Working document QAS/04.068/Rev.2

RESTRICTED

**WORLD HEALTH ORGANIZATION**
**ORGANISATION MONDIALE DE LA SANTE**

# GOOD DISTRIBUTION PRACTICES (GDP)

# FOR PHARMACEUTICAL PRODUCTS

This document has followed the steps given in the schedule on page 2 herein. It has been very widely distributed and numerous comments have been incorporated.

Please address any comments and/or corrections you may have on thereon to Dr S. Kopp, Quality Assurance and Safety: Medicines, Medicines Policy and Standards, World Health Organization, 1211 Geneva 27, Switzerland, fax: (+41 22) 791 4730 or e-mail: kopps@who.int, with a copy to bonnyw@who.int, **by 20 October 2005**.

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**SCHEDULE FOR THE ADOPTION PROCESS OF DOCUMENT QAS/04.068/REV.2: GOOD DISTRIBUTION PRACTICES (GDP) FOR PHARMACEUTICAL PRODUCTS**

| | **Deadline** |
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# GOOD DISTRIBUTION PRACTICES (GDP) FOR PHARMACEUTICAL PRODUCTS

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## 1. INTRODUCTION

Distribution forms an important activity of the integrated supply chain management of pharmaceutical products. Various persons and entities are often responsible for the handling,

storage and distribution of such products. In some cases, however, a person or entity involved in the distribution of pharmaceutical products is only involved in and is responsible for certain elements of the distribution process. This document sets out appropriate steps to assist in meeting the responsibilities involved in the different aspects of the distribution process. The guidelines are intended to apply to all steps in the entire distribution/supply chain. The relevant sections should be considered by various role players as applicable to their particular role in the distribution process. The document does not cover specifically finished products in bulk, distribution of labels and packaging materials, as this is considered to be covered by other guidelines, e.g. GMP.

Practice of repacking, e.g. in pharmacies and other settings, needs to be carried out in accordance with good dispensing practices.

The storage, trade and distribution of pharmaceutical products are activities that are carried out by various companies, institutions and individuals. The nature of the risks involved may generally, however, be the same as those in the manufacturing environment, e.g. mix-ups, contamination and cross-contamination. There are thus aspects in distribution to which the principles of good manufacturing practice (GMP) should be applied. These include, but are not limited to, storage, distribution, transportation, packaging, labelling, documentation and record-keeping practices.

The quality of pharmaceutical products can be affected by a lack of adequate control over numerous activities which occur during the distribution process. Furthermore the distribution process has generally not been well-emphasized with regard to the need for establishment, development, maintenance and control over the activities involved. The objective of these guidelines is to assist in ensuring the quality and integrity of pharmaceutical products during all aspects of the distribution process.

In order to maintain the original quality every activity in the distribution of pharmaceutical products should be carried out according to the principles of GMP, good storage practice (GSP) and good distribution practice (GDP). Although these guidelines are intended to be a stand-alone text they do not deal with all aspects included in the standards for the storage of pharmaceuticals which are covered in the "WHO guide to good storage practices for pharmaceuticals" (*WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-seventh Report*. Geneva, World Health Organization, 2003 (WHO Technical Report Series, No. 908, Annex 9)). It should also be read in conjunction with other guidelines such as "WHO good manufacturing practices: main principles" (*WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-seventh Report*. Geneva, World Health Organization, 2003 (WHO Technical Report Series, No. 908, Annex 4)); "Guidelines for implementation of the WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce (*WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-fourth Report*. Geneva, World Health Organization, 1996 (WHO Technical Report Series, No. 863, Annex 10)); "WHO pharmaceutical starting materials certification scheme (SMACS)" (*WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-eighth Report*. Geneva, World Health Organization, 2004 (WHO Technical Report Series, No. 917, Annex 3)); and the "Guidelines on import procedures

for pharmaceutical products" (*WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-fourth Report*. Geneva, World Health Organization, 1996 (WHO Technical Report Series, No. 863, Annex 12)).

## 2. SCOPE OF THE DOCUMENT

The document lays down guidelines for the distribution of pharmaceutical products . This document does not cover materials such as pharmaceutical starting materials (active pharmaceutical ingredients (API) and excipients), reagents, solvents, process aids, intermediate products, packaging materials and labelling materials. The principles for distribution of starting materials were laid out in the WHO guidances Good Trade and Distribution Practices for pharmaceutical starting materials (TRS 917, Annex 2). …

Different models for the distribution of pharmaceutical products are in place in different countries. Variations may also be seen between systems used in the same country, for example, the public and the private sector. These guidelines are intended to be applicable to all persons and companies involved in any aspect of the distribution of pharmaceutical products from the premises of manufacture to the point of supply to health establishments, e.g. private pharmacies, hospitals, clinics, etc. for supply to the patient. This includes all parties involved in trade and distribution, pharmaceutical manufacturers, including the manufacturers of finished products, brokers, suppliers, distributors, wholesalers, traders, transport companies, forwarding agents, etc. The relevant sections of the guidelines should also be considered for implementation by *inter alia* governments, regulatory bodies, international organizations and donor agencies, certifying bodies, as well as all parties including health care workers involved in any aspect of the trade and distribution of pharmaceutical products. The guidelines can also be used as a tool in the prevention of the distribution of counterfeit and substandard medicines. It must be noted that these are general guidelines which may be adapted to suit prevailing situations/conditions in individual countries.

## 3. GLOSSARY

The definitions provided below apply to the words and phrases used in these guidelines. Although an effort has been made to use standard definitions as far as possible, they may have different meanings in other contexts and documents.

[***Note from WHO Secretariat:***

*We have received an additional comment - received after the consultation discussing all comments received within the deadline:*

*The proposal is to add definitions for brokers, traders, forwarding agent, supply chain, etc.*
*This was discussed at length when developing the GTDP text. The compromise at that time was to include a definition of "supplier". Please kindly comment.*]

*Agreement*
Arrangement undertaken by and legally binding on parties.

*Auditing (new)*

Auditing is an independent, objective assurance and consulting activity designed to add value and improve an organization's operations. It helps an organization accomplish its objectives by bringing a systematic, disciplined approach to evaluate and improve the effectiveness of risk management, control, and governance processes.

(modified, from Professional Practices Framework published by the Institute of Internal Auditors)

*Batch*

A defined quantity of starting material, packaging material or product processed in a single process or series of processes so that it is expected to be homogeneous. (For further details please see *Good manufacturing practices for pharmaceutical products: main principles*. WHO Technical Report Series, No. 908, 2003, Annex 4.)

*Batch number*

A distinctive combination of numbers and/or letters which uniquely identifies a batch on the labels, its batch records and corresponding certificates of analysis, etc.

*Bulk product*

Any product that has completed all processing stages up to, but not including, final packaging.

*Calibration*

The set of operations that establish, under specified conditions, the relationship between values indicated by an instrument or system for measuring (especially weighing), recording, and controlling, or the values represented by a material measure, and the corresponding known values of a reference standard. Limits for acceptance of the results of measuring should be established.

*Consignment (or delivery)*

The quantity of a pharmaceutical(s), made by one manufacturer and supplied at one time in response to a particular request or order. A consignment may comprise one or more packages or containers and may include material belonging to more than one batch.

*Container (new)*

The material employed in the packaging of a pharmaceutical product. Containers include primary, secondary and transportation containers. Containers are referred to as primary if they are intended to be in direct contact with the product. Secondary containers are not intended to be in direct contact with the product.

*Contamination (new: "handling" added)*

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 transport.

*Contract*
Business agreement for the supply of goods or performance of work at a specified price.

*Counterfeit*
A counterfeit medicine is one which is deliberately and fraudulently mislabelled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products and may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging.

*Cross-contamination*
Contamination of a starting material, intermediate product or finished product with another starting material or product during production.

*Distribution*
The division and movement of pharmaceutical products from the premises of the manufacturer of such products, or another central point, to the end user thereof, or to an intermediate point by means of various transport methods, via various storage and/or health establishments.

*Excipient*
A substance or compound, other than the active pharmaceutical ingredient and packaging materials, that is intended or designated to be used in the manufacture of a pharmaceutical product.

*Expiry date*
The date given on the individual container (usually on the label) of a product up to and including which the product is expected to remain within specifications, if stored correctly. It is established for each batch by adding the shelf-life to the date of manufacture.

*FEFO (First Expiry/First Out)*
A distribution procedure that ensures 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; EEFO (Earliest Expiry/First Out) shall have a similar meaning.

*FIFO (First In/First Out)*
A distribution procedure to ensure that the oldest stock is distributed and/or utilized before a newer and identical stock item is distributed and/or utilized.

*Good distribution practices (GDP)* (new)
Good Distribution Practices are that part of quality assurance that ensure that the quality of a pharmaceutical products is maintained through adequate control throughout the numerous activities which occur during the distribution process.

*Good manufacturing practices (GMP )*

That part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.

*Good Storage Practices (new)*
Good Storage Practices are that part of quality assurance that ensure that the quality of a pharmaceutical products is maintained through adequate control throughout the storage.

*Good Trade and Distribution practices (new)*
Good Trade and Distribution Practices are that part of quality assurance that ensure that the quality of a pharmaceutical products is maintained through adequate control throughout the numerous activities which occur during the trade and the distribution process.

*Health establishment*
A health establishment is the whole or part of a public or private facility, building or place, whether operated for profit or not, that is operated or designed to provide health care services including the supply of pharmaceutical products to the end user.

*Importation*
The act of bringing or causing any goods to be brought into a customs territory (national territory, excluding any free zone).

*Intermediate product*
Partly processed product that must undergo further manufacturing steps before it becomes a bulk product.

*Labelling* (new)
Process of identifying a product including the following information, as appropriate: - name, - active ingredient(s): type and amount, - batch number , - expiry date, - special storage conditions or handling precautions, - directions for use, warnings, and precautions, - names and addresses of the manufacturer and/or the supplier.
*(adapted from GMP, chapter 15.11)*

*Manufacture*
All operations of purchase of materials and products, production, quality control, release, storage and distribution of pharmaceutical products, and the related controls.

*Material*
A general term used to denote starting materials (active pharmaceutical ingredients and excipients), reagents, solvents, process aids, intermediates, packaging materials and labelling materials.

*Pharmaceutical product*
Any medicine intended for human use or veterinary product administered to food-producing animals, presented in its finished dosage form or as a starting material for use

in such a dosage form, that is subject to control by pharmaceutical legislation in both the exporting state and the importing state.

*Product recall*
Product recall is a process for withdrawing or removing a pharmaceutical product from the pharmaceutical distribution chain because of defects in the product or complaints of serious adverse reactions to the product. The recall might be initiated by the manufacturer/importer/ distributor or a responsible agency.

*Quality assurance*
Quality assurance is 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 control*
Quality control covers all measures taken, including the setting of specifications, sampling, testing and analytical clearance, to ensure that starting materials, intermediates, packaging materials and finished pharmaceutical products conform with established specifications for identity, strength, purity and other characteristics.

*Quality system*
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*
The status of starting or packaging materials, intermediates, or bulk or finished products isolated physically or by other effective means while a decision is awaited on their release, rejection or reprocessing.

*Sampling*
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, batch release, etc.

*Shelf-life*
The period of time during which a finished 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)*
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). Certain SOPs may be used to supplement product-specific master and batch production documentation.

*Storage*
The storing of pharmaceutical products up to the point of use.

*Transit*
Going, conveying, being conveyed, across, or over or through; passage, route,

*Validation (new)*
A documented programme that provides a high degree of assurance that a specific process, method or system will consistently produce a result meeting pre-determined acceptance criteria.

*Vehicle*
Vehicle refers to trucks, vans, buses, minibuses, cars, trailers, aircraft, railway carriages, boats and other means which are used to convey pharmaceutical products.

## 4. ORGANIZATION AND MANAGEMENT

4.1 The distributor or the organization, to which the distributor belongs, must be an entity that is appropriately authorized to perform the intended function in terms of the applicable legislation, and which can be held liable for its activities.

4.2 There should be an adequate organizational structure defined with the aid of an organizational chart. The responsibility, authority and interrelationships of all personnel should be clearly defined.

4.3 A designated person should be appointed at each distribution point who should have defined authority and responsibility for ensuring that a quality management system is implemented and maintained.

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

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

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

4.7 Individual responsibilities should be clearly defined and understood by the individuals concerned and recorded as written job descriptions. Certain activities may require special attention such as the supervision of performance of activities, in accordance with local legislation.

4.8 Some duties may be delegated or contracted out to suitably designated persons or entities as necessary. There should, however, be no gaps or unexplained overlaps with regard to the application of GDP. These activities should be documented in quality agreements or contracts. There should be periodic audit of such activities with regards to application of GDP.

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

[***Note from WHO Secretariat:***

*We have received an additional comment - received after the consultation discussing all comments received within the deadline:*

*The proposal is to replace 4.6-4.8 by the following paragraph:*

*4.6 Management is responsible for ensuring that distribution practices are put into place to ensure conformance to these GDPs and will take appropriate measure to periodically verify that such procedures are followed to achieve the assurance of quality intended by these GDPs.*"

In addition it is suggested to delete the paras 4.6-4.8 as it is considered that this exceeds the scope of this document.

*Please kindly comment.*]

## 5. PERSONNEL

5.1 All personnel involved in distribution activities should be trained in the requirements of GDP and be capable of meeting these requirements.

5.2 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.

5.3 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.

5.4 National regulations with regard to qualifications and experience of personnel should be followed.

5.5 Personnel should receive initial and continued training relevant to their tasks, including assessment as applicable, in accordance with a written training programme.

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

5.7 Records of all training should be kept.

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

5.9 Procedures relating to personnel hygiene relevant to the activities to be carried out should be established and observed. Such procedures should relate to health, hygiene and clothing of personnel.

5.10 First-aid procedures and equipment for dealing with emergencies involving personnel should be available.

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

5.12 Codes of practice and disciplinary 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, the misappropriation and/or theft thereof.

## 6. QUALITY MANAGEMENT

6.1 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 policies of the distributor regarding quality, as formally expressed and authorized by management.

6.2 Quality management should include:

- an appropriate infrastructure or “quality system”, encompassing the organizational structure, procedures, processes and resources; and

- systematic actions necessary to ensure adequate confidence that a product (or service) and documentation will satisfy given requirements for quality. The totality of these actions is termed “quality assurance”.

6.3 The system should at least cover the principles of quality assurance as embodied in the WHO guidelines on GMP for pharmaceutical products: main principles.

6.4 All parties involved in the distribution of pharmaceutical products should share responsibility for the quality and safety of products to ensure that they are fit for their intended use.

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

6.6 Authorized procurement and release procedures should be in place, to ensure that appropriate pharmaceutical products are sourced from approved suppliers and distributed by approved entities.

6.7 All entities in the supply chain should be traceable as applicable, depending on the type of product, and on the national policies and legislation. There should be written procedures and records to ensure traceability of the products distributed.

6.8 Inspection 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 guidelines and the applicable principles of GMP relating to pharmaceutical products.

6.9 Authorized SOPs for all administrative and technical operations performed should be in place.

## 7. PREMISES, WAREHOUSING AND STORAGE

7.1 Good storage practice (GSP) is applicable in all circumstances where pharmaceutical products are stored throughout the distribution process. For additional guidance relating the general principles of storage of pharmaceutical products, refer to the WHO guideline on good storage practices (*WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-seventh Report*. Geneva, World Health Organization, 2003 (WHO Technical Report Series, No. 908, Annex 9)).

### Storage areas

7.2 Precautions must be taken to prevent unauthorized persons from entering storage areas.

7.3 Storage areas should be of sufficient capacity to allow the orderly storage of the various categories products, namely bulk and finished products, products in quarantine, and released, rejected, returned or recalled products.

7.4 Storage areas should be designed or adapted to ensure good storage conditions. In particular, they should be clean and dry and maintained within acceptable temperature limits. Where special storage conditions are required on the label (e.g. temperature, relative humidity), these should be provided, checked,

monitored and recorded. 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.

7.5 Storage areas should be clean, and free from accumulated waste and 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. 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 the materials and pharmaceutical products. There should be appropriate procedures for the clean up of any spillage to ensure complete removal of any risk of contamination.

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

7.7 Where quarantine status is ensured by storage in separate areas, these areas must be clearly marked and their 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.

7.8 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.

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

7.10 Radioactive materials, narcotics and other hazardous, sensitive and/or dangerous pharmaceutical products, as well as products presenting special risks of abuse, fire or explosion, (e.g. combustible liquids and solids and pressurized gases) should be stored in a dedicated area that is subject to appropriate additional safety and security measures.

7.11 Pharmaceutical products should be handled and distributed according to GMP as defined in this document.

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

7.13 A system should be in place to ensure that pharmaceutical products due to expire first are sold and/or distributed first (FEFO). Where no expiry dates exist for the products, the FIFO principle should be applied. Exceptions may be permitted as

appropriate, provided that adequate controls are in place to prevent the distribution of expired products.

7.14 Rejected pharmaceutical products should be identified and controlled under a quarantine system designed to prevent their use until a final decision is taken on their fate.

7.15 Narcotic drugs should be stored in compliance with international conventions, and national laws and regulations on narcotics.

7.16 Broken or damaged items should be withdrawn from usable stock and separated.

7.17 Storage areas should provide adequate lighting to enable all operations to be carried out accurately and safely.

**Storage conditions**

7.18 Storage conditions for pharmaceutical products should be in compliance with the labelling, which is based on the results of stability testing.

**Monitoring of storage conditions**

7.19 Recorded temperature monitoring data should be available for review. 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 material or product plus one year, or as required by national legislation. 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.

7.20 Equipment used for monitoring should also be calibrated at defined intervals.

**Documentation: written instructions and records**

7.21 Permanent information, 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.

7.22 Procedures should be in place for temperature mapping, security services at the warehouse, destruction of unsaleable stocks and on retention of the records.

**Stock rotation and control**

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

7.24 All significant stock discrepancies should be investigated as a check against inadvertent mix-ups and/or incorrect issue.

## 8. VEHICLES AND EQUIPMENT

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

8.2 The design and use of vehicles and equipment must aim to minimize the risk of errors and permit effective cleaning and/or maintenance, in order to avoid contamination, build-up of dust or dirt and/or any adverse effect on the quality of pharmaceutical products being distributed.

8.3 Dedicated vehicles and equipment should be used, where possible, when handling pharmaceutical products.

8.4 Where non-dedicated vehicles and equipment are used, procedures must be in place to ensure that the quality of the pharmaceutical product will not be negatively influenced. Appropriate cleaning should be performed, checked and recorded.

[***Note from WHO Secretariat:***

*We have received an additional comment - received after the consultation discussing all comments received within the deadline:*

It is suggested to delete the paras 8.3-8.4 as in the commenter's opinion the use of dedicated equipment and vehicles exceed the standard now adhered for drug processing equipment.

*Please kindly comment.*]

8.5 Defective vehicles and equipment should not be used, and should either be removed or labelled as such.

8.6 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.

8.7 Vehicles, containers and equipment should be kept clean and dry and free from accumulated waste. A written cleaning programme should be available, indicating the frequency of cleaning and the methods to be used.

8.8 Vehicles, containers and equipment should be kept free from rodents, vermin, birds and other pests. There should also be written programmes for such pest control. Cleaning and fumigation agents should not have an adverse effect on product quality.

8.9 Equipment used for the cleaning of vehicles should be chosen and used so as not to constitute a source of contamination.

8.10 Special attention should be given 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.

8.11 Where special storage conditions (e.g. temperature and/or relative humidity), different from or limiting the expected environmental conditions, are required during transit 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 national legislation. Recorded monitoring data should be reviewed on receipt of pharmaceutical products to assess whether required storage conditions have been met.

8.12 Equipment used for monitoring conditions within vehicles and containers, e.g. temperature and humidity, should be calibrated.

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

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

8.15 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.

## 9. CONTAINERS AND CONTAINER LABELLING

9.1 All pharmaceutical products should be stored and distributed in containers which do not have an adverse effect on the quality of the products, and which offer adequate protection from external influences, including microbial contamination.

9.2 Labels applied to containers should be clear, unambiguous, permanently fixed to the container and be indelible. Information on the label should comply with applicable

national legislation with regard to the labelling of containers. The labelling should be written in at least one language which is understood by persons involved in the distribution chain.

[***Note from WHO Secretariat:***

*We have received an additional comment - received after the consultation discussing all comments received within the deadline:*

It is suggested to delete the paras 9.1. and 9.2 as in the commenter's opinion paragraph 13.1 (repackaging) sufficiently addresses the issue.

*Please kindly comment.*]

9.3 Shipping containers may not need not to bear labels with full description of the identity of the container's content (in order to prevent theft), but should nonetheless provide sufficient information on handling and storage conditions and precautions to ensure the product is properly handled at all times.

9.4 Special transport and/or storage conditions should be stated on the label. If a pharmaceutical product is intended for transfer 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 label.

9.5 When used, only internationally and/or nationally accepted abbreviations, names or codes should be used in the labelling of containers.

9.6 Special care should be used when using dry ice in 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.

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

## 10. DISPATCH

10.1 Pharmaceutical products should only be sold and/or distributed to persons or entities that are entitled to acquire such products in terms of applicable national, regional and international legislation. Written proof of such authority must be obtained prior to the dispatch of products to such person or entities.

10.2 The supplier of pharmaceutical products should, prior to the dispatch of such products, ensure that the person or entity, e.g. the contract acceptor for transportation of the pharmaceutical products, is aware of and follows the appropriate storage and transport conditions.

10.3 The dispatch and transport of pharmaceutical products should be commenced only after the receipt of a valid delivery order or material replenishment plan which should be documented.

10.4 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.

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

- date of dispatch;
- name and address of the entity responsible for the transportation
- name, address and status of the addressee (e.g. retail pharmacy, hospital, 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;
- assigned batch number and expiry date;
- applicable transport and storage conditions; and
- a unique number to allow identification of the delivery order.

10.6 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 as necessary. Each party involved in the distribution chain has a responsibility to ensure traceability.

10.7 Methods of transportation, including vehicles to be used, should be selected with care, and local conditions should be considered, including the climate of the region and any seasonal variations experienced. Delivery of products requiring controlled temperatures should be done in accordance with the storage and transport conditions.

10.8 Delivery schedules should be established and route planning performed where needed, taking local needs and conditions into account. Such schedules and plans should be realistic and systematic. Care should be taken that the volume of pharmaceutical products ordered should not exceed the capacity of storage facilities at the destination.

10.9 Where applicable vehicles and containers should be loaded carefully and systematically on a first-out/last-in basis in order to save time when unloading and to prevent physical damage. Extra care should be taken during loading and unloading of cartons to avoid breakage.

10.10 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 occur before the products are used by the consumer.

## 11. TRANSPORTATION AND PRODUCTS IN TRANSIT

11.1 The manufacturer should communicate all relevant conditions for storage and transportation to the entity(-ies) responsible for the transportation of pharmaceutical products. Such an entity(-ies) should ensure adherence to these requirements throughout transportation and at any intermediate storage stages.

11.2 Pharmaceutical products should be stored and transported in accordance with procedures in such a way that:

(a) the identity of the product is not lost;

(b) the product does not contaminate and is not contaminated by other products;

(c) adequate precautions are taken against spillage, breakage, misappropriation and theft; and

(d) appropriate temperature and relative humidity conditions are maintained in the case of pharmaceutical products, as appropriate, e.g. using cold chain for thermolabile products.

11.3 The required storage conditions for pharmaceutical products should be maintained within acceptable limits during transportation. The specific storage conditions of the product should thus not be grossly exceeded, or exceeded for an unacceptable period of time during the transit period. Any deviations from storage conditions which are considered to be acceptable should be determined in consultation with the marketing authorization holder and/or the manufacturer.

11.4 Where special conditions are required during transportation which are different from or limit the given environmental conditions (e.g. temperature, humidity) these should be provided, monitored and recorded.

11.5 The transportation process should not have a negative effect on the integrity and quality of pharmaceutical products.

11.6 Written procedures should be in place to investigate and deal with any violations of storage requirements, e.g. temperature violations.

11.7 Products comprising highly active and radioactive materials, other dangerous drugs and substances presenting special risks of abuse, fire or explosion (e.g. combustible liquids, solids and pressurized gases) should be stored and transported in safe, dedicated and secure areas, containers and vehicles. In addition, applicable international agreements and national legislation should be followed.

11.8 Products containing narcotics and other dependence-producing substances should be stored and transported in safe and secure areas, containers and vehicles. In addition, applicable international agreements and national legislation should be applied.

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

11.10 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.

11.11 Products containing toxic and/or flammable substances should be stored and transported in suitably designed, separate and closed containers, taking into account national legislation and international agreements.

11.12 The interior of vehicles and containers should remain clean and dry whilst pharmaceutical products are in transit.

11.13 Packaging materials and transportation containers should be suitable to prevent damage of pharmaceutical products during transport.

11.14 Sufficient security should be provided to prevent theft and other misappropriation of products. Steps should be taken to prevent unauthorized access to pharmaceutical products being transported.

11.15 General international requirements regarding safety, health and environmental aspects (e.g. explosion, contamination of the environment, etc.) should be observed.

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

11.17 A batch tracking system should be used which enables specific batches transported to be traced during the distribution process.

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

## 12. DOCUMENTATION

12.1 Written instructions and records should be available which document all activities relating to the distribution of pharmaceutical products, including all applicable receipts and issues. The name of the applicable entity should appear on all relevant documents.

12.2 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 documents from external sources.

12.3 Documents, 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.

12.4 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.

12.5 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.

12.6 There should be compliance with national legislative requirements with regard to the nature, content and retention of documentation, relating to the distribution of pharmaceutical products. Where such requirements are not in place the documents should be retained for a period equal to the shelf-life of the products where applicable, plus one year.

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

12.8 All records must be readily retrievable, stored and retained using facilities that provide a suitable environment to prevent modification, damage, deterioration and/or loss of documentation.

12.9 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.

12.10 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.

12.11 Records relating to storage of pharmaceutical products should be kept and be readily available upon request in accordance with the WHO guideline on good storage practice (*WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-seventh Report*. Geneva, World Health Organization, 2003 (WHO Technical Report Series, No. 908, Annex 9)).

12.12 In the case of temperature-sensitive pharmaceutical products, records of investigations and actions should be retained for at least one year after the expiry date of the product.

12.13 Where the records are generated and kept in electronic form, their back-ups should, be available to prevent any accidental data loss.

## 13. REPACKAGING AND RELABELLING

13.1 Repackaging (including relabelling) of pharmaceutical products should only be performed by distributors appropriately authorized and/or licensed to do so, and in accordance with GMP principles. Where these functions are performed they should be done in compliance with the applicable national, regional and international guidelines relating to repackaging and relabelling of pharmaceutical products.

## 14. COMPLAINTS

14.1 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.

14.2 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.

14.3 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, original manufacturing process, etc.).

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

14.5 Where necessary, appropriate follow-up action should be taken after investigation and evaluation of the complaint.

## 15. RECALLS

15.1 There should be a system which includes a written procedure to recall promptly and effectively pharmaceutical products known or suspected to be defective, with a designated person(s) responsible for recalls.

15.2 Such procedures should be checked regularly and updated.

15.3 The original manufacturer 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 prior to a recall being instituted.

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

15.5 All recalled pharmaceutical products should be stored in a secure, segregated area pending appropriate action.

15.6 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.

15.7 The 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 product in question.

15.8 All customers and competent authorities of all countries 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.

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

15.10 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.

## 16. REJECTED AND RETURNED PRODUCTS

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

16.2 The necessary assessment and decision regarding the disposition of such products must be taken by a designated 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.

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

16.4 Provision should be made for the proper and safe transport of rejected and waste materials prior to their disposal.

16.5 Pharmaceutical products should be destroyed where necessary in accordance with international, national and local requirements regarding disposal of such products, and with due consideration to protection of the environment.

16.6 Records of all returned, rejected and/or destroyed pharmaceutical products should be kept.

## 17. COUNTERFEIT PHARMACEUTICAL PRODUCTS

17.1 Any counterfeit or suspected counterfeit medicines found in the pharmaceutical supply chain should be segregated immediately from other pharmaceutical products and recorded.

17.2 The holder of the marketing authorization, the appropriate national and/or international regulatory bodies, as well as other relevant competent authorities, should be informed immediately.

17.3 Such products should be clearly labelled in order to prevent further distribution or sale.

17.4 Upon confirmation of the product being counterfeit a formal decision should be taken on the disposal of counterfeit pharmaceutical products and the decision recorded.

## 18. IMPORTATION

18.1 Consideration should be given to the WHO guidelines on import procedures for pharmaceutical products (*WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-fourth Report*. Geneva, World Health Organization, 1996 (WHO Technical Report Series, No. 863, Annex 12)). The following aspects should be given particular attention.

18.2 The number of ports of entry in a country for the handling of imports of pharmaceutical products should be limited by appropriate legislation.

18.3 The most appropriately located and best equipped to handle imports of pharmaceutical products should be chosen as the point(s) of entry when such products are imported into a country.

18.4 At the port of entry consignments of pharmaceutical products should be stored under suitable conditions for as short a time as possible.

18.5 All reasonable steps should be taken by importers to ensure that products are not mishandled or exposed to adverse storage conditions at wharves or airports.

18.6 Where necessary persons with pharmaceutical training should be involved with the customs procedures or should be readily contactable.

18.7 The WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce should be used to provide data regarding quality assessment of imported pharmaceutical products.

## 19. CONTRACT ACTIVITIES

19.1 Any activity relating to the distribution of a pharmaceutical product which is delegated to another person or entity should be performed in terms of a written contract which is agreed upon by the contract giver and the contract accepter.

19.2 The contract should define the responsibilities of each party including observance of the principles of GDP.

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

19.4 Subcontracting may be permissible under certain conditions subject to the written approval of the contract giver.

19.5 Any contract accepter should be audited periodically.

## 20. SELF-INSPECTION

20.1 The system of quality assurance should include self-inspections. These should be conducted in order to monitor the implementation and compliance with the principles of GDP and to trigger necessary corrective and preventive measures.

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

20.3 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 corrective actions taken and recorded.

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