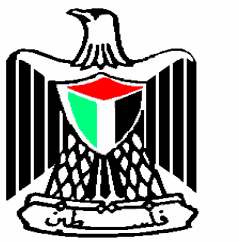

# Good Manufacturing Practices Inspection Aide-Memoir

**Palestinian National Authority**
**Ministry of Health**

General Directorate of Pharmacy
Drug Control &
Registration Department

**2007**

# TABLE OF CONTENTS

| CHAPTER 1: ADMINISTRATION AND GENERAL INFORMATION | |
|---|---|
| 1 | What is the company's name?<br>_____ |
| 2 | What is the company's legal address?<br>_____ |
| 3 | What is the manufacturing site’s address?<br>_____ |
| 4 | What is the name of the responsible pharmacist?<br>_____<br>_____ |
| 5 | Is the responsible, pharmacist present at the time of the inspection?<br>(YES) (NO)<br>_____ |
| 6 | What is the name of the escort(s)/?<br>_____ |
| 7 | Is there evidence of a license to operate, issued by the Regulatory Authority?<br>_____<br>_____ |
| 8 | Does the company manufacture dietary supplements?<br>(YES) (NO) |
| 9 | Does the company manufacture cosmetic products?<br>(YES) (NO) |

| | |
|---|---|
| 10 | Does the company manufacture veterinary products?<br><br>(YES) (NO) |
| 11 | Does the company manufacture other products not indicated above?<br>YES<br>If “YES” indicate below<br>_____<br>_____<br>NO |
| 12 | Does the company manufacture products with beta-lactam active ingredients (penicillins / cephalosporins)?<br>YES<br>If "YES", indicate in which pharmaceutical dosage form<br>_____<br>_____<br>NO |
| 13 | Does the company manufacture products with cytostatic / cytotoxic active ingredients?<br>YES<br>If "YES", indicate in which pharmaceutical dosage form<br>_____<br>_____<br>NO |
| 14 | Does the company manufacture products with hormone active ingredients?<br>YES<br>If "YES", indicate in which pharmaceutical dosage form<br>_____<br>_____<br>NO |
| 15 | Does the company manufacture products with corticosteroids active ingredients?<br>YES<br>If "YES", indicate in which pharmaceutical dosage form<br>_____<br>_____<br>NO |
| 16 | Does the company manufacture products with active ingredients from biological origin?<br>YES<br>If "YES", indicate in which pharmaceutical dosage form<br>_____<br>_____<br>NO |

| | |
|---|---|
| 17 | Does the company manufacture products with active ingredients from biotechnological origin?<br>YES<br>If "YES", indicate in which pharmaceutical dosage form<br>_____<br>_____<br>NO |
| 18 | Is there a list available of current registered products? Attach the list<br><br>(YES) (NO) |
| 19 | Do all marketed products and its pharmaceutical presentations have current (valid) license?<br><br>(YES) (NO) |
| 20 | Does the company have contract production activities?<br><br>(YES) (NO) |

| CHAPTER 2: PERSONNEL | | | | |
|---|---|---|---|---|
| GENERAL | | S | P | I |
| 1 | Is there an organizational chart?<br>What departments are identified?<br>_____<br>_____<br>_____ | | | |
| 2 | Are there job descriptions for key personnel? | | | |
| 2.1 | Are they appropriate to the activities of the department? | | | |
| 3.1 | Number of Quality Assurance staff _____<br>Number sufficient?<br>Qualification adequate?<br>Experience sufficient? | | | |
| 3.2 | Number of Quality Control staff _____<br>Number sufficient?<br>Qualification adequate?<br>Experience sufficient? | | | |
| 3.3 | Number of production staff including packaging_____<br>Number sufficient?<br>Qualification adequate?<br>Experience sufficient? | | | |
| 3.4 | Number of engineering staff ?<br>Number sufficient?<br>Qualification adequate?<br>Experience sufficient? | | | |
| 3.5 | Number of warehousing Staff_____<br>Number sufficient?<br>Qualification adequate?<br>Experience sufficient? | | | |
| 3.6 | Number of R & D Staff_____<br>Number sufficient?<br>Qualification adequate?<br>Experience sufficient? | | | |
| 4 | Is there a clear separation of responsibility for production from QC? | | | |
| 5 | Are the names of the qualifications of those responsible for approving the lot processing records registered with MoH? | | | |

| KEY PERSONNEL | | S | P | I |
|---|---|---|---|---|
| 6 | Are there sufficient key personnel to supervise assigned functions?<br>- Production.<br>- Filling.<br>- Labeling / packaging.<br>- Quality Control.<br>- Engineering.<br>- Maintenance.<br>- Quality Assurance.<br>- Other departments:<br>_____ | | | |
| 6.1 | Are key posts occupied by full time personnel? | | | |
| 7 | Do they posses the qualifications of a scientific education and practical experience (such as biology, microbiology, chemistry, veterinary medicine, chemical or industrial engineering, etc)?<br>- Engineering<br>- Production Department(s)<br>- Filling.<br>- Quality Control.<br>- Quality Assurance.<br>- Animal care.<br>- Other: _____ | | | |
| TRAINING | | S | P | I |
| 8 | Are there on the job training procedures for new employees? | | | |
| 9 | Are training and education records available? | | | |
| 9.1 | Are they current? | | | |
| 9.2 | Are they filed with the supervisor of relevant departments? | | | |
| 10 | Are there an approved training programs? | | | |
| 10.1 | For new employees. | | | |
| 10.2 | For all personnel whose duties are in manufacturing, quality control, maintenance, Cleaning, etc? | | | |
| 10.3 | For other personnel? | | | |
| 11 | Are the training effectiveness periodically assessed? | | | |
| 12 | Are there special training instructions for visitors and consultants programs? | | | |
| 13 | Are there sufficient training materials covering the related subjects? | | | |
| PERSONNEL HYGIENE | | S | P | I |
| 14 | Are appropriate protective gowning required? | | | |
| 14.1 | Are there gowning SOPs for production staff and other staff entering production areas and other areas? | | | |
| 15 | Are staffs instructed to report health or medical problems that may have an adverse affect on the product? | | | |

| | | | | |
|---|---|---|---|---|
| 15.1 | Are they prevented from entering areas in which they may adversely affect the quality of the product or affect their own health? | | | |
| 16 | Is there a medical monitoring program to ensure protection of staff and product?<br>- For all employees?<br>- For contractors?<br>- Periodic eye examinations for personnel conducting visual inspections? | | | |
| 17 | Are personnel required to report health problems? | | | |
| 18 | Do controlled entry requirements exist for:<br>- Production areas?<br>- Testing areas? | | | |
| 18.1 | Do procedures exist for preventing unauthorized entry into:<br>- Production areas?<br>- Storage areas?<br>- Quality Control areas? | | | |
| 18.2 | Are the procedures in writing? | | | |
| 19 | Is smoking, eating, drinking, chewing, food, drinking, smoking materials and personnel medicines prohibited in the areas that might adversely influence product quality? | | | |

| CHAPTER 3: PREMISES | | | | |
|---|---|---|---|---|
| GENERAL CONDITIONS | | S | P | I |
| 1 | Is the building exterior in good conditions? | | | |
| 2 | Are there any sources of environmental contamination in the area surrounding the building? | | | |
| 2.1 | If "YES", are protective measures undertaken? | | | |
| 3 | Are the free and non-productive areas belonging to the company in good clean and orderly conditions? | | | |
| 4 | Are the roads leading to the building tarred and/or built so that dust from the road is not a source of contamination inside the plant? | | | |
| 5 | Is there any protection against the entry of rodents, insects, birds and other animals? | | | |
| 6 | Is there a written pest control program with its respective records? | | | |
| 7 | Is there an SOP for pest control? | | | |
| 7.1 | Does the SOP indicate the substances used for pest control | | | |
| 7.2 | Does the Regulatory Authority authorize the used substances? | | | |
| 7.3 | Does the SOP ensure the avoidance of contamination of starting materials, packaging materials, in process-products and finished products with rodenticides and/or fumigant agents? | | | |
| 8 | Is the flow of personnel and materials such that there are no crossing between than and prevent product contamination? | | | |
| 9 | Are corridors free of in-transit materials? | | | |
| 10 | Are air conditioning and/or ventilation systems for each area in accordance with the operation to be carried out? | | | |
| 11 | Are visible electric installations in good conditions? | | | |
| 12 | Are water, gases, electricity, steam, compressed air and other gas pipelines identified? | | | |
| 13 | Does the company comply with the national legislation on fire control and prevention? | | | |
| 14 | Are there SOPs for waste classification and treatment? | | | |
| 14.1 | Are they followed (or complied with)? | | | |
| 15 | Is waste treatment undertaken in the premises? | | | |
| 15.1 | If "YES", is there a specific area for waste treatment, completely separated from manufacturing areas? | | | |
| | PREMISES | | | |
| 16 | Are premises used for the manufacture of finished products suitably designed and constructed to facilitate good sanitation? | | | |
| 17 | Is there a suitable premises maintenance program? | | | |
| 17.1 | Does it ensure that repair and maintenance do not present any hazard to the quality of products? | | | |
| 18 | Are there SOPs/instructions to remove dust generated during the operations (e.g. during sampling, weighing, weighing, mixing, processing operations, packaging powders,...,etc? | | | |
| 18.1 | If years are measures, taken to avoid cross-contamination and facilitate cleaning? | | | |
| 19 | Are there cleaning and disinfection SOPs for the different premises and areas? | | | |

| | | | | |
|---|---|---|---|---|
| 19.1 | If yes, does the company keep records for this purpose? | | | |
| 20 | Are the lights used in different areas suitable? | | | |
| 21 | Is there a suitable HVAC system in the premises? | | | |
| 22 | Are the lighting, HVAC, water supply, steam supply, and gases systems appropriate and do not adversely affect the products or equipments during manufacturing and storage? | | | |
| | ANCILLARY AREAS | S | P | I |
| 23 | Are there general change rooms in the plant? | | | |
| 24.1 | Are toilets, change rooms and showers separated from manufacturing areas? | | | |
| 24.2 | Are they of easy access, and in good condition with respect to cleanliness, sanitation, order and conservation? | | | |
| 24.3 | Are they adequate for the number of users? | | | |
| 25 | Are the dining room, social areas and cafeteria (rest and snacks) separated from production areas? | | | |
| 26 | Are plant staffs (temporary and permanent) provided with proper working clothes for each area, including protective coverings to avoid direct contact with products and to protect themselves? | | | |
| 27 | Are there SOP's for washing uniforms separately depending on the type of area (sterile, non sterile, maintenance, special products)? | | | |
| 28 | Is there a laundry area for uniforms which is separate from production areas? | | | |
| 29 | If an outside laundry facility is used, are personnel and the person responsible instructed about the corresponding SOP? | | | |
| 29.1 | Are there instruction records? | | | |
| 29.2 | Is this outside laundry facility periodically audited? | | | |
| 29.3 | Are there audit records? | | | |
| | MAINTENANCE | S | P | I |
| 30 | Are the maintenance areas physically separated from production areas? | | | |
| 31 | Is there an SOP of the use, cleaning and maintenance of different service generated equipment? | | | |
| 32 | Are there preventive maintenance programs for equipment and critical support systems? Are performance records for this preventive maintenance program kept? | | | |
| 33 | Is equipment identified as out-of-service or in reparation identified as such? Are they removed from production areas as soon as possible? | | | |
| 34 | Is there a preventive maintenance program for the premises? | | | |
| 34.1 | Are there performance records for this preventive maintenance program? | | | |
| 35 | Are records of the usage of critical equipment showed? | | | |
| 36 | Is there a preventive maintenance program for quality control equipment? Is there a performance record for this preventive maintenance program? | | | |
| | GENERAL SERVICES | S | P | I |
| 37 | Is there a pure steam generator, if necessary? | | | |
| 38 | Is there a compressed air generator free of oil, if necessary? | | | |
| 39 | Is there an electricity generator for the maintenance of critical systems and processes to be used in case of problems with the electricity supply occur? | | | |
| 40 | Are the steam generators for different services separated from production areas? | | | |
| 41 | Do they use gases that will be in direct contact with products? | | | |
| 41.1 | Are gas piping and valves in good conditions and are they dedicated for each gas? | | | |

| CHAPTER 4: WATER SYSTEMS | | | | |
|---|---|---|---|---|
| | POTABLE WATER | S | P | I |
| 1 | What is the source of water used in the company? | | | |
| 2 | If necessary, is any treatment for making water potable undertaken before the water is stored? | | | |
| 2.1 | Does the selected treatment assure potability, according to the country's requirements? | | | |
| 3.1 | Are there schematic drawings for the system? | | | |
| 3.2 | Are the distribution network layouts shown? | | | |
| 3.3 | Are the sampling points shown? | | | |
| 4 | Does the company have water tanks? | | | |
| 4.1 | What materials are the water tanks made of? | | | |
| 5 | Are the cleaning and disinfecting procedures for water tanks documented? | | | |
| 5.1 | Are performance records shown? | | | |
| 6 | Are physicochemical tests of potable water undertaken? | | | |
| 6.1 | Are physicochemical tests of potable water recorded? | | | |
| 6.2 | Is the frequency of testing indicated in the SOPs? | | | |
| 7 | Is potable water used as a source of purified water or water for injection production? | | | |
| 8 | Is microbiological control of potable water undertaken? | | | |
| 8.1 | Is microbiological control of potable water recorded? | | | |
| 8.2 | Is the frequency of testing indicated in the relevant SOPs? | | | |
| 9 | Is potable water used for the initial washing of equipment and tools? | | | |
| 10 | Is the visible piping used for the transportation of potable water maintained in good conditions? | | | |
| 11 | Is there a preventive maintenance program that includes the potable water system? | | | |
| 11.1 | Is there a performance record for this preventive maintenance program? | | | |
| | PURIFIED WATER | S | P | I |
| 12 | Is the purified water used, produced by the company? | | | |
| 13 | Which system is used to obtain purified water? | | | |
| | Ionic exchange resins? | | | |
| | Reverse Osmosis? | | | |
| | Distillation? | | | |
| | Others (specify which)? | | | |
| 14.1 | Are the system schematics shown? | | | |
| 14.2 | Are the distribution network layouts shown? | | | |
| 14.3 | Are the sampling points shown? | | | |
| 15 | What is the production capacity in liters/hour? | | | |
| 15.1 | What is the average consumption? | | | |
| 16 | Are there written procedures for the operation of the system? | | | |
| 17 | Is the purified water stored? | | | |

| | | | | |
|---|---|---|---|---|
| 17.1 | What is the reservoir capacity? | | | |
| 17.2 | Is the reservoir constructed of sanitary type material? | | | |
| 18 | If purified water remains stored longer than 24 hours, is there any treatment to prevent microbiological contamination? | | | |
| 18.1 | Does the selected treatment prevent microbiological contamination? | | | |
| 19 | Are the pipes and valves used to distribute purified water made of sanitary material? | | | |
| 20 | Are the visible piping used in water distribution maintained in good conditions? | | | |
| 21 | Is the distribution system of purified water sanitized? | | | |
| 21.1 | Is there a SOP for the sanitation of purified water storage and distribution system? | | | |
| 21.2 | What is the sanitation method used? | | | |
| 21.3 | In the case of an open distribution system that is not used in 24 hours or more, is sanitation undertaken the day before its use? | | | |
| 21.4 | Are records kept? | | | |
| 21.5 | In the case of chemical sanitation, are sanitizing agent residues tested? | | | |
| 21.6 | Are there records? | | | |
| 22 | Is there any type of filter in the distribution system? | | | |
| 22.1 | In the case that filters exist, are they sanitized? | | | |
| 22.2 | Are the filter sanitation records shown? | | | |
| 22.3 | Are the filter replacement records shown? | | | |
| 22.4 | In the case of open distribution system not used in 24 hours or more, is sanitation done the day before its use? | | | |
| 23 | Is there any other system, to reduce bacterial burden from purified water, used in the distribution system?<br>Which type? | | | |
| 24 | Is the purified water used as a raw material to manufacture non-parenteral products? | | | |
| 25 | Is the purified water used for washing production equipment and utensils? | | | |
| 25.1 | Is the purified water used for the final rinse of the equipment used in the manufacture of non-parenteral products? | | | |
| 26 | Is a non-continuous purified water production system used? | | | |
| 26.1 | Does each batch or production day release, by Quality control, undergo physicochemical test established official pharmacopoeias or by alternative validated methods? | | | |
| 26.2 | Are microbiological controls undertaken on the day of use? | | | |
| 26.3 | Are an action limits established? | | | |
| 26.4 | Is the action limit not more than 100 cfu / mL? | | | |
| 26.5 | When the action limit is exceeded, is an investigation undertaken to ensure quality of the batches of products made with such water? | | | |
| 26.6 | Is the documentation shown? | | | |
| 27 | Is a continuous system of purified water production used? | | | |
| 27.1 | Is there a continuous monitoring of the quality of the purified water? | | | |
| 27.2 | Is there an automatic system to prevent use of the purified water, if this is out of specifications? | | | |
| 27.3 | If there is an automatic system, is this checked to verify that it is functioning properly? | | | |
| 27.4 | Are physicochemical analyses undertaken daily or with an established frequency according to the procedures established by current editions of official pharmacopoeias or by alternative validated methods? | | | |

| | | | | |
|---|---|---|---|---|
| 27.5 | Are microbiological analysis undertaken on the days of use or with an established frequency which is properly validated? | | | |
| 27.6 | Is an action limit established? | | | |
| 27.7 | Is the action limit not more than 100 cfu / mL? | | | |
| 27.8 | When the action limit is exceeded, is an investigation undertaken to ensure quality of the batches of product made with that water? | | | |
| 27.9 | Is the documentation shown? | | | |
| 28 | Are the sampling points rotated to cover all points of use? | | | |
| 29 | Is there a SOP for sampling? | | | |
| 30 | If the water that feeds the system is chlorinated, is there a system to remove the chlorine? | | | |
| 31 | Are ionic exchange resins used? | | | |
| 31.1 | Is there a SOP that considers the criteria to follow for the regeneration of resins and the frequency of regeneration? | | | |
| 31.2 | Are records kept? | | | |
| 32 | Are there SOPs for the sanitation of the purified water system? | | | |
| 32.1 | What is the sanitation system used? | | | |
| 32.2 | What is the sanitation frequency? | | | |
| 32.3 | Are records kept? | | | |
| 33 | Is there a preventive maintenance program that includes the components of the purified water system? | | | |
| 33.1 | Are records kept? | | | |
| | WATER FOR INJECTION | S | P | I |
| 34 | Which treatment system is used to produce Water for Injection? | | | |
| 35 | Are system schematics shown?<br>Are distribution network layouts shown?<br>Are sampling points shown? | | | |
| 36 | Are there written procedures for the operation of the system? | | | |
| 37 | What is the production capacity in liters/hour? | | | |
| 37.1 | What is the average consumption? | | | |
| 38 | If a reverse osmosis system is used: | | | |
| 38.1 | Is a two-steps system or double osmosis system used on line? | | | |
| 38.2 | Is the water that feeds the system pre-treated? | | | |
| 38.3 | What is the pre-treatment system? | | | |
| 38.4 | Is the system sanitized? | | | |
| 38.4.1 | What is the sanitation frequency? | | | |
| 38.4.2 | Are records kept? | | | |
| 38.5 | In case that chemical sanitation is undertaken, are sanitizing agent residues investigated? | | | |
| 38.5.1 | Are records kept? | | | |
| 39 | If distillation is used: | | | |
| 39.1 | Is the water that feeds the system pre-treated? | | | |

| | | | | |
|---|---|---|---|---|
| 39.2 | What is the pre-treatment system?<br>_____<br>_____ | | | |
| 40 | Is there a storage tank for the Water used for injection? | | | |
| 40.1 | Is the tank made of sanitary material? | | | |
| 40.2 | What is its capacity? | | | |
| 40.3 | Does it have a hydrophobic vent absolute filter? | | | |
| 40.4 | Are periodic integrity tests undertaken? | | | |
| 40.5 | Are records kept? | | | |
| 41 | Are pipes used in the distribution of Water for Injection up to the point of use? | | | |
| 41.1 | Are pipes made of sanitary material? | | | |
| 41.2 | Is there any type of heat exchanger in the system? | | | |
| 41.3 | If “YES", are there guarantees that the heat exchanger is not a source of contamination? | | | |
| 42 | Is there a SOP for the sanitation of the water storage and distribution system? | | | |
| 42.1 | What is the sanitation method used? | | | |
| 42.2 | What is the sanitation frequency? | | | |
| 42.3 | Are records kept? | | | |
| 42.4 | In case of chemical sanitation, is the existence of sanitizing agent residues investigated? | | | |
| 42.5 | Are records kept? | | | |
| 42.6 | If sanitation is thermal, is it undertaken periodically by a fluent steam circulation? | | | |
| 42.7 | Are records kept? | | | |
| 43 | If water is not used the same day of its production, is the water maintained above 80 °C or below 4 °C and with constant recirculation through a loop up to points of use? | | | |
| 44 | If recirculation is below 4 $^{o}$C, are additional precautions taken to prevent access of microbial contaminants and its proliferation? | | | |
| 44.1 | What are those precautions?<br>_____<br>_____<br>_____ | | | |
| 44.2 | Do the storage and recirculation of the water at this temperature ensure its quality according to its use? | | | |
| 45 | If the water is produced by reverse osmosis, is there any system to maintain its quality? | | | |
| 46 | If the company manufactures parenteral products, does it use water for injections as a raw material? | | | |
| 47 | If the company manufactures parenteral products, does it use water for injections for the final rinse of equipments and components used in manufacturing? | | | |
| 48 | Is a non-continuous and non-recirculated production system of Water for injection used? | | | |
| 48.1 | If this is the case: is water used only during the day of its production? | | | |
| 48.2 | Is water disposed at end of the day of its production? | | | |

| | | | | |
|---|---|---|---|---|
| 48.3 | Is each batch released by Quality control according to the physicochemical and bacterial endotoxins test results in accordance to the procedures established by current editions of official pharmacopoeias or by alternative methods validated? | | | |
| 48.4 | Are microbiological tests of each batch undertaken? | | | |
| 48.5 | Is an action limit established? | | | |
| 48.6 | Is action limit no more than 10 cfu /100mL ? | | | |
| 48.7 | When the action limit is exceeded, is an investigation of the system always undertaken? | | | |
| 48.8 | Is the investigation report shown? | | | |
| 48.9 | Are measures undertaken? | | | |
| 48.10 | What measures are undertaken? | | | |
| 49 | Is there a continuous system ~~of~~ for the production of water for injections used? | | | |
| 49.1 | Is there a continuous monitoring of the water quality? | | | |
| 49.2 | Is there an automatic system to prevent the use of the water for injection~~s~~, if it is out of specifications? | | | |
| 49.3 | If there is an automatic system to prevent the use of the water for injection~~s~~, if it is out of specifications, is it checked to verify that it is operating properly? | | | |
| 49.4 | Are physicochemical and bacterial endotoxin tests undertaken according to the procedures established by current editions of EP, USP, Pharmacopoeia or by an alternate validated method? | | | |
| 49.5 | Are microbiological tests undertaken daily or with an established frequency which is properly validated? | | | |
| 49.6 | Is an action limit established? | | | |
| 49.7 | Is the action limit no more than 10 cfu / 100mL? | | | |
| 49.8 | When the action limit is exceeded, is an investigation of the system always undertaken? | | | |
| 49.9 | Is the investigation report shown? | | | |
| 49.10 | Were measures taken? | | | |
| 49.11 | What measures were taken? | | | |
| 50 | Are sampling sites rotated so that all points of use are covered? | | | |
| 51 | Is there a SOP for sampling? | | | |
| 52 | Is there a preventive maintenance program that includes the water for injection system? | | | |
| 52.1 | Are records kept? | | | |

## CHAPTER 5: STORAGE AREAS

| | Storage Area | Starting materials | | | Packaging materials | | | Bulk products | | | Finished products | | | Flammable | | | Rejected Prod. and mat. | | | Recalls | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I |
| 1 | If a material enters directly from the outside and products exits directly to the outside, is there a procedure to protect material and products integrity? | | | | | | | | | | | | | | | | | | | | | |
| 1.1 | Is there a system that protects materials and products located inside? | | | | | | | | | | | | | | | | | | | | | |
| 2 | Are the premises of adequate size according to the needs of the company? | | | | | | | | | | | | | | | | | | | | | |
| 2.1 | Are the premises properly identified? | | | | | | | | | | | | | | | | | | | | | |
| 2.2 | Are the premises in order | | | | | | | | | | | | | | | | | | | | | |
| 2.3 | Are floors, walls and roofs well maintained and hygienic? | | | | | | | | | | | | | | | | | | | | | |
| 3 | Are the pipes and drains well maintained and hygienic? | | | | | | | | | | | | | | | | | | | | | |
| 4 | Are visible electric installations in good conditions? | | | | | | | | | | | | | | | | | | | | | |

| | Storage Area | Starting materials | | | Packaging materials | | | Bulk products | | | Finished products | | | Flammable | | | Rejected Prod. and mat. | | | Recalls | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I |
| 5 | Do the storage environmental conditions (including lighting) comply with the established storage requirements? | | | | | | | | | | | | | | | | | | | | | |
| 6 | Is it necessary to control and record the temperature? | | | | | | | | | | | | | | | | | | | | | |
| 7 | If they are needed, is there equipment available to control and /or record temperature? | | | | | | | | | | | | | | | | | | | | | |
| 7.1 | Are there records? | | | | | | | | | | | | | | | | | | | | | |
| 8 | Is it necessary to control and record humidity? | | | | | | | | | | | | | | | | | | | | | |
| 8.1 | If they are needed, is there equipment available to control and /or record humidity? | | | | | | | | | | | | | | | | | | | | | |
| 9 | Do the temperature and humidity, comply with the established parameters for the stored materials and products? | | | | | | | | | | | | | | | | | | | | | |
| 10 | Is a cold room needed? | | | | | | | | | | | | | | | | | | | | | |
| 10.1 | Are there temperature records? | | | | | | | | | | | | | | | | | | | | | |

| | Storage Area | Starting materials | | | Packaging materials | | | Bulk products | | | Finished products | | | Flammable | | | Rejected Prod. and mat. | | | Recalls | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I |
| 10.2 | Is there an alert system to indicate deviations from the established temperature in the cold room? | | | | | | | | | | | | | | | | | | | | | |
| 10.3 | Is there a SOP to handle such deviations? | | | | | | | | | | | | | | | | | | | | | |
| 11 | Are the scales used in the reception and/or dispatch area calibrated periodically? | | | | | | | | | | | | | | | | | | | | | |
| 11.1 | Are the scales checked on a scheduled basis? | | | | | | | | | | | | | | | | | | | | | |
| 12. | Are there areas physically separated or systems in place to prevent mix-ups of materials and products of different categories? | | | | | | | | | | | | | | | | | | | | | |
| 13 | Are there procedures for all the operations of this area receipt of goods, movement of containers, load conditions, dispatches, etc?) | | | | | | | | | | | | | | | | | | | | | |
| 14 | Is there a receiving area? | | | | | | | | | | | | | | | | | | | | | |
| 14.1 | Is the receipt of materials documented and recorded? | | | | | | | | | | | | | | | | | | | | | |

| | Storage Area | Starting materials | | | Packaging materials | | | Bulk products | | | Finished products | | | Flammable | | | Rejected Prod. and mat. | | | Recalls | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I |
| 14.2 | Are these records in an electronic format? | | | | | | | | | | | | | | | | | | | | | |
| 14.3 | Are these written records? | | | | | | | | | | | | | | | | | | | | | |
| 15 | Stock control of materials and products: | | | | | | | | | | | | | | | | | | | | | |
| 15.1 | Is it computerized? | | | | | | | | | | | | | | | | | | | | | |
| 15.2 | Is it manual? | | | | | | | | | | | | | | | | | | | | | |
| 16 | Is the location of in use and not in use goods maintained in a computerized system? | | | | | | | | | | | | | | | | | | | | | |
| 16.2 | Is the location of in use and not in use goods maintained in a manual system? | | | | | | | | | | | | | | | | | | | | | |
| 17 | Is the receiving area designed and equipped to allow for, the cleaning of the containers before storage, if needed? | | | | | | | | | | | | | | | | | | | | | |
| 18 | Is a visual inspection done at receipt, to verify damages or integrity of seal and containers, which could affect product quality? | | | | | | | | | | | | | | | | | | | | | |
| 19 | Is each received container labeled upon receipt? | | | | | | | | | | | | | | | | | | | | | |

| | Storage Area | Starting materials | | | Packaging materials | | | Bulk products | | | Finished products | | | Flammable | | | Rejected Prod. and mat. | | | Recalls | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I |
| 20 | Does the label contain the following information?: | | | | | | | | | | | | | | | | | | | | | |
| 20.1 | Item name and code | | | | | | | | | | | | | | | | | | | | | |
| 20.2 | Supplier name | | | | | | | | | | | | | | | | | | | | | |
| 20.3 | Supplier's lot number | | | | | | | | | | | | | | | | | | | | | |
| 20.4 | Total Number of units | | | | | | | | | | | | | | | | | | | | | |
| 20.5 | Manufacture date | | | | | | | | | | | | | | | | | | | | | |
| 20.6 | Expiry date | | | | | | | | | | | | | | | | | | | | | |
| 20.7 | Internal lot number | | | | | | | | | | | | | | | | | | | | | |
| 20.8 | Special storage conditions | | | | | | | | | | | | | | | | | | | | | |
| 20.9 | Test Date | | | | | | | | | | | | | | | | | | | | | |
| 20.10 | Retest date | | | | | | | | | | | | | | | | | | | | | |
| 21 | Is the label attached to the container body and not to its removable parts? | | | | | | | | | | | | | | | | | | | | | |
| 22 | Are sample containers identified as such? | | | | | | | | | | | | | | | | | | | | | |
| 23 | Before release by quality control, are all items and finished products properly identified as such and maintained in quarantine, either physically or by a system? | | | | | | | | | | | | | | | | | | | | | |

| | Storage Area | Starting materials | | | Packaging materials | | | Bulk products | | | Finished products | | | Flammable | | | Rejected Prod. and mat. | | | Recalls | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I |
| 24 | Is there an area or computerized system to delimit or restrict the use of starting materials, packaging materials, intermediate products and finished products in quarantine? | | | | | | | | | | | | | | | | | | | | | |
| 25 | Are rejected materials properly identified and stored separately in restricted areas? | | | | | | | | | | | | | | | | | | | | | |
| 26 | Is there a procedure for materials destruction? | | | | | | | | | | | | | | | | | | | | | |
| 27 | Are approved items properly identified? | | | | | | | | | | | | | | | | | | | | | |
| 28 | Is there a procedure or system that ensures that starting materials with expired or with expired retest dates are not used? | | | | | | | | | | | | | | | | | | | | | |
| 29 | Are all available starting materials within their valid period? | | | | | | | | | | | | | | | | | | | | | |

| | Storage Area | Starting materials | | | Packaging materials | | | Bulk products | | | Finished products | | | Flammable | | | Rejected Prod. and mat. | | | Recalls | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I |
| 30 | Is the storage layout adequate to preserve the integrity of all items and products? | | | | | | | | | | | | | | | | | | | | | |
| 31 | Is the FIFO /FEFO and the shortest re-test date system followed for the use of starting materials? | | | | | | | | | | | | | | | | | | | | | |
| 32 | Are shelves and/or platforms separated from floors and walls to allow cleaning? | | | | | | | | | | | | | | | | | | | | | |
| 33 | Are activities and operations undertaken in such a manner to ensure that they do not contaminate either the environment or stored materials? | | | | | | | | | | | | | | | | | | | | | |
| 34 | Are packages and containers with items (drums, kegs, boxes, etc.) adequately closed? | | | | | | | | | | | | | | | | | | | | | |
| 35 | Is there an area which is secure or with restricted access which is used to store labels? | | | | | | | | | | | | | | | | | | | | | |

| | Storage Area | Starting materials | | | Packaging materials | | | Bulk products | | | Finished products | | | Flammable | | | Rejected Prod. and mat. | | | Recalls | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I |
| 36 | Are all outdated printed materials destroyed? | | | | | | | | | | | | | | | | | | | | | |
| 37 | Within the storage room, are there distinct areas which are physically separated and with restricted access for psycotropics and narcotic substances? | | | | | | | | | | | | | | | | | | | | | |
| 38 | Are cautions undertaken in the loading of corrosive materials in order of maintaining integrity of other items / materials? | | | | | | | | | | | | | | | | | | | | | |
| 39 | Is there a SOP dealing with spills of corrosive or toxic and active substances? | | | | | | | | | | | | | | | | | | | | | |
| 40 | Are there areas specific for the storage of flammable and explosive products? | | | | | | | | | | | | | | | | | | | | | |
| 41 | Are there established procedures to ensure the identification, sorting, and destruction of expired finished products from the storage area? | | | | | | | | | | | | | | | | | | | | | |
| 41.1 | Are there records of those procedures? | | | | | | | | | | | | | | | | | | | | | |

| | Storage Area | Starting materials | | | Packaging materials | | | Bulk products | | | Finished products | | | Flammable | | | Rejected Prod. and mat. | | | Recalls | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I |
| 42 | Are all drug products available for release, within their valid period? | | | | | | | | | | | | | | | | | | | | | |
| 43 | Is there an area for Finished Product Release? | | | | | | | | | | | | | | | | | | | | | |
| 44 | Is there a distribution control of finished products? | | | | | | | | | | | | | | | | | | | | | |
| 45 | Are all drug products, within their valid period? | | | | | | | | | | | | | | | | | | | | | |

| CHAPTER 6: PRODUCTS RECALL | | | | |
|---|---|---|---|---|
| | | S | P | I |
| 1 | Is there an operating procedure that establishes a system to recall products from the market, if necessary? | | | |
| 2 | Is there a responsible person (independent from the marketing department) designated by or in accordance with the qualified person responsible for the coordination and execution of the recall procedure? | | | |
| 3 | Is Quality control/Quality assurance/Regulatory Affairs notified of undertaken recall operations? | | | |
| 4 | Does the procedure indicate the mandatory requirement of notifying the Health Authority immediately in the event that the cause is for health reasons? | | | |
| 5 | In the case of having distributed products to other countries, is the Health Authority of the recipient country and the recipient of these products informed immediately? | | | |
| 6 | Are distribution records available for a prompt recall of products from the market? | | | |
| 7 | Do those distribution records contain information that allows for the traceability and determination of the receivers of that distribution? | | | |
| 8 | Are there reports about all products recalled from the market, as well as the cause, destination, destruction dates and final reconciliation of quantities? | | | |
| 8.1 | Could the reason(s) for the recall implicate other batches of the product and, if so has an investigation been initiated and appropriate action taken? | | | |
| 9 | Are those reports attached to the product lot record? | | | |
| 10 | Are the recalled products identified as such? | | | |
| 11 | Are these products maintained segregated and orderly in an access restricted area? | | | |

| CHAPTER 7: DOCUMENTATION | | | | |
|---|---|---|---|---|
| | MASTER FORMULA | S | P | I |
| 1. | Specifications for starting materials and packaging materials? | | | |
| 1.1 | Are there updated specifications for starting materials and packaging materials?<br>- Designated name and the internal code reference?<br>- The reference, if any to a pharmacopoeial monograph?<br>- The approved suppliers and the manufacturer?<br>- A sample of printed materials?<br>- Directions for sampling and testing or reference tp procedures?<br>- Qualitative and qualitative requirements with acceptance limits?<br>- Storage conditions and precautions?<br>- The re-testing period? | | | |
| 2 | Specifications for finished products: | | | |
| 2.1 | Are there updated specifications for finished products produced in the premises? | | | |
| 2.2 | Do they include the following:<br>- The designated name of the product and code reference><br>- A description of the pharmaceutical dosage form?<br>- A description of the package details?<br>- Directions for sampling and testing or a reference to procedures?<br>- The qualitative and quantitative requirements?<br>- The storage conditions and special handling precautions, where applicable><br>- The shelf-life. | | | |
| 3 | Specifications for intermediate and bulk products: | | | |
| 3.1 | Are they purchased? | | | |
| 3.2 | Are they produced in the company to be used later in the manufacture of a product? | | | |
| 3.3 | Do they include the following:<br>- The designated name?<br>- The approved suppliers and the manufacturers (where applicable)?<br>- Directions for sampling and testing or reference to procedures?<br>- Qualitative and quantitative requirements with acceptance limits?<br>- Storage conditions and precautions.<br>- The maximum storage period or shelf-life?<br>- The re-testing period? | | | |
| 4 | Is there an updated master formula for each product and size of lot to be manufactured?<br>Does the Technical Director and/or Quality Control/Assurance Director authorize all master formulas? | | | |
| 4.1 | If it is necessary to modify the master formula, are there written procedures on how to do this? | | | |
| 4.2 | Is the Regulatory Health Authority notified of this change? | | | |
| 4.3 | Is authorization from the Health Authority expected before undertaking the change? | | | |
| 5 | Does the qualitative and quantitative formula agree with the authorization given by the Regulatory Health Authority? | | | |
| 5.1 | If a qualitative and quantitative formula change is made, is the corresponding authorization requested? | | | |

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| 6 | Do all products have a master formula containing: | | | |
| 6.1 | Product name, code and product number? | | | |
| 6.2 | Issue date? | | | |
| 6.3 | Description of pharmaceutical dosage form, concentration and/or strength of the active ingredients? | | | |
| 6.4 | Product shelf life? | | | |
| 6.5 | Batch size? | | | |
| 6.6 | Unitary formula? | | | |
| 6.7 | Industrial formula? | | | |
| 6.8 | Starting materials, indicating the quantity of use for each one, with the code or number related to their specifications including those starting materials that are used up during processing and their equivalence to their International Nonproprietary Names (INN)? | | | |
| 6.9 | Theoretical intermediate yield and theoretical final yields with their correspondent limits? | | | |
| 6.10 | Indication of the areas in which each one of the process steps occur and equipment used? | | | |
| 6.11 | Excess active ingredients (if occurs)? | | | |
| 6.12 | Names and signatures of the qualified people involved in the issuance, review, and approval (at least two)? | | | |
| 6.13 | Detailed instructions of the steps to follow for each stage of the process? | | | |
| 6.14 | Instructions concerning controls during the process, of intermediate products and operational variations, indicating specifications? | | | |
| 6.15 | In the master formula, are there references to the SOPs related to different stages of manufacturing, equipment operation, etc. when they correspond? | | | |
| 6.16 | Special precautions that should be taken during the different stages of the process due to the characteristics of the starting materials handled and equipment. | | | |
| 6.17 | The standards for the storage of the intermediate or bulks, including the container, the labeling and any other storage condition when the product requires it? | | | |
| 6.18 | Formula review date. | | | |
| 6.19 | Registration number. | | | |
| 6.20 | Indication of processes (validated) for the manufacture of the product. | | | |
| 6.21 | Forms for record keeping of product specifications during manufacture process (weight, hardness, friability, closure of capsules, disintegration, viscosity, etc.) performed by production and quality control | | | |
| 7 | Is a production order issued for each batch of processed product? | | | |
| 8 | Does the production order issued adjust to the master formula of the product? | | | |
| | BATCH PRODUCTION RECORD (BPR) | S | P | I |
| 9.1 | Is there a process of credible transcription that ensures its exact reproduction? (check the availability of SOPs) | | | |
| 9.2 | Do responsible personnel authorize it? | | | |
| 10 | Does it contain the following data: | | | |
| 10.1 | Product name? | | | |
| 10.2 | Issue date? | | | |
| 10.3 | Batch number? | | | |

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| 10.4 | Expiry date of finished product? | | | |
| 10.5 | The list of raw materials involved (including the ones that are used up during processing) with their code numbers, lot, and/or analysis, theoretical and real quantities utilized for each of them? | | | |
| 10.6 | If it is necessary to adjust the concentration of raw materials, is the modification signed by a qualified person? | | | |
| 10.7 | Are the labels of the raw materials separated, attached? | | | |
| 10.8 | Is the detailed description of each step included in the processed lot record? | | | |
| 10.9 | Are the areas, where each one of the steps occur and the equipment utilized, indicated? | | | |
| 10.10 | Are the procedures, or reference to them, applied to the preparation of equipment and their installations, indicated? | | | |
| 10.11 | Are the areas and equipment/lines released recorded? (line clearance). | | | |
| 10.12 | Are identification labels of areas and of equipment attached? | | | |
| 10.13 | Is the date, the starting and ending time of every step recorded? | | | |
| 10.14 | Are the values of operational deviations to be controlled during process (Ex.: temperature, pH, times, agitation speeds, etc.) recorded?<br>When it corresponds, are records attached? | | | |
| 10.15 | Are the acceptance limits of such deviations indicated? | | | |
| 10.16 | If there are process deviations with regard to the master formula, are they recorded? | | | |
| 10.16.1 | Are they authorized by quality assurance personnel? | | | |
| 1016.2 | Is the management of deviations undertaken as outlined in a SOP which has been previously established? | | | |
| 10.17 | Whenever Quality Control intervenes in some step of the process, are interventions recorded? | | | |
| 10.18 | Are the real yields of the intermediate and end stage recorded? | | | |
| 10.18.1 | Are the yields within the acceptable limits? | | | |
| 10.18.2 | In case of a deviation, is the cause of the deviation investigated according to the SOP? | | | |
| 10.18.3 | Are the investigation findings documented? | | | |
| 10.19 | Are the signatures/ initials of the people who carry out the different operations and of those who supervise them recorded? | | | |
| 10.20 | Is it verified that the data which should appear on the batch process record are completed at the time in which each action is undertaken during the process? | | | |
| 10.21 | Is the reprocessing of products done in accordance with a SOP? | | | |
| 10.22 | Are reprocessing and reworking previously authorized by Control/Quality Assurance? | | | |
| 11 | After the manufacture process is ended, is all the documentation that is part of the batch record, including the certificate of analysis of the Finished Product, filed? | | | |
| 12 | Is the file maintained for at least one year after the Expiry date of the lot? | | | |
| 13 | Is a correlative/sequential and traceable record taken from each production? | | | |
| | PACKAGING | S | P | I |
| 14. | Are there instructions for product packaging, updated and authorized by the qualified person responsible and/or Quality Assurance/Control for each product, size of | | | |

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| | container and dosage form? | | | |
| 15 | Does the company have packaging orders with the following information: | | | |
| 15.1 | Full name and code of the product? | | | |
| 15.2 | Lot number? | | | |
| 15.3 | Presentation unit, dosage forms description and strength/potency? | | | |
| 15.4 | Issue date? | | | |
| 15.5 | Starting date? | | | |
| 15.6 | Finishing date? | | | |
| 15.7 | Expiry date and product shelf life for each batch? | | | |
| 15.8 | Package size, regarding number, weight or product volume in the final container? | | | |
| 15.9 | A full list of all packaging material required for a normal size batch, including quantities, sizes and types, with the lot number, code or reference number related to specifications for every packaging material? | | | |
| 15.10 | Special precautions to be observed, including review of packaging area and equipment for release of production line, as well as, the cleaning requirements of the area and equipment? | | | |
| 15.11 | A process description, including any important supplemental operations, and equipment to be used? | | | |
| 15.12 | Details concerning process control with instructions for the sampling and acceptable limits? | | | |
| 15.13 | Forms for recording product specifications during packaging process (check up process starting, sealing tests, bottle closures, filling volume, lot number, expiry date, etc.) done by packaging and quality control personnel? | | | |
| 15.14 | Signature of the person responsible for the packaging operation? | | | |
| 15.15 | Signature of the person who has dispatched packaging material and of the personnel who has verified this? | | | |
| 15.16 | Signature of the person who has received packaging material? | | | |
| 15.17 | Signature of the Quality inspector during the processes? | | | |
| 15.18 | Yield of packaging operation? | | | |
| 15.19 | Observations (space adequate to note any information or deviation)? | | | |
| | BACTH PACKAGING RECORDS | S | P | I |
| 16 | Is a packaging order for every batch or part batch processed issued? | | | |
| 17 | Does the packaging order conform to the packaging instructions? | | | |
| 18 | Is the release of areas and equipment/ lines recorded? (line clearance) | | | |
| 19 | Are the signatures/initials of the people responsible for the different operations recorded? | | | |
| 20 | Does the batch packaging record contain the following information: | | | |
| 20.1 | The name of the product, the batch number and the quantity of bulk product to be packed, as well as the batch number and the planned quantity of the finished product that will be obtained, the quantity actually obtained, and the reconciliation? | | | |
| 20.2 | The date (s) and time(s) of the packaging operations? | | | |
| 20.3 | The expiry date of the finished product? | | | |
| 20.4 | The name of the responsible person carrying out the packaging operation? | | | |
| 20.5 | The initials of the operators who did the different steps? | | | |
| 20.6 | The controls undertaken with the outcome of verifying the identity and conforming to the packaging instructions, including the results of the in-process controls? | | | |

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| 20.7 | Details of the packaging operations carried out, including references to equipment and the packaging lines used, cleaning records? | | | |
| 20.8 | If necessary, the instructions for keeping the product unpackaged or a record of returning product that has not been packaged to the storage areas? | | | |
| 20.9 | Whenever possible, are samples of the printed packaging materials used, including samples bearing the batch number, expiry date and any additional overprinting kept? | | | |
| 20.10 | Notes on any special problems, including details of any deviation from the packaging instructions, with written authorization by the qualified person responsible? | | | |
| 20.11 | The quantities and reference numbers or identification of all the printed packaging materials and bulk product issued, used, destroyed or returned to stock and the quantities of product obtained to permit an adequate reconciliation? | | | |
| 20.12 | Is there a check to ensure that the data which appears on the batch packaging records are completed at the moment that each action is carried out during the process? | | | |
| 20.13 | Are the reprocessing and reworking of products controlled in a SOP for deviations? | | | |
| 20.14 | Is the intervention of Quality Control included in this SOP? | | | |
| 21 | After the packaging process is ended, is all the documentation that is part of the batch packaging record, including the analytical reports of the Finished Product, filed? | | | |
| 22 | Is the file maintained for at least one year after the Batch expiry date? | | | |
| 23 | Is a correlative/ sequential and traceable record of each production or deviation kept? | | | |
| | GENERAL DOCUMENTATION | S | P | I |
| 24 | All applicable SOPs are available in each area where they are required? | | | |
| 25 | For each procedure, are the purpose, scope, references, and responsibilities clearly defined? | | | |
| 26 | Is there the detailed and precise description, in chronological order of the routine operations? | | | |
| 27 | Are the date issued and the effective date indicated? | | | |
| 28 | Are the procedures available, current? | | | |
| 29 | Are the signatures of the personnel that issue, review, and approve the document indicated? | | | |
| 30 | Are the records indicated within the procedures available? | | | |
| 31 | Are the labels adhered to containers, equipment, and other auxiliary elements of production and areas clear and unambiguous? | | | |
| 32 | Do the labels indicate the condition in which products, equipment, and areas are found? | | | |
| 33 | Is the way in which data is amended due to writing errors defined? | | | |
| 33.1 | Does the use of correction fluid or eraser remain clearly prohibited in the documentation? | | | |
| 33.2 | If there are amendments/changes, are the date and signature recorded? | | | |
| 34 | Is there a SOP for the handling of changes and deviations? | | | |
| 35 | Is there a written procedure for assigning batch/lot numbers? | | | |
| 36 | Are documents designed, prepared and distributed with care? | | | |
| 37 | Are they approved, signed and dated by appropriate and authorized persons (check the availability of an SOP for this purpose?). | | | |
| 38 | Is there an SOP for reproduction of documents? | | | |
| 39 | Is there an SOP for document revision? | | | |
| 39.1 | Are they kept up-to-date. | | | ` |

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| 39.2 | Does the SOP include instructions to prevent the usage of superseded documents? | | | |
| 40 | Are all documents printed, and not handwritten? | | | |
| 40.1 | Where documents require the entry of data, are they made clear, legible? | | | |
| 40.2 | Is there sufficient space for such entries? | | | |
| 41 | Are Alterations to documents made according to the relevant SOP? | | | |
| 42 | How is the data recorded? _____ | | | |
| 42.1 | If it is recorded by electronic means, is the access restricted to only authorized persons? | | | |
| 42.2 | Is it secured by passwords? | | | |
| 42.3 | Is it protected by back-up system? | | | |

| CHAPTER 8: SAMPLING AREA | | | | |
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| SAMPLING AREA | | S | P | I |
| 1 | Is there a physically separated area for sampling? | | | |
| 2 | If there is no area for sampling, is sampling undertaken in such a way as to prevent contamination or cross-contamination? | | | |
| 3 | Does the sampling area have: | | | |
| 3.1 | Sanitary finishes? | | | |
| 3.2 | Dust aspiration/ retention system? | | | |
| 3.3 | Is there a special lighting system, in case that photosensitive raw materials are being handled? | | | |
| 3.4 | Are walls, floors, and ceilings well maintained and hygienic? | | | |
| 3.5 | Is there a place to keep the sampling utensils in an orderly fashion? | | | |
| 3.5.1 | If there is no place available to keep the sampling utensils orderly, where are they kept? | | | |
| 3.6 | Is there a specific washing area, which is separated, for washing the sampling utensils? | | | |
| 3.6.1 | If a specific washing area for the sampling utensils is not available, where are they washed? | | | |
| 4 | In the previous case is there a SOP for the transportation of those sampling utensils to their washing area? | | | |
| 5 | Is there a SOP for the bringing raw materials to be sampled and to transfer them to the quarantine area after sampling? | | | |

## CHAPTER 9: WEIGHING AREA

| WEIGHING AREA | | S | P | I |
|---|---|---|---|---|
| 1 | Is there a physically separated weighing area? | | | |
| 2 | Is there a SOP for the cleaning of the weighing area? | | | |
| 3 | Is the weighing area clean? | | | |
| 4 | Are the necessary precautions taken when working with photosensitive raw materials? | | | |
| 5 | Are special systems for the localized dust extraction available? | | | |
| 6 | Is there a HVAC system with pressure differentials? | | | |
| 7 | Is there an area for the cleaning and sanitation of the containers? | | | |
| 8 | Does it have its own change room, in case the area is not located in the production area? | | | |
| 9 | When orders are not transferred to the plant immediately, are they kept in a suitable place which keeps there integrety and prevents mix-ups? | | | |
| 10 | Are the containers containing raw materials to be weighed transferred safely to the weighing and measuring area? | | | |
| 10.1 | Are these containers cleaned before opening? | | | |
| 11 | Is there a SOP for cleaning the tools/utensils used in weighing and/or measuring? | | | |
| 12 | Are the tools/utensils for weighing and/or measuring clean? | | | |
| 13 | Is there an area for washing the tools/utensils used in weighing and/or measuring? | | | |
| 14 | Are these tools/utensils kept clean and labeled in a safe place? | | | |
| 15 | Are the scales calibrated periodically? | | | |
| 15.1 | Are the scales checked on a defined scheduled basis? | | | |
| 15.2 | Are records kept? | | | |
| 15.3 | Do the capacity and sensitivity of the scales correspond with the quantities that are weighed? | | | |
| 16 | Are containers of raw materials already weighed or measured closed well? | | | |
| 17 | Are the containers used to weigh or measure raw materials reused? | | | |
| 17.1 | If so, are they cleaned very well, free from any previous identification marks and newly labeled? | | | |
| 18 | Are the materials, after being weighed or measured, immediately labeled in order to prevent mix-ups? | | | |
| 19 | On the label, does it state: | | | |
| 19.1 | Name or code and batch of the item? | | | |
| 19.2 | Name or code of the product to which the item is destined? | | | |
| 19.3 | Product Batch number? | | | |
| 19.4 | Quantity that was weighed or measured? | | | |
| 19.5 | Gross weight and tare? | | | |
| 19.6 | Net weight? | | | |
| 19.7 | Signature and date of the worker who carried out the operation? | | | |
| 19.8 | Signature and date of weight verification? | | | |

| | | | | |
|---|---|---|---|---|
| 20 | Are the raw materials of a batch, already weighed or measured, physically separated from those of another batch already weighed? | | | |
| 21 | Are the containers that contain a raw material already weighed, transferred safely to the manufacturing area? | | | |
| 22 | Is there a SOP that describes all the operations of this sector/area? | | | |
| 23 | Is there a special weighing area for sterile materials? | | | |
| 24 | Are weighing areas for potent materials separated? | | | |
| 25 | Which are weighted first, active materials or inactive materials? | | | |

## CHAPTER 10: PRODUCTION

### NON-STERILE PRODUCTS

| | Areas Installations and Equipment | Solid products | | | Semi-solid products | | | Liquid products | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | S | P | I | S | P | I | S | P | I |
| **DOCUMENTATION** | | | | | | | | | | |
| 1 | Are all applicable SOPs available in the area where the activity is performed? | | | | | | | | | |
| 2 | For each procedure, are the purpose, scope, references, and responsibilities clearly defined? | | | | | | | | | |
| 3 | Is there a detailed description, of the precise and sequential operational routine? | | | | | | | | | |
| 4 | Are the date issued and the effective date indicated? | | | | | | | | | |
| 5 | Are the procedures available, current? | | | | | | | | | |
| 6 | Are the signatures /initials of the personnel that issue, review, and approve the document indicated? | | | | | | | | | |
| 7 | Are the records indicated within the procedures available? | | | | | | | | | |
| 8 | Are the labels adhered to the containers, equipment, and other auxiliary elements of production and areas clear and unambiguous? | | | | | | | | | |
| 9 | Do the labels indicate the condition in which the products, equipment, and areas are found? | | | | | | | | | |
| 10 | Is the documentation related to the process that is being carried out in each area kept? | | | | | | | | | |
| 11 | Is the documentation completed at the moment that the action is carried out? | | | | | | | | | |
| 12 | Are procedures on the operation and use of each equipment available? | | | | | | | | | |
| 13 | Are the records of use and maintenance of critical equipment kept? | | | | | | | | | |

| AREAS | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 14 | Is the area physically separated from other areas by walls or another means of separation? | | | | | | | | | |
| 15 | Are the walls, floors and ceiling surfaces smooth and easy to clean? Are joints wall - wall, wall-floor and wall-ceilings of sanitary type? | | | | | | | | | |
| 16 | Are they well maintained and hygienic? | | | | | | | | | |
| 17 | With the exception of the doors, are all openings sealed? | | | | | | | | | |
| 18 | Are the pipes, light fixtures, and points of ventilation and other services designed in such a way to permit their easy cleaning? | | | | | | | | | |
| 19 | Are fixed pipes identified and do they indicate the direction of flow, whenever necessary? | | | | | | | | | |
| 20 | For the pipes of dangerous gases and liquids, are non-interchangeable connections used for each type of fluid? | | | | | | | | | |
| 21 | Are the drains equipped to prevent back-flow and do they have a sanitary cover? | | | | | | | | | |
| 22 | If raw materials and/or the handled products require it, is the ventilation effective and with air control (temperature, humidity and filtration)? | | | | | | | | | |
| 23. | If raw materials and/or the handled products require it, are the temperature and relative humidity measured and recorded? | | | | | | | | | |
| 24 | Is the filter integrity confirmed? | | | | | | | | | |
| 24.1 | Are there records? | | | | | | | | | |
| 25 | Is there a SOP for the renewal and replacement of filters? | | | | | | | | | |
| 26 | Are the necessary precautions taken when working with photosensitive raw materials? | | | | | | | | | |
| 27 | Are visible electrical installations in good condition? | | | | | | | | | |
| 27.1 | Are the outlets duly identified? | | | | | | | | | |
| 28 | Are there special systems for localized dust extraction? | | | | | | | | | |

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| 29 | Are they effective against the quantity of dust generated in the processes? | | | | | | | | | |
| 30 | Is the risk of environmental contamination avoided by the dust extraction system? | | | | | | | | | |
| 31 | Are there security systems in those areas where flammable materials are used? | | | | | | | | | |
| 32 | Are the areas clean? | | | | | | | | | |
| 33 | Is the area cleaned, as per established requirements in the cleaning validation? | | | | | | | | | |
| 34 | Is a cleaning validation period established? | | | | | | | | | |
| 35 | Are the containers for waste collection suitable and identified as such? | | | | | | | | | |
| 36 | Are the containers for waste collection covered? | | | | | | | | | |
| EQUIPMENT | | | | | | | | | | |
| 37 | Are the materials used in the construction of the equipment, non-reactive with the active ingredients handled? | | | | | | | | | |
| 38 | Does the location of the equipment facilitate its cleaning, as well as, the cleaning of the area in which they are found? | | | | | | | | | |
| 39 | Are all the measuring instruments of adequate range and precision? | | | | | | | | | |
| 40 | Are the instruments correctly labeled indicating the validity of calibration? | | | | | | | | | |
| 41 | Is the equipment not in use identified as such and removed from the production areas according to the SOP? | | | | | | | | | |
| 42 | Is the equipment in repair identified as such? | | | | | | | | | |
| 43 | Are there repair records? | | | | | | | | | |
| 44 | Are all the containers, equipment and auxiliary elements cleaned after their use? | | | | | | | | | |
| 45 | Is a validity period for the cleaning of equipment established? | | | | | | | | | |
| 46 | Are these indications established in the SOP for the cleaning of all equipment? | | | | | | | | | |

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| 47 | Is the integrity of the screens/ filters confirmed? | | | | | | | | | |
| 47.1 | Are records kept? | | | | | | | | | |
| 48 | Are there static bed dryers? | | | | | | | | | |
| 49 | Are there fluid bed dryers | | | | | | | | | |
| 50 | For fluid bed dryers: is there a set of sleeves for each product, or is there a cleaning validation process that guarantees no cross-contamination? | | | | | | | | | |
| 50.1 | Are the machinery pieces or parts stored in a safe place? | | | | | | | | | |
| 51 | Are the punches maintained in good condition? | | | | | | | | | |
| 51.1 | Is the access to them restricted? | | | | | | | | | |
| 52 | Is the integrity, measurements, and identity of the punches confirmed? | | | | | | | | | |
| 52.1 | Are records kept? | | | | | | | | | |
| 53 | Are there metal detectors? | | | | | | | | | |
| 54 | Is the air injected in the coating equipment free of impurities? | | | | | | | | | |
| 55 | Are all the hoses, tubes and pipes used to the transfer fluids identified? | | | | | | | | | |
| 55.1 | Are they dedicated by product?<br>If they are not dedicated by product, is the cleaning of hoses, tubes, and pipes validated? | | | | | | | | | |
| 55.2 | Are they maintained in good condition? | | | | | | | | | |
| 56 | Are the filters used disposable? | | | | | | | | | |
| 57 | If they are not, is the shelf life period for them established? | | | | | | | | | |
| 58 | Are the changes recorded? | | | | | | | | | |
| 59 | Are protective elements used for the operations that require them? | | | | | | | | | |
| 59.1 | Which ones? | | | | | | | | | |
| 60 | Are the uniforms worn by personnel, appropriate for the duties they perform? | | | | | | | | | |
| OPEREATION | | | | | | | | | | |
| 61 | Do the workers have uniforms that are clean and in good condition? | | | | | | | | | |

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| 62 | Before initiating the production process, is there verification that the work area and equipment are clean and free from materials used in the previous operation and/or material not pertinent to the current manufacturing process? | | | | | | | | | |
| 63 | Do personnel in production carry out the verification of the weight of the raw materials used in the manufacturing of each lot? | | | | | | | | | |
| 64 | Are the instructions for manufacturing (batch process records) followed and are records taken, including control points? | | | | | | | | | |
| 65 | Are the parameters of the drying operations measured and recorded? | | | | | | | | | |
| 66 | Is there assurance that the drying ovens do not contain lots of different products or different lots from a single product at the same time? | | | | | | | | | |
| 67 | Is there physical separation between different compressing machines? | | | | | | | | | |
| 68 | Is the transfer of semi manufactured/bulks products between one step of the process and another carried out in a manner to prevent their contamination? | | | | | | | | | |
| 69 | Are the containers of semi manufactured products kept closed, and opened only when it is necessary? | | | | | | | | | |
| 70 | Is the mixture of different products or different lots of products avoided through physical separation between the packaging lines? | | | | | | | | | |
| 71 | Is there confirmation that the suspensions and/or emulsions are maintained uniform throughout the bottling process? | | | | | | | | | |
| 72 | Do bottles receive some type of cleaning treatment and/or contaminant removal before being filled? | | | | | | | | | |
| 73 | Is the filling operation carried out on line? | | | | | | | | | |
| 74 | If it is not carried out on line is there a designated filling area? | | | | | | | | | |

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| 74.1 | In that case, are the bottles transferred to the filling area protected against environmental contamination? | | | | | | | | | |
| 75 | Do empty primary containers have a batch number and expiry date? | | | | | | | | | |
| 76 | If so, are the remaining primary containers destroyed? | | | | | | | | | |
| 76.1 | Are the records kept? | | | | | | | | | |
| 77 | If the empty primary containers do not have batch number and expiry date, are they coded manually or automatically? | | | | | | | | | |
| 78 | Are the correct batch number and expiry date confirmed at regular intervals? | | | | | | | | | |
| 79 | Do all finished products have the batch number and expiry date printed on their primary container? | | | | | | | | | |
| 80 | If the labeling and/or packaging operations are conducted outside of the packaging line, is the operation carried out in a designated environment/sector? | | | | | | | | | |
| 81 | Are they coded by an automatic system? | | | | | | | | | |
| 82 | Are the right batch number and expiry date confirmed by authorized personnel? | | | | | | | | | |
| 83 | How are the labels dispensed? | | | | | | | | | |
| 83.1 | Are precautions taken to prevent mix-ups and confusion? | | | | | | | | | |
| 84 | Is the unused printed and coded material destroyed? | | | | | | | | | |
| 84.1 | Are records of this kept? | | | | | | | | | |
| 85 | Is the unused non-coded printed material returned to the warehouse? | | | | | | | | | |
| 85.1 | Are records of this kept? | | | | | | | | | |
| 86 | Is the printed or embossed information legible? | | | | | | | | | |
| 87 | Is the printed or embossed information resistant to fading or erasing? | | | | | | | | | |
| 88 | If automatic machines are used to control dimensions, weights, labels, prospects, bar code, etc., is their proper performance verified? | | | | | | | | | |

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| 89 | In the case of the automatic system, are discarded units which are returned to the line, previously inspected and approved by authorized personnel? | | | | | | | | | |
| 90 | Are process controls performed at each production step? | | | | | | | | | |
| 90.1 | Is the packaging operation carried out on line with the filling operation? | | | | | | | | | |
| 90.2 | If it is not carried out on line, is there a specific area designated for packaging? | | | | | | | | | |

| PRODUCTION:<br>* SEGREGATED PHARMACEUTICAL PRODUCTS: HIGHLY ACTIVE AND SENSITIZING | | | | |
|---|---|---|---|---|
| | | S | P | I |
| 1 | Does the company have designated or independent facilities for the manufacture of highly sensitizing pharmaceutical products, such as?:<br>Penicillin derivatives<br>Cephalosporin<br>Hormones<br>Cytotoxics.<br>Biological preparations of live organisms. | | | |
| 2 | Do production areas have restricted access and only allow access to authorized people? | | | |
| 3 | Are manufacturing steps, from weighing to primary packaging for every group of active ingredient carried out in designated areas or independent facilities? | | | |
| 4 | Do all the areas have their own independent air locks for entry of workers and materials? | | | |
| 5 | Do they have pressure differentials? | | | |
| 6 | Are there manometers to detect pressure differentials? | | | |
| 7 | Is there a schematic drawing of the different areas with their corresponding pressure values? | | | |
| 8 | Is there an air extraction system to avoid discharging contaminants into the environment? | | | |
| 9 | Is there a recirculation of output air? | | | |
| 10 | Does the method use guarantee that the recycled air lacks contamination and that the output fraction that goes to the outside is free of product? | | | |
| 11 | Are there procedures and records of destruction of the waste and filters that were used in these installations/facilities? | | | |
| 12 | Do personnel wear clothing appropriate for the tasks that they perform? | | | |
| 13 | Is clothing of exclusive use? | | | |
| 14 | Does the company have a system for the decontamination, inactivation, washing, and conditioning of the clothing? | | | |
| 15 | Do workers use special protective equipment throughout the production process? | | | |
| 16 | Is a procedure for the cleaning and decontamination of areas and equipment of known effectiveness used? | | | |
| 17 | Is there a distinct and separate area for washing materials and equipment? | | | |

* The requirements are in additional to previous production cheek list?

## PRODUCTION: STERILE PRODUCTS

## DOCUMENTATION

| | Areas | Terminally sterilized products | | | Sterile filtered products | | | Aseptically prepared products | | | Lyophilized products | | | Non-injection products | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | CONDITIONS | S | P | I | S | P | I | S | P | I | S | P | I | S | P | I |
| 1 | Are all the standard operating procedures (SOP) available in the areas where the activity is performed? | | | | | | | | | | | | | | | |
| 2 | For each procedure, are the purpose, scope, references, and responsibilities clearly defined? | | | | | | | | | | | | | | | |
| 3 | Are the issue date and the effective date indicated? | | | | | | | | | | | | | | | |
| 4 | Are the procedures available, current? | | | | | | | | | | | | | | | |
| 5 | Are the signatures of the personnel that issue, review, and approve the document indicated? | | | | | | | | | | | | | | | |
| 6 | Are the records indicated within the procedures available? | | | | | | | | | | | | | | | |
| 7 | Are the labels adhered to the containers, equipment, and other auxiliary elements of production and areas clear and unambiguous? | | | | | | | | | | | | | | | |
| 8 | Do they indicate the condition in which the products, equipment, and areas are found? | | | | | | | | | | | | | | | |
| 9 | Is the documentation related to the process that is being carried out in each area shown? | | | | | | | | | | | | | | | |
| 10 | Is the documentation completed at the moment that the actions are carried out? | | | | | | | | | | | | | | | |
| 11 | Are the procedures for the operation and use of each equipment available? | | | | | | | | | | | | | | | |

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| 11.1 | Are the records of maintenance and use of the critical equipment kept? | | | | | | | | | | | | | | | | |
| AREAS, PREMISES AND EQUIPMENT | | | | | | | | | | | | | | | | | |
| 12 | Is the area separated from other departments? | | | | | | | | | | | | | | | | |
| 13 | Are there physically separated areas for each production step? | | | | | | | | | | | | | | | | |
| 14 | Does the design of the areas, grade A and B, permit a visual view of all the operations from the outside? | | | | | | | | | | | | | | | | |
| TERMINALLY STERILISED: | | | | | | | | | | | | | | | | | |
| 15 | Preparation. | | | | | | | | | | | | | | | | |
| 15.1 | Is preparation of products that are terminally sterilized carried out in grade C then immediate filtration and sterilization are carried out? | | | | | | | | | | | | | | | | |
| 15.2 | If preparation of products that are terminally sterilized done in closed vessels, is it carried out on grade D? | | | | | | | | | | | | | | | | |
| 15.3 | Are non parenteral products prepared in grade C. | | | | | | | | | | | | | | | | |
| 16 | Filling: | | | | | | | | | | | | | | | | |
| 16.1 | Is filling of small and large volume parenterals carried out in a work station under laminar airflow with grade A in an environment of grade C (A/C)? | | | | | | | | | | | | | | | | |
| 16.2 | Are non parenteral products filled in grade C environment? | | | | | | | | | | | | | | | | |
| STERILIZATION BY FILTRATION: | | | | | | | | | | | | | | | | | |
| 17 | Preparation: | | | | | | | | | | | | | | | | |
| 17.1 | Is the preparation of the solutions of small and large volume paranteral products carried out in grade C environment? | | | | | | | | | | | | | | | | |

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| 17.2 | Is the preparation of the solutions, which is done in closed containers, carried out in grade D environment? | | | | | | | | | | | | | | | | |
| 17.3 | Is the preparation of products other than parenterals carried out in grade C environment? | | | | | | | | | | | | | | | | |
| 18 | Filling: | | | | | | | | | | | | | | | | |
| 18.1 | Is the filling operation of SVP and LVP carried out in grade A in an environment of grade B or C (A/B or A/C)? | | | | | | | | | | | | | | | | |
| 18.2 | Is the filling operation of SVP, which are prepared in closed containers carried out in grade B in an environment of grade C (B/C)? | | | | | | | | | | | | | | | | |
| 18.3 | Is the filling operation of products other than parenterals carried out in grade B in an environment of grade C (B/C)? | | | | | | | | | | | | | | | | |
| PRODUCTS PRODUCED FROM STERILE MATERIALS: | | | | | | | | | | | | | | | | | |
| 19 | Preparation: | | | | | | | | | | | | | | | | |
| 19.1 | Is the preparation of SVP and LVP carried out in grade A in an environment of grade B (A/B)? or is it carried out in grade B in an environment of grade C (B/C)? | | | | | | | | | | | | | | | | |
| 19.2 | Is the preparation of products other than parenterals carried out in grade A in an environment of grade B (A/B)? or it is carried out in grade B in an environment of grade C (B/C)? | | | | | | | | | | | | | | | | |
| 20 | Filling: | | | | | | | | | | | | | | | | |
| 20.1 | Is the filling of SVP and LVP products carried out in grade A in an environment of grade B (A/B)? or is it carried out in grade B in an environment of grade C (B/C)? | | | | | | | | | | | | | | | | |

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| 20.2 | Is the filling of products other than parenterals carried out in grade A in an environment of grade B (A/B)? or it is carried out in an grade B in an environment of grade C (B/C)? | | | | | | | | | | | | | | | | |
| ASEPTIC PREPARATIONS: | | | | | | | | | | | | | | | | | |
| 21 | Are handling of materials and all processes of aseptic preparation carried out in grade A in an environment of grade B (A/B)? or are they carried out in grade B in an environment of grade C (B/C)? | | | | | | | | | | | | | | | | |
| 22 | Are the wall surfaces, floors and ceilings smooth and impervious, minimizing the shedding and the accumulation of particles and microorganisms? | | | | | | | | | | | | | | | | |
| 22.1 | Are they easy to clean and maintain sanitary? | | | | | | | | | | | | | | | | |
| 22.2 | Are the finishing of sanitary conditions? | | | | | | | | | | | | | | | | |
| 22.3 | Are they in good conditions and hygienic? | | | | | | | | | | | | | | | | |
| 23 | Are the openings, with the exception of the doors, sealed? | | | | | | | | | | | | | | | | |
| 24 | Are the doors constructed in such ways that they do not contain surfaces that cannot be cleaned? | | | | | | | | | | | | | | | | |
| 25 | In case of existing false ceilings, are they sealed in order to prevent the contamination from the free space above them? | | | | | | | | | | | | | | | | |
| 26 | Are the pipes, lighting fixtures, points of ventilation and other services designed in such a way to permit their easy cleaning and sanitation? | | | | | | | | | | | | | | | | |

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| 27 | Are pipes of dangerous liquids or gases identified and indicate the direction of flow, whenever necessary? | | | | | | | | | | | | | | | | |
| 28 | For the pipes of dangerous gases and liquids, are non-interchangeable connections used for each type of fluid? | | | | | | | | | | | | | | | | |
| 29 | Are the drains equipped to prevent back-flow? | | | | | | | | | | | | | | | | |
| 30 | Are the necessary lighting precautions taken when working with photosensitive raw materials? | | | | | | | | | | | | | | | | |
| 31 | Are the visible electrical installations maintained in good condition? | | | | | | | | | | | | | | | | |
| 32 | Do they have an air supply filtered by HEPA terminal filter in the areas grade A, B and C? | | | | | | | | | | | | | | | | |
| 33 | Do grade D areas have high efficiency filters? | | | | | | | | | | | | | | | | |
| 34 | In the areas of controlled environment (grade B, C and D), is the number of air changes per hour greater than 20? | | | | | | | | | | | | | | | | |
| 35 | Are the integrity and the sealing of the filters confirmed? | | | | | | | | | | | | | | | | |
| 35.1 | Is there a SOP for the review and changing of filters? | | | | | | | | | | | | | | | | |
| 35.2 | Are there records? | | | | | | | | | | | | | | | | |
| 36 | Do the areas have instruments with current calibration, which make it possible to confirm a cascade of pressure differential? | | | | | | | | | | | | | | | | |
| 36.1 | Are there records? | | | | | | | | | | | | | | | | |
| 37 | Do the air flow patterns prevent contamination? | | | | | | | | | | | | | | | | |
| 38 | Is there an alarm system that indicates a deviation in the air supply to the aseptic areas? | | | | | | | | | | | | | | | | |

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| 38.1 | Is there a SOP for how to proceed in the event that this occurs? | | | | | | | | | | | | | | | | |
| 39 | Is there a measure in place to avoid a conveyor belt going from a grade B area to one of lower air quality? | | | | | | | | | | | | | | | | |
| 40 | Are the temperature and relative humidity measured and recorded, if the product requires it? | | | | | | | | | | | | | | | | |
| 41 | Do the temperature and relative humidity correspond with the specifications for the process of every product? | | | | | | | | | | | | | | | | |
| 42 | Are there change rooms exclusive for the controlled environment areas? | | | | | | | | | | | | | | | | |
| 43 | Are the change rooms designed with air locks? | | | | | | | | | | | | | | | | |
| 43.1 | Do these locks have a system of closing interblocking? | | | | | | | | | | | | | | | | |
| 43.2 | Do these locks have filtered air? | | | | | | | | | | | | | | | | |
| 43.3 | Is a bench of sanitary conditions available? | | | | | | | | | | | | | | | | |
| 44 | Is there an area or sector for the washing of containers and/or tools? | | | | | | | | | | | | | | | | |
| 45 | Is there an area or sector for the storage of equipment and clean auxiliary elements? | | | | | | | | | | | | | | | | |
| 46 | Is there an area for storage of clothes especially for controlled areas? | | | | | | | | | | | | | | | | |
| 47 | Is there a separate area for the washing and for the depyrogenation of empty bottles and ampoules? | | | | | | | | | | | | | | | | |
| 48 | Are the operational areas clean? | | | | | | | | | | | | | | | | |
| 49 | Is the area cleaned, within 24 hours after ending the process activities? | | | | | | | | | | | | | | | | |
| 50 | Is a validity period established for cleaning? | | | | | | | | | | | | | | | | |

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| 51 | Are these indications established in the SOP for the cleaning of every area? | | | | | | | | | | | | | | | | |
| 52 | Are containers for waste collection identified as such? | | | | | | | | | | | | | | | | |
| 52.1 | Are they well covered? | | | | | | | | | | | | | | | | |
| 53 | Are the equipments and tools used constructed from compatible materials with the active ingredients handled? | | | | | | | | | | | | | | | | |
| 54 | Does the location of the equipment facilitate their cleaning, as well as, the cleaning of the area in which are found? | | | | | | | | | | | | | | | | |
| 55 | Are all the measuring instruments/equipment of an appropriate range and precision? | | | | | | | | | | | | | | | | |
| 56 | Are there calibration records of the equipment/instruments available? | | | | | | | | | | | | | | | | |
| 57 | Is the unused equipment removed from the production areas? | | | | | | | | | | | | | | | | |
| 58 | Is the equipment in repair identified as such? | | | | | | | | | | | | | | | | |
| 59 | Are all the containers, equipment and auxiliary elements cleaned after their use? | | | | | | | | | | | | | | | | |
| 60 | Is a validity period for the cleaning of the equipment established? | | | | | | | | | | | | | | | | |
| 60.1 | Are these indications established in the SOP for the cleaning of every equipment? | | | | | | | | | | | | | | | | |
| 61 | Are all the hoses, tubes and pipes used in the transfer of fluids identified? | | | | | | | | | | | | | | | | |
| 61.1 | Are they dedicated by product? | | | | | | | | | | | | | | | | |
| 61.2 | When they are not dedicated, is the cleaning validated? | | | | | | | | | | | | | | | | |
| 61.3 | Are they maintained in good working condition? | | | | | | | | | | | | | | | | |

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| 61.4 | Are the connections and valves used of sanitary conditions? | | | | | | | | | | | | | | | | |
| 62 | Are the filters used disposable? | | | | | | | | | | | | | | | | |
| 63 | If they are not disposable, is their usage period established? | | | | | | | | | | | | | | | | |
| 64 | Are the changes recorded? | | | | | | | | | | | | | | | | |
| 65 | Is filter sterilization recorded? | | | | | | | | | | | | | | | | |
| 66 | Are the filters dedicated by active raw material? | | | | | | | | | | | | | | | | |
| OPERATIONS | | | | | | | | | | | | | | | | | |
| 67 | Are protection elements utilized for the operations that require them? Which ones? | | | | | | | | | | | | | | | | |
| 68 | Is the clothing used appropriate for the areas and tasks that are carried out? | | | | | | | | | | | | | | | | |
| 68.1 | Are the uniforms used for work in aseptic areas, clean, in good condition and sterilized prior to their use? | | | | | | | | | | | | | | | | |
| 69 | Are the gloves free of lubricants? | | | | | | | | | | | | | | | | |
| 70 | Is the entry of the personnel into the clean rooms with watches, jewelry, or cosmetics prohibited? | | | | | | | | | | | | | | | | |
| 71 | Are pressure differential values in the different areas measured and recorded? | | | | | | | | | | | | | | | | |
| 71.1 | Are records kept? | | | | | | | | | | | | | | | | |
| 72 | Are particulate counts conducted in the controlled environments? | | | | | | | | | | | | | | | | |
| 72.1 | Are records kept? | | | | | | | | | | | | | | | | |
| 73 | Are microbiological controls conducted in the controlled environments? | | | | | | | | | | | | | | | | |
| 73.1 | Are records kept? | | | | | | | | | | | | | | | | |

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| 74 | Before starting the production process, is it confirmed that the work area and equipment are clean and free from materials from the previous operation and/or materials not pertinent to the current manufacturing process? | | | | | | | | | | | | | | | | |
| 75 | Are the personnel entering the change room already wearing protective clothing? | | | | | | | | | | | | | | | | |
| 76 | Is the weight verification of utilized raw materials in the manufacturing of each lot, carried out? | | | | | | | | | | | | | | | | |
| 77 | Are the instructions for manufacturing followed and are the records taken, including control points? | | | | | | | | | | | | | | | | |
| 78 | Are the materials and equipment sterilized and their containers sanitized? | | | | | | | | | | | | | | | | |
| 78.1 | Do they enter to the aseptic area through air lock? | | | | | | | | | | | | | | | | |
| 79 | Is there a validity time period established for the sterilization of the uniforms, components, containers of products in bulk and other equipment? | | | | | | | | | | | | | | | | |
| 80 | Are sterilizing filtration systems utilized? | | | | | | | | | | | | | | | | |
| 80.1 | Is the integrity of the filters confirmed? | | | | | | | | | | | | | | | | |
| 80.2 | Are records kept? | | | | | | | | | | | | | | | | |
| 81 | For each product, is the maximum time between the starting of the preparation of a solution and its sterilization or filtration through absolute filters established? | | | | | | | | | | | | | | | | |
| 82 | In the case of having a divided batch, is product sterilization carried out by perfectly identified loads? | | | | | | | | | | | | | | | | |

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| 83 | Are records of sterilization and depyrogenation of the container for the filtrate product reception available? | | | | | | | | | | | | | | | | |
| 83.1 | Are records kept? | | | | | | | | | | | | | | | | |
| 84 | Is the operation of washing of empty bottles and ampoules done at least in a grade D area? | | | | | | | | | | | | | | | | |
| 85 | Do the cleaning machines of empty bottles and ampoules use water for injection, for final rinse? | | | | | | | | | | | | | | | | |
| 86 | Are filters utilized for the compressed air used in these washing machines? | | | | | | | | | | | | | | | | |
| 87 | Are filters utilized for the water? | | | | | | | | | | | | | | | | |
| 87.1 | Are records of replacing filters kept? | | | | | | | | | | | | | | | | |
| 88 | Are depyrogenation ovens used? | | | | | | | | | | | | | | | | |
| 89 | Are depyrogenation tunnels used? | | | | | | | | | | | | | | | | |
| 90 | Are depyrogenation cycles validated? | | | | | | | | | | | | | | | | |
| 90.1 | Are records kept? | | | | | | | | | | | | | | | | |
| 90.2 | Are depyrogenation cycles recorded? | | | | | | | | | | | | | | | | |
| 91 | Is the material flow unidirectional? | | | | | | | | | | | | | | | | |
| 92 | What type of sterilization does the containers for non-injection sterile products receive (bottles, flasks, covers, inserts)? | | | | | | | | | | | | | | | | |
| 92.1 | Are records available? | | | | | | | | | | | | | | | | |
| 92.2 | Are they transferred safely to packaging areas? | | | | | | | | | | | | | | | | |
| 93 | Is the transfer of intermediate/bulks between one step and another carried out in a manner which prevents their contamination? | | | | | | | | | | | | | | | | |

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| 94 | Is the maximum time elapsed between the filtration and the product filling determined for products without terminal sterilization? | | | | | | | | | | | | | | | |
| 95 | Do personnel enter to the packaging area through direct access from the change room? | | | | | | | | | | | | | | | |
| 96 | Do personnel wear sterile clothing? | | | | | | | | | | | | | | | |
| 97 | Is the mix-up of different products or different lots of same product avoided by having physical separation among the packaging lines? | | | | | | | | | | | | | | | |
| 98 | Is there a confirmation that the suspensions and/or emulsions are maintained uniform throughout the filling process? | | | | | | | | | | | | | | | |
| 99 | Is the operation carried out on line? | | | | | | | | | | | | | | | |
| 100 | Are aseptic filling test conducted with culture medium, in the normal working conditions, at least on a semiannual frequency? | | | | | | | | | | | | | | | |
| 100.1 | Are these tests carried out in such a way to most accurately reproduce the normal working conditions in the area? | | | | | | | | | | | | | | | |
| 100.2 | Are they carried out in a minimum of 3000 units? | | | | | | | | | | | | | | | |
| 100.3 | Is the test rejected if a figure greater than 0.1% of contaminated units is obtained? | | | | | | | | | | | | | | | |
| 100.4 | Are there records of these tests? | | | | | | | | | | | | | | | |
| 100.5 | Are the causes of any detected contamination investigated? | | | | | | | | | | | | | | | |
| 100.6 | Are there records of this investigation? | | | | | | | | | | | | | | | |

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| 100.7 | Are there records of the corrective actions taken in those cases? | | | | | | | | | | | | | | | | |
| 101 | Do empty primary containers have a batch number and an expiry date? | | | | | | | | | | | | | | | | |
| 102 | If so, are the remaining empty primary containers destroyed? | | | | | | | | | | | | | | | | |
| 103 | Are records of this kept? | | | | | | | | | | | | | | | | |
| 104 | If the empty primary containers do not have a batch number and an expiry date, are they coded manually or automatically? | | | | | | | | | | | | | | | | |
| 105 | If manually coded, are the right batch numbers and expiry dates confirmed at regular intervals? | | | | | | | | | | | | | | | | |
| 106 | Do all finished products have a printed batch number and an expiry date on their primary container? | | | | | | | | | | | | | | | | |
| 107 | If the printing of labels and/or packages is conducted outside the packaging line, is the operation carried out in an environment/ sector which is exclusive, taking one input at a time? | | | | | | | | | | | | | | | | |
| 108 | Are they coded by an automatic system? | | | | | | | | | | | | | | | | |
| 109 | Are the right batch number and expiry date confirmed by authorized personnel? | | | | | | | | | | | | | | | | |
| 110 | Are the labels dispensed in rolls? | | | | | | | | | | | | | | | | |
| 111 | Is the unused printed and coded material destroyed? | | | | | | | | | | | | | | | | |
| 112 | Are records kept? | | | | | | | | | | | | | | | | |
| 113 | Is the remaining unused non-coded printed material returned to the warehouse? | | | | | | | | | | | | | | | | |
| 113.1 | Is there a SOP available for the process of these returns? | | | | | | | | | | | | | | | | |
| 114 | Are records kept? | | | | | | | | | | | | | | | | |

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| 115 | Is the printed or embossed information legible? | | | | | | | | | | | | | | | | |
| 116 | Is the printed or embossed information resistant to fading or erasing? | | | | | | | | | | | | | | | | |
| 117 | If automatic machines are used to control dimensions, weights, labels, prospects, bar code, etc., is their proper performance verified? | | | | | | | | | | | | | | | | |
| 118 | In the case of the automatic systems, are discarded units which are returned to the line, previously inspected and approved by authorized personnel? | | | | | | | | | | | | | | | | |
| 119 | Is the final packaged material identified with the appropriate label? | | | | | | | | | | | | | | | | |
| 120 | Do the autoclave and depyrogenation oven, for taking materials to the aseptic area, have double doors? | | | | | | | | | | | | | | | | |
| 121 | Are mix-ups avoided between the sterile and non-sterile material? | | | | | | | | | | | | | | | | |
| 122 | Are records of time, temperature, and/or pressure of the autoclave and depyrogenation oven maintained? | | | | | | | | | | | | | | | | |
| 123 | Is a validation program for moist heat sterilization cycles maintained? | | | | | | | | | | | | | | | | |
| 123.1 | Are records kept? | | | | | | | | | | | | | | | | |
| 124 | Is clean steam used in the sterilization cycles? | | | | | | | | | | | | | | | | |
| 125 | Are indicators used at each cycle of sterilization? | | | | | | | | | | | | | | | | |
| 125.1 | Are records kept? | | | | | | | | | | | | | | | | |
| 126 | Is sterilized material correctly identified and safely transferred to the inspection area, to avoid mix-ups? | | | | | | | | | | | | | | | | |

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| 127 | Is inspection done automatically? | | | | | | | | | | | | | | | | |
| 127.1 | Is the equipment challenged? | | | | | | | | | | | | | | | | |
| 127.2 | Are records kept? | | | | | | | | | | | | | | | | |
| 128 | Is the inspection done semiautomatically? | | | | | | | | | | | | | | | | |
| 128.1 | Is the inspection done visually? | | | | | | | | | | | | | | | | |
| 128.2 | Is there a changeover of staff carried out? | | | | | | | | | | | | | | | | |
| 128.3 | Are records kept? | | | | | | | | | | | | | | | | |
| 128.4 | Are frequent ophthalmological examinations conducted on the workers in charge of the inspection, at least annually? | | | | | | | | | | | | | | | | |
| 128.5 | Are conditions of lighting and contrast for the inspection controlled? | | | | | | | | | | | | | | | | |
| 129 | Are the containers that contain the already inspected material labeled as such? | | | | | | | | | | | | | | | | |
| 130 | Is the discarded material destroyed? | | | | | | | | | | | | | | | | |
| 130.1 | Are records kept? | | | | | | | | | | | | | | | | |
| 131 | Are process controls undertaken at the different steps of production? | | | | | | | | | | | | | | | | |
| 131.1 | Are records kept? | | | | | | | | | | | | | | | | |

| CHAPTER 11: QUA LITY CONTROL | | | | |
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| GENERAL | | S | P | I |
| 1 | Does the Quality Control laboratory carry out its own: | | | |
| 1.1 | Physicochemical controls? | | | |
| 1.2 | Microbiological controls? | | | |
| 2 | Is the quality control department responsible for approving or rejecting the raw materials, packaging materials, intermediate products, and finished products? | | | |
| 3 | Is there personnel with assigned responsibility to inspect the manufacture processes? | | | |
| 4 | Are there tests conducted on contract basis, because of their dangerousness and/or grade of complexity? | | | |
| 4.1 | Are these tests performed by contracted laboratories or by agreements with official laboratories? | | | |
| 4.2 | What are the tests carried out in these laboratories? | | | |
| 4.3 | Are there technical contracts/agreements? | | | |
| 5 | Are there specifications for: | | | |
| 5.1 | Raw materials? | | | |
| 5.2 | Packaging materials? | | | |
| 5.3 | Intermediate products? | | | |
| 5.4 | Finished products? | | | |
| 6 | Are there SOPs that indicate the frequency of re-analysis and validity of the carried out tests? | | | |
| 6.1 | Are these procedures fulfilled? | | | |
| 7 | Does quality control check if each manufactured lot meets established specifications? | | | |
| 7.1 | Are there records? | | | |
| 8 | Is there an OOS procedure? | | | |
| 8.1 | Is it followed? | | | |
| 8.2 | Are the causes of OOS results investigated? | | | |
| 8.3 | Are there records of the actions taken in those cases? | | | |
| 9 | Is there a procedure for the handling and disposal of chemical and microbial waste? | | | |
| 9.1 | Dose the procedure indicate that accumulation of discarded materials should not be permitted? | | | |
| 9.2 | Are the discarded materials eliminated safely and sanitarily at regular and frequent intervals? | | | |
| 10 | Is there a SOP for approval and rejection of the materials and products? | | | |
| | STANDARD OPERATING PROCEDURES | S | P | I |
| 11 | Are the relevant QC SOPs available? | | | |
| 11.1 | Are they written in the required formats? | | | |
| 11.2 | Is a complete and current index for those SOPs available? | | | |
| 11.3 | Is the set of SOPs currently organized according to the index? | | | |
| 11.4 | Are all the SOPs approved and authorized as required? | | | |
| | PERSONNEL | S | P | I |
| 12 | Are there adequate number of employees? | | | |

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| 12.1 | Are they qualified, including training? (check training records) | | | |
| 12.2 | Have the employees undergone training in the following areas?<br>- SOPs.<br>- Good manufacturing practices.<br>- Good laboratory practices.<br>- Analytical techniques. | | | |
| 13 | Is there an approved QC unit organogram? | | | |
| 14 | Are detailed, written job descriptions available for employees? | | | |
| 15 | Is the group leader (chief analyst) qualified and able to lead the group? | | | |
| | PREMISES: | S | P | I |
| 16 | Is the facility adequate to suit the operations done inside it? | | | |
| 17 | Is the location for the laboratories (other than inspection laboratories) separate from production operations? | | | |
| 18 | Is the location for analytical laboratory separate from microbiological laboratory? | | | |
| 19 | Are there safety installations such as shower, eye washer, fire extinguisher, and protection elements? | | | |
| 19.1 | Is there an operation verification program for the safety equipment? | | | |
| 19.2 | Are records kept? | | | |
| 20 | Is there a special place(s) for documentation and recording purposes? | | | |
| 21 | Is there a designated place for storage of standards and another one for expired materials? | | | |
| 22 | Is there a special and suitable place for instruments? | | | |
| 23 | Is the facility sufficiently and properly lighted? | | | |
| 24 | Is the place properly air conditioned? With suitable air changes? | | | |
| 25 | Is there an emergency exit? | | | |
| 26 | Are there suitable chemical and fumehoods? | | | |
| 27 | Are there sufficient washing systems or washing machines? | | | |
| 27.1 | Are they non-reactive to chemical reagents? | | | |
| 28 | Is the laboratory kept in order and neat? | | | |
| 28.1 | Is there an evidence of good house keeping? | | | |
| | INSTRUMENTATION AND CALIBRATION | S | P | I |
| 29 | Are the equipments and tools adequate and appropriate for each type of product or material?<br>- General service equipments (e.g. hot plates, stirrers, non-volumetric glass ware, ..,etc)<br>- Volumetric equipments.<br>- Measuring equipments.<br>- Physical standards (weights, reference thermometers).<br>- Instrumental analysis equipments.<br>- Computers and data processors. | | | |
| 30 | Is there a list of the available equipments? (Attach the list). | | | |
| 31 | Is there an approved preventive maintenance program for all the equipments used in the laboratory? | | | |
| 31.1 | Is the preventive maintenance conducted according to an approved SOP for each equipment? | | | |
| 31.2 | Are there records showing that the preventive maintenance program is followed? | | | |
| 31.3 | Is the program based on manufactures recommendations? | | | |
| 31.4 | If not, is there documented rational for alteration of the schedule? | | | |
| 31.5 | Is the person who performs the preventive maintenance qualified to do so? | | | |

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| 32 | Are there written procedures for operating the instruments? | | | |
| 33 | Are there written procedures for calibrating the instruments? | | | |
| 34 | Is there a program for equipment calibration? | | | |
| 34.1 | In the program is it indicated, whether it is done externally or internally? | | | |
| 34.2 | Are there records of calibration of each equipment that show program compliance? | | | |
| 34.3 | Are the results within the accepted limits? | | | |
| 35 | Do the calibration certificates or reports indicate the traceability to standards? | | | |
| 36 | Do the calibration certificates or reports indicate the uncertainty of the corresponding measure? | | | |
| 37 | Is there a valid calibration sticker on each instrument? | | | |
| 38 | Dose the laboratory have certified standards? | | | |
| 39 | Are the corresponding certificates available? | | | |
| 40 | Where standards are used to calibrate the instrument, is there a written procedure for that purpose? | | | |
| 41 | Does the laboratory have procedures and protocols for the performance of (IQ, OQ, PQ) of equipment (as appropriate) | | | |
| 41.1 | Are the appropriate qualifications (IQ, OQ, PQ) done for all the equipments requiring that? | | | |
| | SAMPLING, SAMPLE RECEIPT, STORAGE, AND DOCUMENTATIONS: | S | P | I |
| 42 | Is there is a written SOP describing sample receipt and recording? | | | |
| 43 | Is a specific person responsible for the receipt of samples? | | | |
| 44 | Are samples stored in suitable places before and after testing? | | | |
| 45 | Are samples retained after testing is complete? | | | |
| 46 | Is there a time limit on how long a sample may remain in the laboratory prior to testing? | | | |
| 47 | Are samples retained from active raw materials and finished products? | | | |
| 47.1 | Are they kept in enough quantities to carry all the rests? | | | |
| 47.2 | Are they kept according to an SOP? | | | |
| 47.3 | Are the retained samples of finished products kept until a year after the expiry date of the product? | | | |
| 47.4 | Are the retained samples of raw materials kept until a year after the expiry date of the last lot of product prepared from them? | | | |
| 48 | Are there written and approved sampling SOPs for: | | | |
| 48.1 | Raw materials? | | | |
| 48.2 | Packaging materials? | | | |
| 48.3 | Intermediate products? | | | |
| 48.4 | Finished products? | | | |
| 49 | Are the sampling procedures representatives of the totality of the lot or batch? | | | |
| 49.1 | Are these procedures fulfilled? | | | |
| 50 | Are the sampled containers correctly identified | | | |
| 51 | Does the number of sampled containers agree with the sampling plan | | | |
| 52 | Are all incoming packaging materials sampled in accordance with established procedure | | | |
| 53 | Are the elements and tools necessary for sampling available in suitable and sufficient quantities | | | |
| 53.1 | Are they stored in good conditions | | | |
| 53.2 | Is there a written SOP for cleaning and storing the sampling elements | | | |
| | TEST PROCEDURES: | S | P | I |
| 54 | Are approved test procedures available for all tests performed in the laboratory? | | | |

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| 55 | Are the pharmacopoeia procedures updated when a supplemental monograph is issued? | | | |
| 56 | Examine the work currently being performed: | | | |
| 56.1 | Is the test procedure at hand? | | | |
| 56.2 | Is it up-to-date? | | | |
| 56.3 | Is it being accurately followed? | | | |
| 56.4 | Has the method been validated? | | | |
| 56.5 | Is the analysis record in the analyst's notebook including the physical appearance of the sample? | | | |
| 56.6 | Has the analyst recorded the relevant details for the product being tested, including the attachment of printouts or records of weighing? | | | |
| 56.7 | Is there a reference to the test method used in the analysis's notebook? | | | |
| 56.8 | Are records available for the preparation of media used for performing the test? | | | |
| 56.9 | Is the media labeled with expiration date? | | | |
| 58 | Are the testing results investigated before the decision of acceptance or rejection? | | | |
| 59 | How the limits are set inside which the product must satisfy the specification? | | | |
| 60 | Is there a system to investigate laboratory test failures? | | | |
| | REAGENTS, SOLUTIONS & REFERENCE STANDARDS: | S | P | I |
| 61 | Are the reagents/solutions dated when received or prepared? | | | |
| 62 | Are they stored appropriately? | | | |
| 63 | Are there written procedures for the preparation of standards and solutions? | | | |
| 64 | Are the solutions and standard prepared by qualified person(s)? | | | |
| 65 | Are the reagents and standards labeled with following information:<br>- Concentration.<br>- Expire date.<br>- Storage conditions.<br>- The name of the reagent.<br>- The name or signature of the person who prepared them and the re-standardization date (where applicable). | | | |
| 66 | Are there standards and reference materials? | | | |
| 66.1 | Is a records of the primary standards kept? | | | |
| 66.2 | Is a records of the secondary standards kept? | | | |
| 66.3 | Is a records of the reference materials kept? | | | |
| 67 | Does the company have primary standards, coded by pharmacopoeias or internationally recognized agencies, for each active ingredient? | | | |
| 67.1 | Are the primary standards from current lot? | | | |
| 68 | Do all the secondary standards and reference materials have current analytical certificate? | | | |
| 69 | Are there SOPs for the preparation, use and conservation of standards and reference materials? | | | |
| 69.1 | Are those procedures fulfilled? | | | |
| 69.2 | Are the records shown? | | | |
| 70 | Are tests of characterization purity carried out to the samples to be utilized as reference substances of non-coded active ingredients? | | | |
| 71 | Does the company have impurities and related substances standards, officials or non-officials, especially for those considered toxic? | | | |
| | EVALUATION/SUPERVISION OF RESULTS: | S | P | I |
| 72 | Is there an SOP for review of test data and calculations? | | | |

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| 73 | Are raw data reviewed prior to release from the laboratory by a person other than the analyst who performed the test? | | | |
| 74 | Do reviewer sign the notebook to indicate that it has been reviewed? | | | |
| | RECORDS AND DOCUMENTATION SYSTEMS: | S | P | I |
| 75 | Are the following documents available? | | | |
| 75.1 | Specifications for raw materials, packaging materials, finished products, bulk products. | | | |
| 75.2 | Sampling procedures? | | | |
| 75.3 | Test methods and their special records? | | | |
| 75.4 | Reports and certificates analysis? | | | |
| 75.5 | Environmental control methods and results? | | | |
| 75.6 | Calibration and maintenance procedures for laboratory instruments and equipment? | | | |
| 75.7 | Validation records? | | | |
| 76 | Do the analysts have logbooks (analyst's notebook)? | | | |
| 76.1 | Is it a bounded book with numbered pages? | | | |
| 76.2 | Is it neatly filled in and legible? | | | |
| 76.3 | Are any cross-outs initiated and dated? | | | |
| 76.4 | Is there an SOP for notebook maintenance? | | | |
| 76.5 | Is there a record for the instrument used for testing together with any data? | | | |
| 76.6 | Are all calculations recorded? | | | |
| 76.7 | Are all documents and printouts labeled with product name, batch number and date of the test? | | | |
| 76.8 | Are numbers rounded in accordance with an approved SOP? | | | |
| 76.9 | Do the dates on graphs/charts conform to the dates of analysis? | | | |
| 76.10 | Is there a statement in the notebook as to whether or not the sample passes the test? | | | |
| 76.11 | Is the analyst's signature recorded in the notebook? | | | |
| 77 | Do the analysis record(s) contain complete information? | | | |
| 77.1 | Raw materials:<br>- Date receipt raw materials.<br>- Date analysis raw materials.<br>- Date approval raw materials.<br>- Methods of analysis/identification raw material batch number.<br>- Analysis results.<br>- Signature of analyst and group leader.<br>- Sign of approval (release or reject). | | | |
| 77.2 | In-process analysis:<br>- Date receipt sample.<br>- Date analysis sample.<br>- Date approval sample.<br>- Production batch number.<br>- Methods of analysis.<br>- Analysis results.<br>- Signature of analyst and group leader.<br>- Sign of approval (release or reject). | | | |

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| 77.3 | Finished products records:<br>- Date finished product production.<br>- Date analysis finished product.<br>- Date approval finished product.<br>- Production batch number.<br>- Methods of analysis.<br>- Analysis results.<br>- Name of sample.<br>- Sign of approval.<br>- Signature of analyst(s) and group leader. | | | |
| | METHOD VALIDATION: | S | P | I |
| 78 | Have all in-house methods been validated? | | | |
| 79 | Is there written SOP relating to the validation of the analytical methods? | | | |
| 80 | Does methods validation provide data to demonstrate? | | | |
| 80.1 | Linearity? | | | |
| 80.2 | Method precision? | | | |
| 80.3 | Method specificity? | | | |
| 80.4 | Method sensitivity? | | | |
| 80.5 | Method ruggedness? | | | |
| | MICROBIOLOGICAL ANALYSIS: | S | P | I |
| 81 | Are tests of bacterial endotoxins carried out in raw materials and goods declared as pyrogen-free by the supplier, to be used in the injection manufacture? | | | |
| 82 | Are tests of pyrogens or bacterial endotoxins carried out in the finished products for injection, when it corresponds? | | | |
| 83 | Is an official method utilized for bacterial endotoxin control? | | | |
| 84 | Otherwise, is the method validated? | | | |
| 85 | Are pyrogen tests carried out in animals? | | | |
| 85.1 | If "YES": | | | |
| 85.2 | Does the company have its animal house? | | | |
| 85.3 | Does the company use a contracted animal house? | | | |
| 85.4 | In any of both cases, does animal house fulfills with the current regulations on animal operation and management? | | | |
| 85.5 | If the company have animal house, is this separated from the other installations? | | | |
| 86 | Are microbiological controls carried out? | | | |
| 87 | Does the company have separated areas for sterility test and other microbiological controls? | | | |
| 88 | Are there proper areas and laminar flow for carry out the sterility tests? | | | |
| 89 | Are the filters of the laminar flow periodically checked? | | | |
| 90 | Does the company have the materials, culture media and reagents necessary for carrying out the routine microbiological controls? | | | |
| 90.1 | Are the materials, culture media and reagents within the validity period? | | | |
| 91 | Are the dehydrated culture media stored in the conditions of humidity and temperature indicated by the manufacturer? | | | |
| 92 | Are the parameters of every sterilization cycle of culture media recorded? | | | |
| 93 | Is the growth promotion test carried out whenever new lots of culture media are utilized? | | | |
| 94 | Is a standard operating procedure for the preparation of culture media? | | | |

| | | | | |
|---|---|---|---|---|
| 95 | Is there a designated area to perform plate counts, isolations and identifications under a negative air pressure with a means of decontamination? | | | |
| 96 | Does the sterility test area include the following: | | | |
| 96.1 | Pressurization to assure that the tests are carried out under positive pressure? *class A). | | | |
| 96.2 | Smooth cleanable surfaces? | | | |
| 96.3 | Incubators which are controlled to minimize contamination? | | | |
| 96.4 | Separate, controlled environment grown-up area? | | | |
| 97 | Is the clean room maintained in a good state of repair? | | | |
| 98 | Is there an SOP for the cleaning and disinfection of the clean room? | | | |
| 99 | Are there SOPs for the cleaning and disinfection of equipments and tools used for sterility testing? | | | |
| 100 | Are there records for the preparation f disinfectants? | | | |
| 101 | Are disinfectants labeled with expiration dates? | | | |
| 102 | Are the disinfectants used validated for their purposes? | | | |
| 103 | Is the place air conditioned? | | | |
| 104 | Is the laboratory maintained in good state of repair? | | | |
| 105 | Is there evidence of good house keeping? | | | |
| 106 | Are the temperature records attached to all incubators and refrigerators? | | | |
| 106.1 | Are there routine checking and signing of temperature charts? | | | |
| 107 | Is there an SOP defining cleaning and sanitization procedure for the incubators and refrigerators? | | | |
| 108 | Are the autoclave and sterilization cycles validated? | | | |
| 109 | Examine the contents of refrigerators and incubators: | | | |
| 109.1 | Are they clean? | | | |
| 109.2 | Are all test samples recorded in the laboratory logbook? | | | |
| 109.3 | Are all items clearly labeled? | | | |
| 110 | Are there microbial reference strains? | | | |
| 110.1 | If there are reference strains, are they certified by an internationally recognized agency? | | | |
| 110.2 | Is there a record of identification and use of strains? | | | |
| 110.3 | Is the transfer frequency established? | | | |
| 110.4 | Are the transfers recorded? | | | |
| 110.5 | Are periodic controls carried out in order to confirm the viability? | | | |
| 111 | Are sterility tests carried out? | | | |
| 111.1 | For sterility tests, are coded methods utilized? | | | |
| 111.2 | Otherwise, is the method utilized for sterility tests validated? | | | |
| 112 | Is there a record of % of false positive? | | | |
| 112.1 | Is the % of false positive not more than 0.5 % from total? | | | |
| 113 | If the lot fails the sterility test, is a complete investigation of the causes made? | | | |
| 113.1 | Is a second test carried out when it demonstrated that the original test was not valid? | | | |
| 114 | Are antibiotic potency assays carried out? | | | |
| 114.1 | Is the statistical proof of the determination of potency and validity of the test carried out? | | | |
| 115 | Does the company have areas or sectors assigned for the sample preparation? | | | |
| 115.1 | Does the company have areas or sectors assigned for the washing and conditioning of materials? | | | |
| 115.2 | Does the company have areas or sectors assigned for the preparation of culture media? | | | |
| 116 | Does microbiology sector have equipment for bacterial decontamination? | | | |
| 117 | Is there a procedure for the handling and disposal of chemical and microbial waste? | | | |

| | | | | |
|---|---|---|---|---|
| 117.1 | Does the procedure indicate that should not be permitted the accumulation of discarded materials? | | | |
| 117.2 | Are the discarded materials eliminated safely and sanitarily at regular and frequent intervals? | | | |
| 118 | Is there an SOP for monitoring differential pressure? | | | |
| 119 | Are there records of air pressure checked and signed? | | | |
| 120 | Is there an SOP for environmental monitoring in the clean room | | | |
| 121 | Do results conform with the limits stated in the SOP? | | | |
| 122 | Are there records of checking LAF velocities? | | | |
| 123 | Are there records of checking air changes? | | | |
| | STABILITY (GENERAL): | S | P | I |
| 124 | Is there a written stability procedure? | | | |
| 125 | Is there a written stability study protocol: | | | |
| 125.1 | For starting materials? | | | |
| 125.2 | For intermediate products? | | | |
| 125.3 | For finished products? | | | |
| 126 | Does the stability study protocol include: | | | |
| 126.1 | A complete description of the product studied? | | | |
| 126.2 | The controlled parameters? | | | |
| 126.3 | The validated analytical methods? | | | |
| 126.4 | A sufficient number of batches (not less than three). | | | |
| 126.5 | Timetable of the analytical tests to carry out for every product? | | | |
| 126.6 | Special storage conditions? | | | |
| 126.7 | Sufficient quantities of samples in order to fulfill the program? | | | |
| 126.8 | A summary of the obtained data? | | | |
| 126.9 | Evaluations and study conclusions? | | | |
| 127 | Is there a stability study testing program? | | | |
| 128 | Is the program fulfilled? | | | |
| 129 | Are sufficient samples retained from every manufactured batch for shelf-life follow-up? | | | |
| 130 | Is there a program for testing the retained batches? | | | |
| 130.1 | Is the testing frequency according to the requirements? | | | |
| | R & D STABILITY PROGRAM: | S | P | I |
| 131 | Is there a stability program protocol for R & D developed batches? | | | |
| 132 | Does it include the following: | | | |
| 132.1 | Number of batches to be placed on stability for new products. | | | |
| 132.2 | Requirements that all products are stored in the final container to be used for marketing? | | | |
| 132.3 | Is there documented evidence that the program is followed? | | | |
| 133 | Are stability results reviewed by a responsible person? | | | |
| 134 | Are relevant persons informed in writing a bout the out-of-limits stability results, including quality assurance? | | | |
| 134.1 | Does the department conduct investigations in case of out-of-limits results? | | | |
| 135 | Examine the stability storage area(s): | | | |
| 135.1 | Are all instrumentation labeled with a valid calibration stickers? | | | |
| 235.2 | Are there adequate chambers with variety of conditions for storing samples under accelerated stability conditions? | | | |
| 135.3 | Are samples stored in the chambers in order? | | | |
| 135.4 | Are there suitable monitoring and recording systems for the stability chambers? | | | |

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|---|---|---|---|---|
| 135.5 | Are there recording logs describing the stability samples inside storage area(s), including stability chambers? | | | |
| 135.6 | Is a written reconciliation of samples maintained, including the recording of the removal of samples at each testing station? | | | |
| 135.7 | Are corrective actions taken in the event of out-of-limits conditions? | | | |
| 136 | Is there a written SOP describing the destruction of samples at the end of the stability study? | | | |
| 136.1 | Is there a written record of the destruction? | | | |

| CHAPTER 12: QUALITY ASSURANCE | | | | |
|---|---|---|---|---|
| SOPs | | S | P | I |
| 1 | Is a complete index and a complete set of applicable SOPs available in the department? | | | |
| 2 | Are the index and the SOPs current? | | | |
| 3 | Is the set of SOPs correctly organized according to the index? | | | |
| 4 | Are the SOPs reviewed on a regular and defined schedule? | | | |
| 5 | Is there a system for distribution of SOPs and for revocation of outdated SOPs? | | | |
| PERSONNEL | | S | P | I |
| 6 | Are there adequate numbers of employees? | | | |
| 7 | Have the employees undergone training in the following areas? | | | |
| 7.1 | GMPs | | | |
| 7.2 | SOPs. | | | |
| 7.3 | Quality assurance techniques. | | | |
| 8 | Are the employees knowledgeable about their job functions? | | | |
| 9 | Have the employees undergone qualifications according to the relevant SOPs? | | | |
| 10 | Are detailed, written job descriptions available for all employees? | | | |
| 11 | Is an up-to-date organizational chart(s) for the QA department and other departments available? | | | |
| BATCH RECORD REVIEW | | S | P | I |
| 12 | Is there an SOP for batch record review prior to release? | | | |
| 13 | Is there a comprehensive checklist for batch record review prior to release? | | | |
| 14 | Is there a tracking procedure in place to ensure that a batch record with a deviation report attached to it cannot be released prior to the completion of any required investigation? | | | |
| 15 | Examine three recently released batch records:<br>Product: _____ Batch No.: _____<br>Product: _____ Batch No.: _____<br>Product: _____ Batch No.: _____ | | | |
| 15.1 | Are the records complete with respect to the following? | | | |
| 15.2 | The master formula is signed as true copy. | | | |
| 15.3 | Any changes to the master formula are QA authorized prior to manufacturing. | | | |
| 15.4 | All relevant signatures are present. | | | |
| 15.5 | All relevant data are present. | | | |
| 15.6 | All relevant data are accurate. | | | |
| 15.7 | Yield calculation at each stage of production conforms to the SOP. | | | |
| 15.8 | All calculations are verified by a second individual. | | | |
| 15.9 | Any deviations are justified, fully explained, and authorized. | | | |

| DEVIATION REPORT: | | S | P | I |
|---|---|---|---|---|
| 16 | Is there a written deviation (non-conforming) SOP? | | | |
| 17 | Select three manufacturing deviation reports (MDRs) prepared within the last six months.<br><br>Product: _____ Batch No.: _____<br><br>Product: _____ Batch No.: _____<br><br>Product: _____ Batch No.: _____ | | | |
| 17.1 | Were the MDRs completed prior to release of the batch? | | | |
| 17.2 | Does the relevant SOP require a written investigation and follow-up on implementation of recommendations? | | | |
| 17.3 | Are the MDRs filled out in accordance with the SOP? | | | |
| 17.4 | If necessary, is there a fully documented investigation? | | | |
| 17.5 | Have recommendations been made to prevent the deviation from recurring? | | | |
| 17.6 | Have recommendations for corrective action been implemented? | | | |
| 17.7 | Does the SOP required periodic review of MDRs? | | | |
| 18 | Examine the daily deviation reports from the three months preceding the audit. Is there follow-up to ensure that each department sends in a report every day? | | | |
| 18.1 | Select three reports at random. Are they filled out in accordance with the relevant SOP? | | | |
| 19 | Are there deviations that re-occur more than once? | | | |
| CHANGE CONTROL RECORDS: | | S | P | I |
| 20 | Is there a written SOP for change control? | | | |
| 21 | Are all changes that may impact product quality authorized by Quality Assurance prior to implementation? | | | |
| 22 | Examine some recent change control forms: | | | |
| 22.1 | Have the forms been completed and closed? | | | |
| 22.2 | Were any required tests performed and the results evaluated prior to closing the forms? | | | |
| 23 | Has all relevant documentation been updated? | | | |
| ANNUAL REVIEW-PRODUCT QUALITY STANDARDS: | | S | P | I |
| 24 | Is there a written SOP for annual product review? | | | |
| 25 | Examine some product annual reviews completed at least three months prior to the audit.<br>Product: _____ Batch No.: _____<br><br>Product: _____ Batch No.: _____<br><br>Product: _____ Batch No.: _____ | | | |
| 25.1 | Dose the review comment on any out-of-limit or unusual results? | | | |
| 52.2 | Dose the review include special release batches? | | | |

| | | | | |
|---|---|---|---|---|
| 26 | Dose the relevant SOP require that management be informed of problems identified during the review? | | | |
| 27 | Is there a record of examination of reserve samples for the products reviewed? Were the samples found to be satisfactory? | | | |
| 28 | Have recommended corrective actions been implemented? | | | |
| QUALITY AUDITS/ SELF-INSPECTIONS | | S | P | I |
| 29 | Is there a system for regular self-inspections? (Sops, check lists). | | | |
| 30 | Are quality self-inspections and/or audits carried out? | | | |
| 31 | Is Quality assurance responsible for the coordination of quality self-inspections and/or audits? | | | |
| 32 | Are the self-inspections/audits carried out with a pre-established plan? | | | |
| 33 | Are the necessary corrective measures recommended? | | | |
| 34 | Are quality self-inspections and/or audits carried out also in other situations, for example in the event that a product is removed of the market or rejected repeatedly? | | | |
| 35 | Is there a team in charge of quality self-inspections/audits? | | | |
| 36 | Do the written instructions of quality self-inspection/ audits include, at least, the following points: | | | |
| 36.1 | Personnel? | | | |
| 36.2 | Premises and services? | | | |
| 36.3 | Maintenance of buildings and equipment? | | | |
| 36.4 | Storage of materials and finished products? | | | |
| 36.5 | Equipment? | | | |
| 36.6 | Production and controls during the process? | | | |
| 36.7 | Quality control? | | | |
| 36.8 | Documentation? | | | |
| 36.9 | Sanitation and hygiene? | | | |
| 36.10 | Validation and confirmation programs? | | | |
| 36.11 | Calibration of instruments and measurement systems? | | | |
| 36.12 | Procedures of withdrawal of products from the market? | | | |
| 36.13 | Management of claims? | | | |
| 36.14 | Control of labels? | | | |
| 36.15 | Results of previous self-inspections and adopted corrective measures? | | | |
| 36.16 | Follow up any recommendations received from authorities? | | | |
| 37 | The report issued after the self-inspection contains: | | | |
| 37.1 | Results of the self-inspection? | | | |
| 37.2 | Evaluation and conclusions? | | | |
| 37.3 | Corrective measures recommended? | | | |
| 37.4 | Is the monitoring of the corrective measures carried out and registered? | | | |
| AUDIT TO SUPPLIERS | | S | P | I |
| 38 | Is there a system for inspection of suppliers? (SOPs). | | | |
| 39 | Are the suppliers of goods, production and quality control third parties evaluated (if necessary audited) and approved by quality assurance? | | | |
| 40 | Is there a record of approved suppliers available for the areas that require it? | | | |
| 41 | Is there a program for evaluation and audits to suppliers? | | | |

| | | | | |
|---|---|---|---|---|
| 41.1 | Is it fulfilled? | | | |
| 41.2 | Are records of these evaluations and audits kept? | | | |
| 41.3 | Is an assessment of the outcomes made? | | | |
| COMPLAINTS | | S | P | I |
| 42 | Is there an SOP for dealing with complaints? | | | |
| 43 | Is Quality assurance responsible for coordinating the reception and the monitoring of the received claims? | | | |
| 44 | Is there a responsible person assigned? | | | |
| 45 | Does the SOP contain instructions for the reception and investigation of the claims? | | | |
| 45.1 | Is a record of the claims kept? | | | |
| 46 | If necessary, is analytical control made? | | | |
| 47 | Do the decisions made concerning the complaints remain documented? | | | |
| 48 | Are corrective measures adopted? | | | |
| 49 | Examine three recent complains files:<br>Product: _____ Batch No.: _____<br>Product: _____ Batch No.: _____<br>Product: _____ Batch No.: _____ | | | |
| 49.1 | Do the files contain all the relevant data? | | | |
| 49.2 | Have the files been signed by the relevant personnel? | | | |
| 49.3 | Could any of the above complaints affect other batches of the product and, if so, has an investigation been initiated and appropriate action taken? | | | |
| 50 | Examine the list of complaints for the year preceding the audit. Are there products that have several complaints and, if so, has appropriate corrective action been implemented? | | | |
| GOOD DESTRUCTION RECORDS: | | S | P | I |
| 51 | Is there an SOP for destruction of: | | | |
| 51.1 | Product components and packaging materials? | | | |
| 51.2 | Raw materials? | | | |
| 51.3 | In-process materials? | | | |
| 51.4 | Finished product? | | | |
| 52 | Examine the goods destruction records file: | | | |
| 52.1 | Is it identical to that in the warehouse? | | | |
| 52.2 | Are all goods destruction forms QA approved prior to destruction? | | | |
| 52.3 | Is there written evidence that the destruction order has been carried out? | | | |
| 53 | Is the destruction done appropriately as mentioned in the SOP? | | | |
| 54 | Is it done under the supervision of the authority? | | | |
| SPECIAL RELEASE BATCHES: | | S | P | I |
| 55 | Is there an SOP for the special release of batches? | | | |

| | | | | |
|---|---|---|---|---|
| 56 | Examine the list of special releases for the current year:<br>Product: _____ Batch No.: _____<br>Product: _____ Batch No.: _____<br>Product: _____ Batch No.: _____ | | | |
| 56.1 | List the reason(s) for the special release:<br>1.<br>2.<br>3. | | | |
| 56.2 | Is there a written investigation, including conclusions and, if Appropriate, follow-up action for each of the batches? | | | |
| 56.3 | Are there any products that have more than one special release and, if so, is the first batch referred to in the decision to release the later batch? | | | |
| REJECTED BATCHES: | | S | P | I |
| 57 | Is there an SOP for dealing with rejected batches? | | | |
| 58 | Examine the list of rejected batches for the current year: select three batches.<br>Product: _____ Batch No.: _____<br>Product: _____ Batch No.: _____<br>Product: _____ Batch No.: _____ | | | |
| 58.1 | List the reason(s) for the rejection?<br>1.<br>2.<br>3. | | | |
| 58.2 | Specify at which stage of production the batches were rejected? | | | |
| 58.3 | Is there a written investigation, including conclusions as to the cause of the failure and, if appropriate, follow-up action for each of the batches? | | | |
| 58.4 | Are there any products that have more than one rejected batch and, if so, has corrective action been recommended and implemented? | | | |
| RETURNED GOODS: | | S | P | I |
| 59 | Is there a written procedure for holding, testing, and reprocessing of returned drug products? | | | |
| 60 | Examine the list of returned goods for the current year:<br>Product: _____ Batch No.: _____<br>Product: _____ Batch No.: _____<br>Product: _____ Batch No.: _____ | | | |
| 60.1 | Is there a record for each batch, including the following details? | | | |
| 60.1.1 | Name of customer. | | | |
| 60.1.2 | Name and strength of the product. | | | |
| 60.1.3 | Batch number. | | | |
| 60.1.4 | Reason for return. | | | |

| | | | | |
|---|---|---|---|---|
| 60.1.5 | Quantity returned. | | | |
| 60.1.6 | Date of disposition. | | | |
| 60.2 | List the reason(s) for the return:<br>1.<br>2.<br>3. | | | |
| 61 | Is the disposition adequately justified with a documented investigation and conclusions authorized by Quality Assurance? | | | |
| 62 | Could the reason for any of the returns implicate other batches of the product and, if so, has an investigation been initiated and appropriate action taken? | | | |

| CHAPTER 13: VALIDATION | | | | |
|---|---|---|---|---|
| GENERAL ASPECTS | | S | P | I |
| 1. | Is there a master plan covering | | | |
| 1.1 | Validation policy. | | | |
| 1.2 | Organizational structure of validation activities. | | | |
| 1.3 | Responsibilities for validation activities execution. | | | |
| 1.4 | Training requirements. | | | |
| 1.5 | Summary of facilities, systems, equipments and process to be validated. | | | |
| 1.6 | Documentation and standard operating procedures. | | | |
| 1.7 | Validation list: facilities, processes, products. | | | |
| 1.8 | Planning scheduling and validation program, including: | | | |
| 1.8.1 | Chronogram? | | | |
| 1.8.2 | Location of each activity? | | | |
| 1.8.3 | Responsibilities of execution. | | | |
| 1.9 | Acceptance criteria | | | |
| 1.10 | Protocols and reports formats. | | | |
| 1.11 | Change control. | | | |
| 1.12 | Cross reference to documents. | | | |
| 1.13 | Annexes. | | | |
| 2 | Is there a validation committee within the organization? | | | |
| 3 | Has a validation team been conformed? | | | |
| 4 | Are critically important processes validated: | | | |
| 4.1 | Prospectively? | | | |
| 4.2 | Retrospectively? | | | |
| 4.3 | Concurrently? | | | |
| 5 | Are the ratings and/or validations of the following performed and documented: | | | |
| 5.1 | Analytical methods | | | |
| 5.2 | Production and assay equipment | | | |
| 5.3 | Sterile production processes | | | |
| 5.4 | Non-sterile production processes | | | |
| 5.5 | Cleaning procedures | | | |
| 5.6 | Critical support systems (purified water, water for injections, air, vapor, HVAC,…, etc.) | | | |
| 5.7 | Facilities | | | |
| 6 | Is every important modification to the manufacturing process validated, including any change in equipment, manufacturing area, materials, changes in raw materials, packing materials, changes in critical support systems processes and methods that may affect the quality of the product or reproducibility of the process? | | | |
| 6.1 | Are all changes requested formally, documented and approved by representatives of Production, Quality Assurance, Quality Control, Research and Development, Engineering and Regulatory Affairs, as appropriate? | | | |

| | | | | |
|---|---|---|---|---|
| 6.2 | Any product resulting from the changed processes are not released for sale without the full knowledge and consideration of the responsible staff, including (when appropriate) the qualified person? | | | |
| 7 | Are the terms established by the validation and re-validation programs met? | | | |
| 8 | In case electronic data processing systems are used, are these validated? | | | |
| 9 | Is the supply entry recording automated? | | | |
| 9.1 | Is it manual? | | | |
| 9.2 | Is the system reliable? | | | |
| 9.3 | If automated: | | | |
| 9.4 | Is a safety back-up kept? | | | |
| 9.5 | Are safety passwords used for system access? | | | |
| 9.6 | Are these passwords only assigned to authorized personnel? | | | |
| 9.7 | Is there a record of password allocation? | | | |
| 9.8 | Are periodical challenge tests performed on the system to verify reliability? | | | |
| 10 | Is the supply and product stock system automated? | | | |
| 10.1 | Is it manual? | | | |
| 10.2 | If automated: | | | |
| 10.3 | Is a safety back-up kept? | | | |
| 10.4 | Are safety passwords used for system access? | | | |
| 10.5 | Are these passwords only assigned to authorized personnel? | | | |
| 10.6 | Is there a record of password allocation? | | | |
| 10.7 | Are periodical challenge tests performed on the system to verify reliability? | | | |
| 11 | Are the validation studies performed according to pre-defined protocols? | | | |
| 12 | Is a written report summarizing the obtained results and conclusions prepared and filed? | | | |
| 13 | Is the validity of the critical processes and procedures established based on a validation study? | | | |
| 14 | Are the critical points and critical control points of the different Production processes validated in order to obtain a uniform product with the mandated quality as a result? | | | |
| 15 | Does the protocol define the selection criteria for products or groups of products subject to cleaning validation? | | | |
| 16 | Are criteria established to assess the changes originating a re-validation? | | | |
| 17 | Are trend analyses performed to assess the need to re-validate in order to assure the processes and procedures continue to obtain the desired results? | | | |

| Validation of Water System | | Purified Water | | | Water for Injections | | |
|---|---|---|---|---|---|---|---|
| | | S | P | I | S | P | I |
| 1 | Has the water system installation been qualified (IQ)? | | | | | | |
| 2 | Have the system IQ protocol and report been produced? | | | | | | |
| 3 | Does the protocol includes at least the following: | | | | | | |
| 3.1 | Approvals. | | | | | | |
| 3.2 | Statement of purpose. | | | | | | |
| 3.3 | System description. | | | | | | |
| 3.4 | Equipment specification validation system design? | | | | | | |
| 3.5 | Welding roughness testing on pipelines? | | | | | | |
| 3.6 | Absence of dead points/section in the pipeline? | | | | | | |
| 3.7 | Pipe and tank passivation? | | | | | | |
| 3.8 | Standard operating procedures (operation, cleaning and sanitation, preventive maintenance)? | | | | | | |
| 3.9 | Measuring instrument calibration? | | | | | | |
| 3.10 | As built system drawings? | | | | | | |
| 3.11 | Installation check list? | | | | | | |
| 3.12 | Physical verification of material of construction of parts/items? | | | | | | |
| 3.13 | Manufacturer's certifications? | | | | | | |
| 3.14 | Supporting utilities? | | | | | | |
| 3.15 | Final report, includes at least: | | | | | | |
| 3.15.1 | Conclusion/summary? | | | | | | |
| 3.15.2 | Description of the performed methodology? | | | | | | |
| 3.15.3 | Data tablets? | | | | | | |
| 3.15.4 | Results? | | | | | | |
| 3.15.5 | Revision and approvals signatures? | | | | | | |
| 3.16 | Appendix-reference documents? | | | | | | |
| 4 | Has the operation of the water system been qualified (OQ)? | | | | | | |
| 5 | Have the system OQ protocol and report been produced? | | | | | | |
| 5.1 | Approvals? | | | | | | |
| 5.2 | Statement of purpose? | | | | | | |
| 5.3 | System description?? | | | | | | |
| 5.3.1 | System production capacity? | | | | | | |
| 5.3.2 | Flow type and rate? | | | | | | |
| 5.3.3 | Value operation? | | | | | | |
| 5.3.4 | Alarm system operation? | | | | | | |
| 5.3.5 | Equipments description (including name, model No., serial No., manufacturer, supplier, …,etc). | | | | | | |
| 5.3.6 | Component details (name and manufacturers specifications, dimensions, weight, ..,etc). | | | | | | |
| 5.4 | Instrument calibration report? | | | | | | |
| 5.5 | SOPs verification? | | | | | | |
| 5.6 | Control panel functionality? | | | | | | |
| 5.7 | Safety features? | | | | | | |

| Validation of Water System | | Purified Water | | | Water for Injections | | |
|---|---|---|---|---|---|---|---|
| | | S | P | I | S | P | I |
| 5.8 | Final report, includes at least: | | | | | | |
| 5.8.1 | Conclusion/summary? | | | | | | |
| 5.8.2 | Description of the performed methodology? | | | | | | |
| 5.8.3 | Data tablets? | | | | | | |
| 5.8.4 | Results. | | | | | | |
| 5.8.5 | Revision and approval signatures? | | | | | | |
| 6 | Has the water system performance been qualified? | | | | | | |
| 7 | Has the water system performance qualification protocol and report been produced?? | | | | | | |
| 8 | This protocol includes at least: | | | | | | |
| 8.1 | Approval page? | | | | | | |
| 8.2 | Statement of purpose? | | | | | | |
| 8.3 | System description? | | | | | | |
| 8.4 | SOP verification? | | | | | | |
| 8.5 | Sampling plan with details of location for sample collection? | | | | | | |
| 8.6 | Test procedure for microbial quality attributes and analysis of results? | | | | | | |
| 8.7 | Test procedures for chemical and physical quality attributes and analysis of results? | | | | | | |
| 8.8 | Leak test (pressure test) for product water circulation loop? | | | | | | |
| 8.9 | Sanitation program and sanitization frequency determination? | | | | | | |
| 8.10 | Acceptance criteria? | | | | | | |
| 8.11 | Data summary, conclusions, final report and certification? | | | | | | |
| 8.12 | Appendix-reference documents? | | | | | | |
| 9 | Has the water system performance qualification been done in three phases: (Phase 1, Phase 2, Phase 3)? | | | | | | |
| 9.1 | **VALIDATION PHASE 1:** | | | | | | |
| 9.1.1 | Have the operations parameters been defined? | | | | | | |
| 9.1.2 | Are the cleaning and sanitation procedures and frequencies been defined? | | | | | | |
| 9.1.3 | Are the daily sampling records for every pre-treatment point and usage point for a period of 2 – 4 weeks? | | | | | | |
| 9.1.4 | Was the system operating continuously without failure or performance deviation? | | | | | | |
| 9.1.5 | Were the following included in the testing approach? | | | | | | |
| 9.1.5.1 | Chemical and microbiological testing accordance with a defined plan? | | | | | | |
| 9.1.5.2 | Daily sampling for incoming feed-water, after each step in purification process and each point of use and at other defined sample points? | | | | | | |
| 9.1.6 | Have the following been developed?<br>- Appropriate operating ranges?<br>- Finalize operating, cleaning, sanitizating and maintenance procedures? | | | | | | |

| Validation of Water System | | Purified Water | | | Water for Injections | | |
|---|---|---|---|---|---|---|---|
| | | S | P | I | S | P | I |
| 9.1.7 | Have provisional alert and action levels been verified? | | | | | | |
| 9.1.8 | Has a test-failure procedure been developed and refined? | | | | | | |
| 9.2 | **VALIDATION PHASE 2:** | | | | | | |
| 9.2.1 | Are there daily sampling records for every pre-treatment point and usage point for a period of 4 to 5 weeks after Phase 1? | | | | | | |
| 9.2.2 | Were the SOPs deployed and refined after satisfactory completion of Phase 1? | | | | | | |
| 9.2.3 | Were the following demonstrated? | | | | | | |
| 9.2.3.1 | Consistent operation within established ranges? | | | | | | |
| 9.2.3.2 | Consistent production and delivery of water of the required quantity and quality when the system is operated in accordance with the SOPs? | | | | | | |
| 9.2.4 | Are the reports summarizing the results of Phases 1 and 2 of the validation available? | | | | | | |
| 9.3 | **VALIDATION PHASE 3:** | | | | | | |
| 9.3.1 | Are the weekly sampling records available for every usage point for a period of one-year after the satisfactory completion of Phase 2. | | | | | | |
| 9.3.2 | Was it shown that sampling locations, sampling frequencies and tests were reduced to normal routine pattern, based on established procedures proven during Phases 1 and 2? | | | | | | |
| 9.3.3 | Is the case of water for injection systems, are the daily sampling records shown for at least one usage point available, with all the usage points sampled weekly? | | | | | | |
| 9.3.4 | Do the results of these records show that the system is under control? | | | | | | |
| 9.3.5 | Is the validation summary report available? | | | | | | |
| 9.3.6 | Are there personnel training records? | | | | | | |

| | VALIDATION OF HEATING, VENTILATION AND AIR CONDITIONING SYSTEMS **(HVAC)** | S | P | I |
|---|---|---|---|---|
| GENERAL | | S | P | I |
| 1. | Is the validation of HVAC system described in the validation master plan? | | | |
| 1.1 | If yes, does it define the nature and extent of testing and test procedures and protocols to be followed? | | | |
| 1.2 | Are all instillation components subsystems or parameters, critical parameters and non-critical parameters determined? | | | |
| COMISSIONING: | | S | P | I |
| 2 | Does the commissioning process involve at least: | | | |
| 2.1 | Setting up parameters? | | | |
| 2.2 | Balancing? | | | |
| 2.3 | Adjustment and testing entire HVAC system? | | | |
| 3 | Does the data include the following: | | | |
| 3.1 | Design and measured figures for air flows? | | | |
| 3.2 | Design and measured figures for water flows? | | | |
| 3.3 | System pressures and electrical amperages? | | | |
| 4 | Are the above items contained in the operating and maintenance manuals (O&M manuals? | | | |
| 5 | Are all the acceptable tolerances for all system parameters specified prior to commencing the physical installation? | | | |
| 6 | Are personnel provided with the proper training after installation of the system? | | | |
| 6.1 | Does the training include sessions on how to perform operation and maintenance? | | | |
| 7 | Are there properly prepared O&M manuals, schematic drawings, protocols and reports? | | | |
| QUALIFICATION: | | S | P | I |
| 8 | Are the HVAC systems properly qualified? | | | |
| 8.1 | Does it follow the risk-based approach? | | | |
| 9 | Do the qualification stages include design qualification (DQ), installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ)? | | | |
| 10 | Are there (DQ) protocols? | | | |
| 10.1 | Do they contain at least the following: | | | |
| 10.1.1 | Approvals? | | | |
| 10.1.2 | Statement of purpose? | | | |
| 10.1.3 | Design inputs (people, equipments, processes materials, and air quality)? | | | |
| 10.1.4 | Output parameters required (air cleanliness level required, filter efficiencies and air changes required in critical areas, alert and action limits for environmental monitoring, temperature/pressure humidity, particulate level and microbial levels)? | | | |
| 10.1.5 | System description? | | | |
| 10.1.6 | Diagram of complete system? (Copy of drawing given by the supplier). | | | |

| | | | | |
|---|---|---|---|---|
| 10.1.7 | Supplier specifications? | | | |
| 10.1.8 | References? | | | |
| 10.1.9 | Definitions? | | | |
| 11 | Are there (IQ) protocols for critical and non-critical parameters? | | | |
| 11.1 | Do they contain at least the following: | | | |
| 11.1.1 | Approvals? | | | |
| 11.1.2 | Statement of purpose? | | | |
| 11.1.3 | System description? | | | |
| 11.1.4 | Standard operating procedures? (Operating, cleaning and sanitization, calibration and preventive maintenance). | | | |
| 11.1.5 | Calibration review? | | | |
| 11.1.6 | Installation check list? | | | |
| 11.1.7 | Drawings? | | | |
| 11.1.8 | Physical verification of materials of construction of parts/items? | | | |
| 11.1.9 | Supporting utilities? (e.g. power, compressed air, water, steam, vaccum, ..,etc). | | | |
| 11.1.10 | Manufacturer's certification? | | | |
| 11.1.11 | Deficiencies and action report? | | | |
| 11.1.12 | Final report (summary, analysis/evaluation of data, conclusion and certification)? | | | |
| 11.1.13 | Appendix (abbreviations and definitions, reference documents (manufacturers manuals and purchase order)? | | | |
| 12 | Are there (OQ) protocols? | | | |
| 12.1 | Do they contain at least the following: | | | |
| 12.1.1 | Approvals? | | | |
| 12.1.2 | Statement of purpose? | | | |
| 12.1.3 | System description? | | | |
| 12.1.4 | Calibration? | | | |
| 12.1.5 | Operational checks? | | | |
| 12.1.6 | Standard operating procedures verification? | | | |
| 12.1.7 | Control panel functionality? | | | |
| 12.1.8 | Safety features review and check list? | | | |
| 12.1.9 | Final report? (Analysis/evaluation of data, certification). | | | |
| 12.1.10 | Appendix? (Abbreviations and definitions, reference documents). | | | |
| 13 | Are there (PQ) protocols? | | | |
| 13.1 | Do they contain at least the following: | | | |
| 13.1.1 | Approvals? | | | |
| 13.1.2 | Statement of purpose/scope? | | | |
| 13.1.3 | Responsibilities? | | | |
| 13.1.4 | Materials and test equipments? | | | |
| 13.1.5 | Verification of procedures and training? | | | |
| 13.1.6 | Calibration review? | | | |
| 13.1.7 | Sampling plans and acceptance criteria? | | | |
| 13.1.8 | Deviations? | | | |
| 13.1.9 | Reference documents? | | | |
| 13.1.10 | Attachments? | | | |

| | | | | |
|---|---|---|---|---|
| 14 | Are the time intervals between tests defined according on the type of facility? | | | |
| 14.1 | For particle court test (6 months)? | | | |
| 14.2 | For pressure difference (12 months)? | | | |
| 14.3 | For air flow volume to verify air change rates (12 months)? | | | |
| 14.4 | For air flow velocity (12 months)? | | | |
| 15 | Is periodic requalification of parameters done at regular intervals (e.g. annually)? | | | |
| 16 | Is requalification done when any change which could affect system performance, takes place? | | | |
| 17 | Are clean-up times defined? | | | |

| PRODUCTION EQUIPMENT VALIDATION: | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Solids | | | Semi solid | | | Liquids | | | Sterile | | |
| | | S | P | I | S | P | I | S | P | I | S | P | I |
| 1 | Are there equipment installation qualifications SOP's (IQ) in place. | | | | | | | | | | | | |
| 2 | Are the equipment installation qualification (IQ) protocols containing at least: | | | | | | | | | | | | |
| 2.1 | Purpose of the equipment? | | | | | | | | | | | | |
| 2.2 | Description of the equipment? | | | | | | | | | | | | |
| 2.3 | Component and utilities inspection? | | | | | | | | | | | | |
| 2.4 | Control is inspection? | | | | | | | | | | | | |
| 2.5 | General installation? | | | | | | | | | | | | |
| 2.6 | Documentation? | | | | | | | | | | | | |
| 2.7 | Approvals? | | | | | | | | | | | | |
| 3 | Are the equipment operation qualifications SOPs (OQ) in place? | | | | | | | | | | | | |
| 4 | Are the equipment operation qualifications (OQ) protocols containing at least? | | | | | | | | | | | | |
| 4.1 | Purpose of equipment? | | | | | | | | | | | | |
| 4.2 | Responsibilities? | | | | | | | | | | | | |
| 4.3 | Description of the equipment? | | | | | | | | | | | | |
| 4.4 | Description of the equipment operation steps? | | | | | | | | | | | | |
| 4.5 | General installation? | | | | | | | | | | | | |
| 4.6 | Critical parameters functions with acceptance criteria? | | | | | | | | | | | | |
| 4.7 | Documentation? | | | | | | | | | | | | |
| 4.8 | Approvals? | | | | | | | | | | | | |
| 5 | Are there equipment performance qualifications SOPs(PQ) in place? | | | | | | | | | | | | |
| 6 | Are there equipment performance qualifications (PQ) protocols shown, containing at least: | | | | | | | | | | | | |
| 6.1 | Purpose? | | | | | | | | | | | | |
| 6.2 | Responsibilities? | | | | | | | | | | | | |
| 6.3 | Description of the process? | | | | | | | | | | | | |
| 6.4 | Process inputs? | | | | | | | | | | | | |
| 6.5 | Process out puts, with defined acceptance criteria (CPK)? | | | | | | | | | | | | |
| 6.6 | Critical parameters/variables-lis impacting process output and proposal operating ranges? | | | | | | | | | | | | |
| 6.7 | Testing including sampling and testing methods? | | | | | | | | | | | | |

| PRODUCTION EQUIPMENT VALIDATION: | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Solids | | | Semi solid | | | Liquids | | | Sterile | | |
| | | S | P | I | S | P | I | S | P | I | S | P | I |
| 6.8 | Documentation and evaluation of results? | | | | | | | | | | | | |
| 6.9 | Approvals? | | | | | | | | | | | | |
| 7 | Is equipment cleaning validated? | | | | | | | | | | | | |

| | PROCESS VALIDATION:: | S | P | I |
|---|---|---|---|---|
| 1 | What types of process validation are performed? | | | |
| 1.1 | Prospective? | | | |
| 1.2 | Concurrent? | | | |
| 1.3 | Retrospective? | | | |
| 2 | Is process validation include in the validation master plan? | | | |
| 3 | Is process validation performed for each product of different dosage forms? | | | |
| 4 | Are there sufficiently qualified and trained personnel to perform process validation? | | | |
| 4.1 | Are there training records? | | | |
| 5 | Are there process validation protocols and reports? | | | |
| 5.1 | Do the (PV) protocols include at least:<br>- Purpose?<br>- Background/pre-validation activities?<br>- List of equipment and their qualification status?<br>- Facility qualification?<br>- Process flow chart?<br>- Manufacturing procedure?<br>- List of critical processing parameters and critical excipients?<br>- Sampling, tests and specifications?<br>- Acceptance criteria? | | | |
| 5.2 | Do (PV) reports include at least:<br>- Executive summary?<br>- Background?<br>- Presentation and discussion of all results:<br>• Statistical summary of IPC data, control charts?<br>• Critical processing parameters/operating ranges (Optimization)?<br>• Evaluation of data points outside of in-process limits?<br>• Evaluations?<br>- Deviations-impact assessment on validation?<br>- Conclusions?<br>- Recommendations, attachments?<br>- Approvals by protocol approval persons. | | | |
| 6 | Are the analytical methods used in process validation fully validated as required? | | | |
| 7 | Are raw materials validated before performing process validation? (At least 2 separate lots from each supplier). | | | |
| 8 | Are the facilities and equipments used in production qualified? | | | |
| 8.1 | Are equipments calibrated? | | | |
| 8.2 | Do equipments have preventive maintenance program? Is it followed? | | | |
| 9 | Have the key process variables been identified and their operating ranges established? | | | |
| 10 | Are master batch records finalized? | | | |
| 11 | Are relevant SOPs in place? | | | |
| 12 | Are training on equipment operation, manufacturing instructions and sampling strategies completed? | | | |

| | | | | |
|---|---|---|---|---|
| 13 | Are quality systems (i.e. deviations, change control, site quality review committee) in place? | | | |
| 14 | Review a completed process validation protocol and report for one or more products?<br>1. Product Name: _____<br>2. Product Name: _____<br>3. Product Name: _____ | | | |
| 14.1 | Have all the tests required by the validation protocol been performed? | | | |
| 14.2 | Are all the documents correctly filled in and signed by authorized personnel? | | | |
| 14.3 | Are the three validation batches (prospective & concurrent process validation) consecutive? | | | |
| 14.13.1 | If not, is there a documented explanation? | | | |
| 14.4 | Are the conclusions drawn from test results correct? | | | |
| 14.5 | Are there any significant deviations from specifications? | | | |
| 14.5.1 | If yes, specify the deviation, its potential impact on the finished product, and the proposed corrective action? | | | |
| **BATCH RECORDS**: | | | | |
| 14.6 | Are the batch records accurately and completely filled in? | | | |
| 14.7 | Have all the validation batches been reviewed by QA personnel for completeness and accuracy? | | | |
| **DRUG SUBSTANCE TEST RESULTS:** | | | | |
| 14.8 | Are the suppliers of raw materials the same as those registered? | | | |
| 14.9 | Do the results for the raw materials tests conform to specifications? | | | |
| 14.10 | Are the above checked results equipment to those of the biolot? | | | |
| 14.11 | If different, is there a documented explanation? | | | |
| **IN-PROCESS TEST RESULTS:** | | | | |
| 14.12 | Do the in-process test results conform to specifications? | | | |
| **FINISHED PRODUCT:** | | | | |
| 14.13 | Do finished product test results conform to specifications? | | | |
| **EQUIPMENT:** | | | | |
| 14.14 | Has equipment qualification (IQ/OQ and PQ) been performed for all equipment items used in manufacture of the validation batches? | | | |
| **ENVIRONMENTAL CONDITIONS:** | | | | |
| 14.15 | Have the environmental conditions for production of process validation batches been established? | | | |
| 14.15.1 | Are they recorded (temp, RH, ..etc). | | | |
| **RAW DATA VERIFICATION:** | | | | |
| 14.16 | Verify that raw data are available for tests performed? | | | |
| **TEST RESULTS VERIFICATION:** | | | | |
| 14.17 | Review the experiment design methodology? | | | |
| 14.18 | Are the test results obtained verified? | | | |
| 14.19 | Are the test results obtained sufficient for process parameters optimization? | | | |
| 14.20 | Have the different process parameters been optimized? | | | |

| | QUALITY CONTROL VALIDATION: | S | P | I |
|---|---|---|---|---|
| 1 | Does the Validation Master Plan include the Quality Control laboratory? | | | |
| 2 | Does the laboratory have equipment installation qualification (IQ) SOP's and protocols? | | | |
| 2.1 | Are there documents supporting compliance with these SOP's and protocols? | | | |
| 3 | Does the laboratory have equipment operation qualification (OQ) SOP's and protocols? | | | |
| 3.1 | Are there documents supporting compliance with these SOP's and protocols? | | | |
| 4 | Does the laboratory have equipment process qualification (PQ) SOP's and protocols? | | | |
| 4.1 | Are there documents supporting compliance with these SOP's and protocols? | | | |
| 5 | Are there validation programs and procedures for analytical methods not published by internationally recognized pharmacopoeias (BP, USP, Eur.P)? | | | |
| 5.1 | Are all non-pharmacopoeial methods validated? | | | |
| 5.2 | Are there written protocols for validating those methods? | | | |
| 5.3 | Are there documents supporting compliance with those procedures and protocols? | | | |
| 5.4 | Does the criteria for analytical validation include the following as applicable according to the type of the method:<br>- Specificity?<br>- Accuracy?<br>- Linearity?<br>- Range?<br>- Sensitivity?<br>- Limit of detection?<br>- Limit of quantitation?<br>- Ruggedness? | | | |
| 5.5 | Does the analytical method procedure define the data elements required for analytical method validation? | | | |
| 5.6 | Are pharmacopoeial methods verified for their suitability under actual conditions of use? | | | |
| 5.7 | Do the validation procedure and protocol of microbiological assay method include at least the following:<br>- Linearity?<br>- Range?<br>- Accuracy?<br>- Precision? | | | |
| | CLEANING VALIDATION: | S | P | I |
| 1 | Is there a cleaning validation master plan? | | | |
| 2 | Does the validation master plan include at least: | | | |
| 2.1 | Approvals? | | | |
| 2.2 | Purpose and scope? | | | |
| 2.3 | Responsibilities? | | | |
| 2.4 | Cleaning strategy or approach? | | | |
| 2.5 | Equipment description? | | | |
| 2.6 | Product description? | | | |

| | | | | |
|---|---|---|---|---|
| 2.7 | Cleaning method? | | | |
| 2.8 | Sampling methods? | | | |
| 2.9 | Validation test methods? | | | |
| 4 | Are there procedures for the cleaning of equipment used? | | | |
| 4.1 | Do they include at least the following:<br>- Disassembly of equipment?<br>- Visuals inspection for equipment wear, product residuals and foreign materials?<br>- Critical sites of difficult to clean areas?<br>- Assignment of responsibility for cleaning equipment?<br>- Cleaning and sanitization schedules?<br>- A description in detail of the methods, equipment, and materials used in cleaning?<br>- Cleaning/handling and storage of tools used in cleaning (post cleaning)?<br>- Protection of clean equipment?<br>- Inspection of equipment for cleanliness immediately before use? | | | |
| 5 | Are there procedures for the cleaning of facilities used? | | | |
| 6 | Is the cleaning validation performed to confirm cleaning effectiveness? | | | |
| 7 | Is the validation implemented to verify cleaning of: | | | |
| 7.1 | Surfaces in contact with the product? | | | |
| 7.2 | After a change in product? | | | |
| 7.3 | Between shift batches? | | | |
| 8 | Does the validation strategy include contamination risks equipment storage time, the need to store equipment dry and sterile and free of pyrogen if necessary? | | | |
| 9 | Are there cleaning protocols for equipment and facilities? | | | |
| 10 | Does the validation protocol include: | | | |
| 10.1 | Approvals? | | | |
| 10.2 | Purpose and scope? | | | |
| 10.3 | Responsibilities? | | | |
| 10.4 | Equipment design or definition including any monitoring equipment to be used? | | | |
| 10.5 | Cleaning procedures and documentation? | | | |
| 10.6 | Number of consecutive cleaning cycles performed? | | | |
| 10.7 | Qualification of cleaning agent(s)? | | | |
| 10.8 | Sampling methodology? | | | |
| 10.9 | Analytical methodology? | | | |
| 10.10 | Establishing limits? | | | |
| 11 | Are there training records for the personnel performing the validation? | | | |
| 12 | Is the work of the operating personnel effectively supervised? | | | |
| 12.1 | Is it documented? | | | |
| 13 | Is quality control responsible for the sampling for cleaning verification? | | | |
| 14 | Is the personnel responsible for sampling trained on sampling methods *swabs, rinsing, placebo)? | | | |
| 15 | Have acceptance limits been set for both residues and bacteria? | | | |
| 15.1 | Are any they verified? | | | |

| | | | | |
|---|---|---|---|---|
| 16 | Are there limits based on compliance of the following criteria: | | | |
| 16.1 | Visually clean? | | | |
| 16.2 | 10 ppm in another product? | | | |
| 16.3 | 0.1%(0.001) of the therapeutic dose? | | | |
| 16.4 | Below the limit of detection by best available validated analytical methods for allergic, potent, steroids and cytotoxins products? | | | |
| 17 | Are the maximum allowable carry over (MACO) determined for equipments and/production systems? | | | |
| 18 | Are acceptance limits of non-actives residues (detergents, sanitizers, ..etc) determined based on:<br>- NOEL (no observed effect level) and?<br>- NOAEL (no observed adverse effect level)?<br>- LD50 (lethal dose)? | | | |
| 19 | Is the cleaning validation strategy based on? | | | |
| 19.1 | Product grouping? | | | |
| 19.2 | Manufacturing equipment grouping? | | | |
| 19.3 | Cleaning method grouping? | | | |
| 19.4 | Cleaning agents grouping? | | | |
| 20 | Are degradation products verified during validation? | | | |
| 21 | Are analytical methods validated? (including detection limits and quantification limits)? | | | |

| CHAPTER 14: ENGINEERING & MAINTENANCE | | | | |
|---|---|---|---|---|
| SOPs | | S | P | I |
| 1 | Is a complete index and a complete set of applicable SOPs available in the department? | | | |
| 1.1 | Are the index and the SOPs current? | | | |
| 1.2 | Is the set of SOPs correctly organized according to the index? | | | |
| PERSONNEL | | S | P | I |
| 2 | Is there an adequate number of qualified employees? | | | |
| 3 | Select some employees working in the department. Are their training records up-to-date? | | | |
| 3.1 | Have the employees undergone training in the following areas during the last tear? | | | |
| 3.1.1 | GMPs | | | |
| 3.1.2 | SOPs | | | |
| 3.1.3 | Maintenance techniques | | | |
| 3.2 | Have the employees undergone qualification according to the relevant SOP? | | | |
| 3.4 | Are all employees attired according to the appropriate garmenting SOP? | | | |
| CALIBRATION RECORDS | | S | P | I |
| 4 | Is there an approved list of instrumentation included in the calibration program? | | | |
| 4.1 | Is the instrument classification (critical, process control, reference) indicated on the list | | | |
| 4.2 | Is there an approved annual calibration timetable? | | | |
| 4.2.1 | Is there a tracking procedure in place to ensure that every instrument included in the program actually undergoes calibration on time? | | | |
| 4.2.2 | Is there a written procedure in place for informing the relevant QA and production personnel of instruments that have not undergone calibration according to schedule? | | | |
| 4.3 | Are there written SOPs describing in detail how to perform calibrations? | | | |
| 4.4 | Are traceable calibration standards employed? | | | |
| 4.4.1 | Traceable to which agency? | | | |
| 4.4.2 | Are there certificates of calibration available for the standards? | | | |
| 4.4.3 | Is there a written procedure for corrective action in the event that the calibration standard is found to be out-of-limits during recalibration? | | | |
| 4.4.4 | Are the standard instruments stored in a manner that ensures their integrity and accuracy?<br>Physically verify the storage and condition of three reference standards. | | | |
| 4.5 | Examine the calibration history of some critical instruments.<br>1.<br>2.<br>3. | | | |
| 4.5.1 | Is there written evidence that the calibration standards used were within calibration? | | | |
| 4.5.2 | Were the instruments calibrated according to the frequency indicated in the relevant SOP? | | | |

| | | | | |
|---|---|---|---|---|
| 4.5.3 | In the event that the frequency was not adhered to, is there written authorization from Quality Assurance? | | | |
| 4.5.4 | Were the calibrations performed exactly as defined in the relevant procedure? | | | |
| 4.5.5 | Are the forms completely and accurately filled in? | | | |
| 4.5.6 | Were all the calibrations within the defined limits of accuracy? | | | |
| 4.5.7 | If the calibrations were outside the limits, were QA and production personnel informed immediately in writing? | | | |
| PREVENTIVE MAINTENANCE RECORDS | | S | P | I |
| 5.1 | Is there an approved annual preventive maintenance program? | | | |
| 5.2 | Are there written procedures for preventive maintenance for all production equipment? | | | |
| 5.2.1 | Are there written records of performance? | | | |
| 5.3 | Select some equipment items and examine the preventive maintenance history:<br>1.<br>2.<br>3. | | | |
| 5.3.1 | Is there written evidence for each machine that the preventive maintenance was performed in accordance with the relevant SOP? | | | |
| 6.1 | Is there a record of breakdown maintenance for each piece of production equipment? | | | |
| 6.2 | Is there a procedure whereby breakdowns are analyzed so that, if appropriate, the preventive maintenance program is revised to prevent recurrence? | | | |
| LUBRICANTS | | S | P | I |
| 7 | Is there an approved list of food-grade lubricants for use where they may contact product? | | | |
| 7.1 | Is there a written procedure for the receipt and approval of such lubricants? | | | |
| 7.2 | Is a record made of the catalog number of the lubricant used when maintenance is performed? | | | |
| EQUIPMENT QUALIFICATION | | S | P | I |
| 8 | Is there an approved annual program for the qualification of all production equipment? | | | |
| 8.1 | Select some equipment items and examine the IQ/OQ protocols:<br>1.<br>2.<br>3. | | | |
| 8.1.1 | Physically verify that all instruments found on the equipment are included in the protocols? | | | |
| 8.1.2 | Cross-check with the calibration records that the equipment items have the same classification in the qualification protocol as in the calibration report? | | | |
| 8.1.3 | Are the qualification reports approved by all appropriate personnel? | | | |
| 8.1.4 | Are the reports completely and accurately filled out? | | | |

| DRAWINGS | | S | P | I |
|---|---|---|---|---|
| 9 | Is there a complete set of approved drawings for systems and equipment available in the department? | | | |
| 9.1 | Select some equipment items/systems and examine the available drawings:<br>1.<br>2.<br>3. | | | |
| 9.1.1 | Are the drawings the latest edition? | | | |
| 9.1.2 | Are the drawings QA approved? | | | |
| ALARMS PROCEDURES | | S | P | I |
| 10 | Is there an approved alarm system for critical systems? | | | |
| 10.1 | Is there an SOP for responding to alarms for critical systems? | | | |
| 10.1.1 | Is the procedure followed? | | | |
| 10.1.2 | Does the procedure require recording of the alarm and of the corrective action taken in response? | | | |
| RECEIPT OF NEW EQUIPMENT | | S | P | I |
| 11.1 | Is there an SOP describing the receipt and checking of new equipment prior to installation? | | | |
| 11.1 | Is there documented evidence that the procedure is adhered to? | | | |
| 11.2 | Dose the SOP require checking of the equipment according to approved purchasing specifications? | | | |
| FILTER INTEGRITY TEST RECORDS | | S | P | I |
| 12 | Is there an SOP for performing HEPA filter integrity tests? | | | |
| 12.1 | Is the procedure adhered to? | | | |
| 12.2 | Examine records of the most recent tests performed: | | | |
| 12.2.1 | Is there written evidence of corrective action in the event that a filter the test? | | | |
| 12.2.2 | Was the Quality Assurance Department informed of the failure? | | | |
| 12.2.3 | Is the report approved by the Quality Assurance Department? | | | |
| AIRFLOW VELOCITY TEST RECORDS | | S | P | I |
| 13 | Is there an SOP for performing the test? | | | |
| 13.1 | Is the procedure adhered to? | | | |
| 13.2 | Examine records of the most recent tests performed: | | | |
| 13.2.1 | Is there written evidence of corrective action in the event that results are out-of-limits? | | | |
| 13.2.2 | Was the Quality Assurance Department informed of the failure? | | | |
| 13.2.3 | Is the report approved by the Quality Assurance Department? | | | |
| AIR CHANGES TEST RECORDS | | S | P | I |
| 14 | Is there an SOP for performing the test? | | | |
| 14.1 | Is the procedure adhered to? | | | |
| 14.2 | Examine records of the most recent tests performed: | | | |
| 14.2.1 | Is there written evidence of corrective action in the event of out-of-limit results? | | | |

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|---|---|---|---|---|
| 14.2.2 | Was the Quality Assurance Department informed of the failure? | | | |
| 14.2.3 | Is the report approved by the Quality Assurance Department? | | | |
| MAINTENANCE OF TABLET PUNCHES AND DIES | | S | P | I |
| 15 | Is there a written procedure for the maintenance of tablet punches and dies? | | | |
| 15.1 | Examine the history cards of sets of tablet punches and dies:<br>1.<br>2.<br>3. | | | |
| 15.1.1 | Is there written evidence that the table punches and dies were maintained according to the procedure, including:<br>- Dates the set was in use?<br>- Machine in which it was used?<br>- Product name and batch number?<br>- Total quantity of tables made by the set since it was put into use?<br>- Date the set was received back from production? | | | |
| 14.1.2 | Are the sets clean? | | | |
| 15.1.3 | Is there documented evidence that the tablet punches and dies were checked in accordance with the SOP for signs of wear, scoring, or corrosion? | | | |
| 15.1.4 | Is the set stored exactly as defined in the SOP? | | | |
| 15.1.5 | Is a food-grade rust preventive used and approved for use? | | | |
| 15.1.6 | Are specifications for the stated tests available? | | | |
| 15.1.7 | Are there records of destruction of tablet punches and dies that do not conform to the requirements after maintenance? | | | |
| 15.1.8 | Is Quality Assurance informed of out-of-limit results in a timely manner? | | | |

| CHAPTER 15: HVAC SYSTEM | | | | |
|---|---|---|---|---|
| SOPs | | S | P | I |
| 1 | Is a complete index and a complete set of applicable SOPs available:<br>- To the system operator?<br>- In the Maintenance Department? | _____<br>_____ | _____<br>_____ | _____<br>_____ |
| 1.1 | Are the index and the SOPs current? | | | |
| 1.2 | Is the set of SOPs correctly organized according to the index? | | | |
| PERSONNEL | | S | P | I |
| 2 | Is there an adequate and qualified number of employees? | | | |
| 2.1 | Are the training records for the system operator and relevant Maintenance personnel up-to-date? | | | |
| 2.2 | Have the personnel undergone training in the following areas? | | | |
| 2.2.1 | GMPs | | | |
| 2.2.2 | SOPs | | | |
| 2.2.3 | Maintenance techniques | | | |
| 2.3 | Are they knowledgeable about their job functions? | | | |
| 2.4 | Are the employees familiar with all relevant SOPs? | | | |
| 2.5 | Have the employees undergone qualification according to the relevant SOP? | | | |
| SYSTEM DRAWINGS | | S | P | I |
| 3 | Are up-to-date P & ID drawings available covering all elements of the HVAC system in the plant?<br>- Central air handling unit<br>- Each production department | _____<br>_____ | _____<br>_____ | _____<br>_____ |
| 3.1 | Have the drawings been approved by Quality Assurance? | | | |
| 3.2 | Where appropriate, are up-to-date drawings available showing the required pressure differentials in each area? | | | |
| 3.3 | Where appropriate, are up-to-date drawings available showing the required airflow patterns in each area? | | | |
| 3.4 | Where appropriate, are limits for temperature and relative humidity defined in an SOP? | | | |
| SYSTEM MONITORING | | S | P | I |
| 4 | Are there pressure gauges for monitoring the pressure differential across filters? | | | |
| 4.1 | Are readings from pressure gauges for monitoring the pressure differential across filters in the same measuring units? | | | |
| 4.2 | Are limits for differential pressure stated in the relevant SOP in the same measuring units as they appear on the gauges? | | | |
| 4.3 | Is there an SOP for monitoring temperature and relative humidity? | | | |
| 4.4 | Is there an SOP requiring the check of all filters in the system to ensure that they are within approved limits of the pressure differential? | | | |
| 4.4.1 | At what frequency? | | | |
| 4.5 | Are all filters in the system replaced according to the pressure differential or are they replaced according to elapsed time? | | | |

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|---|---|---|---|---|
| 4.6 | Perform a walk-through inspection of the entire system: | | | |
| 4.6.1 | Are all filters labeled with a sticker stating.<br>- Date of last replacement?<br>- Date next replacement due? | _____<br>_____<br>__ | _____<br>___ | _____<br>_____ |
| 4.6.2 | Are all pressure gauges labeled with a valid calibration sticker? | | | |
| 4.6.3 | Examine the differential pressure readings. Do they all conform to the limits stated in the relevant SOP? | | | |
| 4.6.4 | Examine the records for the daily check of filters for the past six months: | | | |
| 4.6.4.1 | How many out-of-limit results are recorded? | | | |
| 4.6.4.2 | Is there documented evidence that corrective action was taken (filter replaced)? | | | |
| 4.6.4.3 | Are there examples of filters that are repeatedly out-of-limits and, if so, has action been taken to investigate the reason? | | | |
| 4.6.4.4 | Where filters are found to be out-of-limit, is an unusual events report form completed? | | | |
| SYSTEM MAINTENANCE | | S | P | I |
| 5 | Is there an approved list of all filters in the system? | | | |
| 5.1 | Are there approved procedures for preventive maintenance of all filters in the HVAC system? | | | |
| 5.1.1 | Central air handling unit | | | |
| 5.1.2 | Each production area | | | |
| 5.2 | Examine the preventive maintenance records for the HVAC system: | | | |
| 5.2.1 | Is there documented evidence that it has been performed according to the frequency stated in the relevant SOP? | | | |
| 5.2.2 | Is there documented evidence of the maintenance of external prefilters in accordance with an approved SOP? | | | |
| 5.2.3 | Are there written records of filter replacement available in the Maintenance Department for replacement as a result of out-of-limit results and not preventive maintenance? | | | |
| SYSTEM VALIDATION | | S | P | I |
| 6 | Are there approved IQ/OQ reports for all elements of the HVAC system?<br>- Central air handling unit.<br>- Each production area. | _____<br>_____ | _____<br>_____ | _____<br>_____ |
| 6.1 | Do the reports include up-to-date diagrams verified as-built? | | | |
| 6.2 | Do the reports include, as necessary, verification of:<br>- Airflow patterns?<br>- Air balancing?<br>- Differential pressures?<br>- Temperature and relative humidity? | _____<br>_____<br>_____<br>_____ | _____<br>_____<br>_____<br>_____ | _____<br>_____<br>_____<br>_____ |
| 6.3 | Are the reports QA approved? | | | |

| CHAPTER 16: RESEARCH AND DEVELOPMENT | | | | |
|---|---|---|---|---|
| SOPs | | S | P | I |
| 1 | Is a complete index and a complete set of applicable SOPs available in the department? | | | |
| 1.1 | Are the index and the SOPs current? | | | |
| 1.2 | Is the set of SOPs correctly organized according to the index? | | | |
| PERSONNEL | | S | P | I |
| 2 | Is there adequate number of employees in the department? | | | |
| 3 | Are their training records up-to-date? | | | |
| 3.1 | Have the employees undergone training in the following areas?<br>- GMPs.<br>- SOPs.<br>- Maintenance techniques.<br>- Performulation and formulation studies?<br>- Production operations techniques? | | | |
| 4 | Are the employees knowledgeable about their job functions? | | | |
| 5 | Are all employees attired according to the appropriate garmenting SOP? | | | |
| R & D ARCHIVES | | S | P | I |
| 6 | Is the R & D archive well maintained so that documents are easily retrievable? | | | |
| 7 | Select two regulatory submissions and examine the available documentation: | | | |
| 7.1 | Is all documentation easily retrievable? | | | |
| 7.2 | Does it include the following?<br>- The original application.<br>- Any amendments and/or supplements.<br>- A copy of any correspondence with the regulatory authorities.<br>- A copy of each annual update submitted since the application was approved. | ____<br>____<br>____<br>____<br>____ | ____<br>____<br>____<br>____<br>____ | ___<br>___<br>___<br>___<br>___ |
| 7.3 | Are the copies of the development reports for these two submissions available and easily and easily retrievable in the archives? | | | |
| 7.4 | Select one performulation experiment referred to in each development report. Is the original experimental data retrievable and available for review? | | | |
| PREFORMULATION STUDIES | | S | P | I |
| 8 | Is there SOP describing how to conduct the preliminary stages of a new R & D project? | | | |
| 8.1 | Dose it include the following?<br>- How to document the project plan.<br>- How to record experiments.<br>- The degree of documentation required prior to performing any performulation experiment.<br>- How to document failed experiments. | ____<br>____<br>____<br>____<br>____ | ____<br>____<br>____<br>____<br>____ | ___<br>___<br>___<br>___<br>___ |
| 9 | Is there an SOP describing how to obtain samples of a new raw material for R | | | |

| | | | | |
|---|---|---|---|---|
| | & D purposes? | | | |
| 9.1 | Does it include the following?<br>- Responsibility for obtaining the examples.<br>- Preliminary information required from the manufacturer prior to the receipt of samples.<br>- Precautions to be taken in the event that the material requires special handling.<br>- Description of how the samples are received and what documentation and/or testing is required prior to R & D use, including material accountability/reconciliation. | ____<br>____<br>____<br><br>____<br>____ | ____<br>____<br>____<br><br>____<br>____ | ___<br>___<br>___<br><br>___<br>___ |
| 10 | Examine the documentation for an experimental batch that is being processed in the R & D facility<br>- Product: _____<br>- Batch No.:_____ | | | |
| 10.1 | Are balances in the facility checked in accordance with an SOP? | | | |
| 10.2 | Are all results within the specifications? | | | |
| 10.3 | If not, is there a record of implementation of corrective action? | | | |
| 10.4 | Is there a written record of the purposes of the experiment? | | | |
| 10.5 | Is the formula to be used written and signed? | | | |
| 10.6 | Is there a record of what testing is to be performed? | | | |
| 10.7 | Does the researcher record his/her observation or comments during the course of the experiment in a numbered notebook? | | | |
| 10.8 | Are corrections made by crossing through, dating, and initialing? | | | |
| 10.9 | Are the environmental conditions (temperature and relative humidity) in the room documented? | | | |
| 10.10 | Is any other experiment being conducted in the room at the same time? | | | |
| 10.11 | Is there a room use log? | | | |
| 10.12 | Is the current batch recorded? | | | |
| 10.13 | Is a record made of what samples are taken from the experimental batch and for what purpose (e.g. physical, analytical, or stability testing)? | | | |
| 10.14 | Is a yield reconciliation made for performulation experiments?<br>- At what stage of the experiment?<br>- Is there an SOP? | ____<br>____<br>____ | ____<br>____<br>____ | ___<br>___<br>___ |
| 10.15 | Upon receipt of all test results, is a written conclusion made for each experiment? | | | |
| 10.16 | Is there an SOP describing the destruction of experimental batches and samples on completion of the experiment? | | | |
| R & D FACILITIES | | S | P | I |
| 11 | Is the department maintained in a good state of repair? | | | |
| 12 | Is the department neat and orderly with sufficient space for equipment and operations? | | | |
| 13 | Examine the area at the end of a day's work. Is it left neat and tidy? | | | |
| 14 | Are all work areas clearly labeled with the name and the batch number of the product being processed? | | | |

| PREVENTION OF CROSS-CONTAMINATION | | S | P | I |
|---|---|---|---|---|
| 15 | Is more than one experiment performed at any one time in each room? | | | |
| 16 | Are doors closed at all times? | | | |
| 17 | Is negative pressure maintained in working areas at all times during work when formulating solid dosage forms? | | | |
| 17.1 | Is there a record of the pressure? | | | |
| 18 | What is the quality of the air in the department (filter designation)? | | | |
| 19 | Are there approved SOPs for the maintenance and replacement of filters? | | | |
| 19.1 | Is there documented evidence that they are followed? | | | |
| 20 | Is dirty equipment covered prior to transfer to the washing room? | | | |
| 21 | Are materials brought into the area clean and free from powder/dust? | | | |
| EQUIPMENT | | S | P | I |
| 22 | Are there sufficient and suitable equipments for all formulation purposes? | | | |
| 23 | Are all instrumentation labeled with a valid calibration sticker? (when necessary). | | | |
| 24 | Is a filled IQ/OQ protocol available for all major equipment items? | | | |
| 24.1 | Examine two such protocols. Are they sufficiently detailed? | | | |
| 25 | Are only approved, food-grade lubricants used where they contact product? | | | |
| 26 | Are equipments neat, clean, and rust free? | | | |
| 27 | When not in use, are equipments covered so as to prevent accidental contamination? | | | |
| 28 | Are equipments constructed so that product contact surfaces are not reactive or absorptive, so that it will not contaminate or in any way affect the product being manufactured? | | | |
| 29 | Are all equipment labeled as to their cleanliness status? | | | |
| 29.1 | How is cleanliness verified (visually or by analytical means)? | | | |
| 30 | Are machine duty cards maintained for all equipments used? | | | |
| 31 | At what stage of product development are cleaning methods validated? | | | |
| 32 | Is cleaning correctly recorded on the room use log as major or minor? | | | |
| EVALUATION / SUPERVISION OF RESULTS | | S | P | I |
| 33 | Is there an SOP requiring the periodic review of researchers notebooks by supervisors? | | | |
| 33.1 | Is there documented evidence that the review is performed? | | | |
| 34 | Is there an SOP requiring the reporting of unusual events? | | | |
| 35 | What documentation is maintained when an experiment is aborted or discarded due to some unforeseen problem? | | | |
| R & D PACKAGING AREA | | S | P | I |
| 36 | Is there a separate packaging area for R & D? | | | |
| 37 | Is the department maintained in a good state of repair? | | | |
| 38 | Is the department neat and orderly with sufficient space for equipment and operations? | | | |
| 39 | Is there adequate physical separation between different packaging lines to prevent mix-ups and/or cross-contamination? | | | |

| | | | | |
|---|---|---|---|---|
| 40 | Is there a written procedure for cleaning the packaging area:<br>- Between batches of the same product?<br>- Between batches of different products? | | | |
| 41 | Is a room duty card used? | | | |
| 42 | Is there a written procedure for cleaning and inspecting the packaging area at the beginning and end of a batch documented in the batch record? | | | |
| 43 | Is the batch yield calculated immediately on completion of the packaging operation and prior to introduction a new batch into the area? | | | |
| R & D WAREHOUSE | | S | P | I |
| 44 | Is there a separate and sufficient storing facilities for R & D? | | | |
| 45 | Is the department maintained in a good state of repair? | | | |
| 46 | Is the department neat and orderly with sufficient space for operations? Examine also the storage area for submission betches. | | | |
| 47 | Is there a record of environmental conditions? | | | |
| 48 | Are all items clearly labeled as to their status? | | | |
| 49 | Is there a separate area for rejected goods/goods destined for destruction? | | | |
| 50 | Are finished goods stored in a separate area from raw materials? | | | |
| 51 | Are inventory control cards maintained for items stored in the warehouse? | | | |