ANNEX

to Recommendation No.
of the Eurasian Economic Commission's Board
dated , 20

GUIDELINES
for filling in the certificate of manufacture conformity to the Eurasian Economic Union's Good Manufacturing Practice

I. Definitions

For the purposes hereof, the concepts having the following meanings shall be used:

“Biological medicinal products” means medicinal products the active substance of which is produced by or extracted from a biological source and that need for their characterization and the determination of their quality a combination of physicochemical-biological testing;

“biotechnology medicinal product” means a medicinal product developed by means of biotechnological processes and methods using recombinant DNA technology, controlled expression of genes coding for biologically active proteins, hybridoma technologies, monoclonal antibodies or other biotechnological processes;

“secondary packing” includes processing operations for packing a medicine contained in primary packaging into secondary (consumer) packaging. This also includes labeling operations or the assembly of other components (pack);

“batch certification” refers to the certification of a finished product batch of medicinal product by a Qualified Person at an authorized manufacturing site before it is released into the internal market or before the product is exported;

“quality control” means a type of laboratory testing for which the manufacturing site is inspected;

“bulk products” means any products which have completed all processing steps, up to but not including, primary and secondary (consumer) packaging or secondary (consumer) packaging;

“primary packing” means processing operations for the primary packing of the finished product. Primary packaging is in direct contact with the medicinal product. Primary packing of sterile medicinal products is part of the finished product manufacturing and shall not be considered separately;

“processing operations” means any or all processing steps in the manufacture of a finished dosage form (medicine) (finished dosage form manufacturing, primary packing, secondary packing, quality control, batch certification, etc.);

“intermediate products” means partly processed raw material that must undergo further processing steps before it becomes a bulk product. For active substances, this means a material produced during steps of the processing of an active substance that undergoes further molecular change or purification before it becomes an active substance. Intermediate products for active substances may or may not be isolated during processing;

“certificate of manufacture conformity to the Eurasian Economic Union's Good Manufacturing Practice” means a document issued by the authorized authority of a Eurasian Economic Union Member State based on the results of pharmaceutical inspections of medicines manufacture for conformity to the Eurasian Economic Union's Good Manufacturing Practice;

“product type” means a type of the active substance and the medicinal product containing it which is determined solely by the sources of the main structural component of the molecule of the active substance (raw material) and its manufacturing methods. The product type of the active substance does not depend on (or change depending on) the step of the processing of the active substance which is performed by the site;

“storage” means any manufacturing site which carries out processing operations or packaging of medicines and has been assessed for conformity to the Eurasian Economic Union's Good Manufacturing Practice in relation to the organization and implementation of the storage process.

The “somatic cell therapy medicinal product” concept is used in the meaning determined by the Rules for Marketing Authorization and Expert Examination of Medicinal Products for Human Use approved by Decision No. 78 of the Eurasian Economic Commission's Council dated November 3, 2016.

II. Guidelines for filling in the certificate form

1. The certificate of manufacture conformity to the Eurasian Economic Union's Good Manufacturing Practice (hereinafter the “certificate”) shall be filled in using electronic printing devices in Russian and, where an appropriate requirement is envisaged in the legislation of the Eurasian Economic Union Member States (hereinafter the “Union” and the “Member States”), in the official language of the Member State in which the issuing authorized authority is located. Where the certificates are to be issued in Russian and the official language of a Member State, these shall be completed using two-sided templates where each side corresponds to the appropriate language.

2. The certificate is a document of strict accountability; the form shall be printed and have security measures in accordance with the relevant Member State legislation.

3. The Form Reference Number field shall specify the number of the accountable form in the accounting system of the Member State.

4. The Certificate Reference Number field shall specify the certificate number generated in the following order:

No. GMP/EAEU/ZZ/XXXXXX-20YY, where:

“GMP” is the relevance of the certificate to the scope of the Good Manufacturing Practice (GMP). This position is followed by a slash, “/”;

“EAEU” is the territory where the certificate is valid – the Eurasian Economic Union (EAEU). This position is followed by a slash, “/”;

“ZZ” is the two-letter country code of the Member State (in accordance with the ISO 3166-1-2013 standard “Codes for the representation of names of countries and their subdivisions — Part 1: Country codes”): Republic of Armenia, AM; Republic of Belarus, BY; Republic of Kazakhstan, KZ; Kyrgyz Republic, KG; Russian Federation, RU.

“No. (XXXXXX)” is a single six-digit serial number of the certificate assigned by the authorized authority of the Member State that conducted the pharmaceutical inspection (from the database on pharmaceutical inspections);

“20YY” is the year of issue of the certificate.

5. The Valid from __ to __* field shall specify the last day of the last inspection plus the period established on the basis of risk analysis results but not more than three years (e.g. certificate valid from July 1, 2022 to June 30, 2025).

6. The field “Full and Abbreviated Names of the Authorized Authority” shall specify in Russian the full name of the authorized authority of the Member State that issued the certificate. Where an appropriate requirement is

envisaged in the legislation of a Member State, the information shall be specified in the official language of the Member State in which the issuing authorized authority is located.

7. The field Full Name of the Manufacturer shall specify the full name of the manufacturer in Russian for manufacturing sites located on the customs territory of the Union. Where an appropriate requirement is envisaged in the legislation of the Member States, the information shall be specified in the official language of the Member State in which the issuing authorized authority is located.

For manufacturing sites located on the territory of third countries, the field shall specify the name of the manufacturer, the address of the manufacturing site and the name of the manufacturing site from its constituent documents (their certified translations into English) using letters of the Latin alphabet and diacritics.

8. The field “Manufacturing Site Address” on the first page of the certificate shall specify in Russian the full address of the place of manufacturing in accordance with the address specified in the special medicines manufacturing authorization (license).

Where an appropriate requirement is envisaged in the legislation of the Member States, the information shall be specified in the official language of the Member State in which the issuing authorized authority is located.

If necessary, the name of the manufacturer, the address of the manufacturing site and the name of the manufacturing site shall be specified (duplicated) using letters of the Latin alphabet.

9. In the subsection of the certificate “Based on (please specify one of the following)”, one of the following should be selected with specification of the following information:

a) the field “Application No. ___ for a medicines manufacturing authorization (license)” shall specify the numerical designation, the reference number of the application;

b) the field “plan for conducting pharmaceutical inspections of the holder of Medicines Manufacturing Authorization (License) No. _____” shall specify the number and approval date of the plan for pharmaceutical inspections of the inspecting pharmaceutical inspectorate;

c) the field “Application No. _____ for the registration of medicines” shall specify the reference number and the date of submission of the application for the registration of medicines to the authorized authority;

d) the field “another basis” shall specify the grounds not listed in subparagraphs a) – c).

For example, at the request of the authorized authority (Expert Committee for Medicinal Products), the date and number of the request, as well as the date and number of the application shall be specified.

10. The field “From the knowledge gained during the pharmaceutical inspection, the latest of which was conducted on _____” shall specify the date or period of the inspection “from ___ to ___” (e.g. from December 10, 2022 to December 12, 2022; or several dates separated by commas).

11. The field “The authenticity (veracity) of this Certificate may be checked in the database of (name of the authorized authority)” shall specify the full name of the Member State's authorized authority and the path to the database (e.g. in the database of “the Ministry of Health of the Republic of Belarus at: http://minzdrav.gov.by/dlya-spetsialistov/lekarstvennaya-politika/index.php”). The path to the database on pharmaceutical inspections should be specified in the following format: “Commission's Website → Technical Regulation and Accreditation Department → Establishment of a

Common Market of Medicines and Medical Products → Medicines → Common Registers and Information Databases → Database on Pharmaceutical Inspections". The national register shall be specified before the database on pharmaceutical inspections.

III. Guidelines for filling in the additional sheet of the certificate

The additional sheet of the certificate shall include only the headings (sections with one-, two- and three-level numbering) and subheadings (subsections with four-level numbering) of manufacturing activities in respect of which the site's activities are assessed and inspected.

The field below shall specify the type of medicines inspected:

☐ Human medicinal products

☐ Human investigational medicinal products

Section 1. "MANUFACTURING OPERATIONS – MEDICINAL PRODUCTS"

1.1. Sterile products

In Section 1.1.1 "Aseptically prepared (processing operations for the following dosage forms)", the type of sterile medicinal products for which inspection was completed shall be specified by selecting the relevant subsection:

1.1.1.1. Large volume liquids;

1.1.1.2. Small volume liquids;

1.1.1.3. Lyophilizates;

1.1.1.4. Solids and implants;

1.1.1.5. Semi-solids;

1.1.1.6. Other aseptically prepared products _____ (please specify).

Subsection 1.1.1.6 shall specify, among other things, cases where sterile intermediates are prepared aseptically.

Subsection 1.1.2 “Terminally sterilized (processing operations for the following dosage forms):” shall specify the sterile medicinal products for which inspection was completed.

Where terminal sterilization of products is not carried out by the inspected manufacturing site but is contracted out to another manufacturing site, a comment such as “terminal sterilization by gamma irradiation is outsourced to another manufacturing site” should be added in relation to that finished dosage form in the section “Any restrictions or clarifying remarks related to the scope of this certificate” (hereinafter the “Restrictions section”) (after Section 4).

In Section 1.1.2 “Terminally sterilized (processing operations for the following dosage forms)”, the type of terminally sterilized medicinal products for which inspection was completed shall be specified by selecting the relevant subsection:

1.1.2.1. Large volume liquids;

1.1.2.2. Small volume liquids;

1.1.2.3. Solids and implants;

1.1.2.4. Semi-solids;

1.1.2.5. Other terminally sterilized prepared products _____ (please specify) (if necessary, a note shall be added regarding a separate site carrying out terminal sterilization).

For these types of products, the Restrictions section shall provide clarifying remarks regarding a separate site carrying out terminal sterilization.

For example, if a site manufactures non-sterile products, contracts out their sterilization to another site and subsequently carries out batch

certification of sterile products, the completed certificate sheet shall be as follows:

1. MANUFACTURING OPERATIONS — MEDICINAL PRODUCTS	
1.1	Sterile products
	1.1.3. Batch certification
1.2	Non-sterile products
	1.2.1. Non-sterile products (processing operations for the following dosage forms):
	1.2.1.15. Other non-sterile medicinal product: *implant which is an intermediate product terminally sterilized at another site*
1.5	Packaging
	1.5.1. Primary packing:
	1.5.1.15. Other non-sterile medicinal product: *implant which is an intermediate terminally sterilized at another site*
	1.5.2. Secondary packing
Any restrictions or clarifying remarks related to the scope of this certificate: "*Sterilization is carried out at another address: <please specify the site's address>*"	

Section 1.1.2.5 "Other terminally sterilized prepared products" shall specify the type of finished products if terminal sterilization is carried out for a product that does not fit into the previously named categories (e.g. a medicated sponge, a film).

This field shall also specify cases where terminally sterilized sterile intermediates are manufactured (the type of intermediate should be specified, e.g. a solution for further processing).

Section 1.1.3 "Batch certification" shall specify the type of finished products for which batch certification is carried out by a Qualified Person at the inspected manufacturing site. This shall apply to all sterile dosage forms.

Section 1.2 “Non-sterile products” shall specify non-sterile medicinal products for which processing operations are carried out at the certified site. The information shall be specified by selecting the relevant subsection:

1.2.1.1. Capsules, hard shell;

1.2.1.2. Capsules, soft shell;

1.2.1.3. Chewing gums;

1.2.1.4. Impregnated matrices;

1.2.1.5. Liquids for external use;

1.2.1.6. Liquids for internal use;

1.2.1.7. Medicinal gases;

1.2.1.8. Other solid dosage forms;

1.2.1.9. Pressurized preparations;

1.2.1.10. Radionuclide generators;

1.2.1.11. Semi-solids;

1.2.1.12. Suppositories;

1.2.1.13. Tablets;

1.2.1.14. Transdermal patches;

1.2.1.15. Other non-sterile medicinal product _____ (please specify).

Subsection 1.2.1.9 “Pressurized preparations” shall specify medicinal products pressurized by a propellant in sealed packaging.

In this section, after the name of the item being completed, the name of the dosage form may be specified in accordance with the Nomenclature of Dosage Forms approved by Decision No. 172 of the Commission's Board dated December 22, 2015, and may be separated from the name of the item by a colon. For example: “*1.2.1.11. Semi-solids: ointment, cream, gel.”*

Entries shall be made under Subsection 1.2.1.15 “Other non-sterile products”, particularly if:

intermediates are manufactured – the type of intermediate should be specified (e.g. powders for further processing);

the assessed type of product does not fit into the previously named categories – for example, an intrauterine delivery system.

Section 1.2.2 “Batch certification” shall specify the type of released products for which batch certification is carried out by a Qualified Person at the inspected manufacturing site. This shall apply to all non-sterile dosage forms.

Section 1.3 “Biological medicinal products” shall specify the type of biological medicinal products in accordance with the subgroups specified in this section.

At the same time, Section 1.1 or 1.2 should be completed to reflect the type of product (sterile, non-sterile) and the finished dosage form if the finished dosage form or intermediate is manufactured.

Section 1.3.1. “Biological medicinal products”

The type of product shall be specified by selecting the relevant subsection:

1.3.1.1. Blood products;

1.3.1.2. Immunological products;

1.3.1.3. Cell therapy products;

1.3.1.4. Gene therapy products;

1.3.1.5. Biotechnology products;

1.3.1.6. Human or animal extracted products;

1.3.1.7. Tissue engineered products;

1.3.1.8. Other biological medicinal products _____ (please specify).

If the inspected manufacturing site is carrying out any processing steps relating to the manufacture of a biological medicinal product, the decision to

include a biological medicinal product in one or another section of the additional sheet of the certificate shall be made subject to two conditions:

if the manufacture of the biological substance may be part of the continuum of processing steps in the manufacture of the finished biological product, these operations should be captured under Section 1.3.1, where appropriate;

If the authorized authority does not consider the processing steps to be partial manufacture of a biological medicinal product, then the activities should be recorded in Sections 3 and 4 of the certificate which relate to manufacturing operations for active substances.

Where the certified operations also include manufacture of the finished dosage form for the biological medicinal product, the relevant finished dosage form should also be selected on the certificate (e.g. “1.1.1.3 Lyophilizates”).

Subsection 1.3.1.1 “Blood products”: This subsection shall be completed where there are processing operations performed in relation to biological products containing an active substance isolated from blood. Examples of such products include albumin, plasma factor VIII or immunoglobulins which are isolated from blood.

Subsection 1.3.1.2 “Immunological products”: This subsection shall be completed where there are processing operations carried out in relation to manufacture of biological medicinal products which have an immunological mode of action (e.g. vaccines, allergens, anatoxins, toxins, sera, bacteriophages).

Subsection 1.3.1.3 “Cell therapy products”: This subsection shall be completed where there are processing operations carried out in relation to the manufacture of cell therapy products.

Subsection 1.3.1.4 “Gene therapy products”: This subsection shall be completed where there are processing operations carried out in relation to the

manufacture of products the active substance of which contains or consists of a recombinant nucleic acid with a view to regulating, repairing, replacing, adding or deleting a genetic sequence.

Subsection 1.3.1.5 “Biotechnology products”: This subsection shall be completed where there are processing operations carried out in relation to the manufacture of biological medicinal products using biotechnology.

Subsection 1.3.1.6 “Human organ (tissue) or animal extracted products”: This subsection shall be completed where there are processing operations carried out in relation to the manufacture of a biological medicinal product containing active substances derived from human or animal sources (cells, tissues, fluids), with specification of the source in the Restrictions section (except for human blood, cells or tissues in which case the products should be more appropriately categorized as “Blood products”, "Cell therapy products” or “Tissue engineered products”).

Subsection 1.3.1.7 “Tissue engineered products”: This subsection shall be completed where there are processing operations carried out in relation to the manufacture of tissue engineered products.

Subsection 1.3.1.8 Other biological medicinal products. This subsection shall be completed where there are processing operations carried out in relation to manufacture of a biological medicinal product which includes a biological active substance which cannot be provided in Section 1.3.1.7 of the additional sheet of the certificate.

This subsection shall also be completed for the manufacture of intermediates (e.g. a biological intermediate for further processing).

Section 1.3.2 “Batch certification”

This section shall be completed if batch certification is carried out for finished products by a Qualified Person at the inspected manufacturing site.

This shall apply to all dosage forms of biological medicinal products. Sections 1.1.3 or 1.2.2 of the certificate should also be completed in accordance with inspected products to reflect the type of finished dosage form being certified. The information shall be specified by selecting the relevant subsection:

1.3.2.1. Blood products;

1.3.2.2. Immunological products;

1.3.2.3. Cell therapy products;

1.3.2.4. Gene therapy products;

1.3.2.5. Biotechnology products;

1.3.2.6 Human or animal extracted products;

1.3.2.7 Tissue engineered products;

1.3.2.8. Other biological medicinal products _____ (please specify);

1.3.2.8. Other biological medicinal products _____ (please specify).

Section 1.4 “Other products or manufacturing activity”

This section shall specify inspected medicinal products that do not fall under Sections 1.1 – 1.3 of the additional sheet of the certificate.

Section 1.4.1 “Manufacture of”

The type of product shall be specified by selecting the relevant subsection:

1.4.1.1. Herbal products;

1.4.1.2. Homeopathic products;

1.4.1.3. Other products _____ (please specify).

Subsection 1.4.1.1 shall determine the type of product and specify the nature of production processes and sources of a particular active substance, which is necessary to identify the inherent potential risks affecting the quality

and safety of the medicinal product, as well as the risks of contamination of other medicines manufactured at this production line.

The type of products shall be determined in accordance with Table 1 in Chapter 9 of the Eurasian Economic Union's Good Manufacturing Practice approved by Decision No. 77 of the Eurasian Economic Commission's Council dated November 3, 2016:

active substances derived from herbal raw materials;

herbal extracts used as active substances;

active substances consisting of comminuted or powdered herbs.

Where a manufacturer carries out processing steps in relation to manufacture of the herbal or homeopathic dosage form of medicinal products (e.g. tablets), sections relevant to these dosage forms (Sections 1.1 to 1.2, 1.5.1) should be completed in addition to items in Section 1.4.

Where the facility is only certified for manufacture of herbal or homeopathic medicinal products, a clarifying remark (e.g. herbal products only or homeopathic products only) should be included in relation to the dosage forms.

Subsection 1.4.1.3 shall specify other inspected types of products: intermediates, cytostatic medicines, cytotoxic medicines, hormones, beta-lactam antibiotics, highly potent products, narcotic medicines, mind-altering medicines and other groups of medicinal products.

Sections relevant to these dosage forms (Sections 1.1 to 1.2, 1.5.1) shall also be completed in addition to items in Section 1.4.

Section 1.4.2. Sterilization of active substances/ excipients/finished product:

This section shall specify the information where these sterilization activities are not carried out as part of the manufacture of a dosage form at the

inspected site or as a processing step in the manufacture of a finished dosage form (e.g. where the certificate holder is a contract sterilization facility performing gamma irradiation of products on behalf of other manufacturers). The information shall be specified by selecting the relevant subsection:

1.4.2.1. Filtration;

1.4.2.2. Dry heat;

1.4.2.3. Moist heat;

1.4.2.4. Chemical;

1.4.2.5. Gamma irradiation;

1.4.2.6. Electron beam.

Section 1.4.3. “Other”

This section shall specify other activities (if necessary). For example, “storage” shall be noted in Section 1.4.3 of the certificate if the medicines manufacturing authorization (license) specifies several addresses: warehouse for storing raw and other materials and finished products; another address where processing steps are carried out in relation to the manufacture of medicines (e.g. laboratory quality control).

It is also allowed to specify here:

storage of stability samples where this is the specific activity which is being carried out at the inspected site;

actual address of implementation of any processing step inspected during the pharmaceutical inspection where the specified address is not reflected in the medicines manufacturing authorization (license) or another form of special authorization.

Section 1.5. “Packaging”

This section shall specify the type of packaging operations performed for inspected medicinal products. This section shall not specify the primary packing of sterile products which is considered part of the processing operations described in Section 1.1 of the additional sheet of the certificate.

For Section 1.5.1 “Primary packing”, the information shall be specified by selecting the relevant subsection:

1.5.1.1. Capsules, hard shell;

1.5.1.2. Capsules, soft shell;

1.5.1.3. Chewing gums;

1.5.1.4. Impregnated matrices;

1.5.1.5. Liquids for external use;

1.5.1.6. Liquids for internal use;

1.5.1.7. Medicinal gases;

1.5.1.8. Other solid dosage forms;

1.5.1.9. Pressurized preparations;

1.5.1.10. Radionuclide generators;

1.5.1.11. Semi-solids;

1.5.1.12. Suppositories;

1.5.1.13. Tablets;

1.5.1.14. Transdermal patches;

1.5.1.15. Other non-sterile medicinal products _____ (please specify the type of products or activities).

Subsection 1.5.1.15 shall be completed, among other things, for the manufacture of non-sterile intermediates and medicinal products not specified in Subsections 1.5.1.1 – 1.5.1.14 (similar to the example of completing Section 1.1.2).

In this section, after the name of the item being completed, the name of the dosage form may be specified in accordance with the Nomenclature of

Dosage Forms approved by Decision No. 172 of the Commission's Board dated December 22, 2015, and may be separated from the name of the item by a colon. For example: "*1.5.1.11. Semi-solids: gel*."

Section 1.5.2 "Secondary packing" shall be completed where secondary packaging is inspected. This shall apply to all finished dosage forms unless otherwise specified in the clarifying remarks.

Section 1.6. "Quality control testing"

The information shall be specified by selecting the relevant section:

1.6.1. Microbiological: sterility;

1.6.2. Microbiological: non-sterility;

1.6.3. Chemical/Physical;

1.6.4. Biological

This section shall be completed if quality control testing as part of manufacturing site inspection shall be carried out according to the categories of Sections 1.6.1 – 1.6.4 One shall specify the types of activities for which there is an authorization to conduct quality control testing directly at the inspected site. If the type of activities is performed by contract laboratories, the categories shall not be specified.

Comment on Section 1. MANUFACTURING OPERATIONS — MEDICINAL PRODUCTS

If a note regarding any restrictions or clarifications is intended as a general comment relating to activities at the manufacturing site, it shall be provided in the field "Any restrictions or clarifying remarks related to the scope of this certificate".

If a note regarding any restrictions or clarifications is not intended as a general comment relating to activities at the manufacturing site, the clarifying

note or restriction (special requirement) shall be provided in this field of the additional sheet of the certificate and accompanied by a reference to the relevant section of the certificate.

Section 2. IMPORTATION OF MEDICINAL PRODUCTS

Section 2.1 “Quality control testing of imported medicinal products” shall be completed where quality control testing is carried out on the territory of the Union Member States in relation to imported medicinal products. This section shall be completed even if entries have been made under Section 1.6 (where applicable).

2.1.1. Microbiological: sterility

2.1.2 Microbiological: non-sterility

2.1.3. Chemical/Physical

2.1.4. Biological

Section 2.2 “Batch certification of imported medicinal products” shall be completed where the manufacturing site is located on the territory of the Union Member States and the Union's Qualified Person carries out batch certification of either an imported finished product or an intermediate (bulk product) which undergoes packing after importation.

For investigational medicinal product manufacturers, batch certification of imported comparator products shall be identified by providing a clarifying remark and selecting the relevant product category.

Permitted types of tests for Section 2.2.1. “Sterile products” shall be specified by selecting the relevant subsection:

2.2.1.1. Aseptically prepared;

2.2.1.2. Terminally sterilized.

For batch certification of non-sterile products, one shall only specify the name of Section 2.2.2. “Non-sterile products" of the additional sheet of the certificate.

In addition to the category of biological medicinal products, Section 2.2.3 “Biological medicinal products” should specify the type of finished medicinal product by selecting the relevant subsection:

2.2.3.1. Blood products;

2.2.3.2. Immunological products;

2.2.3.3. Cell therapy products;

2.2.3.4. Gene therapy products;

2.2.3.5. Biotechnology products;

2.2.3.6. Human or animal extracted products;

2.2.3.7. Tissue engineered products;

2.2.3.8. Other biological medicinal products _____ (please specify).

Section 2.3. “Other importation activities”

The type of other importation activities shall be specified by selecting the relevant section:

2.3.1. Site of physical importation;

2.3.2. Importation of intermediate which undergoes further processing;

2.3.3. Other _____ (please specify).

Section 2.3.1 “Site of physical importation” shall specify that the manufacturing site was inspected for conformity to the Good Manufacturing Practice and is used for receipt and storage of the imported product which is awaiting Qualified Person certification.

Section 2.3.2 “Importation of intermediate which undergoes further processing” shall specify the type of intermediate (e.g. a granulate, a sterile

pharmaceutical ingredient or a partially manufactured biological medicinal product).

Section 2.3.3 “Other” shall specify any restrictions or clarifying remarks relating to importation operations except where a clarifying remark is intended as a general comment on activities at the manufacturing site. In the first case, a reference to the relevant section of the certificate shall be specified.

Unless the clarifying note is intended as a general comment relating to activities at the manufacturing site, a reference to the relevant section of the certificate should be specified wherever a clarifying note or restriction (special requirement) is applied.

Section 3. MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES

The names of the active substance manufactured at the site shall be specified in this section. The applicable manufacturing operations inspected in relation to that active substance shall be specified in Sections 3.1 – 3.6.

This shall be repeated for each active substance manufactured at the site. If the site manufactures only an active substance intermediate, the text “active substance intermediate(s)” shall be entered in the field of Section 3 on the additional sheet of the certificate. The relevant manufacturing operations should be noted as described below. Specific names of active substance intermediates shall be entered as a clarifying remark in the Restrictions section.

Section 3.1. “Manufacture of active substance by chemical synthesis”

The information shall be specified by selecting the relevant section:

3.1.1 Manufacture of active substance intermediates;

3.1.2 Manufacture of crude active substance;

3.1.3 Salt formation/Purification steps: please specify (for example, crystallization);

3.1.4 Other _____ (please specify).

Section 3.1.1 “Manufacture of active substance intermediates” shall specify any steps from manufacture of the defined starting materials until the step prior to manufacture of the crude active substance.

Section 3.1.3 “Salt formation/Purification steps” should specify the types of applicable operations (e.g. crystallization).

Section 3.2. Extraction of active substance from natural sources

The information shall be specified by selecting the relevant section:

3.2.1 Extraction of substance from plant source;

3.2.2 Extraction of substance from animal source;

3.2.3 Extraction of substance from human source;

3.2.4 Extraction of substance from mineral source;

3.2.5. Modification of extracted substance (please specify source from sections 3.2.1 – 3.2.4);

3.2.6. Purification of extracted substance (please specify source from sections 3.2.1 – 3.2.4);

3.2.7 Other _____ (please specify).

Sections 3.2.1 “Extraction of substance from plant source” and 3.2.3 “Extraction of substance from human source” shall be selected where the activities at the manufacturing site are not considered by the pharmaceutical inspectorate to be partial manufacture of a medicinal product and therefore not covered by Section 1.3 of the certificate.

Section 3.2.5 “Modification of extracted substance” relates to the type (physical or chemical) of modification of the extracted active substance.

Activities such as drying or milling shall be captured under Section 3.5 “General finishing steps”.

The term “extraction” used in the title of this section is a general term to cover a number of methods by which an active substance can be isolated from a natural source. The following are some examples:

extraction of a herbal substance from plants should be specified in Section 3.2.1;

purification of a herbal extract by distillation or fractionation should be specified in Section 3.2.6 and the source from which the extract has been obtained (plant) should be specified in Section 3.2.1;

manufacture of an active substance gas by an air separation process shall be specified in Section 3.2.7 “Other”.

Section 3.3. “Manufacture of active substance using biological processes”

This section shall be completed where the production processes in relation to a biological active substance are not specified in Section 1.3 of the certificate. The information shall be specified by selecting the relevant section:

3.3.1 Fermentation;

3.3.2 Cell culture _____ (please specify cell type) (the type of cell cultures means their type specificity, line, strain, etc.);

3.3.3 Isolation/Purification;

3.3.4 Modification;

3.3.5 Other _____ (please specify).

Upon the completion of Section 3.4. “Manufacture of sterile active substance”, Sections 3.1, 3.2, 3.3 shall also be completed as applicable. This section shall be completed in relation to pharmaceutical inspections of those steps in the production process which render an active substance sterile. If the

authorized authority considers the steps in the production process which render an active substance sterile as partial manufacture of the medicinal product, then relevant entries should also be made under Section 1.1. of the certificate.

The type of sterile substances manufactured shall be specified by selecting the relevant section:

3.4.1 Aseptically prepared;

3.4.2 Terminally sterilized.

Section 3.5. "General finishing steps"

The information shall be specified by selecting the relevant section:

3.5.1 Physical processing steps (please specify) _____ (e.g. drying, milling/micronization, sieving)

3.5.2 Primary packaging;

3.5.3 Secondary packaging;

3.5.4. Other (please specify) _____ (for operations not described above).

Section 3.5.1. "Physical processing steps" shall specify particular operations (e.g. drying, milling/micronization, sieving).

Section 3.5.2. "Primary packaging" shall specify the enclosure and/or sealing of the active substance within a packaging material which is in direct contact with the substance.

Section 3.5.3 "Secondary packaging" shall specify the placement of the sealed primary package within an outer packaging material or container.

In addition, this section may reflect any labeling necessary for identification or traceability (lot numbering) of the active substance.

Section 3.5.4. "Other" should be selected for operations that cannot be specified in other parts of Section 3.5.

Section 3.6. “Quality control”

The information shall be specified by selecting the relevant section:

3.6.1 Physical/Chemical testing;

3.6.2 Microbiological testing (including sterility testing);

3.6.3 Microbiological testing (excluding sterility testing);

3.6.4 Biological testing.

This section shall specify activities for quality control testing of the active substance or active substance intermediates at the manufacturing site.

This section shall be completed even if entries have been made under Sections 1.6 and 2.1 of the additional sheet of the certificate relating to medicinal products manufactured at the same site.

A manufacturing site which is certified under item 3.6.3 is also considered having passed a pharmaceutical inspection in relation to microbiological testing activities other than sterility testing (i.e. activities under item 3.6.2) unless a comment to the contrary is included in the Restrictions section.

Section 4. OTHER ACTIVITIES – ACTIVE SUBSTANCES

This section should be completed in relation to activities which are not described in Sections 1–3 of the additional sheet of the certificate. A description of the activity shall be entered in this section.

Field “Any restrictions or clarifying remarks related to the scope of inspected manufacturing operations”

Unless the clarifying note is provided as a general comment relating to activities at the manufacturing site, a reference to the relevant item of the certificate should be included wherever a clarifying note or restriction (special

requirement) is applied. Where remarks apply to a particular active substance, then the name of the active substance should be listed in the remark in addition to the item of the certificate.

Final fields of the additional sheet of the certificate

The field "_____ (full name, title) _____ (signature)" shall specify the last name, first name and patronymic of the person with signing capacity (e.g., Deputy Minister A.V. Ivanov).

The field "(date of signing, DD/MM/YYYY)" shall specify the date of signing the certificate in the day/month/year format (e.g. 04/03/2020).

In the field "L. S.", the seal of the issuing authorized authority should be affixed.

When completing sections of the certificate, it is allowed to enter additional information clarifying the data specified in the certificate.

_____