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FDA CIRCULAR NO. 2020-

Subject: **GUIDELINES FOR THE CLASSIFICATION OF DEFICIENCIES OBSERVED DURING INSPECTION OF DRUG DISTRIBUTORS AND DRUG RETAIL OUTLETS**

I. RATIONALE

Republic Act (RA) No. 3720, as amended by RA No. 9711, declared it a policy of the State to adopt, support, establish, institutionalize, improve and maintain structures, processes, mechanisms and initiatives that are aimed, directed and designed to help establish and maintain an effective health products regulatory system. Pursuant to the foregoing policy, the State, through the Food and Drug Administration, must enhance its regulatory capacity and strengthen its capability with regard to the inspection, licensing and monitoring of establishments, and the registration and monitoring of health products

Consequently, and in order to achieve the objective of RA No. 9711 of ensuring the FDA's monitoring and regulatory coverage over, and providing coherence in FDA's regulatory system for drug establishments and drug products, it is imperative that classification of deficiencies noted during inspection of drug distributors and drug retail outlets is consistent, and guided with distribution and storage practices considered non-compliant to FDA-implemented rules/ standards in the distribution of drug products.

Finally, in compliance with the declared policy of the State laid down in Republic Act No. 11032 or the *Ease of Doing Business and Efficient Government Service Delivery Act of 2018* to promote integrity, accountability, establish effective practices, aimed at efficient turnaround of the delivery of government services and the prevention of graft and corruption in government, the FDA is committed to take appropriate measures to promote transparency.

Hence, this Circular is hereby issued.

II. OBJECTIVE

This Circular is issued to have uniform understanding in the classification of the noted non-conformances during inspection of drug distributors and drug retail outlets and provide guidelines to the drug GDSP inspectorate service of the FDA's Field Regulatory Operations Office. , as well as drug distributors and drug retail outlets for uniformity of regulatory understanding consistent with the provisions of RA No. 3720, as amended by RA No. 9711, RA No. 11032, and relevant national and international standards and policies.

III. SCOPE

These guidelines shall apply to all drug *Good Distribution and Storage Practice (GDSP)* inspectorate and local drug establishments distributing *and retail of* drugs including: household remedy, medicinal gas, traditional and herbal medicines, non-sterile, sterile, vaccines and biologicals and active pharmaceutical ingredients for human and animal use.

IV. GUIDELINES

For uniformity, efficiency and transparency, non-conformances observed during inspections are classified based on the following definitions:

1. **Critical deficiency** - is a departure from the GDSP Guide that leads to a significant risk to the patient or public health. It also refers to a serious situation that could result in regulatory action being considered.

   A deficiency is also considered critical when the establishment is observed to be engaged in fraud, misrepresentation or falsification of pharmaceutical products or ~~data~~ *documents.*

2. **Major deficiency** – is a deficiency which indicates a major deviation from Good Distribution and Storage Practices that has a "direct effect" in the quality/ efficacy of pharmaceutical products.

   A combination of several "other" deficiencies, none of which may be major, but which together present a major deficiency and should be explained and reported as such.

3. **Others** - a deficiency that is not classified as either "Critical" or "Major", but indicates a deviation from GDSP or a deficiency may be judged as "Other" because there is insufficient information to classify it as "Critical" or "Major".

For reference, a list of observations classified according to the above definitions is attached as **Annex A**. The list is non-exhaustive and other observations may be added, removed, or re-classified as appropriate, subject to notice to the concerned stakeholders.

In case of findings classified as critical deficiency (ies) the establishment is directed to initiate outright, <u>any or all</u> of the following (depending on the assessed degree of risk to patient safety):

a. Temporarily stop distribution of affected products

b. Undertake or cause company-initiated recall of affected batches following existing FDA rules and procedure for product recall;

c. Address the deficiencies, including submission of *Corrective Action and Preventive Action* (CAPA) plan and objective evidence of compliance, not later than fifteen (15) calendar days reckoned on the day following the receipt of the inspection report.

Apart from the foregoing, critical findings may result in the FDA imposing subsequent regulatory action, including disapproval of application, suspension or revocation of the issued authorizations.

In case of major and other deficiencies, the inspector is authorized to direct the establishment to address the deficiencies, including the submission of CAPA Plan and objective evidence of compliance, not later than fifteen (15) calendar days reckoned on the day following the receipt of the inspection report.

V. REPEALING AND SEPARABILITY CLAUSES

Any provisions of existing FDA-issued Circulars or Memoranda that are inconsistent with this Circular are hereby repealed, withdrawn and/or revoked accordingly.

If any provision of this Circular or application of such provision to any circumstances is held invalid, the validity of the remainder of the provisions hereof not affected shall continue to be in effect.

VI. EFFECTIVITY

This Circular shall take effect immediately.

USEC. ROLANDO ENRIQUE D. DOMINGO, DPBO
Director General

ANNEX A

List of GDSP Inspection Deficiencies

(The list is non-exhaustive and other observations may be added, removed or reclassified as appropriate)

A. Organization and Management

1. Critical

- There is no registered Pharmacist.

2. Major

- There are no clear and defined duties and responsibilities of personnel involved in the distribution of pharmaceutical products. *(WHO Annex5 TRS 957 6.2)*
- There is no designated person within the organization for ensuring that a quality system is implemented and maintained. *(WHO Annex5 TRS 957 6.3)*
- There are no safety procedures relating to relevant aspects including the safety of personnel and property, environmental protection and product integrity. *(WHO Annex5 TRS 957 6.7)*

B. Personnel

1. Major

- Personnel involved in distribution activities are not trained and qualified in the requirements of GDSP. *(WHO Annex5 TRS 957 7.1)*
- The key personnel involved in the distribution of pharmaceutical products were not able to demonstrate the ability and sufficient knowledge to ensure that pharmaceutical products are distributed properly. *(WHO Annex5 TRS 957 7.2)*
- There is an inadequate number of competent key personnel involved in all stages of the distribution of pharmaceutical products. *(WHO Annex5 TRS 957 7.3)*

2. Others

- Training of personnel was not based on the written standard operating procedure (SOP). *(WHO Annex5 TRS 957 7.1)*
- There is no written training programme for initial and continuing training of personnel involved in distribution activities, relevant to their tasks. *(WHO Annex5 TRS 957 7.1)*
- There is no record of all training with details of subjects covered and participants trained.

C. Quality System

1. Critical

- Distribution of unregistered and substandard / *counterfeit* pharmaceutical products
- Falsification of marketing authorizations

2. Major

- There is no established Quality System. *(WHO Annex5 TRS 957 Chapter 8)*
- There are no records for secure distribution documentation to enable traceability of products distributed. *(WHO Annex5 TRS 957 14.1)*
- Distribution records do not contain the name and address of consignee/customer, lot number and expiry date of drug products. *(WHO Annex5 TRS 957 8.11, 14.2)*
- Distributors or their agents distributed a pharmaceutical product outside a country or territory without appropriate marketing authorization. *(WHO Annex5 TRS 957 7.3, Sec. 11 (k) of RA 3720, as amended by RA 9711)*
- The *drug* distributor/ *retail outlet* obtained their supplies of pharmaceutical products from entities which are not in possession of applicable authorizations to sell or supply such products. *(WHO Annex5 TRS 957 7.3, Sec. 11 (k) of RA 3720, as amended by RA 9711)*

- Distributors supplied pharmaceutical products to persons or entities which are *unauthorized / unlicensed* to acquire such products either in terms of an authorization to act as a distributor or to sell or supply products directly to a patient or to his or her agent. *(WHO Annex5 TRS 957 7.3, Sec. 11 (k) of RA 3720, as amended by RA 9711)*

3. Others

- There is no SOP to ensure document traceability of products received and distributed, to facilitate product recall.
- There is no SOP to be followed when a suspected product is identified which should include provisions for notification of the holder of the marketing authorization, the appropriate national and/or international regulatory bodies, as well as other relevant competent authorities**.**
- The quality system did not describe the procurement and release procedures to ensure that pharmaceutical products are sourced only from ~~a~~approved suppliers and distributed by approved entities.

D. Premises, warehousing and storage

1. Critical

- Storage areas for time- and temperature-sensitive pharmaceutical products (TTSPPs) are not maintained within acceptable temperature limits.
- There were cold chain temperature deviations recorded but no CAPA was done.

2. Major

- Storage areas are insufficient to allow the orderly storage of the various categories of pharmaceutical products. *(WHO Annex5 TRS 957 9.3 & TRS 908 4.2)*
- Storage areas for pharmaceutical products under ambient conditions are not maintained within acceptable temperature limits. *(WHO Annex5 TRS 908 4.17)*
- Temperature mapping had not been conducted to establish the suitability of the storage areas and to determine the appropriate location of the thermometers in the areas where are most likely to show extremes temperature fluctuations. *(WHO Annex9 TRS 961 4.5.1)*
- Monitoring of storage temperature is not conducted. *(WHO Annex9 TRS 961 4.18)*
- There are no separate or defined areas to prevent contamination or mix-ups regarding operations related to the holding of rejected, expired, damaged products before disposition. *(WHO Annex9 TRS 961 4.8, 4.13)*
- The calibration of warehouse thermometer is not done at suitable intervals in accordance with an established written program. *(WHO Annex9 TRS 961 4.8, 4.10.1)*

3. Others

- There is no written programme for pest control.
- There is no documented cleaning schedule for temperature-controlled rooms/equipment. (WHO Annex 9 TRS 961 4.8)
- Pharmaceutical products were not appropriately stored on the shelves/ racks/ pallets assigned for them, and there were products stored directly on the floor.
- Pallets are not kept in a good state of cleanliness and repair.
- Adequate lighting is not provided in all areas.

E. Vehicles and Equipment

1. Major

- Temperature monitoring during transport of time- and temperature-sensitive pharmaceutical products (TTSPPs) is not conducted. *(WHO Annex9 TRS 961 6.4.2, 6.5.1)*
- *Temperature-controlled vehicles directly owned and/or operated are not qualify before it becomes operational.* *(WHO Annex9 TRS 961 6.6)*

2. Others

- There is no SOP in place for the operation and maintenance of all vehicles and equipment involved in the distribution process, including cleaning and safety precautions.
- There is no SOP in place to ensure that the integrity of the products is not compromised during transportation.
- There is no evidence or records that cleaning of vehicles was performed

F. Shipment containers and container labelling

1. Critical

- Shipping containers are not capable of maintaining the time- and temperature-sensitive pharmaceutical products (TTSPPs) within the temperature range needed. *(WHO Annex9 TRS 961 6.8)*

2. Major

- Shipping containers of time- and temperature-sensitive pharmaceutical products (TTSPPs) do not 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. *(WHO Annex9 TRS 961 6.4.2, 6.9)*

3. Others

- There is no SOP for the handling of damaged and/or broken shipping containers.

G. Dispatch and receipt

1. Major

- Shipping containers of cold-chain pharmaceutical products do not 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. *(WHO Annex9 TRS 961 6.4.2, 6.9)*

2. Others

- Records of dispatch do not contain enough information to enable traceability of the pharmaceutical product. (*WHO Annex 9 TRS 802 7.7*)
- There is no SOP for the dispatch of pharmaceutical products.

H. Transportation

1. Major

- Thermometers used to monitor temperature during transport of time- and temperature-sensitive pharmaceutical products (TTSPPs) are not calibrated. *(WHO Annex9 TRS 961 4.10.1)*

2. Others

- SOP on transportation of pharmaceutical products does not include adequate precautions taken against spillage, breakage, misappropriation and theft.
- There is no SOP for investigating and dealing with any failure to comply with storage requirements during transportation of pharmaceutical products.
- There is no SOP for handling spillages during transportation.

I. Documentation

1. Major

- Documentation was not compliant with GDP in that some records had been made in pencil, some temperature records were unsigned**.** *(WHO Annex9 TRS 957 14.6)*
- There were considerable gaps in temperature records. *(WHO Annex9 TRS 961 9.3.1)*
- Records relating to storage of pharmaceutical products are not readily available upon request. *(WHO Annex9 TRS 957 14.1)*

2. Others

- There was no formal process for document control and retention of documents.
- There are no back-ups *for the* records *are generated and kept* in electronic form. *(WHO Annex9 TRS 957 14.15)*
- Backup data is not secured from alteration, erasure or loss through keeping hard copy or alternate systems.

J. Complaints, Returns, Recall and Falsified Medicines

1. Critical

- The company failed to conduct a full recall procedure for the defective pharmaceutical product.

2. Major

- There is no SOP on handling complaints, returns, recalls and counterfeit pharmaceutical products. *(WHO Annex9 TRS 957 16.1, 17.1, 18 .2, 8.7)*

3. Others

- The SOP on handling complaints does not include instructions to notify the Marketing Authorization Holder / Manufacturer and FDA in case of product quality issue.
- The SOP on handling returns from customers was deficient in that it did not indicate that the decision regarding the disposition of such products must only be made by an authorized person.
- The SOP on suspected counterfeit pharmaceutical products did not indicate that all must be reported to the FDA.

K. Importation

1. Critical

- Commercial importation and distribution of pharmaceutical products that are not registered with the FDA.

2. Others

- There is no SOP to ensure that cold-chain pharmaceutical product shipments are cleared through customs as rapidly as possible.

L. Contract Activities

1. Major

- There is no written quality agreement defining the responsibilities of each party including observance of the principles of GDP and relevant warranty clauses with suppliers and sub-distributors. *(WHO Annex9 TRS 957 21)*
- There was no contract/agreement defining the responsibilities of each party for the proposed transportation of pharmaceutical products.
- Written distribution contracts/agreements were not signed or duly authorized by appropriate parties
- The company had insufficient control over outsourced logistic activities. *(WHO Annex9 TRS 957 21.4)*

2. Others

- The distribution contracts/agreements with suppliers and third party warehousing and transportation logistics are not renewed.
- Authorized distributors or third party warehousing logistics were not audited periodically.

M. Self-inspection

1. Major

- The management failed to conduct an evaluation of the audit inspection report and corrective action taken. *(WHO Annex9 TRS 957 22.3)*

2. Others

- The results of self-inspections are not available for review.
- The results of self-inspections do not contain proposals for corrective measures.
- The management failed to conduct evaluation of the audit inspection report and corrective action taken.
- Self-inspection had not been performed as defined in the procedure.

ACRONYMS

GDP – Good Distribution Practice
GDSP – Good Distribution and Storage Practice
CAPA – Corrective Action-Preventive Action
SOP – Standard Operating Procedure