrective actions taken in case the change fails to comply with GDP principles;

c) Within 45 days from the date on which the notification sent by the Department of Health is received, the distributor shall complete corrective actions and send a notification enclosed with evidences (documents, images, videos, certificates) proving that the deficiencies specified in the notification are corrected;

d) Within 10 days from the date on which the notification of corrective actions taken enclosed with evidences (documents, images, videos, certificates) are received, the Department of Health shall assess the correction result and conclude GDP compliance status of the distributor:

- In case results of corrective actions make the distributor comply with GDP principles, the Department of Health shall send a written consent to the change;

- In case results of corrective actions show that the distributor still fails to comply with GDP principles, the Department of Health shall carry out an unscheduled inspection and process inspection result as prescribed in Article 12 of this Circular.

Article 12. Unscheduled inspections and audits of maintenance of compliance with principles of GDP for pharmaceutical products and pharmaceutical starting materials

1. Audits and inspections of maintenance of compliance of a distributor with GDP principles shall be carried out as prescribed by law.

2. The Department of Health shall carry out an unscheduled inspection of maintenance of GDP principles at a distributor in one of the following cases:

a) Results of corrective actions show that the distributor still fails to comply with GDP principles according to Point d Clause 4 Article 11 of this Circular;

b) The distributor that is in GDP degree 2 shall undergo at least 01 scheduled inspection within 3 years from the end of the previous inspection;

c) There are reflections, propositions or inspection/audit results about serious violation of GDP principles.

3. The Director of the Department of Health shall, according to the scope and purposes of the inspection, decide on members of an inspectorate.

4. Procedures for carrying out and processing unscheduled inspection result are specified in Articles 7 and 10 of this Circular.

Chapter V

INSPECTORATE CARRYING OUT INSPECTIONS OF MAINTENANCE OF COMPLIANCE WITH PRINCIPLES OF GDP FOR PHARMACEUTICAL PRODUCTS AND PHARMACEUTICAL STARTING MATERIALS

Article 13. Members and standards to be satisfied by members of an inspectorate

1. Members of an inspectorate include:

Head, secretary and other members selected by the Director of the Department of Health. The number of members shall not exceed 05.

2. An official that joins the inspectorate must satisfy the following standards:

a) He/she must be a public official or public employee of the Department of Health or a public official, public employee or official working under an employment contract in affiliates of the Department of Health;

b) He/she must obtain at least a bachelor's degree or Level 5 of VQF Advanced Diploma or Level 4 of VQF Diploma in pharmacy or medicine;

c) He/she has been provided with training in GPP and audit and inspection of compliance with GPP principles and has mastered GPP principles;

d) He/she must be honest and objective, strictly comply with regulations during the inspection and must not create any conflict of interest with the inspected distributor according to Clause 3 of this Article;

dd) The head of the inspectorate must obtain at least a bachelor’s degree in pharmacy and have at least 02 years’ experience in pharmacy management.

3. Rules for assessing the conflict of interest: a member of the inspectorate shall be deemed to involve a conflict of interest with the inspected distributor in one of the following cases:

a) He/she worked at the inspected distributor in the last 05 years;

b) He/she provided counseling the inspected distributor in the last 05 years;

c) He/she is having financial interests with the inspected distributor;

d) His/her spouse, parent, child, sibling or parent-in-law is working at the inspected distributor.

Article 14. Responsibilities and rights of an inspectorate

1. Responsibilities of an inspectorate

a) Inspect all operations of a distributor according to corresponding GDP principles prescribed in Article 3 of this Circular, updated GDP principles and relevant applicable regulations; specify inspection contents and discovered deficiencies, prepare GDP inspection records.

b) Inform inspection results or provide explanation for the GDP inspection report in case the distributor expresses its dissenting opinions about any content of the GDP inspection record;

c) Secure all information about the inspection and distribution activities of the distributor, unless otherwise agreed by the distributor or at the request of a competent authority in order to serve inspections and audits.

2. Rights of an inspectorate

a) Check entire area, storage facility and equipment of the distributor and check other areas in relation to the distribution of pharmaceutical products and pharmaceutical starting materials by the distributor;

b) Request the distributor to provide documents relating to its business activities, quality control and storage of pharmaceutical products and pharmaceutical starting materials;

c) Collect documentary evidences (by copying documents, taking pictures or recording videos) about the deficiencies discovered during the inspection;

d) Take pharmaceutical product and pharmaceutical starting material samples for quality control in accordance with regulations of law;

dd) Make records, request the distributor to partially or totally suspend distribution activities that commit any violation if violations that seriously affect the quality of one or several pharmaceutical products and pharmaceutical starting materials are found during the inspection; inform a competent person thereof.

Chapter VI

IMPLEMENTATION CLAUSE

Article 15. Effect

1. This Circular comes into force from March 26, 2018.

2. The Circular No. 48/2011/TT-BYT dated December 21, 2011 of the Minister of Health promulgating GDP for pharmaceutical products is null and void from the effective date of this Circular.

Article 16. Reference clause

In the cases where any of the legislative documents and regulations referred to in this Circular is amended or replaced, the newest one shall apply.

Article 17. Transition clauses

1. Regarding the wholesaler of pharmaceutical products or pharmaceutical starting materials that has been issued with the certificate of eligibility for pharmacy business or valid certificate of GDP compliance issued before the effective date of this Circular, the distributor is allowed to distribute pharmaceutical products and starting pharmaceutical products until the expiry of the certificate.

In case the certificate of eligibility for pharmacy business expires, the distributor shall apply for issuance of the certificate of eligibility for pharmacy business as prescribed in the Decree No. 54/2017/ND-CP and inspection of its compliance of GDP principles as prescribed in Chapter III of this Circular.

In case the certificate of GDP compliance expires before the expiry of the certificate of eligibility for pharmacy business, the distributor shall apply for inspection of maintenance of compliance with GDP principles according to Chapter IV of this Circular in order to keep operating until the expiry of the certificate of eligibility for pharmacy business.

2. Regarding the wholesaler of pharmaceutical products or pharmaceutical starting materials that has been issued with the indefinite term certificate of eligibility for pharmacy business, upon the expiry of the certificate of GDP compliance, the distributor shall apply for inspection of maintenance of compliance with GDP principles as prescribed in Chapter IV of this Circular.

3. Regarding the application for issuance of the certificate of eligibility for pharmacy business or application for the periodic inspection of compliance with GDP principles that has been submitted to the Department of Health before the effective date of this Circular, the Department of Health shall keep inspecting the distributor according to the GDP principles issued together with the Decision No. 48/2011/TT-BYT dated December 21, 2011 of the Minister of Health or this Circular.

Article 18. Responsibility for implementation

1. The Drug Administration of Vietnam shall:

a) take charge and cooperate with relevant units in disseminating this Circular;

b) take charge and cooperate with relevant units in providing guidelines for implementation of this Circular for the Departments of Health, health authorities and distributors within its jurisdiction;

c) consolidate and publish the list of nationwide distributors that has been issued with the certificate of eligibility for pharmacy business and certificate of GDP compliance on its website and update the status of the certificate of eligibility for pharmacy business and certificate of GDP compliance, and GDP compliance and other information according to Clause 4 Article 8 of this Circular within its jurisdiction;

d) publish updated GDP documents on its website and the web portal of the Ministry of Health;

dd) take charge or cooperate with the Ministry Inspectorate in inspecting and auditing compliance with GDP principles and take actions against violations within its power.

2. The Traditional Medicine Administration of Vietnam shall:

b) take charge and cooperate with relevant units in providing guidelines for implementation of this Circular for the Departments of Health, health authorities and distributors of traditional pharmaceutical and herbal starting materials and within its jurisdiction;

b) consolidate and publish the list of nationwide distributors that has been issued with the certificate of eligibility for pharmacy business and certificate of GDP compliance on its website and update the status of the certificate of eligibility for pharmacy business, and GDP compliance and other information specified in Clause 4 Article 8 of this Circular within its jurisdiction;

c) Carry out inspections and audits, and take actions against violations within its power.

3. Departments of Health shall:

a) cooperate with relevant units in disseminating this Circular and provide guidelines for its implementation for units within their area;

b) receive applications for issuance of the certificate of eligibility for pharmacy business or applications for inspection of GDP compliance, inspect GDP compliance, issue the certificate of eligibility for pharmacy business and certificate of GDP compliance to distributors within their area;

c) publish the list of distributors that has been issued with the certificate of eligibility for pharmacy business and certificate of GDP compliance and other information specified in Clause 4 Article 8 of this Circular on their website within their jurisdiction;

d) inspect and audit compliance of distributors within their area; take actions against violations within their power;

dd) periodically submit the list of distributors that has been issued with the certificate of eligibility for pharmacy business and status of GDP compliance according to Clause 4 Article 8 of this Circular to the Drug Administration of Vietnam.

4. Distributors shall:

a) organize the compliance with regulations of law on pharmacy and standards specified in this Circular.

b) ensure maintenance of compliance with GDP principles during their operation;

c) distribute pharmaceutical products and pharmaceutical starting materials within the licensed scope in accordance with regulations of law.

Difficulties that arise during the implementation should be reported to the Ministry of Health for consideration./.

PP. THE MINISTER
THE DEPUTY MINISTER

Truong Quoc Cuong

APPENDIX I

GOOD DISTRIBUTION PRACTICES FOR PHARMACEUTICAL PRODUCTS
(Enclosed with the Circular No. 03/2018/TT-BYT dated February 09, 2018 of the Minister of Health)

1. Introduction

2. Scope of the document

3. Glossary

4. General principles

5. Regulation of the distribution of pharmaceutical products

6. Organization and management

1. Introduction

Distribution is an important activity in the integrated supply-chain management of pharmaceutical products. Various people and entities are generally responsible for the handling, storage and distribution of such products. The objective of these guidelines is to assist in ensuring the quality and identity of pharmaceutical products during all aspects of the distribution process. These aspects include, but are not limited to, procurement, purchasing, storage, distribution, transportation, repackaging, relabelling, documentation and record-keeping practices.

This document sets out appropriate steps to assist in fulfilling the responsibilities involved in the different aspects of the distribution process within the supply chain and to avoid the introduction of counterfeits into the marketplace via the distribution chain. The relevant sections should be considered by various participants as applicable to the particular role that they play in the distribution of pharmaceutical products. When the distribution chain is interrupted by manufacturing steps such as repackaging and

relabelling, the principles of good manufacturing practices (GMP) should be applied to these processes.

Counterfeit pharmaceutical products are a real threat to public health and safety. Consequently, it is essential to protect the pharmaceutical supply chain against the penetration of such products. Weak points in the distribution processes of pharmaceutical products provide an avenue for counterfeit as well as illegally imported, stolen and substandard medicines to enter the supply chain. This is a concern in both developed and developing countries. The methods by which such products enter the supply chain have become increasingly complex and have resulted in the development of thriving secondary and grey markets throughout the world. The involvement of unauthorized entities in the distribution and sale of pharmaceutical products is a particular concern. Only a joint approach including all parties involved in the supply chain can be successful in the fight against counterfeit pharmaceutical products and, therefore, all parties active in the market should take an active part in collaborative activities.

These guidelines are intended to be applicable to all persons and outlets involved in any aspect of the distribution of pharmaceutical products from the premises of the manufacturer of the product to the person dispensing or providing pharmaceutical products directly to a patient or his or her agent. This includes all parties involved in trade and distribution of medicines, pharmaceutical manufacturers, including the manufacturers of finished products and pharmaceutical wholesalers as well as other parties such as brokers, suppliers, distributors, logistics providers, traders, transport companies and forwarding agents and their employees.

To maintain the original quality of pharmaceutical products, every party active in the distribution chain has to comply with the applicable legislation and regulations. Every activity in the distribution of pharmaceutical products should be carried out according to the principles of good manufacturing practice (GMP), good storage practice (GSP) and good distribution practice (GDP) as applicable.

2. Scope of the document

This document lays down guidelines for the distribution of pharmaceutical products, including products for which a prescription is required by the patient, products which may be provided to a patient without a prescription, biologicals and vaccines.

The principles for the distribution of starting materials (active pharmaceutical ingredients (APIs) and excipients) are also not covered here. These are laid down in the *WHO guidance Good trade and distribution practices for pharmaceutical starting materials* provided in the Appendix II of this Circular.

3. Glossary

"batch" means a defined quantity of pharmaceutical products supplied to a single order. A batch may include one or more parcels or containers and contain pharmaceutical products handled in one or more batches.

"contamination" means the undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or on to a starting material, intermediate or pharmaceutical product during handling, production, sampling, packaging or repackaging, storage or transportation.

"cross-contamination" means the contamination of a starting material, intermediate product or finished pharmaceutical product with another starting material or product during production, storage and transportation.

"first expiry/first out (FEFO)" means a distribution procedure that ensures that the stock with the earliest expiry date is distributed and/or used before an identical stock item with a later expiry date is distributed and/or used.

"intermediate product" means a partly processed product that must undergo further manufacturing steps before it becomes a bulk finished product

"pedigree" means a complete record that traces the ownership of and transactions relating to a pharmaceutical product as it is distributed through the supply chain.

"product recall" means a process for withdrawing or removing a pharmaceutical product from the pharmaceutical distribution chain because of defects in the product, complaints of serious adverse reactions to the product and/or concerns that the product is or may be counterfeit. The recall might be initiated by the manufacturer, importer, wholesaler, distributor or a responsible agency.

"quality assurance" means a wide-ranging concept covering all matters that individually or collectively influence the quality of a product. It is the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use.

"quality system" means an appropriate infrastructure, encompassing the organizational structure, procedures, processes and resources, and systematic actions necessary to ensure adequate confidence that a product (or services) will satisfy given requirements for quality.

"quarantine" means the status of pharmaceutical products isolated physically or by other effective means while a decision is awaited on their release, rejection or reprocessing.

"sampling" means operations designed to obtain a representative portion of a pharmaceutical product, based on an appropriate statistical procedure, for a defined purpose, e.g. acceptance of consignments or batch release.

"shelf-life" means the period of time during which a pharmaceutical product, if stored correctly, is expected to comply with the specification as determined by stability studies on a number of batches of the product. The shelf-life is used to establish the expiry date of each batch.

"standard operating procedure (SOP)" means an authorized, written procedure giving instructions for performing operations not necessarily specific to a given product but of a more general nature (e.g. equipment operation, maintenance and cleaning, validation, cleaning of premises and environmental control, sampling and inspection).

"storage" means the storing of pharmaceutical products up to the point of use.

"transit" means the period during which pharmaceutical products are in the process of being carried, conveyed, or transported across, over or through a passage or route to reach the destination.

"vehicles" include trucks, vans, buses, minibuses, cars, trailers, aircraft, railway carriages, boats and other means which are used to convey pharmaceutical products.

4. General principles

4.1 All parties involved in the distribution of pharmaceutical products have a responsibility to ensure that the quality of pharmaceutical products and the integrity of the distribution chain is maintained throughout the distribution process from the site of the manufacturer to the entity responsible for dispensing or providing the product to the patient or his or her agent.

4.2 The principles of GDP shall be treated as a means of establishing minimum standards applied to pharmaceutical product distributors.

4.3. The principles of GDP are applicable both to pharmaceutical products moving forward in the distribution chain from the manufacturer to the entity responsible for dispensing or providing pharmaceutical products to the patient and to products which are moving backwards in the chain, for example, as a result of the return or recall thereof.

4.4. The principles of GDP should also be adhered to in the case of pharmaceutical products which are donated.

4.5. All entities involved in the distribution process should apply due diligence with adherence to the principles of GDP, for example, in procedures relating to traceability and in recognition of security risks.

4.6. There should be collaboration between all parties including governments, customs agencies, law enforcement agencies, regulatory authorities, manufacturers, distributors and entities responsible for the supply of pharmaceutical products to patients to ensure the quality and safety of pharmaceutical products and prevent the exposure of patients to

counterfeit pharmaceutical products and pharmaceutical products that are not licensed to be sold or used.

5. Regulation of the distribution of pharmaceutical products

5.1. National legislation should be in place to regulate the activities of persons or entities involved in the distribution of pharmaceutical products.

5.2. The distributor or should be an entity that is appropriately authorized in terms of applicable legislation to perform the function(s) that it intends to perform and held accountable for the activities that it performs which relate to the distribution of pharmaceutical products.

5.3. Only distributors which hold the marketing authorization or import license should be entitled to distribute pharmaceutical products.

5.4. Distributors may only purchase pharmaceutical products from the establishment that possesses licenses for manufacturing, wholesaling or distribution of pharmaceutical products.

5.5. Distributors may only supply pharmaceutical products to other establishments licensed to supply pharmaceutical products or to health facilities or retailers.

5.6. When necessary, duties and responsibilities may only be delegated to entities which are suitably authorized in line with the national legislation. Duties and responsibilities should be specified in a written agreement. These delegated and contracted out activities should be documented in agreements or contracts. There should be a periodic audit of such activities with regard to application of GDP.

6. Organization and management

6.1. There should be an adequate organizational structure for each entity defined with the aid of an organizational chart. The responsibility, authority and interrelationships of all personnel should be clearly indicated.

6.2. Duties and responsibilities should be clearly defined and understood by the individuals concerned and recorded as written job descriptions. Employees in charge of storage and distribution of controlled pharmaceutical products should satisfy qualification requirements prescribed in relevant legislation. At every level of the supply chain, employees should be fully informed and trained in their duties and responsibilities.

6.3. A designated person should be appointed within the organization, who has defined authority and responsibility for ensuring that a quality system is implemented and maintained.

6.4. Managerial and technical personnel must have the authority and resources needed to carry out their duties and to set up and maintain a quality system, as well as to identify and correct deviations from the established quality system.

6.5. The responsibilities placed on any one individual should not be so extensive as to present any risk to product quality.

6.6. There should be arrangements in place to ensure that management and personnel are not subject to commercial, political, financial and other pressures or conflict of interest that may have an adverse effect on the quality of service provided or on the integrity of pharmaceutical products.

6.7. Safety procedures relating to all relevant aspects including the safety of personnel and property, environmental protection and product integrity, should be in place.

7. Personnel

7.1. All personnel involved in distribution activities should be trained and qualified in the requirements of GDP, as applicable.

Personnel should receive initial and continuing training relevant to their tasks, and be assessed as applicable, in accordance with a written training programme. In addition, training of the personnel should include the topic of product security, as well as aspects of product identification, the detection of counterfeits and the avoidance of counterfeits entering the supply chain. A record of all training, which includes details of subjects covered and participants trained, should be kept.

7.2. Key personnel involved in the distribution of pharmaceutical products should have the ability and experience appropriate to their responsibility for ensuring that pharmaceutical products are distributed properly.

7.3. There should be an adequate number of competent personnel involved in all stages of the distribution of pharmaceutical products in order to ensure that the quality of the product is maintained.

7.4. Regulations relating to the qualifications and experience of personnel should be adhered to.

- The warehouse-keeper for a storage facility must obtain at least an intermediate professional education diploma in pharmacy. Regarding the distributor of traditional pharmaceutical products, the warehouse-keeper must obtain at least an intermediate professional education diploma in traditional medicine or Certificate of traditional physician or pharmacist. Regarding the distributor of controlled pharmaceutical products (narcotics, psychotropics, and drug and radiopharmaceutical precursors), the warehouse-keeper must comply with relevant legislation. Personnel responsible for

inspection and control of pharmaceutical product quality must obtain at least a bachelor's degree in pharmacy.

- Regarding the distributor of vaccines and biologicals, the warehouse-keeper must obtain at least an intermediate professional education diploma in medicine/pharmacy. Personnel responsible for transport must obtain at least an intermediate professional education diploma in pharmacy. Personnel responsible for dispensation must obtain at least a basic diploma in medicine/pharmacy.

7.5. Personnel dealing with hazardous pharmaceutical products (such as highly active materials, radioactive materials, narcotics, and other hazardous, environmentally sensitive and/or dangerous pharmaceutical products, as well as products presenting special risks of abuse, fire or explosion) should be given specific training.

Personnel must be physically fit and be entitled to undergo periodic health check-ups. Personnel with infectious diseases should be isolated from storage and transport areas. First-aid procedures and equipment should be in place to handle potential incidents that may affect the safety of personnel.

7.6. Personnel involved in the distribution of pharmaceutical products should wear garments suitable for the activities that they perform. Personnel dealing with hazardous pharmaceutical products, including products containing materials that are highly active, toxic, infectious or sensitizing, should be provided with protective garments as necessary.

7.7. Appropriate procedures relating to personnel hygiene, relevant to the activities to be carried out, should be established and observed. Such procedures should cover health, hygiene and clothing of personnel.

7.8. Procedures and conditions of employment for employees, including contract and temporary staff, and other personnel having access to pharmaceutical products must be designed and administered to assist in minimizing the possibility of such products coming into the possession of unauthorized persons or entities.

7.9. Codes of practice and punitive procedures should be in place to prevent and address situations where persons involved in the distribution of pharmaceutical products are suspected of, or found to be implicated in, any activities relating to the misappropriation, tampering, diversion or counterfeiting of any product.

8. Quality system

8.1 Within an organization, quality assurance serves as a management tool. There should be a documented quality policy describing the overall intentions and requirements of the distributor regarding quality, as formally expressed and authorized by management.

8.2 The quality system should include an appropriate organizational structure, procedure, processes and resources and systematic actions necessary to ensure adequate confidence

that a product or service and its documentation will satisfy given requirements for quality. The totality of these actions is described as the quality system

8.3. The quality system should include provisions to ensure that the holder of the marketing authorization, entity identified on the label (the manufacturer, importer or distributor), the medicine/pharmacy authorities, as well as other relevant competent authorities, would be informed immediately in a case of confirmed or suspected counterfeiting of a pharmaceutical product. Such products should be stored in a secure, segregated area and clearly identified to prevent further distribution or sale.

8.4. Where electronic commerce (e-commerce) is used, i.e. electronic means are used for any of the distribution steps, defined procedures and adequate systems should be in place to ensure traceability and confidence in the quality of the pharmaceutical products concerned. Electronic transactions (including those conducted via the Internet), relating to the distribution of pharmaceutical products, should be performed only by authorized persons or entities.

8.5. Authorized procurement and release procedures for all administrative and technical operations performed should be in place to ensure that appropriate pharmaceutical products are sourced only from approved suppliers and distributed by approved entities.

8.6. Inspection, auditing and certification of compliance with a quality system (such as the applicable International Standardization Organization (ISO) series, or national or international guidelines) by external bodies is recommended. Such certification should not, however, be seen as a substitute for compliance with these GDP guidelines and the applicable principles of GMP relating to pharmaceutical products.

8.7. If measures to ensure the integrity of the pharmaceutical products in transit are in place, they should be managed properly. For example, if seal control programmes for transit shipment are used, numbers should be issued in a tracked and sequential manner, the integrity of seals should be monitored and numbers verified during transit and upon receipt. Written procedures should be in place for use in situations where pharmaceutical products are suspected of being or are found to be counterfeit.

8.8. Distributors should from time to time conduct risk assessments to assess potential risks to the quality and integrity of pharmaceutical products. The quality system should be developed and implemented to address any potential risks identified. The quality system should be reviewed and revised periodically to address new risks identified during a risk assessment.

Traceability of pharmaceutical products

8.9. Regulations should foster a safe, transparent and secure distribution system which includes product traceability throughout the supply chain. This is a shared responsibility among the parties involved. There should be procedures in place to ensure document traceability of products received and distributed, to facilitate product recall.

8.10. All parties involved in the supply chain should be identifiable, depending on the type of product and in accordance with regulations of law.

8.11. Measures should be in place to ensure that pharmaceutical products have documentation that can be used to permit traceability of the products throughout distribution channels from the manufacturer/importer to the entity responsible for selling or supplying the product to the patient or his or her agent. Records including expiry dates and batch numbers may be part of a secure distribution documentation enabling traceability.

Records for each batch should contain at least following information to ensure traceability:

- Receipt: Name and address of shippers/manufacturer, shipper's contact point, date of receipt, quantity received;

- Dispatch: List of name, address and contact point of the recipient, date of dispatch, quantity dispatched, inventory.

8.12. Ideally there should be a procedure in place for the creation and maintenance of a pedigree for pharmaceutical products.

Provision should be made for a visual and/or analytical identification of potential counterfeit products. The procedure to be followed when a suspected product is identified should include provisions for notification, as appropriate, of the holder of the marketing authorization, entity identified on the label (the manufacturer, importer or distributor), the appropriate medicine/pharmacy authorities, as well as other relevant competent authorities (see also section 19).

8.13. A suitable and, to the extent possible, internationally compatible product coding, identification system should be in place and developed in collaboration with the various parties involved in the supply chain.

9. Premises, warehousing and storage

9.1. Good storage practices (GSP) are applicable in all circumstances where pharmaceutical products are stored and throughout the distribution process. For additional guidance relating to the general principles of storage of pharmaceutical products, refer to the *WHO guide to good storage practices for pharmaceuticals*.

Storage areas:

9.2. Precautions must be taken to prevent unauthorized persons from entering storage areas. Employees should comply with the company policies to maintain a safe, secure and efficient working environment.

9.3. Storage areas should be of sufficient capacity to allow the orderly storage of the various categories of pharmaceutical products, namely commercial and non-commercial products, products in quarantine, and released, rejected, returned or recalled products as well as those suspected to be counterfeits. A storage area should be at least 30 m^2 with a capacity of 100m^3. In the case of a wholesaler of herbal ingredients and traditional pharmaceutical products, there should be a storage facility with a total area of at least 200m^2 and capacity of at least 600 m^3.

9.4. Storage areas should be designed or adapted to ensure appropriate and good storage conditions. In particular, they should be clean and dry and maintained within acceptable temperature limits. Pharmaceutical products should be stored off the floor and suitably spaced to permit cleaning and inspection. Pallets should be kept in a good state of cleanliness and repair.

9.5. Storage areas should be clean and free from accumulated waste and vermin. Organizations in charge of distribution must ensure that premises and storage areas are cleaned regularly. There should also be a written programme for pest control. The pest control agents used should be safe and there should be no risk of contamination of pharmaceutical products. There should be appropriate procedures for the clean-up of any spillage to ensure complete removal of any risk of contamination.

9.6. If sampling is performed in the storage area, it should be conducted in such a way as to prevent contamination or cross-contamination. Adequate cleaning procedures should be in place for the sampling areas.

9.7. Receiving and dispatch bays should protect pharmaceutical products from the weather. Receiving areas should be designed and equipped to allow incoming containers of pharmaceutical products to be cleaned, if necessary, before storage.

9.8. Where quarantine status is ensured by storage in separate areas, these areas must be clearly marked and access restricted to authorized personnel. Any system replacing physical quarantine should provide equivalent security. For example, computerized systems can be used, provided that they are validated to demonstrate security of access.

9.9. Physical or other equivalent validated (e.g. electronic) segregation should be provided for the storage of rejected, expired, recalled or returned products and suspected counterfeits. The products and the areas concerned should be appropriately identified.

9.10. Unless there is an appropriate alternative system to prevent the unintentional or unauthorized use of quarantined, rejected, returned, recalled or suspected counterfeit pharmaceutical products, separate storage areas should be assigned for their temporary storage until a decision as to their future has been made.

9.11. Pharmaceutical products, radioactive materials, controlled pharmaceutical products and starting materials (narcotic, psychotropics and precursors) and other hazardous, sensitive and/ or dangerous pharmaceutical products, as well as products presenting

special risks of abuse, fire or explosion (e.g. combustible or flammable liquids and solids and pressurized gases) should be stored in a dedicated area(s) that is subject to appropriate additional safety and security measures in accordance with relevant regulations specified in legislative documents.

Toxic pharmaceutical products, toxic pharmaceutical starting materials, pharmaceutical products and active ingredients on the list of banned substances in certain fields should be stored in a dedicated area(s), separated from other pharmaceutical products and arranged neatly to avoid any confusion, displayed recognizably and packaged in a manner that ensures no leakage of toxic pharmaceutical products and toxic pharmaceutical starting materials during transit.

9.12. Pharmaceutical products should be handled and stored in such a manner as to prevent contamination, mix-ups and cross-contamination.

9.13 A system should be in place to ensure that the pharmaceutical products due to expire first are sold and/or distributed first (first expiry/ first out (FEFO)). Exceptions may be permitted as appropriate, provided that adequate controls are in place to prevent the distribution of expired products.

9.14. Broken or damaged items should be withdrawn from usable stock and stored separately.

9.15. Storage areas should be provided with adequate lighting to enable all operations to be carried out accurately and safely.

Storage conditions and stock control:

9.16. Storage and handling conditions should comply with applicable national and local regulations.

9.17. Storage conditions for pharmaceutical products should be in compliance with the recommendations of the manufacturer.

9.18. Facilities should be available for the storage of all pharmaceutical products under appropriate conditions (e.g. environmentally controlled when necessary). Records should be maintained of these conditions if they are critical for the maintenance of the characteristics of the pharmaceutical product stored.

9.19. Records of temperature monitoring data should be available for review. There should be defined intervals for checking temperature. The equipment used for monitoring should be checked at suitable predetermined intervals and the results of such checks should be recorded and retained. All monitoring records should be kept for at least the shelf-life of the stored pharmaceutical product plus one year, or as required by law. Temperature mapping should show uniformity of the temperature across the storage facility. It is recommended that temperature monitors be located in areas that are most

likely to show fluctuations determined according to the results of an assessment of uniformity of the temperature across the storage facility. There should be at least 01 self-recording temperature monitor with an appropriate recording interval (once or twice an hour depending on season).

Regarding pharmaceutical products or pharmaceutical starting materials (e.g. vaccines and biologicals) that require special storage conditions, it is required to use equipment for monitoring of conditions (e.g. temperature) during storage and transportation. The use of monitoring equipment and data shall be recorded.

9.20. Equipment used for monitoring of storage conditions should also be calibrated at defined intervals.

9.21. Periodic stock reconciliation should be performed by comparing the actual and recorded stocks.

9.22. Stock discrepancies should be investigated in accordance with a specified procedure to check that there have been no inadvertent mix-ups, incorrect issues and receipts, thefts and/or misappropriations of pharmaceutical products. Documentation relating to the investigation should be kept for a predetermined period.

10. Vehicles and equipment

10.1. Vehicles and equipment used to distribute, store or handle pharmaceutical products should be suitable for their purpose and appropriately equipped to prevent exposure of the products to conditions that could affect their stability and packaging integrity, and to prevent contamination of any kind.

10.2. The design and use of vehicles and equipment must aim to minimize the risk of errors and permit effective cleaning and/or maintenance to avoid contamination, build-up of dust or dirt and/or any adverse effect on the quality of the pharmaceutical products being distributed. Appropriate cleaning should be performed, checked and recorded.

10.3. Where feasible, consideration should be given to adding technology, such as global positioning system (GPS) electronic tracking devices and engine-kill buttons to vehicles, which would enhance the security of pharmaceutical products while in the vehicle.

10.4. Dedicated vehicles and equipment should be used, where possible, when handling pharmaceutical products. Where non-dedicated vehicles and equipment are used, procedures should be in place to ensure that the quality of the pharmaceutical product will not be compromised.

10.5. Vehicles, equipment and containers should be selected and assessed appropriately to ensure that pharmaceutical products and pharmaceutical starting materials are stored under required conditions during transportation.

10.6. Procedures should be in place to ensure that the integrity of the products is not compromised during transportation.

10.7. Where third-party carriers are used, distributors should develop written agreements with carriers to ensure that appropriate measures are taken to safeguard pharmaceutical products, including maintaining appropriate documentation and records. Such agreements should be in line with regulatory requirements.

10.8. Defective vehicles and equipment should not be used and should either be labelled as such or removed from service.

10.9. There should be procedures in place for the operation and maintenance of all vehicles and equipment involved in the distribution process, including cleaning and safety precautions.

10.10. Vehicles, containers and equipment should be kept clean and dry and free from accumulated waste. Organizations in charge of distribution must ensure that vehicles used are cleaned regularly.

10.11. Vehicles, containers and equipment should be kept free from rodents, vermin, birds and other pests. There should be written programmes and records for such pest control. The cleaning and fumigation agents used should not have any adverse effect on product quality.

10.12. Equipment chosen and used for the cleaning of vehicles should not constitute a source of contamination. Agents used for the cleaning of vehicles should be approved by management.

10.13. Special attention should be paid to the design, use, cleaning and maintenance of all equipment used for the handling of pharmaceutical products which are not in a protective shipping carton or case.

10.14. Where special storage conditions (e.g. temperature and/or relative humidity), different from, or limiting, the expected environmental conditions, are required during transportation, these should be provided, checked, monitored and recorded. All monitoring records should be kept for a minimum of the shelf-life of the product distributed plus one year, or as required by law. Records of monitoring data should be made available for inspection by the regulatory or other oversight body.

10.15. Equipment used for monitoring conditions, e.g. temperature and humidity, within vehicles and containers should be calibrated at regular intervals.

10.16. Vehicles and containers should be of sufficient capacity to allow orderly storage of the various categories of pharmaceutical products during transportation.

10.17. Where possible, mechanisms should be available to allow for the segregation during transit of rejected, recalled and returned pharmaceutical products as well as those suspected of being counterfeits. Such goods should be securely packaged, clearly labelled, and be accompanied by appropriate supporting documentation.

10.18. Measures should be in place to prevent unauthorized persons from entering and/or tampering with vehicles and/or equipment, as well as to prevent the theft or misappropriation thereof.

11. Shipment containers and container labelling

11.1. Pharmaceutical products should be stored and distributed in shipment containers that have no adverse effect on the quality of the products, and that offer adequate protection from external influences, including contamination.

11.2. Shipping containers should bear labels providing sufficient information on handling and storage conditions and precautions to ensure that the products are properly handled and secure at all times. The shipment container should enable identification of the container's contents and source.

11.3. The need for any special transport and/or storage conditions should be stated on the shipment container label. If a pharmaceutical product is intended for transfer to areas outside the control of the manufacturer's products management system, the name and address of the manufacturer, special transport conditions and any special legal requirements, including safety symbols, should also be included on the container label.

11.4. Normally, internationally and/or nationally accepted abbreviations, names or codes should be used in the labelling of shipment containers.

11.5. Special care should be taken when using dry ice in shipment containers. In addition to safety issues it must be ensured that the pharmaceutical product does not come into contact with the dry ice, as it may have an adverse effect on the quality of the product.

11.6. Written procedures should be available for the handling of damaged and/or broken shipment containers. Particular attention should be paid to those containing potentially toxic and hazardous products

12. Dispatch and receipt

12.1. Pharmaceutical products should only be sold and/or distributed to persons or entities that are authorized to acquire such products in accordance with the applicable regulations of law. Written proof of such authority must be obtained prior to the distribution of products to such persons or entities.

12.2. Prior to the dispatch of the pharmaceutical products, the supplier should ensure that the person or entity, e.g. the contract acceptor for transportation of the pharmaceutical

products, is aware of the pharmaceutical products to be distributed and complies with the appropriate storage and transport conditions.

12.3. The dispatch and transportation of pharmaceutical products should be undertaken only after the receipt of a valid delivery order or material replenishment plan, which should be documented.

12.4. Written procedures for the dispatch of pharmaceutical products should be established. Such procedures should take into account the nature of the product as well as any special precautions to be observed. Pharmaceutical products under quarantine will require release for dispatch by the person responsible for quality (see 6.3).

12.5. Records for the dispatch of pharmaceutical products should be prepared and should include at least the following information:

- date of dispatch;

- complete business name and address (no acronyms), type of entity responsible for the transportation, telephone number and names of contact persons;

- complete business name, address (no acronyms), and status of the addressee (e.g. retail pharmacy, hospital or community clinic);

- a description of the products including, e.g. name, dosage form and strength (if applicable);

- quantity of the products, i.e. number of containers and quantity per container (if applicable);

- applicable transport and storage conditions;

- a unique number to allow identification of the delivery order; and

- assigned batch number and expiry date (where not possible at dispatch, this information should at least be kept at receipt to facilitate traceability).

12.6. Records of dispatch should contain enough information to enable traceability of the pharmaceutical product. Such records should facilitate the recall of a batch of a product, if necessary, as well as the investigation of counterfeit or potentially counterfeit pharmaceutical products.

12.7. In addition, the assigned batch number and expiry date of pharmaceutical products should be recorded at the point of receipt to facilitate traceability.

12.8. Methods of transportation, including vehicles to be used, should be selected with care, and local conditions should be considered, including the climate and any seasonal

variations experienced. Delivery of products requiring controlled temperatures should be in accordance with the applicable storage and transport conditions.

12.9. Delivery schedules should be established and routes planned, taking local needs and conditions into account. Such schedules and plans should be realistic and systematic. Security risks should also be taken into account when planning the schedules and routes of the delivery.

12.10. Care should be taken to ensure that the volume of pharmaceutical products ordered does not exceed the capacity of storage facilities at the destination.

12.11. Vehicles and containers should be loaded carefully and systematically, where applicable on a first-out/last-in basis, to save time when unloading, prevent physical damage and reduce security risks. Extra care should be taken during loading and unloading of cartons to avoid damage.

12.12. Pharmaceutical products should not be supplied or received after their expiry date, or so close to the expiry date that this date is likely to be reached before the products are used by the consumer.

12.13. Incoming shipments should be examined to verify the integrity of the container/closure system, ensure that tamper-evident packaging features are intact, and that labelling appears intact

13. Transportation and products in transit

13.1. Products and shipment containers should be secured to prevent or provide evidence of unauthorized access. Vehicles and operators should be provided with additional security, as appropriate, to prevent theft and other misappropriation of products during transportation.

13.2. Product shipments should be secured and include the appropriate documentation to facilitate identification and verification of compliance with regulatory requirements. Policies and procedures should be followed by all persons involved in the transportation, to secure pharmaceutical products.

13.3. The people responsible for the transportation of pharmaceutical products should be informed about all relevant conditions for storage and transportation. These requirements should be adhered to throughout transportation and at any intermediate storage stages.

13.4. Pharmaceutical products should be stored and transported in accordance with procedures such that:

- The identity of the product is not lost;

- The product does not contaminate and is not contaminated by other products;

- Adequate precautions are taken against spillage, breakage, misappropriation and theft;

- Appropriate environmental conditions are maintained, e.g. using cold chain for thermolabile products.

13.5. The required storage conditions for pharmaceutical products should be maintained within acceptable limits during transportation. If a deviation has been noticed during transportation by the person or entity responsible for transportation, this should be reported to the distributor and recipient. In cases where the recipient notices the deviation, it should be reported to the distributor. Where necessary, the manufacturer of the pharmaceutical product should be contacted for information about appropriate steps to be taken.

13.6. Where special conditions are required during transportation that are different from or limit the given environmental conditions (e.g. temperature and humidity) these should be provided by the manufacturer on the labels, monitored and recorded.

13.7. Written procedures should be in place for investigating and dealing with any failure to comply with storage requirements, e.g. temperature deviations.

13.8. Transportation and storage of pharmaceutical products containing hazardous substances, such as toxic, radioactive material, and other dangerous pharmaceutical products presenting special risks of abuse, fire or explosion (e.g. combustible or flammable liquids, solids and pressurized gases) should be stored in safe, dedicated and secure areas, and transported in safe, suitably designed, secured containers and vehicles. In addition, the requirements of applicable international agreements and laws should be met.

13.9. Products containing narcotics and other dependence-producing substances (psychotropics and precursors) should be transported in safe and secure containers and vehicles and be stored in safe and secure areas. In addition, the requirements of applicable international agreements and laws should be complied with.

13.10. Spillages should be cleaned up as soon as possible to prevent possible contamination, cross-contamination and hazards. Written procedures should be in place for the handling of such occurrences.

13.11 Physical or other equivalent (e.g. electronic) segregation should be provided for the storage and distribution during transit of rejected, expired, recalled or returned pharmaceutical products and suspected counterfeits. The products should be appropriately identified, securely packaged, clearly labelled and be accompanied by appropriate supporting documentation.

13.12. The interiors of vehicles and containers should remain clean and dry while pharmaceutical products are in transit.

13.13. Packaging materials and shipment containers should be of suitable design to prevent damage of pharmaceutical products during transport. Seal control programmes should be in place and managed properly.

13.14. Drivers of vehicles should identify themselves and present appropriate documentation to demonstrate that they are authorized to transport the load.

13.15. Damage to containers and any other event or problem that occurs during transit must be recorded and reported to the relevant department, entity or authority, and investigated.

13.16. Pharmaceutical products in transit must be accompanied by the appropriate documentation.

14. Documentation

14.1. Written instructions and records which document all activities relating to the distribution of pharmaceutical products, including all applicable receipts and issues (invoices) should be available. Records should be kept for seven years, unless otherwise prescribed by law.

14.2. Distributors should keep records of all pharmaceutical products received. Records should contain at least the following information:

- Name of the pharmaceutical product; strength, content, packing specifications, marketing authorization, certificate of analysis, manufacturing date, batch number, expiry date.

- Name of the manufacturer/importer (if any), supplier, quantity received, date of receipt; receipt record.

- Name and address, telephone, email (if any) if the buyer, quanity dispatched for sale, date of dispatch, pharmaceutical product delivery record.

14.3. Procedures should be established and maintained for the preparation, review, approval, use of and control of changes to all documents relating to the distribution process. Procedures must be in place for both internally generated documents and those from external sources.

14.4. Documents, and in particular instructions and procedures relating to any activity that could have an impact on the quality of pharmaceutical products, should be designed, completed, reviewed and distributed with care.

14.5. The title, nature and purpose of each document should be clearly stated. The contents of documents should be clear and unambiguous. Documents should be laid out in an orderly fashion and be easy to check.

14.6. All documents should be completed, approved, signed (as required) and dated by an appropriate authorized person(s) and should not be changed without the necessary authorization.

14.7. The nature, content and retention of documentation relating to the distribution of pharmaceutical products and any investigations conducted and action taken, should comply with relevant regulations of law. Where such regulations are not in place, the documents should be retained for at least one year after the expiry date of the product concerned.

14.8. The distributor must establish and maintain procedures for the identification, collection, indexing, retrieval, storage, maintenance, disposal of and access to all applicable documentation.

14.9. All records must be readily retrievable, and be stored and retained using facilities that are safeguarded against unauthorized modification, damage, deterioration and/or loss of documentation.

14.10. Documents should be reviewed regularly and kept up to date. When a document has been revised, a system should exist to prevent inadvertent use of the superseded version.

14.11. There should be computers connected to the Internet and software should be used to manage distribution activities. Mechanisms should exist to allow for transfer of information, including quality or regulatory information, between a manufacturer and a customer, as well as the transfer of information to the relevant regulatory authority as required.

14.12. Records relating to storage of pharmaceutical products should be kept and be readily available upon request in accordance with the *WHO guidelines on good storage practice for pharmaceuticals.*

14.13. Permanent records, written or electronic, should exist for each stored product indicating recommended storage conditions, any precautions to be observed and retest dates. Pharmacopoeial requirements and current national regulations concerning labels and containers should be respected at all times.

Documents relating to narcotic, psychotropics, precursors, combined pharmaceutical products containing narcotic active ingredients, combined pharmaceutical products containing psychotropic active ingredients, combined pharmaceutical products containing precursors; toxic pharmaceutical products, toxic pharmaceutical starting materials, pharmaceutical products and active ingredients on the list of banned substances in certain fields are prescribed by law.

14.14. Procedures should be in place for temperature mapping, security services to prevent theft or tampering with goods at the storage facilities, destruction of unsalable or unusable stocks and on retention of the records.

14.15. Where the records are generated and kept in electronic form, back ups should be maintained to prevent any accidental data loss.

15. Repackaging and relabelling

15.1. Repackaging and relabelling of pharmaceutical products should be limited, as these practices may represent a risk to the safety and security of the supply chain.

15.2. Where they do occur, they should only be performed by entities appropriately authorized to do so and in compliance with the applicable GMP principles.

15.3. In the event of repackaging by companies other than the original manufacturer, these operations should result in at least equivalent means of identification and authentication of the products.

15.4. Procedures should be in place for the secure disposal of original packaging.

16. Complaints

16.1. There should be a written procedure in place for the handling of complaints. A distinction should be made between complaints about a product or its packaging and those relating to distribution. In the case of a complaint about the quality of a product or its packaging, the original manufacturer and/or marketing authorization holder should be informed as soon as possible.

16.2. All complaints and other information concerning potentially defective and potentially counterfeit pharmaceutical products should be reviewed carefully according to written procedures describing the action to be taken, including the need to consider a recall where appropriate.

16.3. Any complaint concerning a material defect should be recorded and thoroughly investigated to identify the origin or reason for the complaint (e.g. repackaging procedure or original manufacturing process).

16.4. If a defect relating to a pharmaceutical product is discovered or suspected, consideration should be given to whether other batches of the product should also be checked.

16.5. Where necessary, appropriate follow-up action should be taken after investigation and evaluation of the complaint. There should be a system in place to ensure that the complaint, the response received from the original product manufacturer, or the results of the investigation of the complaint, are shared with all the relevant parties.

16.6. Product quality problems or suspected cases of counterfeit products should be documented and the information should be shared with the competent authorities.

17. Recalls

17.1. There should be a system, which includes a written procedure, to effectively and promptly recall pharmaceutical products known or suspected to be defective or counterfeit, with a designated person(s) responsible for recalls. The system should comply with the guidance issued by the regulatory authority. This procedure should be checked regularly and updated as necessary.

17.2. The original manufacturer and/or marketing authorization holder should be informed in the event of a recall. Where a recall is instituted by an entity other than the original manufacturer and/or marketing authorization holder, consultation with the original manufacturer and/or marketing authorization holder should, where possible, take place before the recall is instituted.

Information on a recall should be shared with the appropriate regulatory authority. If a recall of the original product is necessary because of a counterfeited product which is not easily distinguishable from the original product, the manufacturer of the original product and the relevant health authority should be informed.

17.3. The effectiveness of the arrangements for recalls should be evaluated at regular intervals. All recalled pharmaceutical products should be stored in a secure, segregated area pending appropriate action.

17.4. Recalled pharmaceutical products should be segregated during transit and clearly labelled as recalled products. Where segregation in transit is not possible, such goods must be securely packaged, clearly labelled, and be accompanied by appropriate documentation.

17.5. The particular storage conditions applicable to a pharmaceutical product which is subject to recall should be maintained during storage and transit until such time as a decision has been made regarding the fate of the product in question.

17.6. All customers and competent health authorities of the area to which a given pharmaceutical product may have been distributed should be informed promptly of any intention to recall the product because it is, or is suspected to be, defective or counterfeit.

17.7. All records should be readily available to the designated person(s) responsible for recalls. These records should contain sufficient information on pharmaceutical products supplied to customers (including exported products).

17.8. The progress of a recall process should be recorded and a final report issued, which includes a reconciliation between delivered and recovered quantities of products.

17.9. When necessary emergency recall procedures should be implemented.

18. Returned products

18.1. A distributor should receive pharmaceutical product returns or exchanges pursuant to the terms and conditions of the agreement between the distributor and the recipient. Both distributors and recipients should be accountable for administering their returns process and ensuring that the aspects of this operation are secure and do not permit the entry of counterfeit products.

18.2. The necessary assessment and decision regarding the disposition of such products must be made by a suitably authorized person. The nature of the product returned to the distributor, any special storage conditions required, its condition and history and the time elapsed since it was issued, should all be taken into account in this assessment. Where any doubt arises over the quality of a pharmaceutical product, it should not be considered suitable for reissue or reuse.

18.3. Provision should be made for the appropriate and safe transport of returned products in accordance with the relevant storage and other requirements.

18.4. Rejected pharmaceutical products and those returned to a distributor should be appropriately identified and handled in accordance with a procedure which involves at least:

- the physical segregation of such pharmaceutical products in quarantine in a dedicated area; or

- other equivalent (e.g. electronic) segregation.

This is to avoid confusion and prevent distribution until a decision has been taken with regard to their disposition. The particular storage conditions applicable to a pharmaceutical product which is rejected or returned should be maintained during storage and transit until such time as a decision has been made regarding the product in question.

18.5. Provision should be made for the appropriate and safe transport of rejected pharmaceutical products prior to their disposal.

18.6. Destruction of pharmaceutical products should be done in accordance with regulations of law regarding disposal of such products, and with due consideration to protection of the environment.

18.7. Records of all returned, rejected and/or destroyed pharmaceutical products should be kept for a predetermined period.

19. Counterfeit pharmaceutical products

19.1. Counterfeit pharmaceutical products found in the distribution chain should be kept apart from other pharmaceutical products to avoid any confusion. They should be clearly labelled as not for sale. Pharmacy authorities, competent authorities and the holder of the marketing authorization for the original product should be informed immediately.

19.2. The sale and distribution of a suspected counterfeit pharmaceutical product should be suspended and the regulatory authority notified without delay.

19.3. Upon confirmation of the product being counterfeit, a formal decision should be taken on its disposal, ensuring that it does not re-enter the market, and the decision recorded.

20. Contract activities

20.1. Any activity relating to the distribution of a pharmaceutical product which is delegated to another person or entity should be performed by parties appropriately authorized for that function and in accordance with the terms of a written contract.

20.2. The contract should define the responsibilities of each party including observance of the principles of GDP and relevant warranty clauses. It should also include responsibilities of the contractor for measures to avoid the entry of counterfeit medicines into the distribution chain, such as by suitable training programmes.

20.3. All contract accepters should comply with the requirements in these guidelines.

20.4. Subcontracting may be permissible, under certain conditions and subject to the written approval of the contract giver; however, the subcontractors should be authorized for the function.

20.5. Contract accepters should be audited periodically.

21. Self-inspection

21.1. The quality system should include self-inspections. These should be conducted to monitor implementation and compliance with the principles of GDP and, if necessary, to trigger corrective and preventive measures.

21.2. Self-inspections should be conducted in an independent and detailed way by a designated, competent person.

21.3. The results of all self-inspections should be recorded. Reports should contain all observations made during the inspection and, where applicable, proposals for corrective measures. There should be an effective follow-up programme. Management should evaluate the inspection report and the records of any corrective actions taken./.

APPENDIX II

GOOD DISTRIBUTION PRACTICES FOR PHARMACEUTICAL STARTING MATERIALS

(Enclosed with the Circular No. 03/2018/TT-BYT dated February 09, 2018 of the Minister of Health)

1. Introduction

Good manufacturing practices for active pharmaceutical ingredients were published in 2000 by The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), in ICH Q7. Section 17 of this ICH text includes guidelines for agents, brokers, traders, distributors, repackers and relabellers. This section was written based on the outcome of the World Health Organization (WHO) investigation into deaths resulting from the intentional relabelling of industrial grade ethylene glycol as pharmaceutical grade material. This material was

subsequently formulated into a paediatric medicine that caused many deaths. Section 17 of this good manufacturing practice (GMP) guide for active pharmaceutical ingredients (APIs) applies to any party other than the original manufacturer which may trade and/or take possession, repack, relabel, manipulate, distribute or store an API or API intermediate. The scope of ICH Q7 does not include excipients.

Following a number of incidents involving diethylene glycol and a World Health Assembly resolution (WHA52.19), WHO published the *Good trade and distribution practices for pharmaceutical starting materials* in 2004 (*2*). At the time of publication of these guidelines, WHO had not yet adopted the text from ICH Q7 as GMP for APIs. The WHO guidance for excipients, published in 1999, did not cover trade and distribution practices for excipients.

In 2010, WHO published *Good manufacturing practices for active pharmaceutical ingredients*, which reflect the text from ICH Q7 and include Section 17 of that document, to replace the existing WHO GMP for APIs.

The WHO Expert Committee on Specifications for Pharmaceutical Preparations discussed the revision of the *Good trade and distribution practices for pharmaceutical starting materials* at several meetings. The scope of this WHO guidance on *Good trade and distribution practices for pharmaceutical starting materials* is applicable to any ingredient that is used in the manufacture of a medicinal product, including APIs, excipients and any others.

Note: Material deriving from non-pharmaceutical grades, such as food, industrial or technical grades, should not be designated as pharmaceutical grade when it is not produced under the required manufacturing conditions and quality system. For finished pharmaceutical products (FPPs), details can be found in the WHO good distribution practices for pharmaceutical products.

2. Quality management

2.1 Within an organization, quality assurance serves as a management tool. In contractual situations, quality assurance also serves to generate confidence in the supplier. There should be a documented quality policy describing the overall intentions and direction of the distributor regarding quality, which should be formally expressed and authorized by management. The quality policy should clearly indicate that the distributor implements and maintains good trade and distribution practices (GTDP) as described in these guidelines, within the organization and its services.

2.2. Quality management should include:

a) an appropriate infrastructure or “quality system”, encompassing the organizational structure, procedures, processes and resources. The size, structure and complexity of the distributor and its activities should be taken into consideration when developing or modifying the quality system;

b) an independent quality unit (or designee), which is responsible for all quality-related matters;

c) an appropriate quality risk management (QRM) system to enable a systematic process for the assessment, control, communication and review of risks to the quality of the product. The extent of application of the QRM system should reflect the operations performed;

d) a validation/qualification system to ensure that the resulting product is capable of meeting the requirements for the specified application;

dd) systematic actions necessary to ensure adequate confidence that a material (or service) and relevant documentation will satisfy given requirements for quality – the totality of these actions is termed quality assurance;

e) a clear documented procedure for selecting, approving, disqualifying and re-approving suppliers of pharmaceutical starting materials and services;

g) a robust deviation management and change control programme designed to ensure that quality is continually assessed and maintained: these should include a customer notification where appropriate;

h) a system ensuring traceability of products and associated documentation throughout the entire supply chain.

2.3. The system should cover for example, but not be limited to, the quality assurance principles in these guidelines.

2.4. All parties involved in the manufacture and supply chain must exercise responsibility to ensure the quality and safety of the materials and products, and that they are fit for their intended use in accordance with their specifications.

2.5. The responsibilities placed on any one individual should not be so extensive as to present any risk to quality. In the event of a supplier having a limited number of staff, some duties may be delegated or contracted out to designated persons who are appropriately qualified. There should, however, be no gaps or unexplained overlaps related to the application of GTDP for pharmaceutical starting materials as described in these guidelines.

2.6. Where electronic commerce (e-commerce) is used, defined procedures and adequate systems should be in place to ensure confidence in the quality of the material and its traceability.

2.7. Authorized release procedures should be in place to ensure that when material is released for its intended purpose, it is of an appropriate quality, meets its specifications and is sourced from approved suppliers.

2.8. Implementation of QRM principles using appropriate tools such as hazard analysis and critical control point (HACCP); inspection and certification of compliance with an appropriate quality system such as applicable International Organization for Standardization (ISO) series, and recognition of compliance with national and/or regional standards by external bodies is recommended. However, this should not be seen as a substitute for the implementation of these guidelines or for conforming, for example, to pharmaceutical GMP and good storage practices (GSP) requirements, as applicable.

2.9. A system should be in place for the performance of regular internal audits with the aim of continuous improvement. The findings of the audit and any corrective and preventive actions taken, including verification of their effectiveness, should be documented and brought to the attention of the responsible management.

3. Organization and personnel

3.1. There should be an adequate organizational structure and a sufficient number of personnel should be employed to carry out all the tasks for which the supplier is responsible

3.2. There should be sufficient organizational structure and personnel in place for the performance of tasks within the jurisdiction of the supplier. All personnel should be aware of the principles of the appropriate guidelines, including but not limited to GTDP.

3.3. Individual responsibilities should be clearly defined, understood by the individuals concerned and recorded in writing (as job descriptions or in a contract). Certain activities, such as supervision of performance of activities in accordance with local legislation, may require special attention. Personnel should be suitably qualified, trained and authorized to undertake their duties and responsibilities.

3.4. Personnel should receive initial and continuing training relevant to their tasks. Training should be provided by qualified trainers in accordance with a training programme. The effectiveness of training should be verified where appropriate. Training records should be maintained. All personnel should be motivated to support the establishment and maintenance of quality standards.

3.5. Personnel dealing with hazardous materials (such as highly active, toxic, infectious or sensitizing materials) should be given specific training and should be provided with the necessary protective equipment. Documented policies and procedures for the use of personal protective equipment should be followed to decrease exposure of workers working directly with products and those in the immediate environment.

3.6. Personnel who may be exposed to materials from open containers should maintain good hygiene, have no open wounds and should wear appropriate protective garments, gloves, masks and goggles

4. Premises

4.1. Premises, including laboratory facilities, must be located, designed, constructed, adapted and maintained to suit the operations to be carried out. Their layout and design must aim to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid contamination, cross-contamination, mix ups, build-up of dust, dirt or waste and, in general, any adverse effect on the quality of materials.

4.2. Measures should be in place to prevent unauthorized persons from entering the premises.

4.3. Premises should be designed, equipped and maintained so as to afford maximum protection against the entry of insects, rodents or other animals. A pest control programme should be implemented and maintained. Its effectiveness should be monitored.

4.4. Suitable supporting facilities and utilities (such as air control, ventilation and lighting) should be in place and appropriate to the activities performed, in order to avoid contamination, cross-contamination and degradation of the material. Utilities that could affect product quality should be identified and monitored.

4.5. If sampling of pharmaceutical starting materials is performed, the sampling area should be separate and in a controlled environment. Sampling should only be performed in a storage area if it can be conducted in such a way that there is no risk of contamination or cross-contamination. Adequate cleaning procedures should be in place for the sampling areas.

5. Procurement, warehousing and storage

Note: GSP are applicable in all circumstances in which, and in all areas where, materials are stored.

5.1. Materials should be purchased from approved suppliers in accordance with mutually agreed formal specifications.

5.2. Actions should be taken to minimize the risk of falsified or non-conforming materials entering the supply chain.

5.3. There should be authorized procedures describing the activities relating to the receipt, storage and distribution of materials. Steps should be taken to ensure and document that the arriving consignment is correct and that the products originate from approved suppliers. Deliveries should be examined to check that containers have not been damaged, altered or tampered with, and that closures and security seals are intact.

5.4. Storage areas should have sufficient capacity to allow orderly storage of the various categories of materials.

5.5. Receipt and dispatch bays should be equipped with the means to protect materials from adverse environmental conditions. Reception areas should be designed and equipped to allow containers of incoming materials to be cleaned before storage if appropriate. Upon receipt, material should be segregated until released by the quality unit.

5.6. Segregated areas should be provided for the storage of received, quarantined, rejected, recalled and returned material, including materials with damaged packaging. Any system replacing physical segregation, such as electronic segregation based on a computerized system, should provide equivalent security and should be appropriately qualified and validated.

5.7. The storage areas should be kept clean and dry.

5.8. Segregated areas and materials should be appropriately identified.

5.9. The required storage conditions, as specified for the material, should be maintained within acceptable limits at all times during storage. Appropriate checks to confirm that required shipping conditions have been met should be conducted as soon as possible after receipt.

The product should be transferred to appropriate storage facilities immediately after checks to be made in the goods receiving area have been conducted.

5.10. Where special storage conditions are required (e.g. particular temperature, humidity or protection from light) these should be provided, monitored and recorded as appropriate.

Temperature mapping should show uniformity of the temperature across the storage facility. It is recommended that temperature monitors be located in areas that are most likely to show fluctuations determined according to the results of an assessment of uniformity of the temperature across the storage facility. There should be at least 1 self-recording temperature monitor with an appropriate recording frequency (once or twice an hour depending on season).

5.11. Radioactive materials, controlled pharmaceutical starting materials (narcotic drugs, psychotropic drugs and precursors) and other hazardous, sensitive and/or dangerous active ingredients, as well as active ingredients presenting special risks of abuse, fire or explosion (e.g. combustible or flammable liquids and solids and pressurized gases) should be stored in a dedicated area(s) that is subject to appropriate additional safety and security measures in accordance with relevant regulations specified in legislative documents.

Toxic pharmaceutical starting materials and active ingredients on the list of banned substances in certain fields should be stored in a dedicated area(s), separated from other pharmaceutical products and arranged neatly to avoid any confusion, displayed

recognizably and packaged in a manner that ensures no leakage of toxic pharmaceutical products and toxic pharmaceutical starting materials during transportation.

5.12. Special attention should be given to the design, use, cleaning and maintenance of all equipment for bulk handling and storage, such as tanks and silos.

5.13. Products should be packed in such a way as to avoid breakage, contamination, tampering or theft. The packing should be adequate to maintain the quality of the product during transport. If special shipping conditions have to be met they should be defined, provided and controlled. The containers in which products are shipped should be sealed and should clearly indicate the authenticity of the product and its supplier.

5.14. Spillages should be cleaned up as soon as possible to prevent possible cross-contamination and hazard.

5.15. Provision should be made for the proper and safe storage of waste materials awaiting disposal. Toxic substances and flammable materials should be stored in suitably designed, separate, closed containers in enclosed areas, taking into account the relevant national legislation.

5.16 A default system should be in place to ensure that those materials due to expire first are sold or distributed first (earliest expiry/first out). Where no expiry dates are specified for the materials, the first in/first out principle should be applied.

5.17. A process should be in place to ensure that materials that have reached their expiry or retest date should be withdrawn immediately from saleable stock. Materials with a retest date should be retested according to the appropriate specifications. Materials with an expiry date should not be retested or used after that date.

5.18. Stock inventory should be checked regularly, at least for quantity, overall condition and retesting or expiration dates. Any discrepancies should be investigated.

5.19. Controls should be in place to ensure that the correct product is picked, packed and distributed. The material should have an appropriate remaining shelf life. All batch numbers should be recorded.

5.20. Storage areas should be clean and free from accumulated waste and from vermin. A written sanitation programme should be available, indicating the frequency of cleaning and the methods to be used to clean the premises and storage areas.

6. Equipment

6.1. Equipment must be located, designed, constructed, adapted, qualified, used, cleaned and maintained to suit the operations to be carried out. Its layout, design and use should aim to minimize the risk of errors and permit effective cleaning and maintenance so as to

avoid cross-contamination, build-up of dust or dirt and any adverse effect on the quality of materials.

6.2. Defective equipment should not be used and should either be removed or labelled as defective. Equipment should be disposed of in such a way as to prevent any misuse.

6.3. The status of the equipment should be readily identifiable.

6.4. Fixed pipework should be clearly labelled to indicate the contents and, where applicable, the direction of flow.

6.5. All services, piping and devices should be adequately marked and special attention paid to the provision of non-interchangeable connections or adaptors for dangerous gases, liquids and other materials.

6.6. Balances and other measuring equipment of an appropriate range and precision should be available and should be calibrated in accordance with a suitable schedule.

6.7. Dedicated equipment should be used where appropriate when handling and/or processing pharmaceutical starting materials. Where non-dedicated equipment is used cleaning validation should be performed.

6.8. Closed equipment should be used when possible. If open equipment is used, suitable measures should be taken to prevent contamination.

6.9. Procedures should be in place for the operation and maintenance of equipment. Lubricants and other materials used on surfaces that come into direct contact with the materials should be of the appropriate grade, e.g. food-grade oil, and should not alter the quality of the materials.

6.10. Washing and cleaning equipment should be chosen and used such that it cannot be a source of contamination.

7. Documentation

7.1. Documents, in particular instructions and procedures relating to any activity that might have an impact on the quality of materials, should be designed, completed, reviewed and distributed with care. Documents should be completed, approved, signed and dated by appropriate authorized persons and should not be changed without authorization. Specifications for materials, including packaging materials, should be available, reviewed and revised on a regular basis.

7.2. Documents should have unambiguous contents: their title, nature and purpose should be clearly stated. They should be laid out in an orderly manner and be easy to check.

7.3. Certificates of analysis (COAs) issued by the original manufacturer should be provided. If additional testing is done, all COAs should be provided.

COAs should document product traceability back to the manufacturer by naming the original manufacturer and the manufacturing site. COAs should indicate which results were obtained by testing the original material and which results came from skip-lot testing or other testing and should specify the organization responsible for issuing the COA.

7.4. Before any material is sold or distributed, the supplier should ensure that the COAs and results are available and that the results meet the required specifications.

7.5. The original manufacturer and the intermediaries handling the material should always be traceable and transparent; and this information should be made available to authorities and end-users, downstream and upstream, when requested.

7.6. Depending upon risk assessment, and in accordance with the national requirements, quality agreements should form the basis of the relationship for all parties involved in the supply chain. The agreements should include mechanisms to allow transfer of information, e.g. quality or regulatory information and change control.

7.7. Labels applied to containers should be clear, unambiguous, permanently fixed and should be printed in the company's agreed format. The information on the label should be indelible.

7.8. Each container should be identified by labelling bearing at least the following information:

- the name of the pharmaceutical starting material (including grade and reference to pharmacopoeias where relevant);

- if applicable, the International Nonproprietary Name (INN);

- the amount (weight or volume);

- the batch number assigned by the original manufacturer or the batch number assigned by the repacker, if the material has been repacked and relabeled;

- the retest date or expiry date (where applicable);

- the storage conditions;

- handling precautions, where necessary;

- identification of the original manufacturing site;

- name and contact details of the supplier.

7.9. Relevant storage and handling information and safety data sheets should be available.

7.10. Records should be kept and must be readily available upon request in accordance with GMP and GSP.

8. Repackaging and relabelling

8.1. Operations, such as combining into a homogeneous batch, repackaging and/or relabelling, are manufacturing processes and are not recommended. In circumstances where they are to be conducted, their performance should be in compliance with GMP.

Note: It is important to note that any party who engages in repackaging or blending of an API is considered to be a manufacturer and must submit appropriate registration documents for such manufacturing. They must also comply with the GMP for APIs as set out in WHO Technical Report Series, No. 957, Annex 2, 2010.

8.2. Special attention should be given to the following points:

- prevention of contamination, cross-contamination and mix ups;

- appropriate environmental conditions for dispensing, packaging and sampling;

- security of stocks of labels, line clearance checks, online inspections, destruction of excess batch-printed labels and label reconciliation;

- good sanitation and hygiene practices;

- maintaining batch integrity (mixing of different batches of the same solid material should normally not be done);

- as part of batch records, all labels that were removed from the original container during operations, and a sample of the new label, should be kept;

- if more than one batch of labels is used in one operation, samples of each batch should be kept;

- maintaining product identity, integrity and traceability.

8.3. Upon receipt, packaging materials should be placed in quarantine and should not be used prior to release. There should be procedures for the inspection, approval and release of the packaging materials.

8.4. When different batches of a material from the same original manufacturing site are received by a distributor and combined into a homogeneous batch, the conformity of each batch with its specification should be confirmed before it is added.

8.5. Only materials from the same manufacturing site, received by a distributor and conforming to the same specifications, can be mixed. If different batches of the same material are mixed to form a homogeneous batch it should be defined as a new batch, tested and supplied with a batch certificate of analysis. In such cases the customer should be informed that the material supplied is a mixture of manufacturers' batches.

8.6. In all cases, traceability back to the manufacturer should be documented by identifying the original manufacturer of the specific batch of the material and its manufacturing site.

8.7. If batches are combined or mixed, the oldest batch should determine the expiry or retest date assigned to the combined or mixed batch.

8.8. If the integrity and quality of the batch is maintained during repackaging and relabelling, then the original COA of the original manufacturer should be provided.

If retesting is done, both the original and the new COA should be provided as long as the batch integrity is maintained. The batch referred to on the new COA should be traceable to the original COA.

8.9. Repackaging of materials should be carried out using approved packaging materials for which the quality and suitability have been established as being equal to or better than those of the original container.

8.10. The reuse of containers should be discouraged unless they have been cleaned using a validated procedure. Recycled containers should not be used unless there is evidence that the quality of the material packed in them will not be adversely affected.

8.11. Materials should be repackaged only if efficient environmental control exists to ensure that there is no possibility of contamination, cross-contamination, degradation, physicochemical changes and/or mix ups. The quality of air supplied to the area should be suitable for the activities performed, e.g. there should be efficient filtration.

8.12. The quality of air supplied to the area should be suitable for the activities performed, e.g. there should be efficient filtration.

8.13. Containers of repackaged material and relabelled containers should bear both the name of the original manufacturing site and the name of the distributor/repacker.

8.14. Procedures should be in place to ensure maintenance of the identity and quality of the material by appropriate means, both before and after repackaging operations.

8.15. Each batch of repackaged material should be tested to ensure that the material conforms to documented specifications.

8.16. There should be a procedure to ensure that appropriate repackaging documentation, in addition to the test results, is evaluated prior to release of the repackaged material.

8.17. Sampling, analytical testing and batch release procedures should be in accordance with GMP.

8.18. Only official pharmacopoeial methods or validated analytical test methods should be used for the analysis. Where alternatives to the test methods specified in a monograph are used to provide test results, those alternative methods should be demonstrated to be suitable and equivalent.

8.19. Out-of-specification test results should be investigated and documented.

8.20. Samples of pharmaceutical starting materials in appropriate quantities should be kept for at least one year after the expiry or retest date, or for three years after distribution is complete.

8.21. The repacker and relabeller should ensure that the stability of the material is not adversely affected by the repackaging or relabelling. Stability studies to justify assigned expiration or retest dates should be conducted if the pharmaceutical starting material is repackaged in a container different from that used by the original manufacturer. It is recognized that some excipients may not need additional stability studies.

9. Complaints

9.1. All complaints and other information concerning potentially defective materials must be carefully reviewed according to written procedures that describe the action to be taken and specify the criteria on which a decision to recall a product should be based. Records of complaints should be retained and evaluated for trends at defined intervals.

9.2. Any complaint concerning a material defect should be recorded and thoroughly investigated to identify the origin or reason for the complaint (e.g. the repackaging procedure or the original manufacturing process). Corrective and preventive actions should be taken where appropriate, and recorded.

9.3. If a defect in a pharmaceutical starting material is discovered or suspected, consideration should be given to whether other batches should be checked.

9.4. Where necessary, appropriate follow-up action, possibly including a recall, should be taken after investigation and evaluation of the complaint.

9.5. The manufacturer and customers should be informed if action is needed following possible faulty manufacturing, packaging, deterioration or any other serious quality problems with a pharmaceutical starting material.

10. Recalls

10.1. There should be a system for recalling promptly and effectively from the market, materials known or suspected to be defective.

10.2. The original manufacturer should be informed in the event of a recall.

10.3. There should be detailed written procedures for the organization of any recall activity. These procedure(s) should be regularly reviewed and updated.

10.4. All recalled materials should be stored in a secure area while their fate is decided.

10.5. In the event of serious or potentially life-threatening situations, all customers and competent authorities in all countries to which a given material may have been distributed should be promptly informed of any intention to recall the material.

10.6. All records should be readily available to the designated person(s) responsible for recalls. These records should contain sufficient information on materials supplied to customers (including exported materials).

10.7. The effectiveness of the arrangements for recalls should be evaluated at regular intervals.

11. Returned goods

11.1. Goods returned to the supplier should be appropriately identified and quarantined. The conditions under which returned goods have been stored and shipped should be evaluated to determine the quality of the returned goods.

11.2. The quality unit or designee should decide on the disposition of the returned goods following a formal and documented investigation process. Corrective and preventive actions should be taken where appropriate.

12. Handling of non-conforming materials

12.1. Non-conforming materials should be handled in accordance with a procedure that will prevent their introduction or reintroduction into the market. Records covering all activities, including destruction, disposal, return and reclassification, should be maintained.

12.2. An investigation should be performed to establish whether any other batches are also affected. Corrective and preventive measures should be taken where necessary.

12.3. The disposition of the material, including downgrading to other suitable purposes, should be documented.

13. Dispatch and transport

13.1. Materials should be loaded, unloaded and transported in a manner that will ensure the maintenance of controlled conditions where applicable (e.g. temperature, protection from the environment). The transport process should not adversely affect the materials. Any carrier used for transport should be approved according to a written procedure unless the carrier has been selected by the customer.

13.2. Requirements for special transport and/or storage conditions should be stated on the label and/or in the transport documentation. If the pharmaceutical starting material is intended to be transferred outside the control of the manufacturer's materials management system, the name and address of the manufacturer, quality of contents, special transport conditions and any special legal requirements should also be included on the label and/or in the transport documentation.

13.3. The supplier of the materials should ensure that the contract acceptor for transportation of the materials is aware of and provides the appropriate storage and transport conditions, e.g. through audits.

13.4. Procedures should be in place to ensure proper cleaning and prevention of cross-contamination when liquids (tanks) and bulk or packed materials are transported.

13.5. The bulk transport of pharmaceutical starting materials requires numerous precautions to avoid contamination and cross-contamination. The best practice is to use dedicated equipment, tanks or containers.

Where non-dedicated vehicles and equipment are used, procedures should be in place to ensure that the quality of the pharmaceutical starting material will not be compromised. Appropriate cleaning should be performed, checked and recorded.

10.5. Vehicles, equipment and containers should be selected and assessed appropriately to ensure pharmaceutical products and pharmaceutical starting materials are stored under required conditions during transportation.

13.6. Packaging materials and transportation containers should be suitable to prevent damage to the pharmaceutical starting materials during transport.

13.7. For bulk transport, validated cleaning procedures should be used between loadings, and a list of restricted previous cargoes must be supplied to the transport companies.

13.8. Steps should be taken to prevent unauthorized access to the materials being transported.

13.9. General international requirements regarding safety aspects (e.g. prevention of explosion and of contamination of the environment) should be observed.

14. Contract activities

14.1. Any activity performed, as referenced in the GMP and GTDP guidelines, delegated to another party, should be agreed upon in a written contract.

14.2. The contract giver should evaluate the proposed contract acceptor's compliance with GTDP before entering into an agreement.

14.3. All contract acceptors should comply with the requirements in these guidelines. Special consideration should be given to the prevention of cross-contamination and to maintaining traceability.

14.4. There should be a written and approved contract or formal agreement between the contract giver and contract acceptor that addresses and defines in detail the responsibilities with respect to GTDP and which party is responsible for which quality measures.

14.5. Subcontracting may be permissible under certain conditions, subject to approval by the contract giver, especially for activities such as sampling, analysis, repacking and relabeling./.

APPENDIX III

CLASSIFICATION OF DEGREE OF DEFICIENCIES AND COMPLIANCE OF DISTRIBUTORS OF PHARMACEUTICAL PRODUCTS AND PHARMACEUTICAL STARTING MATERIALS

(Enclosed with the Circular No. 03/2018/TT-BYT dated February 09, 2018 of the Minister of Health)

I. Classification of degree of deficiencies

1. Critical deficiency means a deviation from GDP standards, resulting in producing a pharmaceutical product or pharmaceutical starting material in a manner that adversely affects the quality, safety and efficacy and leading to a risk of seriously affecting life and health of the user or community; or means a combination of several major deficiencies, which indicates a serious system failure. This includes an activity which increases the risk of counterfeit pharmaceutical products reaching users.

2. Major deficiency means a non-critical deficiency but may lead to the storage of products and starting materials being out of compliance with storage guidelines of the manufacturer; or indicates a major deviation from GDP or storage conditions; or indicates

a failure to carry out satisfactory storage procedures or a failure of the qualified person to fulfill his/her legal duties; or means a combination of several "other" deficiencies, none of which on their own may be major, but which may together represent a major deficiency and should be explained and reported as such.

3. Minor deficiency means a deficiency, which cannot be classified as either critical or major one, but which indicates a deviation from GDP.

II. Classification of degree of compliance with GDP principles

1) Degree 1: the distributor does not have any critical and major deficiencies.

2) Degree 2: the distributor does not have any critical deficiencies and has major deficiencies.

3) Degree 3: the distributor has critical deficiencies.