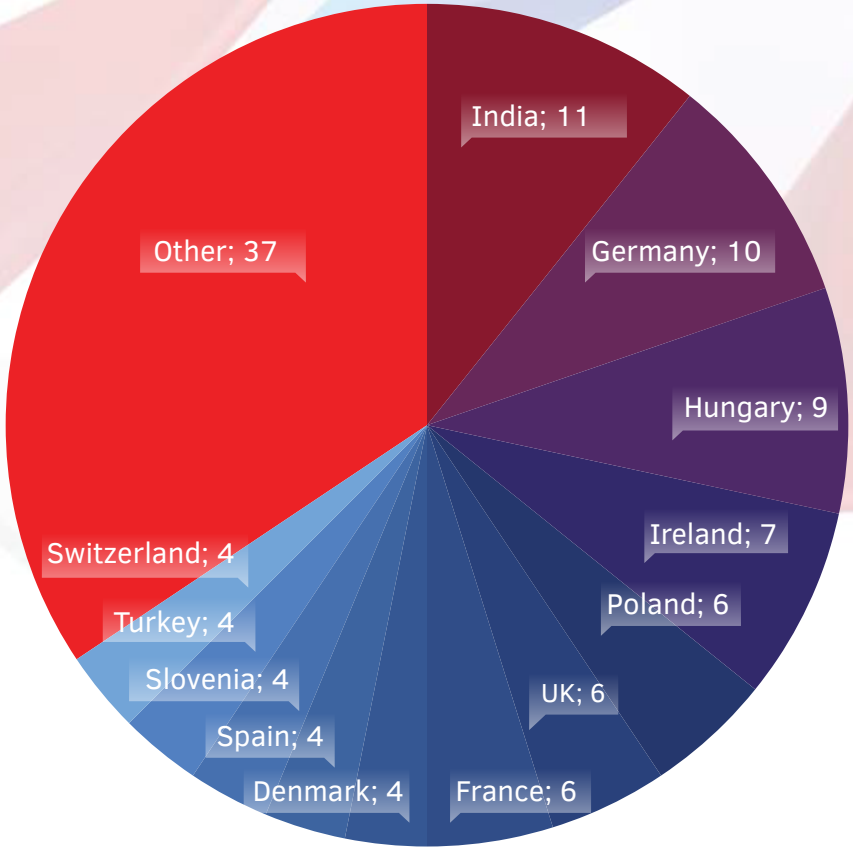
MINISTRY OF INDUSTRY AND TRADE OF THE RUSSIAN FEDERATION

Comments on manufacturers' questions of present interest

Federal State Institution
“State Institute of Drugs and Good Practices”
(FSI “SID & GP”)

Follow-up inspection

Preliminary expectations : 112 companies (from 38 countries) may submit an application for issuing of the certificate by the end of 2018.



GOVERNMENT OF THE RUSSIAN FEDERATION
DECISION dated December, 3 2015 г. No. 1314

…"inspection" means the activities of the Ministry of Industry and Trade of the Russian Federation (with respect to medicinal products for medical use) and the Federal Service for Veterinary and Phytosanitary Supervision (for medicinal products for veterinary use) (hereinafter referred to as authorized bodies) or the federal state institution, subordinated to the authorized body (hereinafter referred to as an authorized institution), aimed at confirming the compliance of the manufacturer of medicinal products with the rules of good manufacturing practice …

…19. The inspection of foreign manufacturers is carried out by an authorized institution …

Follow-up inspection

Decision Matrix

Inspection

All non-conformities found during the previous inspection should be closed, CAPA fulfilled.

If not, the status of the non-conformity increases.

Reduction of the time from the moment of filing an application to the issuance of a Certificate

At the moment, the average time for inspecting the site / processing the report from the date of the decision in the MI&T of Russia is

110-112

working days.

In January 2018, it was decided that the institute together with the report prepares and submits a draft of the certificate to the Ministry of Industry and Trade of the Russian Federation. The draft of the certificate is prepared by the examination department in the event that the report indicates that the results of the inspection allow the manufacturer to be assessed for compliance with the requirements of the Rules of Good Manufacturing Practice.

The possibility of considering CAPA as an inspection phase

The decision to conduct inspections is taken by the Ministry of Industry and Trade of the Russian Federation

Decision of the Government of the Russian Federation of 03.12.2015 No. 1314 "On determining the compliance of the manufacturers of medicines with the requirements of the rules of good manufacturing practice"

- It is not considered to assess CAPA during forming of the report after conducted inspection.
- It is provided by the rules that it may be possible for the manufacturing site to submit additional materials which for reasons beyond control were not provided during inspection: http://gilsinp.ru/?news=informatsiya-o-ponyatii-dopolnitenye-materialy-posle-provedeniya-inspektirovaniya-inostrannogo-proizvoditelya

Decision of 03.11.2016 No. 83 “On the Approval of the Rules of Pharmaceutical Inspection Conduction”

- It is considered to assess the CAPA-materials.

Emphasis on preparing manufacturers for inspection

Generally, more time is required for riddance of the findings, than the period of the follow-up inspection. For instance, in the absence of equipment, lack of validation / transfer of the process or analytical techniques.

PRE-INSPECTION preparation to inspection: analysis of the "real" situation at the time of inspection - the availability of equipment, premises and relevant documentation for the declared stages of production of medicines (List - Form 3).

Please note, that after an Agreement for carrying out the inspection and the Inspection Plan are signed, changes to the List are not allowed.

Decision on issuing of the Certificate

Weekly data is updated on the official web-site of the Ministry of Industry and Trade of the Russian Federation

http://minpromtorg.gov.ru/docs/list/

Lists register

(tag page «Lists register» - «Register of GMP Certificates»)

In case of extension of the List of medicinal products produced on the site

Analysis of submitted documents (internal procedure), for assessing the risks for the quality of medicinal products in the production of the extended List:

- co-production on the same production lines, equipment, in the same premises, using the same flows and engineering systems;
- risks of cross-contamination.

In the case of a follow-up inspection, they try to organize it as soon as possible.

Categorization of the findings

Each inspection is individual:

special characteristics of manufactured medicinal products;

technology features,

particular qualities of the organization of production and the Pharmaceutical Quality System in general, etc.

non-conformance that refer to the same paragraph of the GMP Rules, depending on the above features, may carry a different level of risk of impact on product quality, and therefore, a different categorization.
For example, different rates of contamination risks in the case of the production of "sterile" and "non-sterile" products.

Categories of non-conformance (Order of Minpromtorg of Russia of 04.02.2016 No. 261)

Critical non-conformance –

violation (non-conformance) of the requirements of the Rules of Good Manufacturing Practice or the requirements of the registration dossier for a medicinal product for medical use, which led or may lead to the production of a poor-quality medicinal product for medical use,

which caused or may cause harm to human health or life.

Categories of non-conformance (Order of Minpromtorg of Russia of 04.02.2016 No. 261)

Major non-conformity–

· violation (non-conformity) of the requirements of the Rules of Good Manufacturing Practice, which **led or may lead to the production of a poor-quality medicinal product for medical use,**

which can not cause harm to human health or life,

or violation (non-conformity) of the requirements of the registration dossier for a medicinal product for medical use,

or a set of several other violations (non-conformities), none of which can not be classified as major, but which together constitute a major violation (non-conformity) and should be construed as a major violation (non-conformity).

Categories of non-conformance (Order of Minpromtorg of Russia of 04.02.2016 No. 261)

Other non-conformities

- *violations (non-conformities) of the requirements of the Rules of Good Manufacturing Practice*, which are not referred to either critical or major violations

Status of availability to conduct inspections on compliance with EAEU rules

MI&T of Russia has been given appropriate powers since October 2017. To start the inspection for compliance with the requirements of the EAEU Rules FSI "SID & GP" needs a legislative act.

FSI "SID & GP" is working to prepare for the implementation of this activity. Internal procedures have been developed, staff training has been conducted, interaction with colleagues from the EAEU countries has been established.

Within the framework of the WHO educational program, for the first time on the basis of the FSI "SID & GP", training was conducted for the participants on the part of the regulatory bodies of the EAEU countries (Russia, Armenia, Kazakhstan, Kyrgyzstan) on the organization of inspection for compliance with GMP rules.

Legislation in the framework of EAEU

1. Rules of Good Manufacturing Practice EAEU (Decision Eurasian Economic Commission Council No. 78 dated November 3, 2016)	Requirements for manufacturing of medicinal products
2. Rules of Good Distribution Practice EAEU (Decision Eurasian Economic Commission Council No. 80 dated November 3, 2016)	Requirements for distribution of medicinal products
3. On approval of the inspection results for the production of medicinal products (Decision Eurasian Economic Commission Council No. 93 dated November 3, 2016)	Considerations of recognition of national inspections carried out for the national market
4. On mechanism of accreditation of authorized persons of manufacturers of medicinal products (Decision Eurasian Economic Commission Council No. 73 dated November 3, 2016)	Issues of confirmation of the competence of authorized persons
5. Rules of Pharmaceutical Inspection Conduction (Decision Eurasian Economic Commission Council No. 83 dated November 3, 2016)	Regulation of the inspection process, the documenting of inspections
6. Procedure for ensuring the conduction of joint pharmaceutical inspections (Decision Eurasian Economic Commission Council No. 91 dated November 3, 2016)	Regulation of joint and unscheduled inspections within the Union
7. General requirements for the quality system for pharmaceutical inspectorates of member-states EAEU (Decision Eurasian Economic Commission Council No. 82 dated November 3, 2016)	Regulating procedural issues related to inspection

Mutual recognition of GMP certificates

Federal Law No. 61 - FZ “On circulation of the medicines” dated 12.04.2010.

Decision of the Eurasian Economic Commission Council No. 93 “On approval of the inspection results for the production of medicinal product” dated 03.11.2016

GMP certificate	National level, mutual recognition	Supranational level (EAEU), mutual recognition
National certificate Non-EAEU resident	**Non valid**	**Non valid**
National certificate EAEU resident	Valid through 31.12.2020	Valid through 31.12.2018
Certificate of compliance with EAEU rules Non-EAEU resident	**Non valid**	Valid
Certificate of compliance with EAEU rules EAEU resident	Valid through 31.12.2020	Valid

Thank you for your attention!

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