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Guidelines on Good Distribution Practices of Medicinal Products

EUROPEAN INDUSTRIAL PHARMACISTS GROUP

GUIDELINES ON GOOD DISTRIBUTION PRACTICES OF MEDICINAL PRODUCTS
European Industrial Pharmacists Group

Contents

The European Industrial Pharmacists Group (GPIE/EIPG) is the European Association representing the national professional organisations of pharmacists employed in the pharmaceutical and allied industries of the member states of the European Union.
Further information can be found on their website http://www.eipg.eu

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These guidelines have been prepared in accordance with Council Directive 2001/83/EC of 6 November 2001 on the Community code relating to medicinal products for human use. They do not cover commercial relationships between parties involved in distribution of medicinal products nor questions of safety at work.

1. Introduction

The Community pharmaceutical industry operates at a high level of quality assurance, achieving its pharmaceutical quality objectives by observing Good Manufacturing Practice to manufacture medicinal products which must then be authorised for marketing. This policy ensures that products released for distribution are of the appropriate quality.

This level of quality should be maintained throughout the distribution network so that authorised medicinal products are distributed to retail pharmacists and other persons entitled to sell medicinal products to the general public without any alteration of their properties. The concept of quality management in the pharmaceutical industry is described in Chapter I of the Community Guide to Good Manufacturing Practice for medicinal products and should be considered when relevant for the distribution of medicinal products. The general concepts of quality management and quality systems are described in the CEN standards (series 29 000).

In addition, to maintain the quality of the products and the quality of the service offered by wholesalers, Directive 2001/83/EEC provides that wholesalers must comply with the principles and guidelines of good distribution practices published by the Commission of the European Communities.

The quality system operated by distributors (wholesalers) of medicinal products should ensure that medicinal products that they distribute are authorised in accordance with Community legislation, that storage conditions are observed at all times, including during transportation, that contamination from or of other products is avoided, that an adequate turnover of the stored medicinal products takes place and that products are stored in appropriately safe and secure areas. In addition to this, the quality system should ensure that the right products are delivered to the right addressee within a satisfactory time period. A tracing system should enable any faulty product to be found and there should be an effective recall procedure.

2. General Principles

2.1 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/her agent.

2.2 The principles of GDP should be included in national legislation and guidelines for the distribution of medicinal products, in a Member State as applicable, as a means of establishing minimum standards.

2.3 The principles of GDP are applicable both to medicinal products moving forward in the distribution chain from the manufacturer to the entity responsible for dispensing or providing medicinal 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.

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

2.5 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.

2.6 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 medicinal products to patients to ensure the quality and safety of medicinal products and prevent the exposure of patients to counterfeit medicinal products.

3. Regulation of the Distribution of Medicinal Products

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

3.2 The distributor or the organization to which the distributor belongs should be an entity that is appropriately authorized in terms of applicable legislation to perform the function(s) that it intends to perform. The distributor or the

organization to which it belongs should be held accountable for the activities that it performs which relate to the distribution of pharmaceutical products.

3.3 Only persons or entities that are authorized to distribute medicinal products by wholesale are entitled to engage in such activity. Such authorization may either be through the holding of a wholesale distribution authorization or in the form of a manufacturing authorization, the latter including an authorization to distribute by wholesale the medicinal product covered by the authorization,

3.4 The holder of an authorisation to distribute medicinal products by wholesale, or his/her agent, must comply with certain obligations in relation to the wholesale distribution of medicinal products. These obligations are set out in Title VII of Directive 2001/83/EC. They require that the holder of the authorisation:

a. Must comply with the principles and guidelines for good distribution practices.

b. Shall only distribute medicinal products within or to a Member State in respect of which a marketing authorization has been granted, that allows the use of said medicinal products in that Member State, and shall furthermore ensure that said distribution is in accordance with the provisions of the authorization.

c. Must have suitable and proper staff, premises, installations and equipment, so as to ensure proper conservation and distribution of medicinal products, and shall make such premises, installations and equipment accessible at all times to the persons responsible for inspecting them.

d. Must have a qualified person designated as responsible (known as the Responsible Person).

e. Must obtain supplies of medicinal products only from persons or entities that are in possession of a distribution authorization or who are exempt from obtaining such authorization by virtue of being in possession of a manufacturing authorization.

f. Must supply medicinal products only to persons or entities that are themselves in possession of a distribution authorization or who are authorized or entitled to sell or supply medicinal products directly to a patient or to his/her agent.

g. Must have an emergency plan which ensures effective implementation of any recall from the market ordered by the competent authorities or carried out in cooperation with the manufacturer or marketing authorization holder for the medicinal product concerned

h. Must keep records either in the form of purchase/sales invoices, or on computer, or in any other form, giving for any transaction in medicinal products received or dispatched at least the following information: the date, the name of the medicinal product, the quantity received or supplied, the name and address of the supplier or consignee, as appropriate. Such records must be kept available to the competent authorities for inspection purposes for a period of five years.

i. Shall, for all supplies of medicinal products to a person authorized or entitled to supply medicinal products to the public, enclose a document that makes it possible to ascertain the date, the name and pharmaceutical form of the medicinal product, the quantity supplied, and the name and address of the supplier and consignor.

j. Shall ensure, within the limits of their responsibilities, appropriate and continued supplies of medicinal products to pharmacies and persons authorised to supply medicinal products so that the needs of patients are covered.

3.5 The distribution of medicinal products via the Internet should be limited to registered and authorized mail-order pharmacies or other authorized entities.

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 accountable 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 indicated.

4.3 A management representative or Responsible 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. He/she should be appropriately qualified, should preferably be a licensed pharmacist, and should fulfil his/her responsibilities personally.

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 established 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 or on the integrity of medicinal products.

4.7 Individual duties and 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. At every level of the supply chain, employees should be fully informed and trained in their duties and responsibilities.

4.8 Some duties and responsibilities, such as equipment maintenance and calibration, and transport services, may be delegated or contracted out to suitably designated persons or entities as authorised and as necessary. There should, however, be no gaps or unexplained overlaps with regard to the application of GDP. These delegated and contracted out activities, and the respective duties and responsibilities, should be documented in written 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.

4.10 Wholesalers wishing to distribute or distributing medicinal products in Member State(s) other than the Member State in which the authorisation was granted should make available on request to the competent authorities of the other Member State(s) any information in relation to the authorization granted in the Member State of origin, namely the nature of the wholesaling activity, the address of sites of storage and distribution point(s) and, if appropriate, the area covered. Where appropriate, the competent authorities of this (these) other Member State(s) will inform the wholesaler of any public service obligation imposed on wholesalers operating on their territory.

5. Personnel

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

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

5.3 There should be an adequate number of competent and qualified personnel involved in all stages of the distribution of medicinal products in order to ensure that pharmaceutical quality assurance objectives are achieved, and that the quality of the product is maintained.

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

5.5 Training should be based on written standard operating procedures. Personnel should receive initial and continuing training relevant to their tasks, and be assessed as applicable, in accordance with a written training programme.

5.6 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.

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

5.8 Records of all training should be kept.

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

5.10 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. They

should also ensure that all members of staff are trained in, and observe high levels of, personal hygiene and sanitation.

5.11 Procedures and conditions of employment for employees, including contract and temporary staff, and other personnel having access to medicinal 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 medicinal products are suspected of, or found to be implicated in, any activities relating to the misappropriation, tampering, diversion, theft and/or counterfeiting 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 quality system should at least cover the main principles of quality assurance as embodied in the European Union's principles and guidelines of good manufacturing practice (GMP) in respect of medicinal products.

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

6.5 The quality system should include provisions to ensure that the holder of the marketing authorisation and the manufacturer (if different from the marketing authorisation holder) identified on the packaging material, the appropriate national and/or international regulatory bodies, as well as other relevant competent authorities, would be informed immediately in a case of confirmed or suspected counterfeiting of a medicinal product. Such products should be

stored in a secure, segregated area and clearly identified to prevent further distribution or sale.

6.6 Where electronic commerce (e-commerce) is used, namely, 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 medicinal products. Electronic transactions (including those conducted via the Internet) relating to the distribution of medicinal products should be performed only by authorised persons or entities,

6.7 Authorized procurement and release procedures for all administrative and technical operations performed should be in place, to ensure that appropriate medicinal products are sourced only from approved suppliers and distributed by approved entities. The approval should originate from the competent authority of the individual country where the legal entity is registered.

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 medicinal products.

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

6.10 If measures to ensure the integrity of the medicinal products in transit are in place, they should be managed properly. Thus, 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 medicinal products are suspected of being or are found to be counterfeit.

6.11 Distributors should from time to time conduct risk assessments to assess potential risks to the quality and integrity of medicinal 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 medicinal products

6.12 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.

6.13 All entities in the supply chain should be identifiable and 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.

6.14 Measures should be in place to ensure that medicinal 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.

6.15 Ideally there should be a procedure in place for the creation and maintenance of a pedigree for medicinal 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 authorisation and the manufacturer (if different from the marketing authorisation holder) identified on the packaging material, the appropriate national and/or international regulatory bodies, as well as other relevant competent authorities.

6.16 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. While it is understood that a differentiated approach may be necessary for different products and regions, pedigree and/or track-and-trace technologies provide possible options to ensure traceability.

7. Premises, Warehousing and Storage

7.1 Good storage practices (GSP) are applicable in all circumstances where medicinal products are stored and throughout the distribution process.

Storage areas

7.2 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 effi cient working environment.

7.3 Medicinal products should normally be stored apart from other goods and in agreement with national regulations.

7.4 Storage areas should be of sufficient capacity to allow the orderly storage of the various categories of medicinal products, namely products in quarantine, and released, rejected, returned or recalled products, as well as those suspected to be counterfeit.

7.5 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 specified temperature limits. Where special storage conditions are required on the packaging material (e.g. temperature, relative humidity), these should be provided, checked, monitored and recorded. Medicinal 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.

7.6 Storage areas should be clean, and free from accumulated waste and vermin. A written sanitation programme should be available indicating a regular 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 medicinal products. There should be appropriate procedures for the cleanup of any spillage to ensure complete removal of any risk of contamination. All sanitation, pest-control and spillage cleanup should be recorded and the records should be kept for at least five years.

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

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

7.9 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.

7.10 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 areas concerned should be appropriately identified.

7.11 Radioactive materials, narcotics and other hazardous, sensitive and/or dangerous medicinal 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 areas that are subject to appropriate additional safety and security measures.

7.12 Medicinal 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 stock is appropriately rotated, and that medicinal 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. Adequate controls should be in place to ensure that products beyond their expiry date or shelf life are separated from usable stock and neither sold nor supplied. In the presence of such controls, exceptions to the FEFO system may be permitted as appropriate.

7.14 Rejected medicinal products, such as those with broken seals, damaged packaging or suspected of possible contamination, should be identified and controlled under a quarantine system designed to ensure their withdrawal from saleable stock.

7.15 Unless there is an appropriate alternative system to prevent the unintentional or unauthorized use of quarantined, rejected, returned, recalled or suspected counterfeit medicinal products, such products should be stored in a clearly separated area so that they cannot be sold in error or contaminate other goods, until a final decision is taken on their fate.

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

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

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

Storage conditions

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

7.20 Storage conditions for medicinal products should be in compliance with the recommendations of the manufacturer and the instructions on the label, which are based on the results of stability testing.

7.21 Facilities should be available for the storage of all medicinal products under appropriate conditions.

Monitoring of storage conditions

7.22 Records should be maintained of the storage conditions of medicinal products if they are critical for the maintenance of the characteristics of the medicinal product stored.

7.23 Records of temperature monitoring data should be clear and 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 medicinal product plus one year, or as required by national legislation; a minimum period of five years is recommended.

7.24 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, and an alarm system constantly connected with at least two individuals should be in place to provide alerts when such fluctuations exceed established limits.

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

Stock rotation and control

7.26 Periodic stock reconciliation should be performed by comparing the actual and recorded stocks. This should be done at defined intervals.

7.27 All significant stock discrepancies should be investigated to check that there have been no inadvertent mix-ups, incorrect issues and receipts, thefts and/or misappropriations of medicinal products. Documentation relating to the investigation should be kept for a predetermined period.

7.28 Damaged medicinal products should not be issued and should be brought to the attention of the person responsible for distribution. Any action taken should be documented.

7.29 All stocks should be checked regularly for obsolete, outdated or expired medicinal products. All due precautions should be observed to prevent the issue of expired medicinal products.

7.30 Sales representatives should not be provided with samples of medicinal products which they retain for onward distribution, unless it is established that such samples are kept by the sales representative under conditions which are GDP complaint, in appropriate storage and/or transport facilities that comply with the labelled storage requirements of the medicinal product at all times, using procedures, security and controls to maintain the quality of the medicinal product and provide an audit trail and accountability for any stock, and supplied only to persons qualified to prescribe the medicinal product in accordance with national, regional and international legislation.

8. Vehicles and Equipment

8.1 Vehicles and equipment used to distribute, store or handle medicinal 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 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 to avoid contamination, build-up of dust or dirt and/or any adverse effect on the quality of medicinal products being distributed.

8.3 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 medicinal products while in the vehicle.

8.4 Dedicated vehicles and equipment should be used, where possible, when handling medicinal products.

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

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

8.7 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 national and regional regulatory requirements.

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

8.9 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.

8.10 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. A written cleaning programme should be available, indicating the frequency of cleaning and the methods to be used.

8.11 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 medicinal product quality.

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

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

8.14 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 at least the shelf-life of the stored medicinal product plus one year, or as required by national legislation; a minimum period of five years is recommended. Recorded monitoring data should be reviewed on receipt of medicinal products to assess whether the required storage conditions have been met.

8.15 Equipment used for monitoring conditions within vehicles and containers, e.g. temperature and humidity, should be calibrated and/or validated, as applicable, at regular intervals.

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

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

8.18 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.

9. Shipment Containers and Container Labelling

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

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

9.3 The need for any special transport and/or storage conditions should be stated on the shipment container label. If a medicinal 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.

9.4 All containers should be clearly labelled with at least the name of the material, the batch number, the expiry date, and the specified storage conditions, where applicable. Unauthorized abbreviations, names or codes should not be used. Only internationally and/or nationally accepted abbreviations, names or codes should be used in the labelling of containers.

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

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

10. Orders and Receipt of Incoming Medicinal Products

10.1 Orders from wholesalers should be addressed only to persons authorised to supply medicinal products as wholesalers or holders of a manufacturing or importing authorisation granted in accordance with Directive 2001/83/EC.

10.2 On receipt, each incoming delivery should be checked against the relevant purchase order and the batch release certificate, and each container physically verified, e.g. by the label description, batch number, type of medicinal product and quantity.

10.3 The assigned batch number and expiry date of medicinal products should be recorded at the point of receipt to facilitate traceability.

10.4 The consignment should be examined for uniformity of the containers and, if necessary, should be subdivided according to the supplier's batch number should the delivery comprise more than one batch.

10.5 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. Each container should be carefully inspected for possible contamination, tampering and damage, and any suspect containers or, if necessary, the entire delivery should be quarantined for further investigation.

10.6 When required, samples of medicinal products should be taken only by appropriately trained and qualified personnel and in strict accordance with written sampling instructions. Containers from which samples have been taken should be labelled accordingly. The samples should be stored in accordance with the instructions on the label and retained for at least one year after the expiry date.

10.7 All incoming medicinal products should be subject to quarantine and clearly labeled accordingly. Batch segregation should be maintained during quarantine and all subsequent storage.

10.8 Medicinal products should remain in quarantine until an authorized release or rejection is obtained. Medicinal products which are so released or rejected should be clearly labeled accordingly.

10.9 Measures should be taken to ensure that rejected medicinal products cannot be distributed. They should be stored separately from other materials and medicinal products while awaiting destruction or return to the supplier.

11. Dispatch

11.1 Medicinal products should only be sold and/or distributed to persons or entities that are authorised to acquire such products as demonstrated by the applicable national, regional and international legislation. Written proof of such authority must be obtained prior to the dispatch of products to such persons or entities.

11.2 The supplier of medicinal products should, prior to the dispatch of such products, ensure, by means of a quality agreement and audits, that the person or entity, e.g. the contract acceptor for transportation of the medicinal products, is aware of the medicinal products to be distributed and complies with the appropriate storage and transport conditions.

11.3 The dispatch and transportation of medicinal products should be commenced only after the receipt of a valid delivery order or material replenishment plan which should be documented.

11.4 Written procedures for the dispatch of medicinal products should be established. Such procedures should take into account the nature of the product, as well as any special precautions to be observed. Medicinal products under quarantine will require release for dispatch by the Responsible Person.

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

- date of dispatch;
- complete business name and address, type of entity responsible for the transportation, telephone number and names of contact persons;
- complete business 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 (if applicable);
- assigned batch number and expiry date (where not possible at dispatch, this information should at least be kept at receipt to facilitate traceability);
- the batch release certificate;
- applicable transport and storage conditions; and
- a unique number to allow identification of the delivery order.

11.6 Records of dispatch should contain enough information to enable traceability of the medicinal 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 medicinal products. Each party involved in the distribution chain has a responsibility to ensure traceability.

11.7 All records should be clear, readily accessible and available upon request.

11.8 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.

11.9 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.

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

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

11.12 Medicinal 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.

12. Transportation and Products in Transit

12.1 The transportation process should not compromise the integrity and quality of medicinal products.

12.2 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 medicinal products.

12.3 The people responsible for the transportation of medicinal 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.

12.4 Medicinal 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; and
- appropriate environmental conditions are maintained e.g. using cold chain for thermolabile products.

12.5 A batch tracking system should be used to enable specific batches to be traced during the distribution process.

12.6 The required storage conditions for medicinal products should be maintained within acceptable limits during transportation. There should be no gross deviation from the specific storage conditions for the product, or deviation for an unacceptable period of time, during the transit period. 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 medicinal product should be contacted for information about appropriate steps to be taken. 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.

12.7 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 by the manufacturer on the labels, monitored and recorded.

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

12.9 Products containing hazardous substances, such as highly active, toxic, radioactive materials, and other dangerous medicinal products presenting special risks of abuse, fire or explosion (e.g. combustible liquids, solids and pressurized gases) should be stored in safe, dedicated and secure areas, and transported in safe, suitably designed, dedicated and secure containers and vehicles. In addition, the requirements of applicable international agreements and national legislation should be complied with.

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

12.11 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.

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

12.13 Products containing toxic and/or flammable substances should be stored and transported in suitably designed, separate and closed containers, in accordance with national legislation and international agreements.

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

12.15 Packaging materials and transportation containers should be of suitable design to prevent damage of medicinal products during transport. Seal control programmes should be in place and managed properly.

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

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

12.18 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.

12.19 Medicinal products in transit must be accompanied by the appropriate documentation.

13. Documentation

13.1 Written instructions and records should be available which document all activities relating to the distribution of medicinal products, including all applicable receipts and issues (invoices). The name of the applicable entity should appear on all relevant documents. Records should be kept for seven years, unless otherwise specified in national or regional regulations.

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

- date;
- name of the medicinal product;
- quantity received, supplied, traded or brokered;
- name and address of the supplier or consignee, as appropriate;
- assigned batch number and expiry date;
- national identification number, where appropriate.
- the batch release certificate;

13.3 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 documents from external sources.

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

13.5 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.

13.6 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.

13.7 The nature, content and retention of documentation relating to the distribution of medicinal products should comply with national legislative requirements. The documents should be retained for at least one year after the expiry date of the product concerned; a minimum period of five years is recommended.

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

13.9 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.

13.10 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.

13.11 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 competent authority as required.

13.12 Records relating to storage of medicinal products should be kept, and be clear and readily available upon request. Written instructions and records should be available which document all activities in the storage areas including the handling of expired stock. These should adequately describe the storage procedures and define the route of medicinal products and information through the organization in the event of a product recall being required.

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

13.14 Records should be kept for each delivery. They should include the description of the goods, quality, quantity, supplier, supplier's batch number, the date of receipt, assigned batch number and the expiry date. Such records should be retained for at least one year after the expiry date of the product concerned; a minimum period of five years is recommended.

13.15 Comprehensive records should be maintained showing all receipts and issues of medicinal products according to a specified system, e.g. by batch number.

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

13.17 In the case of temperature-sensitive medicinal products, records of investigations and actions should be retained for at least one year after the expiry date of the product concerned; a minimum period of five years is recommended.

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

13.19 All documentation should be made available on request of the competent authorities.

14. Repackaging and Relabelling

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

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

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. Safety features should be replaced by ones which are qualitatively and quantitatively equivalent as regards the possibility to ascertain identification, authenticity and uninterrupted traceability of the medicinal product, and without opening the immediate packaging.

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

15. Complaints

15.1 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.

15.2 A person should be designated responsible for handling the complaints and deciding the measures to be taken together with sufficient supporting staff to assist him. If this person is not the Responsible Person, the latter should be made aware of any complaint, investigation or recall.

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

15.4 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).

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

15.6 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.

15.7 Product quality problems or suspected cases of counterfeit products should be documented and the information shared with the appropriate national and/or regional regulatory authorities.

15.8 All the decisions and measures taken as a result of a complaint should be recorded and referenced to the corresponding batch records.

15.9 Complaints records should be reviewed regularly for any indication of specific or recurring problems requiring attention and possibly the recall of marketed products.

15.10 Special attention should be given to establishing whether a complaint was caused because of counterfeiting.

16. Recalls

16.1 There should be a system which includes a written procedure, to recall promptly and effectively medicinal products known or suspected to be defective or counterfeit. The system should comply with the guidance issued by the national or regional regulatory authority.

16.2 Such procedures should be checked regularly and updated as necessary.

16.3 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.

16.4 Information on a recall should be shared with the appropriate national or regional 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.

16.5 A person should be designated as responsible for execution and co-ordination of recalls and should be supported by sufficient staff to handle all the aspects of the recalls with the appropriate degree of urgency. This responsible person should normally be independent of the sales and marketing organisation. If this person is not the Responsible Person, the latter should be made aware of any recall operation.

16.6 Recall operations should be capable of being initiated promptly and at any time.

16.7 The recall message approved by the holder of the marketing authorisation and, when appropriate, by the competent authorities, should indicate whether the recall should be carried out also at retail level. The message should request that the recalled products be removed immediately from the saleable stock and stored separately in a secure area until they are sent back according to the instructions of the holder of the marketing authorisation.

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

16.9 Recalled medicinal 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.

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

16.11 The particular storage conditions applicable to a medicinal 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.

16.12 All customers (other wholesalers, retail or hospital pharmacists and persons entitled to sell medicinal products to the public) and competent authorities of all countries to which a given medicinal product may have been distributed should be informed promptly and with the appropriate degree of urgency of any intention to recall the product because it is, or is suspected to be, defective or counterfeit.

16.13 All records should be readily available to the designated person(s) responsible for recalls. These records should contain sufficient information (addresses, phone and/or fax numbers inside and outside working hours, batches and amounts delivered) on medicinal products supplied to customers (including exported products and medical samples) to enable all destinees of a medicinal product, or those having received only the batch to be recalled, to be immediately identified and contacted.

16.14 The progress of a recall process should be recorded at the time it is carried out and a final report issued, which includes a reconciliation between delivered and recovered quantities of products. The records should be made available to the competent authorities of the Member States on whose territory the products were distributed.

16.15 When necessary emergency recall procedures should be implemented.

17. Rejected and Returned Products

17.1 Rejected medicinal products and those returned to a distributor should be appropriately identified and handled in accordance with an approved

procedure which involves at least the physical segregation of such medicinal products in quarantine in a dedicated area, or other equivalent (e.g. electronic) segregation, to avoid confusion and prevent return to saleable stock and distribution until a decision has been taken with regard to their disposition. The storage conditions applicable to a medicinal 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.

17.2 A wholesale distributor should receive medicinal product returns or exchanges from a pharmacy or other persons authorized to administer or dispense drugs pursuant to the terms and conditions of an agreement between the wholesale distributor and the pharmacy or authorized person. Both wholesale distributors and pharmacies or other persons authorized to administer or dispense drugs shall be accountable for administering their returns process and ensuring that the aspects of this operation are secure and do not permit the entry of adulterated or counterfeit product

17.3 Returned products should only be returned to saleable stock if the goods are in their original unopened containers and in good condition, if it is known that that the goods have been stored and handled under proper conditions and if the remaining shelf life is acceptable.

17.4 The necessary assessment and decision regarding the disposition of such products must be taken by a nominated, 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 medicinal product it should not be considered suitable for reissue or reuse.

17.5 Medicinal products returned from patients to pharmacies should not be taken back as stock, but should be destroyed.

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

17.7 Any returned stock reissued should be so identified and recorded in stock records. Products returned to saleable stock should be placed such that the FEFO or FIFO system operates effectively.

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

17.9 When medicinal products are destroyed this should be done in accordance with international, national and local requirements regarding disposal of such products, and with due consideration to protection of the environment.

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

18. Counterfeit Pharmaceutical Products

18.1 The sale and distribution of any counterfeit or suspected counterfeit medicinal products found in the distribution chain should be suspended and the medicinal product segregated immediately from other medicinal products to avoid any confusion, and recorded.

18.2 The holder of the marketing authorization, and the appropriate national and/or international competent authorities should be informed immediately.

18.3 Counterfeit or suspected counterfeit medicinal products should be clearly labelled as not for sale, to prevent further distribution or sale.

18.4 Upon confirmation of the medicinal 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.

19. Cross-Border Movement of Medicinal Products

19.1 Consideration should be given to procedures for cross-border movement of medicinal products. The following aspects should be given particular attention.

19.2 The number of ports of entry in a country for the handling of cross-border movement of medicinal products should be limited by appropriate legislation. Such ports could be designated by the state.

19.3 The most appropriately located and best equipped to handle cross-border movement of medicinal products should be chosen as the port(s) of entry for the import of such products into a country.

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

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

19.6 Where necessary, people with pharmaceutical training should be involved with the customs procedures or should be readily contactable.

19.7 The quality of medicinal products moving in international commerce should be established using data regarding quality assessment of medicinal products which is compliant with international and national legislation.

19.8 Customs, enforcement agencies and regulatory agencies responsible for supervision of medicinal products should establish means for cooperation and information exchange in order to prevent importation of counterfeit medicinal products.

20. Contract Activities

20.1 Some duties and responsibilities may be delegated or contracted out to suitably designated persons or entities as authorized and as necessary. Duties and responsibilities may only be delegated to entities which are suitably authorized to perform the contracted activity in line with national legislation.

20.2 Any activity relating to the distribution of a medicinal product which is delegated to another person or entity should be performed by parties appropriately authorized for that function and according to the terms of a written contract which is agreed upon by the contract giver and the contract accepter. The contract giver should seek the approval for the delegation of the activity, and the evaluation and approval of the written contract, from the marketing authorisation holder of any medicinal product whose quality may be affected by the delegation of the activity.

20.3 The contract should define the respective responsibilities of each party including observance of the principles of GDP and relevant warranty clauses. Technical aspects of the contract should be drawn up by competent persons suitably knowledgeable in GDP. There should be no gaps or unexplained overlaps with regard to the application of GDP. The contract should also include responsibilities of the contract accepter for measures to avoid the entry of counterfeit medicinal products into the distribution chain, such as by suitable training programmes.

20.4 The contract giver should be responsible for assessing the competence of the contract acceptor to carry out successfully the work required and for ensuring

by means of the contract that the principles and guidelines of GDP as interpreted in this guide are followed.

20.5 The contract giver should provide the contract acceptor with all the information necessary to carry out the contracted operations correctly in accordance with the marketing authorisation and any other legal requirements. The contract giver should ensure that the contract acceptor is fully aware of any problems associated with the product or the work which might pose a hazard to his premises, equipment, personnel, other materials or other products.

20.6 The contract giver/acceptor should ensure that all medicinal products delivered to him by the contract acceptor/giver comply with their specifications and have been released for such delivery by a Qualified Person or Responsible Person.

20.7 The contract acceptor must have adequate premises and equipment, knowledge and experience, and competent personnel to carry out satisfactorily the work ordered by the contract giver.

20.8 Subcontracting may be permissible, under certain conditions. However, the contract acceptor should not pass to a third party any of the work entrusted to him under the contract (subcontracting) without the contract giver's prior evaluation and written approval of the arrangements. All subcontractors should be authorized for the functions subcontracted to them. Arrangements made between the contract acceptor and any third party should ensure that information is made available in the same way as between the original contract giver and contract acceptor.

20.9 The contract acceptor should refrain from any activity which may adversely affect the quality of the medicinal product.

20.10 All distribution records and samples should be kept by, or be available to, the contract giver. Any records relevant to assessing the quality of a product in the event of complaints or a suspected defect must be accessible and specified in the defect/recall procedures of the contract giver.

20.11 The contract should permit the contract giver to visit the facilities of the contract acceptor.

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

20.13 Any contract accepter should be audited periodically.

21. Self-Inspection

21.1 The system of quality assurance 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 Personnel matters, premises, equipment, documentation, distribution of medicinal products, arrangements for dealing with complaints and recalls, and self inspection, should examined at intervals following a pre-arranged programme in order to verify their conformity with the principles of quality assurance.

21.3 Self-inspections should be conducted in an independent and detailed way by a designated, competent person. Independent audits by external experts may also be useful.

21.4 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.

22. Bibliography

22.1 Guidelines on Good Distribution Practice of Medicinal Products for Human Use (Text with EEA Relevance) (94/C 63/03)

22.2 WHO guide to good storage practices for pharmaceuticals. In: *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-seventh report.* Geneva, World Health Organization, 2003 (WHO Technical Report Series, No. 908), Annex 9.

22.3 WHO guide to good distribution practices for pharmaceuticals. In: *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth report.* Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 5.

22.4 WHO good distribution practices for pharmaceutical products. In: *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-*

fourth report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No, 957), Annex 5.

22.4 Guidelines for Good Manufacturing Practices for Medicinal Products for Human and Veterinary Use. In: *The Rules Governing Medicinal Products in the European Union*, Volume 4.

22.5 UK Guidance on Wholesale Distribution Practice. In: *Rules & Guidance for Pharmaceutical Manufacturers & Distributors*, Medicines and Healthcare products Regulatory Agency (MHRA), 2007.

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ANNEX I
Glossary of terms

agreement
Arrangement undertaken by and legally binding on parties.

auditing
An independent and objective activity designed to add value and improve an organization's operations by helping an organization to accomplish its objectives by using a systematic, disciplined approach to evaluate and improve the effectiveness of risk management, control and governance processes.

batch
A defined quantity of medicinal products processed in a single process or series of processes so that it is expected to be homogeneous.

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

batch release certificate
A certificate confirming that, in respect of a batch of medicinal product, the activities referred to in Article 51 of Directive 2001/83/EC have been carried out by the Qualified Person referred to in Article 49 of Directive 2001/83/EC.

broker
A person or an entity whose activity involves the broker entering independently and on behalf of a third party into a contract with a person or entity whereby the broker receives a commission for any business he brings to the person or company calculated as a percentage of the transaction mediated between that entity and the third party. However, the broker normally does not actually take physical control of the medicines.

consignment (or delivery)
The quantity of medicinal products 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
The material employed in the packaging of a medicinal 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
The undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or on to a medicinal product during handling, sampling, packaging, storage or transport.

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

counterfeit medicinal product
A counterfeit medicinal product is one with a deliberate and fraudulently false or misleading representation of its identity (including its packaging and labelling, name, composition in respect of any of its components, including excipients, and strength) and/or its source (including the manufacturer, country of manufacture, country of origin, marketing authorisation holder) and/or its history (including the records and documents relating to distribution channels). Counterfeiting can apply to both branded and generic products, and counterfeit medicinal products may include products with the correct ingredients, with the wrong ingredients, without active ingredients, with an incorrect quantity of active ingredients or with fake packaging. It does not include unintentional manufacturing errors.

cross-contamination
Contamination of a starting material, intermediate product or finished medicinal product with another starting material or product during production, storage and transportation.

distribution
All activities consisting of procuring, purchasing, holding, storing, selling, supplying, importing, exporting or movement of medicinal products, with the exception of the dispensing or providing medicinal products directly to a patient or his/her agent. Such activities are carried out with manufacturers or their depositories, importers, other wholesale distributors or with pharmacists and persons authorized or entitled to supply medicinal products to the public.

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 medicinal product to aid in the processing of the drug delivery system during its manufacture, protect, support or enhance stability, bioavailability, or patient acceptability, assist in product identification, or enhance any other attribute of the overall safety and effectiveness of the drug during storage or use. Excipients include

fillers, disintegrants, lubricants, colouring matters, antioxidants, preservatives, adjuvants, stabilisers, thickeners, emulsifiers, solubilisers, permeation enhancers, flavouring and aromatic substances, as well as the constituents of the outer covering of the medicinal products, such as gelatin capsules.

expiry date
The date given on the individual container (usually on the label) of a product up to and including the date on 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.

first expiry/first out (FEFO)
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; earliest expiry/first out (EEFO) has a similar meaning.

first in/first out (FIFO)
A distribution procedure to ensure that the oldest stock is distributed and/or used before a newer and identical stock item is distributed and/or used.

forwarding agent
A person or entity engaged in providing, either directly or indirectly, any service concerned with clearing and forwarding operations in any manner to any other person and includes a consignment agent.

good distribution practices (GDP)
Good distribution practices are that part of quality assurance that ensures that the quality of a medicinal product is maintained by means of adequate control of the numerous activities which occur throughout the distribution process as well as providing a tool to secure the distribution system from counterfeits, unapproved, illegally imported, stolen, counterfeit, substandard, adulterated, and/or misbranded medicinal products..

good manufacturing practices (GMP)
That part of quality assurance which ensures that medicinal products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.

good pharmacy practice (GPP)
The practice of pharmacy aimed at providing and promoting the best use of medicines and other health care services and products, by patients and members of the public. It requires that the welfare of the patient is the pharmacist's prime concern at all times.

good storage practices (GSP)

That part of quality assurance that ensures that the quality of medicinal products is maintained by means of adequate control throughout the storage thereof.

good trade and distribution practices (GTDP)
That part of quality assurance that ensures that the quality of medicinal products is maintained by means of 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 medicinal products to the end user.

intermediate product
Partly processed product that must undergo further manufacturing steps before it becomes a bulk finished product.

labelling
Information on the immediate or outer packaging which permits the process of identifying a medicinal 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.

manufacture
All operations of purchase of materials and products, production, quality control, release, storage and distribution of medicinal 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.

marketing authorisation
A legal document issued by the competent medicines regulatory authority for the purpose of marketing or free distribution of a product after evaluation for safety, efficacy and quality. It must set out, inter alia, the name of the product, the pharmaceutical dosage form, the quantitative formula (including excipients) per unit dose (using INNs or national generic names where they exist), the shelf-life and storage conditions, and packaging characteristics. It specifies the information on which authorization is based (e.g. “The product(s) must conform to all the details provided in your application and as modified in subsequent correspondence”). It also

contains the product information approved for health professionals and the public, the sales category, the name and address of the holder of the authorization, and the period of validity of the authorization. Once a product has been given marketing authorization, it is included on a list of authorized products — the register — and is often said to be "registered" or to "have registration". Market authorization may occasionally also be referred to as a "licence" or "product licence".

medicinal product
Any substance or combination of substances presented as having properties for treating or preventing disease in human beings or animals, or which may be used in or administered to human beings or animals either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.

name of the medicinal product
The name, which may be either an invented name not liable to confusion with the common name, or a common or scientific name accompanied by a trade mark or the name of the marketing authorization holder. The common name is the international non-proprietary name recommended by the World Health Organization, or, if one does not exist, the usual common name.

package leaflet
A leaflet containing information for the user which accompanies the medicinal product.

packaging material
Any material, including printed material, employed in the packaging of a medicinal product, but excluding any outer packaging used for transportation or shipment. Packaging materials are referred to as immediate (or primary) or outer (or secondary). Immediate packaging constitutes the container or other form of packaging immediately in contact with the medicinal product, while outer packaging is the packaging into which the immediate packaging is placed.

parallel trader
A person or entity involved in the purchase, repackaging, relabelling and resale of medicines. The profits of a parallel trader are mainly based on arbitrage business which he realizes by the purchase of medicines in a low-price country and the sale of medicines in a higher priced country.

pedigree
A complete record that traces the ownership and transactions of a medicinal product as it is distributed through the supply chain.

product recall
A process for withdrawing or removing a medicinal 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.

production
All operations involved in the preparation of a medicinal product, from receipt of materials, through processing, packaging and repackaging, labelling and relabelling, to completion of the finished product.

public service obligation
The obligation placed on wholesalers to guarantee permanently an adequate range of medicinal products to meet the requirements of a specific geographical area and to deliver the supplies requested within a very short time over the whole of the area in question.

quality assurance
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 medicinal 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 medicinal 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 medicinal products isolated physically or by other effective means while a decision is awaited on their release, rejection or reprocessing.

Responsible Person
The qualified person designated as responsible in terms of Article 79 of Directive 2001/83/EC, with regards to the minimum requirements to obtain an authorization for the wholesale distribution of medicinal products.

retention sample
A sample of a fully packaged unit from a batch of finished product. It is stored for identification purposes. For example, presentation, packaging, labelling, patient information leaflet, batch number, expiry date should the need arise during the shelf life of the batch concerned.

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

shelf-life
The period of time during which a medicinal 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 medicinal products and materials up to their point of use.

supplier
A person or company engaged in the activity of providing products and/or services.

trading
All activities consisting of negotiating independently on behalf of another person the sale or the purchase of medicinal products, or billing or brokering medicinal products, apart from supplying medicinal products to the public, and not falling under the definition of wholesale distribution.

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

validation
Action of proving and documenting that any process, procedure or method actually and consistently leads to the expected results.

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