Resolution No. 482/2002

This Resolution establishes that the manufacture of veterinary products shall comply with the Good Manufacturing Practices Regulation on Veterinary Products.

Having regard to Docket File No. 18638/2001 of the National Service for Agri-Food Health and Quality, and considering:

That in the 1st Ordinary Session of the Permanent Working Group on Veterinary Products of the Animal Health Commission of the Common Market of the South (MERCOSUR, by its initials in Spanish), which took place in the Autonomous City of Buenos Aires between April 13 and 17, 1998, a project of Good Manufacturing Practices was agreed.

That, although there exist international rules on this matter, it is necessary to adapt them to the national reality of the countries of the Region, to what defines their cultural, social and economic characteristics.

That a tool of such characteristics is essential for a future forecast of the national industry to the rest of the world, since it is a prerequisite, demanded by most of the countries of the world, to authorize the import of veterinary medicine.

That, in addition, it is essential to have a national standard, with the aforementioned characteristics, to be implemented as a requirement for imports to our country.

That the industry of this sector has actively participated in the development and debate of this standard, and agreed with all its contents.

That the Directorate for Legal Affairs has issued its opinion on this matter and expressed no legal objection.

That the undersigned is empowered to issue this Resolution, pursuant to the provisions in Section 8 paragraph i), of Decree No. 1585 of December 19, 1996, replaced by Decree No. 394 of April 1st, 2001.

Therefore, the President of the National Service for Agri-Food Health and Quality resolves:

Section 1— The manufacture of veterinary products must comply with the Good Manufacturing Practices Regulation on Veterinary Products included in the Annex of this Resolution.

Section 2— Manufacturing companies shall have a maximum time of three (3) years from the passage of this Resolution to present an adaptation project of their production processes to the standard set in the preceding Section.

Section 3— Manufacturing companies shall have a maximum time of six (6) years from the passage of this Resolution, to bring their production processes into condition to be certified by the General Coordination Office for Pharmacological and Veterinary Products and Feedstuff of the Department of Agricultural Chemicals and Pharmacological and Veterinary Products of this National Service, pursuant to the standard set in Section 1 of this Resolution.

Section 4— Companies may implement Good Manufacturing Practices for Veterinary Products at any time from the passage of this Resolution and request a certificate of compliance to this National Service through the General Coordination Office for Pharmacological and Veterinary Products and Feedstuff of the Department of Agricultural Chemicals and Pharmacological and Veterinary Products.

Section 5— Have it notified, published, transferred to the National Official Registry and filed. — Bernardo G. Cané.

Annex

Standards for Good Manufacturing Practices of Veterinary Products

1. Overview:

When manufacturing medicinal products a full inspection of the production is essential to guarantee the quality of the products to the client. Should the produced substances may be critical to save, preserve or recover animal health, no operation shall be left to chance.

Some of the best practices for the manufacture of medicinal products with the desired quality are described below. The implementation of such practices, along with the diverse inspections carried out throughout lead time, will largely contribute to ensure high and homogeneous quality of medicinal products batches.

The manufacturer shall be responsible for the quality of products since he is empowered to avoid mistakes and accidents by carefully monitoring control and manufacturing processes.

The implementation of the following requirements is extended to all the manufacturing processes, including packing and labeling, until the product reaches its final presentation form.

2. Personnel:

2.1 The manufacturer shall have a well defined organization represented in a well-known and updated organization chart. Individual responsibilities shall be clearly defined, registered and transmitted through the description of the duties and positions.

2.2 The manufacturer shall employ enough skilled and competent personnel for production.

2.3 The manufacturer shall have an initial and continuous training program in Good Manufacturing Practices (GMP) and have it registered and evaluated.

2.4 The manufacturer shall properly train all the personnel for the appointed tasks and responsibilities and for the GMP.

2.5 The manufacturer shall clearly inform to the "Competent Official Body" who the line manager is.

2.6 All responsible personnel shall have their specific tasks in writing, and sufficient authority to carry them out.
Such tasks may be delegated to appointed substitutes with a satisfactory qualification level. There shall not be flaws related to

the application of GMP, neither can be overlapping personnel's responsibilities.

2.7 Among the key-personnel that shall carry out their tasks full-time, there are: managers responsible for production, and quality and line managers.
Personnel responsible for production and quality control shall be independent. Should there arise the need to delegate certain tasks, the responsibility shall not be delegated.

2.8 The manufacturer shall implement hygiene programs and adapt them to his activities.

3. Facilities:

3.1. Overview.

3.1.1. The manufacturer shall have located, planned, constructed, adapted and maintained facilities in such a way that they adjust to operations to be performed. Their design shall minimize risk and allow effective cleaning and maintenance in such a way that they avoid cross contamination, dirt and dust build-up and any adverse effect on the products quality.

3.1.2. The manufacturer shall have appropriate and continuous facilities maintenance processes, without risking people, equipment or products.

3.1.3. The facilities shall have appropriate lightening, temperature, humidity, ventilation, and noise conditions that do not unfavorably, directly or indirectly affect people, manufactured products nor equipment performance.

3.1.4. Facilities must be designed and equipped in such a way that they allow maximum protection against insects or any other animal.

3.2. Auxiliary facilities.

3.2.1. Break and dining rooms, if any, shall be separated from the other areas.

3.2.2. Locker rooms, washrooms and restrooms shall be easily accessible and appropriate for all users. Restrooms shall be directly connected to production and storage areas.

3.2.3. Maintenance areas shall be placed in facilities separated from the production area. Should there is a need to keep tools and pieces in the production area, they shall be kept in rooms or cabinets reserved for that purpose.

3.3. Storage areas.

3.3.1. Storage areas shall be big enough to orderly store various types of materials and products in sectors: raw materials, packing materials, intermediate materials, in bulk products, finished products, in quarantine materials or products, approved products, reproved products, returned products or products collected from market.

3.3.2. Storage areas shall be designed to ensure the right conditions for storage. They shall be cleaned, dried and maintained within accepted temperature and humidity storage limits, as well as stocked, monitored and registered.

3.3.3. Reception areas shall be designed and equipped in such a way that they protect equipment and products from climatic variations before being stored, and allow their cleaning, when necessary.

3.3.4. Should there be a separated area for sample collection, it shall be designed and equipped in such a way that it avoids contamination.

3.3.5. In accordance with the relevant legislation, for substances covered under the special control system, such as psychotropics, narcotics or similar, there shall exist storages or closed facilities with restricted access.
3.3.6. In accordance with the relevant legislation, substances presenting fire or explosion risks shall be stored in isolated, secure and ventilated areas.
3.3.7. There shall exist a separated and secure area for printed packing material storage, in such a way that it maintains its integrity and avoids confusions and mistakes.
3.4. Weighing and measuring areas.
3.4.1. Weighing and measuring of raw materials must be carried out with proper extractor fans in separated areas for that purpose.
3.5. Production area.
3.5.1. There shall be exclusive or separated installations with independent air conditioning system for: cephalosporins, penicillanic acids and hormones.
3.5.2. In areas where products containing avermectins, or any other endectocine obtained through fermentation processes, are manufactured, production cycles shall be accepted within the same facilities, whenever specific precautions are adopted and the necessary approvals are granted.
3.5.3. There shall be separated areas for the manufacture of pesticides.
3.5.4. Facilities must be located in such a way that they allow production to be carried out following a logical and concordant order regarding production operations sequence. Likewise, such facilities shall meet cleaning requirements.
3.5.5. The adaptation of the workspace shall allow a logical and organized arrangement of equipment and material, with the purpose of minimizing contamination risks and avoiding misunderstandings and mistakes.
3.5.6. Primary packing materials and in bulk or intermediary products which are exposed to the environment shall be located in rooms with smooth, cracks-free, and easy cleaned and sanitized, if necessary, surfaces (walls, floors and ceilings).
3.5.7. Plumbing, lightening, ventilation points and other services shall be planed and placed in such a way that they avoid difficult to clean places. Its maintenance shall be carried out outside the productive areas. Areas where visual checks are conducted shall be illuminated.
3.5.8. Drains, when allowed, shall have a trap, the right size and shall not allow reflows. Should there be gutters, they shall not be deep, but easy to clean and sanitize.
3.5.9. Productive areas shall be adequately aired for manipulated products, operations and external environment. For that purpose, temperature, humidity and filtering control units will be needed, when necessary.
3.5.10. In those operations where dust is produced (for example during sampling, weighing, mixing, manufacturing, or dry products packing operations) specific measures shall be taken with the purpose of avoiding cross contamination and facilitating cleaning.
3.5.11. Areas intended for the production of products containing pesticides in their formulation shall adjust to specific regulations.
3.6. Quality control area.

3.6.1. Quality control laboratories shall be separated from the production area. Those areas where microbiological, biological and radioisotopical material is employed shall be separated from one another.
3.6.2. Quality control laboratories shall be designed in such a way that they adapt to operations carried out therein, and they shall have enough space for minimizing cross contamination and avoiding misunderstandings and mistakes.
Provision should be made for the extraction of fumes and vapors, and the adequate ventilation, temperature and humidity. Independent air conditioning systems and other necessary measures shall be applied in laboratories manipulating special substances, such as radioisotopics and certain microbiological and biological samples.
3.6.3. There shall be enough and adequate space for the following activities:
a) Samples storage and reference standards.
b) Glassware, reactives and auxiliary material storage.
c) Flammables and corrosives storage.
d) Filing and filing of documents area.
e) Closed and locked area with restricted access for substances covered under the special control system, in accordance with the relevant legislation.
f) Isolated area, with restricted access for radioactive materials, in accordance with the relevant legislation.
3.6.4 Quality control laboratories facilities shall ensure the protection of machines sensitive to vibrations, electrical or magnetic interferences, heat and humidity.
3.7 Vivarium.
3.7.1. Vivarium facilities shall be separated from the other areas and shall be equipped with independent air systems.
3.7.2. Vivarium facilities shall possess the following sectors:
3.7.2.1. Nursery/breeding and maintenance.
a) Quarantine sector.
b) Cultivation and maternity sector.
c) Animals growth sector.
3.7.2.2. Hygiene separated in:
a) Cleaning and garbage dump sectors.
b) Personal hygiene sector, including locker rooms, washrooms and restrooms.
3.7.2.3. Administrative containing:
a) Animals delivery sector.
b) Office.
c) Material storage.
3.7.2.4. Laboratories intended for biological assays.
3.7.3. Vivarium construction designs shall consider:
a) Walls, floors and ceilings shall be smooth, impermeable and covered with washable materials.
b) Windows shall have mosquito nets and systems to control sunlight interference.
c) Corners between the walls, the ceiling and the floor shall be round.
d) Doors shall be wide and have glass windows and springs that return them to their original position.
e) There shall not be unevennesses on the floor.

3.7.4. Vivarium facilities shall have temperature, humidity and ventilation control devices.
3.7.5. Lightning devices shall provide a controlled light intensity.
3.7.6. There shall be noise control devices in order to avoid disturbances in animal behavior.

4. Equipments.

4.1. Equipment shall be placed, designed, adapted and maintained in order to be fit for developed operations.

4.2. Equipment design and structure shall be aimed at minimizing cross contamination, avoiding mistake risks and allowing their cleaning and sanitizing.

4.3. Those parts of the equipment that are in contact with the product shall not be reactive, additive or absorbent.

4.4. Fixed drains shall be clearly identified, indicating content and flow direction, when appropriate.

4.5. Measurement, weighing and registering equipment shall be calibrated and tested to defined intervals. These tests shall be registered.

4.6. Washing and cleaning equipment shall be chosen and used in such a way that they are not a source of contamination.

4.7. Defective equipment that cannot be moved out from a manufacturing area shall be identified as such.

5. Hygiene, health sanitization and safety:

5.1. Written hygiene processes shall exist, they must cover personnel and facilities, equipment and machines, production materials and containers, cleaning and sanitizing products, and any aspect that may constitute a contamination source for the manufactured product.

5.2. In accordance with laws relevant to the sector, the manufacturer shall have processes for:

a) Medical entrance, periodic and resignation exams.

b) Diseases, injuries and specific allergies controls.

c) Vaccine and monitoring program, according to the type of manufactured product.

d) Contamination prevention and monitoring of people manipulating biological, chemical and physical agents that may be detrimental for health.

5.3. Any employee with injuries or diseases that may affect the quality and safety of products shall be excluded from the activity.

5.4. Employees shall use working clothes in accordance with the conducted activity. Such clothes shall be cleaned and frequently changed.

5.5. Smoking, drinking, eating, chewing or having plants, food, drinks, cigarettes and personal medicines in production, laboratory, and storing areas, or any other area where such actions may have adverse effects on the product quality, shall not be allowed.

5.6. Personal hygiene processes, even the usage of protective clothing shall also be applied to people who do not belong to the aforementioned areas.

5.7. There shall exist a sanitization program with the following descriptions:

a) Enforcement frequency;

b) Methods and materials used and approved by Health Care Institutions;

c) People responsible for such enforcement.

5.8. There shall exist written safety processes, according to the relevant laws, containing a written description of individual or collective safety equipments necessary for the development of activities.

5.9. There shall exist written processes for conflagration or emergency situations, containing a written description of fire extinguishers and hydrants location. The quantity and type of fire extinguishers and hydrants shall be sufficient and of open access.

6. Documentation:

6.1. Basic concepts.

6.1.1. The aim of appropriate documentation is to define material specifications and manufacturing and control methods in order to ensure that all personnel involved in manufacturing knows what to do and when. It is also intended to ensure that authorized persons have the necessary information to decide about the release to sell of one (1) product batch/consignment and allowing its tracking for an investigation of the record of any consignment under any suspicion of mistake.

6.1.2. Documentation shall be carefully separated, revised and distributed.

6.1.3. Documents shall be approved, signed and dated by authorized people. No document shall be modified without previous authorization.

6.1.4. The content of such documents shall not be ambiguous: title and nature of its aim shall be presented clearly, legible and arranged in such a way that it allows easy verification. Work documents reproduction from template documents shall be carried out in such a way that it prevents mistakes from being reproduced.

6.1.5. Documentation shall be regularly reviewed and updated; there shall be a system that prevents the inadvertent use of a substitute version when it has been modified.

6.1.6. Any alteration of the documentation shall be signed and dated in such a way that it allows reading the original information. When applicable, the motive of the alteration shall be registered.

6.1.7. Data may be registered through automatic processing systems, of electronic data, photographs or any other reliable source. Detailed formula or operational processes samples, concerning the used system shall be available and the accuracy of the records shall be verified. Should documentation be done through electronic processing systems, only authorized personnel may access or modify data contained in the computer, therefore, there shall be an eliminations or modifications record. Access shall be restricted by codes or other means and the result of information entry shall be independently verified. Electronic documentation shall be protected by copies in magnetic tapes, microfilms, and prints on paper or other means. It is important that data be available during the archiving period.

6.2. Sample formula shall include the following:

6.2.1. The name of a product with one (1) product reference code belonging to its specification.

6.2.2. Pharmaceutical formulation description, product activity, batch or consignment size and expiration date.

6.2.3. A list of every raw material, and packing and auxiliary material to be used with their respective quantities nomination, and an exclusive reference for each one of them; any substance that may disappear through manufacturing shall be mentioned.

6.2.4. Declaration of forecasted final performance with its acceptance limits and of significant intermediate performances, when appropriate.

6.3. Sample process shall include:

6.3.1. A declaration of plant location and main used machinery.

6.3.2. Methods, or their reference, to be used for preparing essential machinery (for example, cleaning, assembling, calibrating, sterilization) and others, if applicable.

6.3.3. Detailed instructions of step by step process (for example, material inspection, forecasted treatments, raw materials addition sequence, mixing times, temperatures) and others, if applicable.

6.3.4. Instructions of every control and its limits during procedure.

6.3.5. Storage requirements for in bulk products, including packing, labeling, and special storage conditions, when applicable.

6.3.6. Processes graphic records shall be annexed.

6.3.7. Heavy and/or measured raw materials identification labels shall be annexed when there is not an equivalent safety system.

6.3.8. The label of the final product shall be annexed together with its consignment or batch number and expiration date.

6.3.9. Any special precaution that shall be taken into account.

6.4. Manufacturing order.

6.4.1. Every consignment or batch of one (1) product shall be produced according to the written manufacture order containing relevant information of the sample formula, including the following data at the end of the production:

a) Product name;

b) Number of consignment or batch being manufactured;

c) Data and starting and finishing time of every intermediate production stage;

d) Name of the operator responsible for the different production stages and of the person authenticating such operations;

e) Identification number and quantity of each used material, including number and quantity of any added returned or reprocessed material;

f) Process controls, signature of the people who carried them out, and obtained results;

g) Obtained performance and observations of any significant mistake of the expected performance;

h) Comments on special problems including details such as a signed authorization for each production formula alteration or manufacturing instructions;

i) Quality control evidence and its result. Shall the batch/consignment be rejected, an indication of its elimination or employment shall be needed as well.

6.5. Log file and reference samples.

6.5.1. Records shall be maintained in such a way that they allow a tracking of the activities related to products manufacturing and quality control.

6.5.2. Records and reference samples of finished products and, when necessary, of intermediate products shall be retained for no less than one (1) year after expiration date of its validity.

7. Agreements with third parties:

7.1. Production and quality control by agreements with third parties shall be defined, mutually agreed, and have the purpose of avoiding misunderstandings that may result in an insufficient product, work or analysis. Both parties shall enter into a written contract in which the obligations of each party are clearly stipulated. In such agreement, the way in which the person in charge of authorizing the circulation of each

product batches/consignments intended for sale, or of issuing the analysis certificate, shall meet his responsibilities shall be elucidated.

7.2. Manufacturing agreement shall only be entered into by manufacturers with the Operation Authorization of the Competent Official Body. The service provider shall not transfer to third parties the entrusted services.

8. Materials:

8.1. Every received material and finished products shall be put in quarantine immediately after reception or production, or until they are released for their use or distribution.

8.2. Every material shall be stored under the adequate conditions in an organized manner, in order to allow the separation of batches and stock rotation, following the "first in first out" and the "first expired first out" rules.

8.3. Every used material shall be received, put in quarantine, sampled, identified, analyzed for the meeting of established specifications, approved or rejected, stored, labeled, and released for use, in accordance with the written processes.

8.4. If a materials delivery were composed by different supplier batches, every batch shall be considered independent for sampling, analysis and release.

8.5. In each reception, the integrity and correspondence between the order form and the delivery note, and the identification of packing containing materials shall be verified.

8.6. Should, during reception, be any packing-caused damage that may adversely affect material quality, it shall immediately be informed to quality control for the corresponding investigations.

8.7. Every material shall be sampled by quality control, through adequate and reliable systems. Sampling programs shall be constant.

8.8. Raw materials.

8.8.1. Manufacturer shall have written and approved specifications that have already been agreed with raw materials suppliers.

8.8.2. Stored raw materials shall be identified with, at least, the following information:

a) Name and internal reference code, when applicable;

b) Batch number(s) assigned by supplier and registered reception number;

c) Raw material internal situation, i.e. if it is in quarantine, approved, rejected or returned;

d) Validity date, when appropriate, manufacturing date and second analysis date;

e) This situation shall be registered in the packing from where the samples were taken;

f) There shall exist just one identification system and it shall be either electronic or manual.

8.8.4. Only raw material approved by quality control and inside their validity period shall be used.

8.8.5. Raw materials subject to control special system shall be stored in closed storages or facilities, with restrictive access.

8.8.6. Toxic, flammable, explosive, corrosive, and radioactive raw materials shall be stored in separated areas with restrictive access.

8.9 Packing material: Primary and secondary.

8.9.1. Packing materials shall not be detrimental for the substance and shall ensure the right protection against external influences and potential contaminations. Adequate specifications shall be available.

8.9.2. Special attention shall be paid to printed materials. Such materials shall be securely stored and shall prevent unauthorized access.

8.9.3. Packing materials shall only be acquired from approved suppliers and should be registered, when necessary, in the specification sheet.

8.9.4. Every packing material shall be sampled by Quality Control through adequate and reliable programs. Such programs shall be constant.

8.9.5. Primary or secondary packing materials that are not used shall be removed from stock and this action shall be registered.

8.9.6. Packing materials shall be identified by, at least, the following information:

a) Name ad internal reference code, when applicable;

b) Batch number(s) assigned by supplier and registered reception number;

c) Raw material internal situation, i.e. if it is in quarantine, approved, rejected or returned;

d) In packing where these samples have been taken, this action shall be registered.

9. Production:

9.1 Every product manufacture as material manipulation, reception, quarantine, sampling, storing, production, packing, quality control and expedition, shall be carried out in accordance with written and registered processes.

9.2. Should deviations in instructions or processes occur, they shall be approved in writing by an authorized person, with participation of the Quality Control area, when necessary.

9.3. Material count and verified outputs shall be made. Any discrepancy in pre-established limits shall be informed, investigated and registered.

9.4. Operations with various products shall not take place simultaneously or consecutively in the same sector, unless there is not risk of mix or cross contamination.

9.5 During production materials, in bulk products, main equipment, and unused areas shall be labeled and identified regarding product, material in process, its concentration (when applicable) and batch or consignment number. When this indication is applicable, the state of production shall also be mentioned.

9.6. The access to production area shall be limited to authorized persons.

9.7. Controls in process carried out in production areas shall not represent any risk for product quality.

9.8. Cross contamination shall be minimized through adequate processes or organization measures, such as:

a) Each production area shall have one (1) independent air conditioning system, or cycles (by periods of time), accompanied by validated cleaning processes;

b) Usage of appropriate air chambers, air pressure or extraction differences, when applicable;

c) Usage of protective clothing in areas where products are being processed and it represents a special risk of cross contamination;

d) Usage of validated cleaning or contamination processes;

e) Adoption of one (1) closed production system;

f) Usage of residue detection tests;

g) Usage of labels indicating cleaning state in areas and equipments.

9.9. During packing process, the risk of misunderstandings or substitution of various products or of batches or consignments of the same product, through lines separations.

9.10 Packing lines shall be verified, before the commencement of operations through one (1) registered operation, related to the lack of previous products batch or consignment remaining materials.

9.11. The product name and consignment or batch number in the process shall be indicated in each of the stages or in the packing line.

9.12. The product control in process during packing shall include, at least, the verification of the following items:

a) General aspect of packing;

b) If packing is complete;

c) If the right products and packing materials are being used;

d) If inscriptions are correct;

e) The proper functioning of the process monitors in packing line;

9.13. After the end of each operation, every packing material marked with batch/consignment code that was not used shall be destroyed, this action shall be registered. Non-codified printed materials shall be returned to stock through written processes.

9.14. Water.

9.14.1. The manufacturer may use drinking water for his facilities as supply source, for cleaning and purification processes.

9.14.2. Every process for obtaining drinking water shall be efficient, with the appropriate facilities, in order to ensure a high standard of physicochemical and microbiological quality.

9.14.3. Manufacturer shall periodically proceed to a physicochemical and microbiological assessment of the drinking water supply and of water resulting from purification processes and used in products formulation.

9.14.4. Drinking water and water resulting from purification processes quality parameters shall be established in officially accepted standards.

9.15. Weighing and measurement processes.

9.15.1. Weighing scales and measuring containers shall be periodically calibrated and weighing scales shall be officially controlled in a regular way. These processes shall be registered.

9.15.2. Measuring and weighing containers shall be cleaned and free from the previous identifications before re-use.

9.15.3. After materials weighing or measuring, they shall be immediately labeled so as to avoid misunderstandings.

9.15.4. This label shall contain:

a) Input name;

b) Input consignment number;

c) Name of the product to which the input is destined;

d) Product consignment/batch number;

e) Weighed or measured quantity;

f) Gross weight;

g) Signature of the person who weighed and verified.

9.15.5. Weighed or measured materials for each product batch/consignment shall be physically separated.

9.15.6. There shall exist one (1) system for minimizing cross contamination during weighing or measuring.

10. Finished products:

10.1. Every finished product shall be put in quarantine immediately after being received or produced, and until being released for their use or distribution.

10.2. Every finished product shall be stored in adequate conditions in an organized way so as to allow the separation of consignments or batches and stock rotation, obeying the "first in first out" and the "first expired first out" rules.

10.3. Every finished product shall be received, put in quarantine, sampled, identified, analyzed for the meeting of established specifications, approved or rejected, stored, labeled, and released for use, in accordance with the written processes.

10.4. One (1) system for entry and stock of every batch/consignment and finished product shall be maintained, existing periodic inventories.

10.5. Finished products shall be subject to control special systems and stored in closed storages or facilities, with restrictive access.

10.6. Storing and distribution.

10.6.1. Only products finished within their validity date shall be stored. Finished products with expired validity date shall be removed from storage and subsequently destroyed. These processes shall be registered.

10.6.2. The company shall have a policy concerning stored finished products with validity date near expiration date.

10.6.3. Distribution system shall work in such a way that older batches/consignments be dispatched first.

10.6.4. Storage, dispatch, and distribution conditions (temperature, humidity, and lightning) shall be compatible with the ones required by the product, and they shall match the ones indicated in the label of such product.

10.6.5. Products needing special storing conditions (temperature and/or controlled humidity) require areas equipped for the purpose of maintaining such conditions with their correspondent records.

10.6.6. Distribution records shall be maintained for every finished product consignment or batch, with the purpose of easing, if necessary, the removal of the batches/consignments from the market, in accordance with written processes. Records shall contain, at least, consignee's name and address, consignment or batch number, quantity and dispatch date.

11. Quality control.

11.1. The function of quality control is not limited to laboratory operations, it shall cover every activity and decision that may affect product quality.

11.2. Every manufacturer shall have one (1) independent person responsible for quality control, who shall directly report to senior management of the company.

11.3. The main responsibilities of quality control are:

11.3.1. To approve:

a) Specifications and testing methods for raw materials, intermediary products, packing materials and finished products;

b) Specifications and analytical methodologies for controls in process;

c) Sampling processes;

d) Processes concerning hygiene and health measures;

e) Other quality product related instructions.

11.3.2. To be responsible for the approval or rejection of raw materials, packing materials, finished products and, if necessary, intermediate products.

11.4 Every manufacturer shall have one (1) control laboratory, of his own or of a third party, with enough, qualified and equipped personnel for carrying out every necessary quality control test. Tests shall be carried out in accordance with written and validated controls. Tools shall be calibrated in adequate intervals and reactives shall be of the appropriate quality.

11.5. Quality control personnel shall have open access to production areas so as to carry out samplings and verifications.

11.6. Quality control sector shall have the following documentation available:

a) Specifications;

b) Sampling processes;

c) Analysis and register activities (including analytical sheets, notebooks or any other annotations);

d) Bulletins or certificates of analysis containing, at least, the following information;

d.1) Material or product name and, when applicable, in pharmaceutical nomenclature;

d.2) Batch/Consignment number and, when applicable, manufacturer and/or supplier name;

d.3) Reference to specifications and relevant analysis procedures;

d.4) Analysis results, including observations, specifications calculations and references (limits);

d.5) Analysis dates;

d.6) Signature and typed or printed name of the people who carried out the analysis;

d.7) Signature and typed or printed name of the people who verified analysis and calculations, when applicable;

d.8) Clear indication of authorization or rejection (or any other disposition about the condition of the material or product) and date, signature and typed or printed name of the person appointed as responsible.

e) Environmental monitoring records (when specified);

f) Method validation records, when applicable;

g) Tools record and calibration processes and equipment maintenance.

11.7. Any Quality Control documentation related to consignment/batch records shall be maintained by one (1) year after the consignment/batch expiration day.

11.8. Sampling shall be carried out in accordance with approved written procedures describing the following:

a) Sampling method or criteria;

b) Equipment to be used for sampling and/or individual protection, when necessary;

c) Sampling size;

d) Instructions for any subdivision required in the sample;

e) Type and condition of the packing to be used for placing the sample in;

f) Sample volume identification;

g) Any special precaution to be observed, especially in relation with the sampling of sterile and harmful products;

h) Sampling equipment cleaning and storing instructions;

i) Samples storing condition;

j) Sampling residues destination.

11.9. Retention samples for future references shall meet the following requirements:

a) Have a label indicating its content, batch/consignment number, sampling date and analysis number;

b) Be enough for carrying out, at least, two (2) full reanalysis;

c) Finish product samples shall be kept in their final sell packing and stored in conditions specified by manufacturer;

d)Should the finished product have presentations per quantity and/or large volumes and/or in bulk, retention sample shall not be less than a hundred (100) milliliters or a hundred (100) grams and shall be kept in packs with the same characteristics that the ones intended for market and stored in conditions specified by the manufacturer.

12. Stability tests:

12.1. One (1) written stability study program for products shall be established using schedules and analytical methods indicating stability.

12.2. Samples shall be kept in their final market packing or other packing with the same characteristics, at room or recommended temperature, or accelerated stability tests shall be carried out.

13. Self-inspection and quality audits:

13.1. Self-inspections shall be periodically carried out for verification and compliance of GMPs in every production and quality control aspect.

13.2. A self-inspection program shall be planned in order to detect any drift in the implementation of GMPs and to recommend appropriate corrective actions.

13.3. The manufacturer shall appoint a team conducting the self-inspection, made up by internal servants or external people, experts in their field, familiarized with GMPs.

13.4. Self-inspections frequency shall depend on the needs of the company. Procedures and records for self-inspection shall be registered and shall still be in the execution program.

13.5. The self-inspection conclusions shall include: self-inspection results, evaluations and conclusions, recommended corrective actions.

13.6. Self-inspections shall be complemented with quality audits, which consist in an exam and an evaluation of a whole or of one (1) system, with the specific aim of improving it.

13.7. Quality audit may be carried out by external or independent specialists or by one (1) team appointed by the administration.

13.8. Quality audit may be extended to suppliers and third parties.

14. Quality complaints and drifts:

14.1. The manufacturer shall have written instructions to deal with complaints concerning products quality.

14.2. Every necessary action shall be taken quickly and complaints shall be fully investigated and registered.

14.3. Manufacturer shall have one (1) system allowing the investigation of every product that may have been affected by one (1) repetitive mistake or one (1) failure in the processes of the company.

14.4. Every complaint concerning quality drifts of one (1) product shall be registered and investigated. The person responsible for quality control shall be involved in the study of such problems and records shall include, at least, the following information: product name, consignment/batch name; name of the person who complained; reason of such complaint; answer.

14.5. Every measure and decision taken as a result of one (1) complaint shall be registered, signed, dated, and annexed to the corresponding records of such consignment/batch.

15. Withdrawal of products from market:

15.1. In order to withdraw a product from market, appropriate and updated written procedures are necessary.

15.2. Data contained in distribution records shall be of easy access for personnel responsible for withdrawal.

15.3. Withdrawn products shall be identified and stored in separated and secure areas while their destination is decided.

14.4. Competent authorities of every country, to which one (1) product has been sent to, shall be immediately informed of any decision of withdrawal of products under the suspicion of quality drift.

16. Rejected products and materials:

16.1. Manufacturer shall have written procedures concerning the manipulation of rejected materials, whether it be raw materials, packing materials or finished products.

16.2. Rejected materials and products shall be visibly identified as such and stored in a controlled way while they wait to be destructed, reprocessed or returned to suppliers.

17. Returns:

17.1. Products returned by market and which are within their validity period shall be retested in accordance with the data informed by the person responsible for quality control. Taking into account the nature of the product, demanded storing conditions, its record and conditions, and the time passed from their dispatch to market, will suffer the following treatments:

a) Destruction;

b) Reprocessing;

c) Repacking;

d) Incorporation into the following in bulk consignment or batch.

17.2. Any adopted decision concerning returning shall be registered and approved by authorized personnel and documentation shall be annexed to the records of the consignment or batch.

17.3. Non returned products with an expired validity period shall be destroyed and this action shall be registered.