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FEDERAL STATE INSTITUTION
STATE INSTITUTE OF DRUGS AND GOOD PRACTICES
(FSI SID & GP)

SELF-MONITORING SHEETS

for Verifying Compliance of the Company with the Requirements of the Rules of Good Manufacturing Practice

Source: Order of the Ministry of Industry and Trade of Russia No. 916

"On Approval of the Rules of Good Manufacturing Practice" dated June 14, 2013 (as amended on December 18, 2015)

Developed by the Center for Good Engineering Practices
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RULES OF GOOD MANUFACTURING PRACTICE

Order of the Ministry of Industry and Trade of Russia No. 916 "On Approval of the Rules of Good Manufacturing Practice" dated June 14, 2013 (as amended on December 18, 2015)

PHARMACEUTICAL QUALITY SYSTEM (CHAPTER 1)

Pharmaceutical Quality System

The manufacturer must manufacture medicinal products so as to ensure that they are fit for their intended use, comply with the requirements of the Marketing Authorization File or Clinical Trial Protocol and do not place patients at risk due to inadequate safety, quality or efficacy. The attainment of these objectives is the responsibility of senior management. To achieve these objectives reliably there must be a comprehensively designed and correctly implemented Pharmaceutical Quality System incorporating Good Manufacturing Practice and Quality Risk Management.

Self-monitoring sheet

- Does the manufacturing facility have a documented pharmaceutical quality system?
- Are the efficacy and suitability of the pharmaceutical quality system evaluated on a regular basis?
- Does the senior management participate in periodic reviews of the pharmaceutical quality system?
- Is there a procedure for self-inspection and/or quality audit?
- Is there a system for improving quality indicators at the manufacturing facility?
- Is there continual improvement through the implementation of improvements?
- Are measures being taken to assess the planned changes forward?
- Is there an assessment of the changes after implementation?
- Are quality risk management principles used to establish the reasons for assumptions of product defect and other problems?
- Are there clearly defined areas of responsibility and duties for the staff?
- Is there a control system in place regarding the manufacturing process efficiency and the medicinal product quality?
- Have the production and control operations been checked to ensure meeting the appropriate requirements?
- Have measures been taken to ensure production control?
- Have measures been taken to ensure the appropriate raw materials and packaging materials to be supplied and used?
- Have measures been taken to select and control suppliers?
- Are the results of medicinal product and process monitoring evaluated during batch release?
- Are the results of medicinal product and process monitoring evaluated when investigating deviations and for taking preventive measures?
- Is the necessary control of intermediate products carried out?
- Is the necessary control carried out during the manufacturing process?
- Is validation performed?

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PHARMACEUTICAL QUALITY SYSTEM (CHAPTER 1)

Organization of Manufacturing and Quality Control of Medicinal Products

The manufacturer must manufacture medicinal products so as to ensure that they are fit for their intended use, comply with the requirements of the Marketing Authorization File or Clinical Trial Protocol and do not place patients at risk due to inadequate safety, quality or efficacy. The attainment of these objectives is the responsibility of senior management. To achieve these objectives reliably there must be a comprehensively designed and correctly implemented Pharmaceutical Quality System incorporating Good Manufacturing Practice and Quality Risk Management.

Self-monitoring sheet

- Are all manufacturing processes described in the company's regulations?
- Does the company have a system for revising manufacture regulations?
- Are critical stages of the manufacturing process validated?
- Are all procedures and instructions in writing and unambiguous?
- Are all personnel appropriately educated and trained to perform procedures properly?
- Is there a recording system (handwritten or technical) documenting the actual steps required by established procedures and guidelines?
- Is there a recording system (handwritten or technical) documenting that the quantity and quality of the products used meet the established standards?
- Is there a system (handwritten or technical) recording deviations from the established standards?
- Are investigations carried out and the reasons for deviations found out?
- Are corrective and preventive actions taken when deviations are detected?
- Does the Batch Processing Record allow you to track the complete manufacturing history of the batch in a convenient and understandable form?
- Is there an organized system for recalling any batch of medicinal products from circulation?
- Are complaints regarding the quality of the medicinal products marketed under consideration?
- Are causes of defects investigated?
- Are appropriate measures taken after investigation of the causes of defects in relation to medicinal product of inadequate quality as well as for preventing similar cases?

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Quality Control

The manufacturer must manufacture medicinal products so as to ensure that they are fit for their intended use, comply with the requirements of the Marketing Authorization File or Clinical Trial Protocol and do not place patients at risk due to inadequate safety, quality or efficacy. The attainment of these objectives is the responsibility of senior management. To achieve these objectives reliably there must be a comprehensively designed and correctly implemented Pharmaceutical Quality System incorporating Good Manufacturing Practice and Quality Risk Management.

Self-monitoring sheet

- Are there adequate facilities, equipment and trained personnel for the control and testing of raw materials and packaging materials, intermediate, bulk and finished products?
- Are there approved procedures for sampling, inspection and testing of raw materials and packaging materials, intermediate, bulk and finished products?
- Do the staff take samples of raw materials and packaging materials, intermediate, bulk and finished products in accordance with the methods approved by the Quality Control Department?
- Are quality control test procedures validated?
- Is there a record system (handwritten or technical) documenting that all necessary sampling, inspection and test procedures have actually been taken?
- Is there a system (handwritten or technical) recording deviations?
- Are records generated in accordance with the requirements of the specifications based on the results of control and testing of raw materials and packaging materials, intermediate, bulk and finished products?
- Are the relevant manufacturing documents and deviations from established procedures evaluated?
- Is the introduction of a batch of products into civil commerce monitored in accordance with the requirements?
- Is there a sufficient number of control samples of raw materials, packaging materials and finished products being preserved, which will allow, if necessary, testing in the future?
- Are quality reviews of all medicinal products manufactured, including medicinal products manufactured only for export, carried out on a regular basis to confirm the consistency of the existing process?
- Are the results of the product quality review evaluated and conclusions drawn about the need for corrective and preventive action or revalidation?

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PHARMACEUTICAL QUALITY SYSTEM (CHAPTER 1)

Quality Risk Management

The manufacturer must manufacture medicinal products so as to ensure that they are fit for their intended use, comply with the requirements of the Marketing Authorization File or Clinical Trial Protocol and do not place patients at risk due to inadequate safety, quality or efficacy. The attainment of these objectives is the responsibility of senior management. To achieve these objectives reliably there must be a comprehensively designed and correctly implemented Pharmaceutical Quality System incorporating Good Manufacturing Practice and Quality Risk Management.

Self-monitoring sheet

- Is a quality risk management procedure carried out?
- Is the quality risk assessment based on scientific knowledge, experience with the process and ultimately aimed at protecting the patient?
- Is the level of risk consistent with the level of effort, formalization and documentation of the quality risk management process?

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Responsible Personnel

The organization and operation of a proper quality assurance system and proper manufacturing of medicinal products depend on the human aspect. For this reason, the manufacturer has a sufficient number of qualified personnel to carry out all the tasks which are the responsibility of the manufacturer. Individual responsibilities should be clearly understood by the individuals and recorded.

Self-monitoring sheet

- Does the company have documentary evidence that the manufacturing process complies with these Rules?
- Is it reflected in the Company's Charter that the Production Manager and the Quality Control Manager are responsible persons?
- Do responsible employees (the Production Manager and the Quality Control Manager) work independently of each other?
- Does the company have a well-defined corporate structure?
- Does the company have approved job descriptions?
- Is there any unreasonable duplication of job descriptions at the manufacturing facility?
- Are all the rules and requirements of this order assigned to employees?
- Is there a sufficient number of personnel at the manufacturing facility?
- Is the responsibility for each batch of medicinal products manufactured in accordance with the current legislation and the requirements of the Marketing Authorization File recorded in the job descriptions of authorized persons?
- Do the job descriptions of authorized persons specify responsibility for medicinal products manufactured outside the Russian Federation, that each imported batch of products has been tested in accordance with the procedure established in the Russian Federation?
- Does the qualification of the authorized person meet the requirements established by the current legislation?
- Is manufacturing and storage of products ensured in accordance with approved documentation to achieve the required quality?
- Is the exact implementation of instructions for manufacturing operations ensured?
- Does the QC Manager's job description define responsibility for the quality of raw materials, packaging materials, as well as intermediate, bulk and finished products?
- Does the QC Manager's job description define the need to evaluate the Batch Processing Record?
- Does the QC Manager's job description define the need to ensure all necessary tests to be carried out?
- Does the QC Manager's job description define the need to approve specifications, sampling instructions, test methods, and other QC procedures?
- Does the QC Manager's job description define the need to ensure appropriate validation to be carried out?
- Is appropriate validation ensured?

Training

The organization and operation of a proper quality assurance system and proper manufacturing of medicinal products depend on the human aspect. For this reason, the manufacturer has a sufficient number of qualified personnel to carry out all the tasks which are the responsibility of the manufacturer. Individual responsibilities should be clearly understood by the individuals and recorded.

Self-monitoring sheet

- Is a continuous training system provided at the manufacturing facility for personnel whose duties take them into production and storage areas or into control laboratories (including the technical, maintenance and cleaning personnel), and for other personnel whose activities could affect the quality of the product?
- Is the practical effectiveness of the continuous training system evaluated?
- Is there primary on-the-job training for newly recruited employees in accordance with their assigned responsibilities?
- Is information about training kept at the manufacturing facility?
- Is special training at the manufacturing facility given to personnel working in areas where contamination is a hazard, e.g. clean areas or areas where highly active, toxic, infectious or sensitizing materials are handled?
- Is information in advance given to visitors or untrained workers at the manufacturing facility, in particular about personal hygiene and the prescribed protective clothing?
- Are principles of quality assurance and any measures capable of improving its understanding and implementation fully discussed during the training sessions at the manufacturing facility?

Personnel Hygiene

The organization and operation of a proper quality assurance system and proper manufacturing of medicinal products depend on the human aspect. For this reason, the manufacturer has a sufficient number of qualified personnel to carry out all the tasks which are the responsibility of the manufacturer. Individual responsibilities should be clearly understood by the individuals and recorded.

Self-monitoring sheet

- Is there a developed and implemented set of measures for industrial hygiene at the manufacturing facility?
- Have specific features of the company been taken into account when developing measures for industrial hygiene?
- Are there special hygiene requirements for personnel involved in the manufacture of special groups of products?
- Have procedures for compliance with health, sanitary and clothing requirements for personnel been developed?
- Are personal hygiene requirements communicated to each employee whose job responsibilities involve staying in production and quality control areas?
- Do personnel receive medical examination upon recruitment?
- Are there regular medical examinations for employees whose duties take them into the production and quality control areas?
- Are there instructions at the manufacturing facility to ensure that personnel are aware of the health conditions that could affect product quality?
- Have any measures been developed at the manufacturing facility to ensure that no person affected by an infectious disease or having open lesions on the exposed surface of the body is engaged in the manufacture of medicinal products?
- Does every person entering the production areas wear protective garments appropriate to the operations to be carried out?
- Is eating, drinking, chewing or smoking, or the storage of food, drink, smoking materials or personal medication prohibited in the production and storage areas?
- Is direct contact avoided between the operator’s hands and the exposed product as well as with any part of the equipment that comes into contact with the products?
- Are personnel instructed to use the hand-washing facilities?

Production Area

Premises and equipment must be located, designed, constructed, adapted and maintained to suit the operations to be carried out. Their layout and design must aim to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build up of dust or dirt and, in general, any adverse effect on the quality of products.

Self-monitoring sheet

- Are premises laid out in a logical order corresponding to the sequence of the operations?
- Are premises laid out in a logical order corresponding to the requisite cleanliness levels?
- Are risks to human health due to industrial cross-contamination fully minimized?
- Are all the necessary measures at the manufacturing facility followed to minimize the risk of contamination of materials and products from the environment?
- Is manufacturing of sensitizing and highly active substances in the same premises avoided?
- Is the risk of confusion between different medicinal products or their components minimized?
- Has the risk of mix-ups and cross-contamination in premises for packaging medicinal products been considered?
- Is there a separate area for weighing raw materials, sampling?
- Is the ventilation system in production areas equipped with air control facilities (temperature, humidity, filtration)?
- Are utility systems accessible from outside the production area?
- Does the design of utility systems permit easy cleaning and disinfection?
- Drains should have trapped gullies.
- Have the requirements for the materials of interior surfaces (walls, ceilings, floors) been taken into account?
- Are production areas well lit, particularly where visual on-line controls are carried out?

Storage Areas

Premises and equipment must be located, designed, constructed, adapted and maintained to suit the operations to be carried out. Their layout and design must aim to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build up of dust or dirt and, in general, any adverse effect on the quality of products.

Self-monitoring sheet

- Have storage areas been designed to ensure good storage conditions? (Temperature, humidity, monitoring)
- Are storage areas of sufficient capacity to allow orderly storage of the various categories of materials and products: starting and packaging materials, intermediate, bulk and finished products, products in quarantine, released, rejected, returned or recalled products?
- Is quarantine status is ensured by storage in separate areas?
- Are raw materials, packaging materials and products protected from the weather?
- Are reception areas designed and equipped to allow containers of incoming starting and packaging materials to be cleaned before storage?
- Are there separate sampling areas for starting materials and primary packaging materials?
- Are risks of contamination during sampling fully minimized?
- Is a segregated area provided for the storage of rejected, recalled or returned starting materials, packaging materials or products?
- Have special storage conditions been taken into account for highly active materials?
- Is special attention paid to the safe and secure storage of printed packaging materials as they are considered critical to the conformity of the medicinal product?

Quality Control Area

Premises and equipment must be located, designed, constructed, adapted and maintained to suit the operations to be carried out. Their layout and design must aim to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build up of dust or dirt and, in general, any adverse effect on the quality of products.

Self-monitoring sheet

- Are control laboratories designed to suit the operations to be carried out in them?
- Is there sufficient space in the laboratory to avoid mix-ups and cross-contamination, as well as storage space for samples and records?
- Are quality control laboratories separated from production areas?
- Are there separate rooms to protect sensitive instruments from vibration, electrical interference, humidity, etc.?
- Are special requirements met in laboratories handling particular substances, such as biological or radioactive samples?

Ancillary Areas

Premises and equipment must be located, designed, constructed, adapted and maintained to suit the operations to be carried out. Their layout and design must aim to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build up of dust or dirt and, in general, any adverse effect on the quality of products.

Self-monitoring sheet

- Are rest and refreshment rooms separated from other areas?
- Is the size of ancillary areas appropriate for the number of personnel?
- Are toilets directly connected to production or storage areas?
- Are maintenance workshops separated from production areas?
- Is an animal house well isolated from other areas?
- Does the animal house have a separate entrance?
- Has the need for separate air handling facilities for the animal house been considered?
- Is manufacturing equipment designed, located and maintained to suit its intended purpose?
- Do repair and maintenance operations present any hazard to the quality of the products?
- Are there approved manufacturing instructions for cleaning the equipment?
- Is the risk of contamination from washing and cleaning equipment and tools minimized?
- Is equipment installed in such a way as to prevent any risk of error or of contamination?
- Is the effect of the production equipment (parts of the production equipment that come into contact with the product) on the product quality evaluated?
- Are an appropriate range and precision of balances and measuring equipment controlled?
- Are balances, measuring equipment, recording and control equipment calibrated and checked at defined intervals?
- Are adequate records of calibration and checks maintained?
- Is fixed pipework clearly labeled to indicate the contents and the direction of flow?
- Are pipes for purified water, water for injection and, where appropriate, other water pipes sanitized?
- Are there factory-approved instructions for sanitizing the pipes for purified water, water for injection and, if necessary,
- the pipes for other water, indicating the limits of microbial contamination and measures to be taken if they are exceeded?
- Is there defective equipment in the production area?

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DOCUMENTATION (CHAPTER 4)

Instructive Documents and Recording Documents

Documentation constitutes an essential part of the Pharmaceutical Quality System and is key to organizing of production and quality control in compliance with the GMP requirements. The various types of documents and media used should be fully defined in the manufacturer's Quality Management System.

Self-monitoring sheet

- Has the Site Master File been implemented at the manufacturing facility?
- Does the Site Master File define the manufacturing process and quality control process?
- Has a Batch Processing Record been implemented at the manufacturing facility?
- Does the Batch Processing Record define the manufacturing process and quality control process?
- Does the Batch Processing Record define the issuance of a Batch Release Certificate?
- Are all factors affecting the quality of the finished product given in the Batch Processing Record?
- Are the requirements (specifications) that must be met by the starting materials, packaging materials and products used or obtained during manufacturing regulated at the company?
- Has the master formula been developed at the company?
- Has the processing instruction been developed at the company?
- Have the packaging instructions been developed at the company?
- Have test procedures for raw materials, equipment and computerized systems been developed at the company?
- Have the instructions for process, packaging, sampling and testing been developed?
- Have the procedures/instructions to provide guidance on how to conduct and record individual operations (e.g. validation protocol, master validation plan) been developed?
- Is there a record of each product batch history, including sales?
- Are all the source data of the product batch recorded, at least all the data on which the quality solutions are based?
- Has the document flow been developed at the manufacturing facility to confirm the quality of products (data sheets, analytical sheets, executive summary and deviation reports)?

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DOCUMENTATION (CHAPTER 4)

Generation, Control and Retention of Documents

Documentation constitutes an essential part of the Pharmaceutical Quality System and is key to organizing of production and quality control in compliance with the GMP requirements. The various types of documents and media used should be fully defined in the manufacturer's Quality Management System.

Self-monitoring sheet

- Is the responsibility of the authorized person defined in the job description for the development of all types of necessary documentation?
- Is there a procedure for the development, execution, issue, withdrawal of documents and amending them?
- Do the documents comply with the requirements of the Marketing Authorization File, as well as the documents submitted for obtaining a Manufacturing Authorization for medicinal products?
- Are appropriate controls for electronic documents such as templates, forms, and master documents implemented?
- Is there a retention system for documents containing critical information, including source data (for example, regarding validation or stability), confirming the information of the Marketing Authorization File, during the period of validity of the Marketing Authorization?
- Is complete destruction or replacement of complete sets of new documents containing critical information documented?
- Are appropriate controls in place to ensure the integrity of the records during the retention period?
- Are instructive documents signed by authorized signatories with a date indication?
- Are the validity periods of the instructive documents set?
- Are the documents regularly reviewed and updated?
- Is the possibility of using outdated versions of documents excluded?
- Are changes made to the documents saved, are they signed on time?
- Is it clearly defined which record is related to each manufacturing activity?
- Are there controls in place to ensure the integrity of the record throughout the retention period?
- Is the retention of documentation carried out in accordance with the requirements and depending on the type and purpose of the documentation?

Specifications

Documentation constitutes an essential part of the Pharmaceutical Quality System and is key to organizing of production and quality control in compliance with the GMP requirements. The various types of documents and media used should be fully defined in the manufacturer's Quality Management System.

Self-monitoring sheet

- Are specifications for starting and packaging materials, and finished products authorized?
- Is there the designated name and the internal code reference in the approved specification?
- Is there a reference to a pharmacopoeial monograph or regulatory document in the approved specification?
- Are there names of the approved suppliers and original manufacturer of the starting and packaging materials in the approved specification?
- Is there a specimen of printed materials in the approved specification?
- Does the approved specification contain directions for sampling and testing?
- Are there qualitative and quantitative requirements with acceptance limits in the approved specification?
- Are there storage conditions and precautions in the approved specification?
- Is there the expiration date in the approved specification?
- Are specifications for intermediate and bulk products similar to specifications for raw materials or finished products?
- Does the approved specification for finished products contain a description of the dosage form and details of the packaging?
- Does the approved specification contain directions for sampling and testing?
- Does the approved specification for finished products contain storage conditions and any special handling precautions?
- Does the approved specification for finished products contain the expiration date?

Manufacturing Formula and Processing Instructions

Documentation constitutes an essential part of the Pharmaceutical Quality System and is key to organizing of production and quality control in compliance with the GMP requirements. The various types of documents and media used should be fully defined in the manufacturer's Quality Management System.

Self-monitoring sheet

- Do the approved Manufacturing Formula and Processing Instructions exist for batch size to be manufactured?
- Does the Manufacturing Formula include a description of the technological process and control methods at all stages of drug manufacturing?
- Does the structure and content of master formulae comply with those established by the relevant regulatory legal acts of the Russian Federation?
- Do the Processing Instructions include a statement of the processing location and the principal equipment to be used?
- Do the Processing Instructions include methods, or reference to the methods, to be used for preparing the critical equipment (e.g. cleaning, assembling, calibrating, sterilizing)?
- Do the Processing Instructions include methods to check that the equipment and work station are clear of previous products?
- Do the Processing Instructions include methods for checking the cleanliness of the equipment and its readiness for the next process?
- Do the Processing Instructions include the detailed stepwise processing instructions?
- Do the Processing Instructions include any in-process controls with the limits of control parameters?
- Do the Processing Instructions include the requirements for bulk storage of the products; including the container, labeling and special storage conditions?
- Have special precautions been taken into account when developing the Processing Instructions?

Packaging Instructions

Documentation constitutes an essential part of the Pharmaceutical Quality System and is key to organizing of production and quality control in compliance with the GMP requirements. The various types of documents and media used should be fully defined in the manufacturer's Quality Management System.

Self-monitoring sheet

- Do the approved Packaging Instructions exist at the manufacturing facility?
- Do the Packaging Instructions include the name of the product; including the batch number of bulk and finished product?
- Do the Packaging Instructions include the description of its dosage form and strength?
- Do the Packaging Instructions include the pack size expressed in terms of the number, weight or volume of the product in the final container?
- Do the Packaging Instructions include a complete list of all the packaging materials required?
- Do the Packaging Instructions include directions to check that the equipment and work station are clear of previous products?
- Do the Packaging Instructions include special precautions to be observed, including a careful examination of the packaging area and equipment?
- Do the Packaging Instructions include a description of the packaging operation?
- Do the Packaging Instructions include details of in-process controls with instructions for sampling and acceptance limits?

Batch Processing Record

Documentation constitutes an essential part of the Pharmaceutical Quality System and is key to organizing of production and quality control in compliance with the GMP requirements. The various types of documents and media used should be fully defined in the manufacturer's Quality Management System.

Self-monitoring sheet

- Is there an approved Batch Processing Record at the manufacturing facility?
- Does the Batch Processing Record contain data confirming batch production in accordance with these rules?
- Are batch production data retained at the manufacturing facility?
- Does the Batch Processing Record contain dates and times of commencement and completion of production?
- Does the Batch Processing Record contain last name(s) and initials of the operator(s) who performed each significant step of the process?
- Does the Batch Processing Record contain the batch number and/or analytical control number?
- Does the Batch Processing Record contain any relevant processing operations or events, and major equipment used?
- Is there a record of the in-process controls and the initials of the person(s) carrying them out, and the results obtained, in the Batch Processing Record?
- Does the Batch Processing Record contain notes on any deviation from the Manufacturing Formula and Processing Instructions, signed by an authorized person and dated?
- Is the Batch Processing Record signed by the person responsible for the processing operations, and dated?

Procedures and Records

Documentation constitutes an essential part of the Pharmaceutical Quality System and is key to organizing of production and quality control in compliance with the GMP requirements. The various types of documents and media used should be fully defined in the manufacturer's Quality Management System.

Self-monitoring sheet

- Are there approved procedures for the receipt of each delivery of each starting material, (including bulk, intermediate or finished goods) as well as primary, secondary and printed packaging materials?
- Are the records of the receipts maintained?
- Do the records of the receipts include the name of the material on the delivery note and the containers?
- Do the records of the receipts include the date of receipt?
- Do the records of the receipts include the supplier’s name and manufacturer’s name?
- Do the records of the receipts include the manufacturer’s batch?
- Do the records of the receipts include the total quantity of materials and number of containers received?
- Are there approved procedures for the internal labeling?
- Are there approved procedures for the quarantine and storage of starting materials, packaging materials and other materials?

Testing

Documentation constitutes an essential part of the Pharmaceutical Quality System and is key to organizing of production and quality control in compliance with the GMP requirements. The various types of documents and media used should be fully defined in the manufacturer's Quality Management System.

Self-monitoring sheet

- Is there a documented sampling procedure at the manufacturing facility?
- Does the sampling instruction contain information on the methods and equipment to be used?
- Does the sampling instruction contain information on the amounts to be taken?
- Are there written procedures for testing starting and packaging materials and products at different stages of manufacture?
- Are logbooks kept for major or critical production and analytical testing equipment?
- Are logbooks kept for premises where product has been processed?

Prevention of Cross-Contamination in Production

Production operations must follow clearly defined procedures, comply with these Rules in order to obtain products of the required quality and be in accordance with the relevant Manufacturing Authorization and Marketing Authorization File.

Self-monitoring sheet

- Is contamination of a starting material or of a product by another material or product prevented?
- Is a risk of uncontrolled release of dust, gases, vapors, aerosols, or organisms at the manufacturing facility prevented?
- Is there dedicated manufacturing facility for products such as penicillins, live bacteria, medicinal products containing live microorganisms, and some other biological medicinal products?
- Does the manufacturing facility have airlocks and exhaust plant to the full extent?
- Has the risk of contamination caused by recirculation or re-entry of untreated or insufficiently treated air been fully minimized?
- Is it prohibited to keep specific protective clothing inside the areas where products are processed?
- Are the cleaning and decontamination techniques used proven to be effective?
- Are "closed systems" used at the manufacturing facility?
- Is there a check for the presence of residues?
- Are cleaning status labels used on the equipment?
- Is there a monitoring and evaluation of the effectiveness of measures aimed at preventing contamination?

Validation

Production operations must follow clearly defined procedures, comply with these Rules in order to obtain products of the required quality and be in accordance with the relevant Manufacturing Authorization and Marketing Authorization File.

Self-monitoring sheet

- Are there developed and approved validation procedures at the manufacturing facility?
- Are validation results and conclusions recorded?
- Is suitability assessed when a new Manufacturing Formula or a new production method is introduced for batch production?
- Does the existing manufacturing process provide the ability to yield a product consistently of the required quality?
- Are all significant changes in the manufacturing process (including any change in equipment or raw materials and packaging materials) validated?
- Do processes and procedures undergo revalidation?

Starting Materials

Production operations must follow clearly defined procedures, comply with these Rules in order to obtain products of the required quality and be in accordance with the relevant Manufacturing Authorization and Marketing Authorization File.

Self-monitoring sheet

- Are starting materials purchased only from approved suppliers specified in the relevant specification?
- Have specification forms for starting materials been agreed with the suppliers of starting materials?
- Have all aspects of starting material production and control been agreed upon with regard to handling, labeling, packaging, rejection procedures?
- Have all aspects of claim handling been agreed between the manufacturer of medicinal products and the supplier?
- Is the integrity of the packaging and seals checked at the stage of each delivery, the compliance of the information specified in the delivery note with the supplier's labels?
- Is the correct labeling of the starting materials in the storage area checked?
- Are there appropriate procedures or measures at the manufacturing facility to assure the identity of the contents of each container of starting material?
- Are the containers, from which the samples were taken, labeled?
- Is the process of issuing starting materials regulated at the manufacturing facility?
- Is each dispensed starting material as well as its weight or volume independently checked?
- Are the check results documented?

Processing Operations: Intermediate and Bulk Products

Production operations must follow clearly defined procedures, comply with these Rules in order to obtain products of the required quality and be in accordance with the relevant Manufacturing Authorization and Marketing Authorization File.

Self-monitoring sheet

- Is there a system for monitoring the cleaning of the work area and equipment before starting any process operation?
- Are intermediate and bulk products kept under appropriate conditions?
- Have all critical processes been validated?
- Are in-process environmental controls carried out?
- Is any significant deviation from the expected yield recorded?
- Are causes of any significant deviation from the expected yield investigated?

Packaging Materials and Packaging Operations

Production operations must follow clearly defined procedures, comply with these Rules in order to obtain products of the required quality and be in accordance with the relevant Manufacturing Authorization and Marketing Authorization File.

Self-monitoring sheet

- Are packaging materials purchased only from approved suppliers specified in the relevant specification?
- Have the packaging material specification forms been agreed with suppliers?
- Have all aspects of packaging material production and control been agreed upon with regard to handling, labeling, packaging, rejection procedures?
- Have all aspects of claim handling been agreed between the manufacturer and the supplier?
- Are printed materials stored in adequately secure conditions such as to exclude unauthorized access?
- Are cut labels transported and distributed in separate closed containers so as to avoid mix-ups?
- Is there a person authorized to issue the approval for use of packaging materials at the manufacturing facility?
- Are outdated or obsolete packaging material destroyed at the manufacturing facility?
- Is the risk of cross-contamination minimized when designing scheduled packaging operations?
- Aren't different products packaged in close proximity unless there is physical segregation?
- Is there a system for monitoring the cleaning of the work area and equipment before starting packaging?
- Are the name and batch number of the product being handled displayed at each packaging station or line?
- Are all products and packaging materials to be used checked on delivery to the Packaging Department?
- Are appropriate procedures applied to ensure that no mix-ups or mislabeling can occur?
- Is control and documentary support of any printing operations provided?
- Are checks made to ensure that all electronic code readers, label counters or similar devices operate correctly?
- Are any causes of significant or unusual discrepancy observed during reconciliation of the amount of bulk product and printed packaging materials and the number of units produced recorded and investigated at the manufacturing facility?
- Are any remaining packaging materials destroyed and the destruction recorded?

Finished Products

Production operations must follow clearly defined procedures, comply with these Rules in order to obtain products of the required quality and be in accordance with the relevant Manufacturing Authorization and Marketing Authorization File.

Self-monitoring sheet

- Are finished products held in quarantine before their final release certificate is issued?
- Is the quality assessment of the finished product carried out before the final release certificate is received?
- Is the required documentation assessed in accordance with appropriate regulations before the finished product release certificate is received?
- Is there a storage area for usable finished products after the release certificate has been issued?
- Is there a separate storage area for rejected materials and products?
- Are rejected materials and products clearly marked as such?
- Is there a need for additional controls on any processed finished product or a product into which a recovered product has been incorporated?
- Are products, returned from the market and which have left the control of the manufacturer, to be destroyed?

QUALITY CONTROL (CHAPTER 6)

Quality Control is concerned with sampling, testing and checking for compliance with the requirements of specifications, instructions and other documents, organizing work, documenting and issuing release certificates. The purpose of Quality Control is to prevent the use or sale of materials or products that do not meet specified requirements. Quality Control is not confined to laboratory operations, but must be involved in all decisions which may concern the quality of the product.

Self-monitoring sheet

- Is there a Quality Control Department independent from other departments within the company?
- Are production laboratories provided with sufficient resources to ensure that all quality control activities are carried out efficiently and reliably?
- Are quality control personnel provided access to production areas for sampling and testing?
- Does the Quality Control Department have simple access to the following documentation: specifications, sampling procedures, test procedures and documents, results of monitoring of the production environment, test method validation protocols?
- Are batch records retained following the principles on retention of batch documentation?
- Have all special requirements and procedures been taken into account for sampling?
- Are other samples also taken to monitor the most stressed part of a process (e.g. beginning or end of a process)?
- Have quality control procedures been validated?
- Are the obtained test results recorded and checked to be consistent with each other?
- Are all testing operations carried out according to the methods approved by Quality Control Department?
- Has the company developed and approved instructions for the preparation and use of laboratory reagents, volumetric laboratory glassware and titrated solutions, standard samples and culture media?
- Is the correct labeling of laboratory solutions and reagents used?
- Are animals maintained and controlled in a manner that assures their suitability for the intended use?
- Are animals identified? Are adequate records maintained, showing the history of their use?
- Is the stability of the finished medicinal product tested?
- Is the stability of intermediate and bulk products tested?
- Are all the necessary parameters shown and analyzed in the on-going stability program?
- Are the results of on-going stability studies kept at the place of production for submission to the authorized federal executive body?
- Are out-of-specification cases and significant abnormal trends in quality control analyzed?
- Are there periodic reviews of the stability data?

RULES OF GOOD MANUFACTURING PRACTICE

Order of the Ministry of Industry and Trade of Russia No. 916 "On Approval of the Rules of Good Manufacturing Practice" dated June 14, 2013 (as amended on December 18, 2015)

OUTSOURCED ACTIVITIES

(CHAPTER 7)

Any activity covered by these Rules and transferred to another company for outsourcing is properly identified, agreed and monitored in order to avoid misunderstandings that may lead to unsatisfactory quality of products or operations performed.

Self-monitoring sheet

- Are the obligations of the parties clearly specified out in the contract between the customer and the contractor?
- Does the contract specify the procedure and responsibility of the person authorized to issue release certificates for each product batch?
- Has a manufacturing license for medicinal products been received when organizing the manufacturing process through another company?
- Is the company working on the formation of the Marketing Authorization File?
- Does the contract under which the outsourced activities are carried out, as well as all the proposed changes to technical or other agreements, comply with the legislation of the Russian Federation?
- Does the contract under which the outsourced activities are carried out, as well as any proposed changes to technical or other agreements, comply with the Marketing Authorization File for the relevant product?
- Can you control and audit the pharmaceutical quality system and any outsourced activities?
- Have the contractor's legal capacity (including whether it has a license required in accordance with the legislation of the Russian Federation) and its competence been checked?
- Is the contractor fully aware of all the factors associated with the products or outsourced activities that may pose a danger to its premises, personnel, equipment, starting materials or other products?
- Do you initiate and/or control the actions of the contractor regarding the necessary improvements?
- Are the actions of the contractor controlled?
- Is it considered that the agreement between the contractor and the third party must ensure that information, including the data about the third party's conformity assessment, is provided in the same way as between the original customer and the contractor?
- Is there transmission of information related to product quality assessment in the event of complaints, suspected non-conformity, or investigating in the case of a suspected falsified product?

COMPLAINS AND PRODUCT RECALLS (CHAPTER 8)

All complaints and information regarding potentially poor-quality medicinal products are thoroughly investigated in accordance with approved procedures. The manufacturer has a system of quick and effective recall from the market of products with identified or suspected quality violations.

Self-monitoring sheet

- Has a person responsible for handling complaints and making decisions been appointed at the manufacturing facility?
- Is an authorized person notified of all complaints, investigations and product recalls?
- Are there approved procedures for actions to handle complaints for potentially poor-quality medicinal products and to decide on products recall?
- Are all quality complaints recorded indicating the source data at the manufacturing facility?
- Is an inspection of similar batches carried out if a non-conformity of the quality of any batch of products with the established requirements is found or suspected?
- Is a review conducted to identify specific and recurring factors that require special attention and may lead to product recalls?
- Is there sufficient consideration in the assessment and investigations of cases where the cause of the complaint is product counterfeiting?
- Has a person in charge of production been appointed for the timely recall of products from the market?
- Are the shipping records available to the responsible person?
- Is there a developed scheme for the immediate notification of the competent authorities of all countries where the products were sent, about the decision to recall the products?
- Are recalled products labeled?
- Are recalled products stored separately in a safe area until a decision is made on its further use or destruction?