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# Sample plan of EAEU GMP inspection (excerpt)

## Objects of inspection (sections of the Rules of Good Manufacture Practice)

| **Part I. General requirements** | |
|---|---|
| **1. Pharmaceutical quality system** | ☑ |
| Quality Manual | ☑ |
| Responsibilities and duties of the management | ☑ |
| Analysis conducted by the management | ☑ |
| System of changes management | ☑ |
| Suppliers and contractors relationship management system | ☑ |
| Work with defects and non-correspondences | ☑ |
| System of corrective and preventive actions | ☑ |
| System of batch release | ☑ |
| Reviews of product quality | ☑ |
| Quality risk management system | ☑ |
| **2. Personnel** | ☑ |
| Organizational structure | ☑ |
| Key personnel | ☑ |
| Learning & trainings system | ☑ |
| Hygiene of personnel | ☑ |
| Consultants | ☑ |
| **3 Premises and Equipment** | ☑ |
| Project and qualification of premises, equipment, and engineering systems | ☑ |
| Monitoring, cleaning and maintenance | ☑ |
| Warehouse, production and supplementary areas | ☑ |
| Quality control areas | ☑ |
| **4. Documentation** | ☑ |
| Documents and records administration | ☑ |
| Documents and records storage | ☑ |
| Procedures and notes | ☑ |
| **5. Manufacturing** | ☑ |
| Prevention of crossover contamination | ☑ |
| Validation of processes and cleaning procedures | ☑ |
| Starting (raw) and packaging materials | ☑ |
| Technological process and in-process controls | ☑ |
| Packaging | ☑ |
| Manufacturing documentation and records | ☑ |
| Finished products: storage and distribution | ☑ |
| Handling of non-conforming products | ☑ |
| **6. Quality Control** | ☑ |
| Quality Control system | ☑ |
| Documentation for quality control | ☑ |
| Sampling | ☑ |
| QC testing procedures | ☑ |
| Control samples and retain samples | ☐ |
| Program of the ongoing stability studies | ☑ |

| | |
|---|---|
| Validation and transfer of QC testing methods | ☑ |
| **7. Activity transferred to other companies/persons (outsourcing)** | ☑ |
| **8. Reclamations, quality defects, and product recalls** | ☑ |
| **9. Self-inspection** | ☑ |
| **Part II. Main requirements to active pharmaceutical substances used as raw materials** | ☐ |
| **Part III. Documents related to the Rules of Good Manufacturing Practice** | |
| **Appendix No. 1** Requirements to manufacturing of sterile dosage forms | ☐ |
| **Appendix No. 2** Requirements to manufacturing of biological (including immunobiological) active pharmaceutical substances and medicinal products for human use | ☐ |
| **Appendix No. 3** Requirements to manufacturing of radiopharmaceuticals | ☐ |
| **Appendix No. 4** Requirements to manufacturing of medicinal products for veterinary use (except for immunobiological products for veterinary use) | ☐ |
| **Appendix No. 5** Requirements to manufacturing of immunobiological products for veterinary use | ☐ |
| **Appendix No. 6** Requirements to manufacturing of medicinal gases | ☐ |
| **Appendix No. 7** Requirements to manufacturing of herbal medicinal products | ☐ |
| **Appendix No. 8** Requirements to sampling of raw materials and packaging materials | ☑ |
| **Appendix No. 9** Requirements to manufacturing of liquid and semisolid dosage forms | ☑ |
| **Appendix No. 10** Requirements to manufacturing of pressurized aerosol products for inhalation with metering valves | ☐ |
| **Appendix No. 11** Requirements to computer systems | ☑ |
| **Appendix No. 12** Requirements to use of ionizing radiation for manufacture of medicinal products | ☐ |
| **Appendix No. 13** Requirements to medicinal products for clinical trials | ☐ |
| **Appendix No. 14** Requirements to medicinal products received from donated blood and plasma | ☐ |
| **Appendix No. 15** Requirements to qualification and validation | ☑ |
| **Appendix No. 16** Requirements to confirmation of the conformity of the batch for its release by qualified person | ☑ |
| **Appendix No. 17** Requirements to parametric release | ☐ |
| **Appendix No. 18 (19)** Requirements to control samples and retain samples | ☑ |

**Inspection Schedule**

| Time | Inspection Stage and Scope | Inspector's Name |
|---|---|---|
| | **Day 1** | |
| 09.00 – 18.00 | **Presentation of the Enterprise (optionally).**<br>**Enterprise's documentation verification:**<br>1.1. Valid license and GMP Certificate.<br>1.2. Valid version of the Site Master File.<br>1.3. Validation Master Plan of the enterprise. List of planned validation and qualification activities for 2019 and 2020 with their accomplishment status indicated.<br>1.4. Reviews of qualification status of clean rooms, equipment, and engineering systems; reviews of validation status of | |

| Time | Inspection Stage and Scope | Inspector's Name |
|---|---|---|
| | processes, equipment cleaning methods and analytical procedures related to the production of medicinal products declared for inspection.<br>1.5. Review of the current status of production of the medicinal products declared for inspection, including the following information: name of a medicinal product, production stages , production facilities being used, main production equipment with its type, name, and model indicated.<br>1.6. Detailed layouts of production facilities being used for the manufacture of medicinal products declared for inspection, with personnel, starting and raw materials flows, differential pressure and cleanliness classes (high resolution diagrams).<br>1.7. Documents confirming the implementation of CAPA for elimination of non-conformities identified as a result of the previous inspection carried out during the period from ___ to ___ (Inspection Report No. ____). | |
| | **Verification of the Pharmaceutical Quality System documents**<br>1.8. Pharmaceutical Quality System analysis procedure. Pharmaceutical Quality System assessment report for 2019.<br>1.9. Presentation on documents management: documents development, introduction, distribution, storage, withdrawal from circulation, and update. Document management procedures.<br>1.10. Change control procedure. List of major changes in respect of the medicinal products declared for inspection for 2019-2020. Example of change review and assessment (at the discretion of the panel of inspectors).<br>1.11. Deviations, Corrective Action and Preventive Action (CAPA) Management procedure. List of major and critical deviations relating to the medicinal products declared for inspection for 2019-2020. Trend analysis on the recurrent deviations. Example of an investigation of deviation and implementation of CAPA (at the discretion of the panel of inspectors).<br>1.12. Finished product release procedure. List of the Authorized Persons of the enterprise.<br>1.13. Complaint management procedure. List of complaints relating to the medicinal products declared for inspection for 2019-2020. Example of a complaint investigation and CAPA implementation (at the discretion of the panel of inspectors).<br>1.14. Product recall procedure. Review of medicinal product recalls (if any) for 2019-2020. In case of actual recalls, records on carrying out of a mock recall. | |
| | 1.15. Risk management procedure. Risk analysis reviews performed/updated at the site since the previous inspection. | |

| Time | Inspection Stage and Scope | Inspector's Name |
|---|---|---|
| | 1.16. Risk analysis and cross-contamination prevention policy. Procedure for verification of the cross-contamination prevention activities implementation and efficiency.<br>*1.17.* Product quality review preparation procedure. Quality reviews for the following medicinal products: *product 1 ; product 2*<br>1.18. Presentation describing the supplier selection and periodical assessment process; audit frequency carrying out. Procedures describing the supplier selection and qualification and audit carrying out.<br>1.19. Updated version of the list of approved suppliers of starting and packing materials used for the manufacture of medicinal products declared for inspection; list of approved suppliers of GxP services.<br>1.20. Plans of audits of suppliers for 2019-2020 with their execution indicated.<br>1.21. Reports on audit of the supplier of *product's 1* pharmaceutical substance (front page, audit participants, information on the inspected object, conclusions based on the audit findings).<br>1.22. Report of periodic audit report of the company performing the preparation of workwear intended for operation in cleanrooms (front page, audit participants, information on the inspected object, conclusions based on the audit findings).<br>1.23. Self-inspection (internal audit) procedure. Schedule of self-inspections for 2020. Schedule of self-inspections for 2019 and documents confirming the implementation of the planned self-inspections. Recent self-inspection report of the quality assurance department. | |
| **Day 2** | | |
| 09.00 – 18.00 | **Video recordings review. The records may be presented on-line or in the form of reference links to the respective video files:**<br>- Warehouses review, including sampling room;<br>- Clean rooms for the manufacture of the medicinal products declared for inspection; personnel and material airlocks;<br>- Major technological stages of production of the medicinal products declared for inspection;<br>- Major equipment used for the manufacture of medicinal products declared for inspection;<br>- Quality control laboratory premises. | |
| | **Verification of warehouse management documents:**<br>2.1. Detailed layouts of warehouses, raw/other materials sampling rooms with an indication of their cleanliness classes (high-resolution diagrams). | |

| Time | Inspection Stage and Scope | Inspector's Name |
|---|---|---|
| | 2.2. Procedure for receipt and storage of starting/other materials. Records on the receipt of the latest deliveries of *product 1 and product 2* drug substances.<br>2.3. Procedure for the starting/other material statuses management in the warehouse. Exact computerized system data on movement and status changes of the latest deliveries of *product 1 and product 2* drug substances.<br>2.4. Starting and other materials sampling procedure. Sampling plans. Sampling records relating to the latest deliveries of *product 1 and product 2* drug substances.<br>2.5. Sampling rooms cleaning/disinfection procedure. Copies of records on cleaning/disinfection of rooms before and after the sampling of records before and after sampling of the latest deliveries of the latest deliveries of *product 1 and product 2* drug substances.<br>2.6. Procedure of monitoring of climatic parameters in the storage premises and areas. Warehouse climatic parameters control records for August, 2020.<br>2.7. Recent warehouse temperature mapping protocol and report for the summer period. | |
| | **Review of documents on engineering systems and production environment monitoring:**<br>2.8. Maintenance procedure for the cleanrooms air preparation systems (HVAC). HVAC system filters control and change records for 2020.<br>2.9. Reports on the recent qualification of HVAC system for the D class cleanrooms used from the production of medicinal products declared for inspection.<br>2.10. Cleanroom microbiological monitoring procedure, microbial and particle count requirements applicable to the production and packaging rooms and starting material sampling areas. Report on the results of monitoring of the production environment for the last inspection period with trend analysis.<br>2.11. Purified water production, storage and distribution system flow diagram with the parameter control sensors indicated.<br>2.12. Purified water production, storage and distribution system sanitization procedure. Two recent sanitizations records.<br>2.13. Purified water physicochemical and microbiological parameters monitoring procedure. Reports on the monitoring results for the last inspection period with trend analysis.<br>2.14. Compressed air quality control procedures. Reports of the compressed air quality monitoring for the last inspection period. | |
| **Day 3** | | |
| 09.00 – 18.00 | **Production documents review:** | |

| Time | Inspection Stage and Scope | Inspector's Name |
|---|---|---|
| | 3.1. Batch formulas for the medicinal products declared for inspection. Production and packaging process flow diagrams with the critical process parameters and in-process controls indicated.<br>3.2. Possibility of reworking and reprocessing in relation to the medicinal products declared for inspection.<br>3.3. Production, packaging and quality control records on the latest manufactured and packaged batches of *product 1 and product 2*.<br>3.4. Packaging residues with printed variable information and rejected products handling procedures.<br>3.5. Production equipment cleaning procedure: mixer and filling line used for the manufacture of *product 2*. | |
| | **Validation documents consideration:**<br>3.6. Equipment qualification procedure. Report on qualification of the mixer being used for the manufacture of *product 2*<br>3.7. Process validation procedure. *Product 1 and product 3* manufacture and packaging processes validation reports.<br>3.8. An overview of the maximum allowable hold time for the intermediate and unpackaged products at different stages of the production process for all medicinal products declared for inspection. Reports on validation of the maximum allowable hold time for the intermediate and bulk products (at the discretion of the panel of inspectors). Assessment of the impact of long-term storage of bulk products up to the stage of primary packaging on the stability of finished products of medicinal products declared for inspection.<br>3.9. Validation of the equipment cleaning procedure. Cleaning validation approach. Worst case conditions selection (if applicable). Equipment cleaning, Cleaned Equipment Hold Time (CEHT), Dirty Equipment Hold (DEHT) validation reports: mixer and filling line used for the manufacture of *product 2*<br>3.10. Register of computerized systems being used at the enterprise with their validation status indicated. Computerized system validation report (at the discretion of the panel of inspectors). | |
| | **Quality control documents consideration:**<br>3.11. Internal analytical control specifications for starting and raw materials, intermediate and finished products for *product 1 and product 4*<br>3.12. Media growth promotion properties control procedure. Growth promotion test records for 2 batches of media used for the control of absence of *Escherichia coli* in finished products.<br>3.13. OOS investigation procedure. List of OOS's for the medicinal products declared for inspection for 2019-2020. Trend analysis for the cases of recurrent OOSs Example of | |

| Time | Inspection Stage and Scope | Inspector's Name |
|---|---|---|
| | OOS investigation (at the discretion of the panel of inspectors).<br>3.14. Post-approval stability study programs and reports for the shelf-life period of *product 1 and product 4.*<br>3.15. Validation reports of assay and related substances determination methods used for quality control of *product 2*.<br>3.16. Documents confirming the control of active substance and *product 1 f*or the absence of _____ impurity. | |
| **Day 4** | | |
| 09.00 – 10.00 | **Personnel management documents consideration:**<br>4.1. Personnel training procedure. Quality control department's chemist training procedure for 2020 with the completion status indicated.<br>4.2. Requirements to the workwear used in the cleanrooms. Types of workwear. Quality agreement concluded with the company performing the preparation of workwear.<br>4.3. Personnel gowning procedure. Production area enter and exit procedures. Personnel hygiene. | |
| 10.00 – 13.00 | **Videoconferencing with the representatives of the manufacturer.**<br>Discussion of open issues from the previous days of the inspection. | |
| 13.00 – 14.00 | **Lunch Break** | |
| 14.00 – 17.00 | **Verification of additional documentation requested in the course of inspection.**<br>Information concerning the possibility of labelling of products intended for the market of the Russian Federation with control and identification marks (serialization). Availability and type of the respective equipment and software, format code. System validation status and its connectivity to the information system of the Russian Federation. | |
| 17.00 – 18.00 | **Internal conference of the panel of inspectors on the inspection findings.** | |

**7.** The Inspection Schedule may be changed at the discretion of the inspectors according to the on-site circumstances.