MINISTRY OF PUBLIC HEALTH

ORDER
on approval of the Guideline on Good Distribution Practice of Wholesale Medicinal Products

On seeing the Approval Report of the Pharmaceutical Directorate No. EN 12.412 of 2 December 2008,

Taking into account provisions of Title XVII – The medicinal product of Law No. 95/2006 on healthcare reform, with further amendments and completions,

Based on Government Decision No. 862/2006 on organisation and functioning of the Ministry of Public Health, with further amendments and supplementations,

the Minister of Public Health hereby issues the following Order:

Art. 1. – The Guideline on Good Distribution Practice of Wholesale Medicinal Products is approved, in accordance with the Annex which is integral part of this Order.

Art. 2. - On the present Order coming into force, Minister of Public Health Order No. 892/2006 is repealed, in view of approval of the Good Distribution Practice of Wholesale Medicinal Products, published in the Official Gazette of Romania, Part I, No. 653 of 28 July 2006.

Art. 3. – This Order is carried out by the National Medicines Agency and is to be published in the Official Gazette of Romania, Part I.

Minister of Public Health,

Gheorghe Eugen Nicolăescu

Bucharest, 2 December 2008.
No. 1.963.

ANNEX

GUIDELINE
on Good Distribution Practice of Wholesale Medicinal Products

CHAPTER I

Art. 1. - This Guideline represents the translation and adaptation of the Guideline on Good Distribution Practice of medicinal products for human use (94/C63/03), issued by the European Commission based on the provisions of Art. 10 of the European Commission Council Directive No. 92/25/EEC of 31 March 1992 concerning the wholesale distribution of medicinal products for human use, amended with provisions of the Guideline on Good Distribution Practice for Pharmaceutical Products (WHO Technical Report Series No. 937, 2006), issued by the World Health Organisation. This Guideline refers neither to the commercial relations between the parts involved in the distribution of medicinal products for human use, nor to the aspects concerning labour protection.

CHAPTER II
Principles

Art. 2. - (1) The 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.

(2) This level of quality should be maintained throughout the distribution network so that authorised medicinal products are distributed to pharmacies without any alteration of their properties.

(3) 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, approved through the NMA Scientific Council Decision No. 38/2006, and applies for the distribution of medicinal products for human use.

(4) To maintain the quality of the products and of the services provided by wholesalers, title XVII of Law No. 95/2006, as amended, provides that wholesalers must comply, in addition, with the Guideline on Good Distribution Practice published by the Commission of the European Community.

(5) The quality system operated by distributors (wholesalers) of medicinal products should ensure that medicinal products that they distribute are authorised for marketing in accordance with the legislation in force, that contamination from or of other products is avoided, that an adequate turnover of the stored medicinal products takes place and that medicinal products are stored in appropriately safe and secure areas.

(6) In addition to this, the quality system should ensure that the right medicinal 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.

CHAPTER III
Definitions

Art. 3. - The terms and notions given below apply to the terms used in this Guideline (they may have different meanings in other contexts):

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

2. *Batch (lot)* - 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;

3. *Batch (lot)* number – a specific combination of numbers and/or letters specifically identifying a batch;

4. *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.

5. *Contamination* - The undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or on to a finished product during handling, production, sampling, packaging or repackaging, storage or transport;

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

7. *Cross-contamination* - Contamination of a material or product with another material or product;

8. *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.

9. Distribution (delivery) – quantity of medicinal products provided once, as an answer to a certain demand or order; a delivery may consist of one or several packages or containers and may include several batches of the same product;

10. 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.

11. 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.

12.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;

13.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.

14.Good distribution practices (GDP) - that part of quality assurance ensuring that the quality of a medicinal products is maintained through adequate control throughout the numerous activities which occur during the distribution process up to the final user, and also ensuring that all measures are taken in order to prevent the occurrence of counterfeited, unauthorised or illegally produced medicinal products;

15.Health establishment - 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.

16.Intermediary agent – physical natural or juridical legal person entity whose tasks include the signing of a contract with another natural or legal entityphysical or juridical person, for which the intermediate agent receives a commission for each service provided to that person or company, calculated as a percentage of the transaction between the company and its partner; normally, the intermediate agent does not take over the physical control of medicinal products.

17.Intermediate product - Partly processed product that must undergo further manufacturing steps before it becomes a finished product.

18.IT service provider – physical or juridical person ensuring IT services for other juridical persons (manufacturers or providers) for all operations included in the distribution chain or only for certain operations within the distribution chain. Usually, third part IT service providers are specialised in integrated transportation and storage services which may adapt to the clients' delivery needs and requirements. An IT service provider has no proprietary rights on the stored or distributed medicinal products.

19.Labelling - Process of identifying a medicinal product including the following information, as appropriate: - name, - active substance(s) 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.

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

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

22.Parallel distributor – physical or juridical person involved in the acquirement, repackaging, relabelling and remarketing of medicinal products; the parallel distributor gains profit mainly by acquiring medicinal products at low prices from certain countries and selling them for a higher price in other countries;

23.Product recall - a process for withdrawing or removing a medicinal 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 competent authority;

24.Provider – person or entity involved in the delivery of products and/or services;

25.Quality assurance - the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use.

26.Quality control - Quality control covers all measures taken, including the setting of specifications, sampling, testing and release of the quality certificate, to ensure that starting materials, intermediates, packaging materials and finished products conform with established specifications for identity, strength, purity, shelf-life, storage conditions and other characteristics;

27.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.

28.Quarantine - The status of starting or packaging materials, intermediates, bulk or finished products isolated physically or by other effective means while a decision is awaited on their release or rejection;

29.Sampling – operations in view of obtaining a representative sample of a medicinal product, based on an adequate statistical procedure, aiming for a defined purpose, e.g. testing in view of the quality batch release;

30.Shelf-life - The period of time during which a finished 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;

31.Standard Operating Procedure (SOP) - An authorizauthorised, 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, cleaning, validation, cleaning of premises, environmental control, sampling and inspection); certain SOPs may be used to supplement product-specific master and batch production documentation.

32.Transit - period of time in which the product is transported to its destination;

33.Validation - 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.

34.Vehicle – means of transport which are used to convey pharmaceutical products (trucks, vans, buses, minibuses, cars, trailers, aircraft, railway carriages, boats etc.)

35.Wholesale chain distribution (total) – wholesale distribution activity consisting in acquiring, marketing, storage, set up of the order and delivery of medicinal products;

CHAPTER IV
Organisation and management

Art. 4. - (1) Each wholesale distribution unit should own an adequate organizational structure defined with the aid of an organizational chart.

(2) The responsibility, authority and interrelationships of all personnel should be clearly defined in the approved job descriptions, available in written form.

(3) The employees' duties should be compliant with their competence.

Art. 5. - (1) The leading personnel should have the authority and own the necessary resources in order to accomplish the given tasks, the enforcement and maintenance of a management quality system, as well as to identify and check the deviations from the established quality management system.

(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.

Art. 6. - (1) Some duties may be delegated or contracted out to suitably designated persons.

(2) There should, however, be no gaps or unexplained overlaps with regard to the application of this Guideline.

(3) There should be periodic audit of such activities with regards to application of this Guideline.

Art. 7. - Safety procedures relating to all relevant aspects including the safety of personnel and property, environmental protection and product integrity, should be in described in standard operating procedures.

CHAPTER V
Personnel

Art. 8. - All personnel involved in distribution activities should be competent and sufficient in number in view of ensuring the quality's maintenance.

Art. 9. - (1) The personnel should be trained when hired and periodically, in accordance with an annual instruction programme; the training's efficacy should be assessed.

(2) The training should be carried out in accordance with standard procedures and records of this training should be stored, mentioning the participants and the themes exposed.

(3) Apart from general provisions concerning the good manufacturing practice, training should include themes specific to the type of activity which is being carried out, such as: medicinal product safety, aspects referring to the identification of medicinal products, ways of avoiding the entrance into the distribution chain of counterfeit medicinal products.

(4) The personnel handling medicinal product presenting a certain risk degree (e.g. strongly active, radioactive, psychotropes, narcotics, sensitising agents and/or hazardous ones) should benefit of targeted training.

Art. 10. - (1) The personnel involved in the distribution of medicinal products should wear the appropriate working/safety equipment, in accordance with the activities carried out.

(2) If needed, the personnel handling medicinal products presenting a certain risk should use protective gloves.

(3) Adequate procedures relating to the healthcare status, hygiene and personnel equipment should be conceived and enforced, in accordance with the activities carried out by the personnel.

Art. 11. - The wholesale distributor should enforce and apply an internal regulation describing the measures required in the circumstance under which the employees can be involved in the illegal appropriation of a medicinal product.

CHAPTER VI
Quality management

Art. 12. - The distributor should elaborate his documented quality policy, officially authorised by the highest manager, describing the overall intentions and the quality standards requested by the organisation.

Art. 13. – The distributor should own and apply procedures concerning the supply and delivery of medicinal products, including those related to the administrative and technical operations undertaken, attesting the fact that the acquisition of necessary medicinal products is done with the help of authorised providers and that their distribution is done by authorised distribution units.

Art. 14. - (1) The quality system of a wholesale distributor should contain provisions concerning the must of immediate information of the marketing authorisation holder, national and/or international competent authorities, in case of the identification of medicinal products suspected of counterfeiting or counterfeited.

(2) Such products should be stored in a secured, separate area, and they should be clearly marked, in order to prevent a subsequent distribution or sale.

Art. 15. - (1) 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.

(2) All entities in the supply chain should be traceable; and on the national policies and legislation; there should be records to ensure traceability of the products distributed from the manufacturer/importer to the retail distributor.

Art. 16. - (1) The compliance of the quality system implemented by a distributor may be certified in accordance with the international standards (e.g. ISO standards) by the accredited entities, however such certification can absolutely not be a substitute for the obligation to respect the legislation concerning the wholesale distribution of medicinal products for human use.

(2) The ISO certification cannot be seen as a substitute for the distribution authorisation released by the National Medicines Agency (NMA), the Romanian competent authority in the healthcare field.

CHAPTER VII
Premises

Art. 17. - (1) Premises must be located, designed, constructed, adapted, and maintained to suit the operations to be carried out; the purpose of these measures is to avoid any kind of undesired or unexpected effect on the quality of medicinal products.

(2) The layout of premises should be appropriate in order to permit effective maintenance of medicinal products depending on their status (“quarantine”, “released”, “recalled”, “withdrawn”, “returned”, as well as those products suspected of counterfeit).

(3) Measures should be taken in order to prevent the entering of unauthorised persons; storage areas should not be used as passing premises for the personnel who does not work there.

Art. 18. - Storage areas should be properly illuminated in order to permit the correct and safe course of all operations.

Art. 19. - (1) Storage areas should include their own safety temperature and humidity system in view of a proper maintenance of medicinal products in the conditions mentioned by the manufacturer and should have monitoring devices of the created conditions.

(2) Most medicinal products are stored under normal conditions: a maximum temperature of 25 degrees Celsius, relative humidity ranging between 60 ± 5%; when particular maintenance conditions are required, these should also be ensured, assessed and monitored.

(3) The uniformity of the temperature and humidity values of the storehouse should be assessed by editing a distribution map indicating the points where the monitoring devices of the two parameters shall be placed.

(4) The climatisation device should comprise warning functions, in case the specified temperature and humidity intervals are surpassed (visual/auditive alarm).

(5) The special devices used in view of the monitoring of the temperature and humidity conditions should be calibrated at established intervals, and the calibration's results should be kept.

(6) Records concerning the monitoring of conservation parameters should be periodically assessed; these are kept at least one year after the expiry of the availability period of a medicinal product in that storehouse, unless the legislation mentions otherwise.

Art. 20. - Premises should be designed and equipped so as to afford maximum protection against the entry of insects, birds or rodents; the rodenticides used should be safe and not be subject to contamination risk for the medicinal products.

Art. 21. - (1) At premises and storehouses, cleaning is done in accordance with an established procedure and programme.

(2) Adequate measures should be taken in order to prevent leaks or breakings, bacterial or crossed contamination; in case of leaks, there should be adequate cleaning procedures, so as to prevent any contamination risk.

Art. 22. - (1) Reception and expedition areas should ensure the protection of materials and products from bad weather.

(2) These areas should be segregated from the area meant for storage.

(3) An adequate space should be assigned in the reception area in order to clean up, when needed, the recipients containing medicinal products, prior to storage.

Art. 23. - Storage premises should contain fireproof stands, metal racks or made of other adequate materials, in view of the storage of recipients containing medicinal products, placed in order to allow the normal flow of the staff and handling equipment.

CHAPTER VIII
Storage

Art. 24. - (1) Storage and handling of medicinal products should be done in such manner that it prevents contamination and mix-ups.

(2) Normally, medicinal products should be stored away from other products.

(3) A defined storage area should be assigned for each medicinal product, so as to allow easy identification and handling of packagings by operators; to this

purpose, a valid electronic system or any other system leading to the same result may be used (e.g. the set up of a disposition map).

Art. 25. - (1) At the time of the reception, the recipients containing products should be examined relating to their integrity and compliance with the given order.

(2) Medicinal products with broken seals, damaged packaging or suspected to be contaminated should be withdrawn from the marketing stock and, in case they are not disposed immediately, should be stored in a dedicated area, clearly delimited, in order to not be marketed by mistake and to not contaminate other products.

Art. 26. - (1) When the quarantine status of the products is ensured through storage in physically delimited areas, these should be clearly marked, and access should only be permitted to the authorised staff.

(2) Any system replacing the physical quarantine should provide an adequate insurance degree; for example, computer systems may be used, provided that they are valid in order to assess the ability of securing access.

Art. 27. - (1) Physical or other equivalent validated (e.g. electronic) segregation should be provided for the storage of rejected, expired, recalled or returned materials or products.

(2) Recalled, expired, withdrawn or returned medicinal products, as well as products suspected of counterfeit and the areas where they are stored should be appropriately identified.

Art. 28. - Radioactive products, psychotropes, narcotics and other hazardous, sensitive and/or dangerous materials and pharmaceutical products, as well as substances presenting special risks of fire or explosion, (e.g. combustible liquids and solids and pressurized and inflammable gases) should be stored in dedicated areas that are subject to appropriate additional safety and security measures.

Art. 29. - (1) The medicinal products requiring special storage conditions (i.e. controlled medicinal products, medicinal products which require storage at certain temperatures) should be immediately identified and stored in accordance with written instructions and legal provisions in such cases.

(2) When the storage conditions aren’t specified on the labelling, the provisions of other standards in force should be followed. (e.g. pharmacopoeias)

Art. 30. - (1) There should be a procedure and a recording system ensuring that medicinal products having the most recent expiry date should be marketed and/or distributed in the first place (according to the "first expired, first out" principle - FEFO).

(2) The stocks should be refilled periodically by comparing the stored ones with the recordings.

(3) Any deviation observed concerning the situation of the stocks should be investigated, in order to check up whether unintentional mix-ups occurred, incorrect releases or illegal possession of medicinal products.

CHAPTER IX
Vehicles and equipment

Art. 31. - (1) Vehicles and equipment used to distribute, store, or handle medicinal 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.

(2) Measures should be taken in order to prevent the access of unauthorised persons (including by breaking and entering) in means of transport and/or at the handling equipment, as well as in order to prevent theft or illegal possessions of medicinal products transported.

Art. 32. - 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 or any adverse effect on the quality of medicinal products being distributed.

Art. 33. - (1) The means of transport and the recipients to be transported should have sufficient capacity in order to allow proper maintenance of medicinal products during transportation.

(2) There should be a system allowing segregation during transport of rejected, recalled, returned medicinal products and other products suspected of counterfeit.

(3) 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 delivered in a protective shipping carton or case.

Art. 34. - (1) The means of transport should have their own system meant to ensure the temperature and humidity needed for the storage of medicinal products under the specific conditions mentioned by the manufacturer and should have specific devices in order to monitor those conditions.

(2) Most of the medicinal products are stored and transported under normal conditions: temperature of maximum 25 degrees Celsius, relative humidity of 60 ± 5%; when special storage conditions are required, these should also be ensured, controlled and monitored.

(3) The devices used for the monitoring of temperature and humidity conditions should be calibrated at established intervals, and the results should be kept.

(4) The distributor should bring the proof of the monitoring of parameters such as temperature and humidity during the transportation of medicinal products, by keeping the recordings at least one year as of the expiry of a distributed medicinal product, unless the legislation specifies otherwise.

Art. 35. - (1) If possible, the transport and handling of medicinal products should be done by using means of transport and dedicated equipment.

(2) When non-dedicated means of transport and handling equipment are used, there should be procedures ensuring that medicinal product's quality shall not be compromised; adequate operations should be carried out, which should subsequently be checked and registered.

(3) Cleaning and fumigation agents should not influence negatively the products' quality.

(4) The equipment used for cleaning the vehicles should be chosen and used so as to not represent a contamination source.

Art. 36. - Defective means of transport and equipment should not be used: these should be labelled as "defective" or withdrawn from the distribution unit.

Art. 37. - The access of rodents, insects, birds and such in the means of transport, recipients and handling equipment; there should be written programs exposing the ad hoc measures taken by the wholesale distribution unit.

Art. 38. - The wholesale distribution unit should take into account the use of additional technology (e.g. satellite electronic devices, Global Positioning System (GPS)), if such means may lead to considerable safety of medicinal products during transportation.

CHAPTER X
Containers and container labelling

Art. 39. - All medicinal 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.

Art. 40. - (1) Special transport and/or storage conditions should be stated on the label, if needed.

(2) If a medicinal 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.

(3) Recipients to be transported may both be labelled with complete information concerning the recipient's content (in order to prevent theft), but should provide sufficient information relating to the handling and maintenance conditions and with the measures which should be taken in order to guarantee that the product is being handled appropriately every moment.

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

Art. 41. - Special care should be used when using dry ice in containers; in addition to safety issues it must be ensured that the product does not come into contact with the dry ice, as it may have an adverse effect on the quality of the product.

Art. 42. - 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.

CHAPTER XI
Dispatch

Art. 43. - (1) Pharmaceutical products should only be sold and/or distributed to juridical persons that are entitled to acquire such products that are authorised in Romania to distribute such products (wholesale, retail), in accordance with the law.

(2) Before distributing medicinal products, the wholesale distribution unit should obtain from the applicant the written proof attesting the existence of a valid marketing authorisation, released in accordance with the law.

Art. 44. - The distributor should provide adequate means of transport for the medicinal products being transported, which meet the requirements specified in Chapter IX, or may sign a contract with a transporter, if he makes sure that the latter meets the requirements imposed for the transport of medicinal products.

Art. 45. - The distributor and transport of medicinal products may be initiated only after receiving an available order in written form.

Art. 46. - There should be written procedures for the dispatch of pharmaceutical products, taking into account the nature of the product, as well as any special precautions to be observed.

Art. 47. - Records for the dispatch of pharmaceutical products should be prepared and should include at least the following information:

- date of dispatch ;
- full name (without abbreviations) and address of the wholesale distributor (juridical person), information about the transporter (telephone number, contact persons);
- full name (no abbreviations) and address of the juridical person/addressee (wholesale distribution unit, retail distribution unit);
- a description of the products including, e.g. name, pharmaceutical form and
strength (if applicable);
- quantity of the products, (i.e. number of containers and quantity per container – where required);
- assigned batch number and expiry date;
- applicable transport and storage conditions (if applicable);
- a unique number to allow identification of the delivery order.

Art. 48. - (1) Records of dispatch should contain enough information to enable traceability of the pharmaceutical product.

(2) Such records should facilitate the recall of a batch of a product as necessary; moreover, it should facilitate the discovery of counterfeited medicinal product sources, if required.

(3) Each party involved in the distribution chain has a responsibility to ensure the medicinal product's traceability.

Art. 49. - In case of emergency, wholesale distributors should be able to immediately deliver the medicinal products that they usually provide to those authorised to release them to the public.

Art. 50. - Delivery schedules should be established and route planning should be realistic.

Art. 51. - 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 medicinal products are used by the consumer.

Art. 52. - (1) Medicinal products may only be released in view of distribution after they have been released by the person responsible for the products' quality.

(2) Medicinal products in quarantine may be transferred to another wholesale distribution unit of the same company only if the person(s) responsible for the medicinal products' quality have authorised this transfer and if the necessary check-ups concerning the needed documentation have been carried out.

Art. 53. - There should be a system aiming for the rapid reconstitution of the distribution list for each batch of medicinal product, in order to allow its recall.

CHAPTER XII
Transportation and products in transit

Art. 54. - (1) Medicinal products should be protected during transportation, in order to prevent unauthorised access or providing proof, if the unauthorised access occurred.

(2) The transport of medicinal products should be secured and accompanied by an adequate documentation, in order to identify these and check the conformity with the authorities' requirements should be secured and accompanied by an adequate documentation, in order to ensure their identification and check-up of the compliance with the authorities' requirements, in harbours, airports, customs and storehouses.

Art. 55. - Pharmaceutical products should be transported 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 or materials;

c) adequate precautions are taken against spillage, breakage and theft.

Art. 56. - (1) Transport conditions should be ensures (temperature, relative humidity) corresponding to each category of medicinal product, and should be recorded throughout the entire transport and transit period.

(2) The devices used in order to monitor the temperature and humidity conditions should be calibrated at established intervals, and calibration results should be kept.

(3) The distributor should assess the monitoring of the temperature and humidity parameters during the transport of medicinal products, by keeping the records at least one year as of the expiry date of a distributed medicinal product, unless the legislation imposes otherwise, which shall be made available during the inspections carried out by the NMA.

(4) There should be written procedures for the investigation of any situation of non-compliance with the transport conditions.

Art. 57. - (1) The transportation means and recipients should be carefully and properly loaded, by following, if possible, the "first in first out" rule (FIFO), in order not to waste time with loading and to prevent the disposal of the containers.

(2) Special attention should be given to the loading-unloading of carton packages, in order to avoid their disposal.

Art. 58. - (1) Products comprising highly active and radioactive materials, other dangerous medicinal products and dangerous substances presenting special risks of abuse, fire or explosion (e.g. combustible liquids, pressurized gases) should be stored and transported in safe, dedicated and secure areas, containers and vehicles; the same measures should be taken for medicinal products containing narcotics and other addictive substances.

(2) In addition, applicable international agreements and national legislation should be applied.

Art. 59. - Products containing narcotics and other addictive substances should be stored and transported in safe and secure areas, containers and vehicles, in accordance with the national legislation and international agreements.

Art. 60. - (1) Spillages during transportation should be cleaned as soon as possible to prevent possible contamination, cross-contamination and hazards.

(2) Written procedures should be in place for the handling of such occurrences.

Art. 61. - (1) 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.

(2) The medicinal products should be appropriately identified, securely packaged, clearly labelled, and accompanied by appropriate supporting documentation.

Art. 62. - (1) Packaging materials and recipients which must be transported should be adequate in order to prevent the disposal of medicinal products during transportation.

(2) There should be adequately implemented control programmes concerning the sealing manner (i.e. the issued seals should be analysed; seals should be intact during transit and reception).

Art. 63. - (1) Drivers should not be allowed to enter the storehouse, but only the reception/expedition areas.

(2) Moreover, the driver should be identified and submit the documentation attesting that he is authorised for the transport.

Art. 64. - The disposal of recipients, as well as any other event or problem that occurs during transit should be recorded and reported to the authorities involved, as required, then investigated.

CHAPTER XIII
Documentation

Art. 65. - The distributors should identify their products and transactions using a control number similar to the batch numbers.

Art. 66. - (1) Written instructions and records documenting the entire activity concerning the distribution of medicinal products, including all receptions and releases, should be made available; the name of the wholesale distributor should appear on all relevant documents.

(2) Procedures such as the set up, approval, use and control of changes in case of documents referring to the distribution process should be established.

(3) Moreover, procedures concerning the access to the distribution documents should be established and enforced, as well as procedures describing the archiving and disposal modality, as required, following the expiry of the documents' availability date.

(4) Procedures should be made available not only for the internally-generated documents, but for the external ones as well.

Art. 67. - (1) All documents should be filled in, approved, signed and dated by an authorised person(s) and cannot be modified without the necessary authorisation.

(2) The title, type and scope of each document should be clearly stated.

(3) The content of the documents should be unambiguously clear.

(4) Documents should be kept in order, in order to be easily checked.

Art. 68. - (1) The nature and content of the documentation related to distribution, as well as it maintenance period should be compliant with the national legislation.

(2) When there are no such requirements, documents should be kept for a while equalling the availability period of the medicinal products, plus one year.

Art. 69. - All documents should be easily recovered and maintained via methods ensuring that non-authorised modifications, disposals and or document losses do not occur.

Art. 70. - (1) Documents should be regularly revised and kept up-to-date.

(2) When a document has been revised, there should be a system preventing the inappropriate use of the previous version.

Art. 71. - There should be mechanisms allowing the information transfer, including those referring to quality or legal regulations, between a distributor and a client, as well as the information transfer to the NMA, upon request.

Art. 72. - There should be updated records on paper or in electronic format, for each stored product, including the recommended storage conditions, any other precautions which should be taken and restore data, if required.

Art. 73. - There should be procedures for setting up a map representing the distribution of the temperature's values, the disposal of unsealed/non-usable stocks and storage of recordings.

Art. 74. - In case of medicinal products sensible to temperature or humidity, the records of investigations and actions carried out in case of neglecting the specified conditions should be stored at least one year as of the product's expiry date.

Art. 75. - When records are generated and kept in electronic format, these should be saved and kept in order to prevent a potential data loss.

Art. 76. - Wholesale distribution authorisation holders should keep records of any transaction of received or expedited medicinal products, containing at least the information mentioned under Art. 47.

CHAPTER XIV
Repackaging and relabelling

Art. 77. - (1) Any repackaging and re-labelling operation of medicinal products for human use are considered partial manufacturing operations and should be carried out in accordance with provisions of Art. 748 of Law No. 95/2006, as amended, and with those of the Guideline on the Good Manufacturing Practice of medicinal products for human use, approved through the NMA Scientific Council Decision No. 38/2006.

(2) Since the repackaging and re-labelling represent a risk in view of the interruption of the distribution chain's security (because the safety system of the original manufacturer is not maintained, nor is the authentication of the medicinal product as close to the patient as possible), these operations should be limited as much as possible.

(3) Conditions concerning repackaging should be clearly described.

(4) In case of a repackaging carried out by a company, other than the initial manufacturer, the product resulted should be at least equivalent to the initial product.

(5) The same technical and regulation requirements apply for the distributor carrying out repackaging and re-labelling operations, as well as for the manufacturer.

CHAPTER XV

Complaints

Art. 78. - The NMA should be informed about the recalls referring to the medicinal products' quality, which may lead to their recall.

Art. 79. - (1) There should be a written procedure in place for the handling of complaints; a distinction should be made between complaints about a medicinal product or its packaging and those relating to distribution.

(2) In the case of a complaint about the quality of a medicinal product or its packaging the original manufacturer and/or marketing authorisation holder should be informed as soon as possible.

(3) Any complaint concerning the quality of a medicinal product should be recorded and investigated to identify the origin or reason for the complaint.

Art. 80. - (1) 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 quick and efficient recall where appropriate.

(2) If a defect relating to a medicinal product is discovered or suspected consideration should be given as to whether other batches of the product should also be checked.

Art. 81. - (1) Where necessary, intermediate agents, distributors, those responsible for repackaging and relabelling should analyse the complaint together with the initial manufacturer of the medicinal product in order to establish whether subsequent actions involving other clients who have received the non-compliant medicinal product (and the NMA) should be initiated.

(2) The investigation of the complaint/recall's reason should be carried out and documented by the most involved part.

(3) When a complaint is forwarded to the original product's manufacturer, the records kept by intermediate agencies, distributors, those carrying out the repackaging and re-labelling should include all answers received by the original product's manufacturer (including the date when the information about non-compliance has been received).

CHAPTER XVI
Recalls

Art. 82. - 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.

Art. 83. - Such procedures should be checked regularly and updated, if necessary.

Art. 84. - (1) The original manufacturer and/or marketing authorisation holder should be informed in the event of a recall.

(2) Where a recall is instituted by an entity other than the original manufacturer and/or marketing authorisation holder, consultation with the original manufacturer and/or marketing authorisation holder should, where possible, take place prior to a recall being instituted.

(3) Information concerning the recall should be forwarded to the NMA.

Art. 85. - (1) The effectiveness of the arrangements for recalls should be evaluated at regular intervals.

(2) All recalled pharmaceutical products should be stored in a secure, segregated storage area belonging to the distributor pending appropriate action.

Art. 86. - (1) Recalled medicinal products should be segregated during transit and clearly labelled as recalled products.

(2) Where segregation in transit is not possible, such goods must be securely packaged, clearly labelled, and be accompanied by appropriate documentation.

Art. 87. - The storage conditions applicable to a pharmaceutical product which is subject to recall should be maintained during storage and/or transit until such time as a decision has been made regarding the medicinal product in question.

Art. 88. - All customers and competent authorities of all countries to which a given medicinal 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.

Art. 89. - (1) All records should be readily available to a designated person(s) responsible for recalls.

(2) These records should contain sufficient information on pharmaceutical products supplied to customers (including exported products).

Art. 90. - 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.

Art. 91. - The original manufacturer and the NMA should be informed in the event of a recall of an original product, as a consequence of the identification of a counterfeited medicinal product, which cannot be by the original product.

Art. 92. - Intermediate agents, commerciants, distributors, those carrying out the repackaging and re-labelling should keep records of the complaints and recalls which have been forwarded to them.

CHAPTER XVII
Returned products

Art. 93. - (1) A wholesale distributor should follow the terms and conditions receiving recalled medicinal products from a retail distribution unit or from other persons authorised for providing medicinal products.

(2) The wholesale distributor, as well as the retail distribution units (or other persons authorised to provide medicinal products) are responsible for the management of their own recall processes and for the safety of the operations, in order not to allow the marketing of counterfeit and falsified medicinal product.

Art. 94. - (1) The necessary assessment and decision regarding the disposition of such medicinal products must be taken by an authorised person.

(2) 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.

Art. 95. - Provision should be made for the proper and safe transport of returned products in accordance with the relevant storage conditions and other requirements.

Art. 96. - Provision should be made for the proper and safe transport of rejected and waste materials prior to their disposal.

Art. 97. - Medicinal products should be disposed where necessary in accordance with international and national requirements regarding disposal of such products, and with due consideration to protection of the environment.

Art. 98. - Records of all returned, rejected and/or disposed medicinal products should be kept.

Art. 99. – Any situation in which the recalled medicinal products are considered counterfeited should be immediately reported to the authorities; all measures should be taken in order to grant that these products shall never be marketed again.

CHAPTER XVIII
Counterfeit medicinal products

Art. 100. - All parties involved in the supply chain should cooperate in order to successfully fight against counterfeits.

Art. 101. - (1) Holders of a wholesale distribution authorisation should buy medicinal products only from persons/bodies who are holders of a manufacturing/wholesale distribution authorisation, depending on the case.

(2) The MAHs of wholesale distributions should only provide medicinal products to authorised persons owning a wholesale distribution authorisation, or to those persons authorised for providing medicinal products to the population.

Art. 102. - The distributor should own the appropriate procedures in order to notify the NMA, in case a medicinal product is suspected of being counterfeited or identified.

Art. 103. - Any counterfeit or suspected counterfeit medicinal product found in the pharmaceutical supply chain should be segregated immediately from other medicinal products and recorded.

Art. 104. - Such products should be clearly labelled in order to prevent further distribution or sale.

Art. 105. - Upon confirmation of the medicinal product being counterfeit a formal decision should be taken on the disposal of counterfeit pharmaceutical products and the decision recorded.

Art. 106. - Procedures concerning the emergency recall of counterfeit medicinal products found in the supply chain should be established.

CHAPTER XIX
Contract activities

Art 107. - Any activity relating to the distribution of a medicinal product 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.

Art. 108. - (1) The contract should define the responsibilities of each party, in accordance with the legislation in force, including observance of the principles of this Guideline

(2) The contract should also include the responsibility of the contract giver concerning the measures which should be taken (such as training) in order to discard the possibility of introducing counterfeit medicinal products in the supply chain.

Art. 109. - (1). Subcontracting may be permissible under certain conditions subject to the written approval of the contract giver.

(2) Subcontracting of transport activities is not accepted.

Art. 110. - Any contract accepter should be audited periodically.

CHAPTER XX
Self-inspection

Art. 111. - (1) The system of quality assurance should include self-inspections.

(2) 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.

Art. 112. - Self-inspections should be conducted in an independent and detailed way by a competent person, designated by the distributor.

Art. 113. - (1) The results of a self-inspection should be recorded as reports.

(2) Reports should contain all observations made during the inspection and, where applicable, proposals for corrective measures.

(3) There should be an effective follow-up programme during self-inspection.

(4) Management should evaluate the self-inspection report, and corrective actions taken and recorded.