

INSTRUCTION

ON HANDLING THE REPORTS OF MEDICINES QUALITY DEFECT

1. **INTRODUCTION**

This Instruction describes the procedure for reporting, informing and documentation evaluating on deviations from the quality standard of a medicine (hereinafter: medicine quality defect), as well as the measures and activities taken in relation to the class of quality defect.

This Instruction refers to medicines for human and veterinary use (hereinafter: medicine) marketed in Montenegro, including those that are clinically tested, substances used in the manufacture and packaging, and which deviate or may deviate from quality standards, as well as falsified medicines.

The Instruction does not apply to incidents/errors in use of the medicine, adverse reaction, quality defects or incidents related to medical devices.

This Instruction is intended for patients, healthcare professionals, marketing authorisation holders, manufacturers, importers of unauthorised medicines and sponsors of clinical trials for medicines being tested.

The most common reasons for reporting medicine quality defects are as follows:

* chemical contamination;
* microbiological contamination;
* mechanical impurities (presence of particles);
* non-compliance with marketing authorisation;
* OOT, or OOS results within the stability study obtained by the manufacturer;
* OOS results obtained in the procedure of laboratory quality control conducted in the OMCL or other competent regulatory body of the EU Member States;
* non-compliance of the manufacture of the medicine with applicable Guidelines of Good Manufacturing and/or Distribution Practice identified by the competent inspection, i.e. the competent regulatory bodies of the EU Member States, or by international bodies (e.g. ''*Warning Letters*'' by FDA, ''*Notices of concerns*'' by WHO, EDQM);
* suspension or recall of CEP;
* adverse reaction to a medicine (pharmacovigilance) connected to the medicine quality defect;
* suspected falsified medicine.
  1. **Classes of medicine quality defects**

Depending on the degree of risk for the patient-user, the quality defect may be:

1. Class I, potentially life-threatening defects, or defects with serious consequences for health, such as:
   * Wrong medicine (labeling and composition/ingredients do not refer to the same medicine);
   * Right medicine, but wrong strength, which can lead to serious medical consequences;
   * Microbiological contamination in sterile injectable or ophthalmic medicines;
   * Chemical impurities which can lead to serious medical consequences;
   * Mix-up of some products (rogues) with more than one container involved
   * Wrong active substance in a medicine with several active substances with serious medical consequences.
2. Class II, defects that can cause diseases or improper treatment, but are not life-threatening, i.e. they do not fall within class I, for example:
   * Incorrect labeling, e.g. incorrect or omitted text/picture on the packaging of the medicine;
   * Patient leaflet is missing, or it contains incorrect information;
   * Microbiological contamination of sterile products that do not belong to the group of injectable or ophthalmic sterile products, with possible medical consequences;
   * Chemical or physical contamination (higher amount of contamination, contamination with other medicines - cross-contamination, particles);
   * Mix up of products in containers (rogues);
   * non-compliance with the specification (content/stability or filling/mass for single-dose containers, related substances)
   * unsafe closure with serious medical consequences (cytotoxic medicines, strong-acting medicines, containers with the protection for children).
3. Class III, defects that cannot cause serious consequences for health, but marketing of the medicine may be suspended or the medicine may be recalled from the market, for other reasons, such as:
   * Errors in labelling of the packaging, e.g. incorrect or omitted batch number or expiration date;
   * Improper closure (non-sterile medicine);
   * Microbiological or physical or chemical contamination that is unlikely to have medical consequences.
   1. **Activities (measures), recall levels and deadlines in relation to the quality defect class**

The decision that CInMED makes based on the evaluation of the Report of the medicine quality defect and the reporter’s documentation may be to undertake one or more of the activities that are listed below:

* temporary suspension of marketing of the medicine/batch of the medicine
* recall of the medicine/batch of the medicine
* limitation of use
* sending the Caution in use notification
* investigation of the marketing authorisation holder, i.e. the manufacturer, and the implementation of corrective and preventive measures
* extraordinary quality control of the batch of medicine
* archiving without undertaking activities
* other actions assessed as being necessary (e.g. inspection, variation of the marketing authorisation and other regulatory measures).

Mentioned measures are described in more detail in item 4. Activities (measures) taken in relation to the quality defect.

There are three recall levels:

* level of the patient/medicine user
* level of institutions that dispense the medicine to the person using/administering the medicine (public and hospital pharmacies)
* level of the wholesale.

Deadlines for the recall of the medicine from the market, in relation to the quality defect class:

* 24h for class I;
* 48h for class II;
* 5 days for class III.

1. **Report of the medicine quality defect**

CInMED may recieve the report of the medicine quality defect from one of the following sources:

* Marketing authorisation holder
* Manufacturer
* Wholesaler/Importer
* Healthcare professionals
* Veterinary professionals
* Clinical trials sponsors
* Ministry of Health, administrative body responsible for inspection affairs, administrative body competent for veterinary affairs, Customs dministration, Ministry of Internal Affairs or other state institutions
* whistleblowers - (usually employed in the medicine manufacture or in the quality control laboratory of medicine manufacturers).

The same applies to the report of suspected falsified medicine.

* 1. **Report of the quality defect by the patient and/or healthcare professional**

When the patient doubts the efficacy of the medicine, notices unexpected adverse reactions that are not described in the Packaging Leaflet, or notices defects in the quality or packaging of the medicine, it is necessary to contact a pharmacist or doctor.

The patient may report medicine quality defect to the healthcare professional who prescribed the medicine, i.e., dispensed it at the pharmacy. It is important that the patient does not stop the therapy voluntarily and that he/she consults a doctor or pharmacist.

Healthcare professional who has noticed a medicine quality defect or who received a report on suspected medicine quality defect by a patient, shall immediately stop dispensing the medicine of the same batch to patients and without delay complete and submit a report on the medicine quality defect to CInMED. A veterinary professional who has noticed a medicine quality defect shall immediately suspend the application/dispensing of the medicine of the same batch and without delay complete and submit a report on the medicine quality defect to CInMED. The batch of the medicine for which a suspected quality defect has been noticed or reported shall be separated from other available batches of the same medicine and placed in quarantine.

The reporting form is provided in the *Form for reporting the medicine quality defect* available on CInMED portal in the section *Medicines quality defects.* The batch of medicine for which the suspected quality defect has been noticed or reported shall be separated from other available batches of the same medicine and placed in quarantine.

* + 1. **Initial assessment of quality defects by a healthcare/veterinary professional**

When healthcare/veterinary professionals notice a medicine quality defect or receive a report from a patient, they shall carry out an initial assessment of the quality defect. Healthcare/veterinary professionals may also contact CInMED to request additional information regarding the mentioned quality defect.

Responsibility of the healthcare/veterinary professional includes the following:

* distinguishing adverse events caused by the medicine that deviates from quality standards from adverse reactions to the medicine, i.e.s, caused by an incident or error;
* distinguishing adverse events caused by a medicine that deviates from quality standards, from those caused by a medical device that was used to administer the medicine;
* providing all necessary information before reporting a medicine quality defect (when a serious risk to human health is reported, it is important to inform CInMED as soon as possible, and in the next step to provide complete information);
* preventing further use of the medicine for which a quality defect has been reported;
* storage of samples of medicine the quality defect of which has been reported.
* if it is suspected that an adverse event in a patient may be related to the medicine quality defect, the healthcare/veterinary professional should check the following:
* whether the product has been stored properly (to rule out that improper storage is the cause of the medicine quality defect)
* if the quality defect is visible, whether it is identified in a new, unopened packaging or has the package already been used (to rule out user errors such as product substitutions)?
* if there are other unopened packagings of the same batch of the medicine available that could be checked?
* if the medicine requires prior preparation, such as the addition of a solvent, whether this procedure was carried out properly and/or whether the proper solvent was used?
* whether the medicine was used according to the instructions provided by the doctor and pharmacist and according to the instructions for Packaging Leaflet for the particular medicine?
* if the medicine was used along with a medical device, whether the medical device could have caused an adverse event?

It is necessary to carefully evaluate the case to clarify whether there is a suspicion of a quality defect. In case it is determined that there is doubt about the quality of the medicine, it must be reported.

* 1. **Report of the medicine quality defect by the marketing authorisation holder, manufacturer, wholesaler/importer of unauthorised medicine and clinical trial sponsor**

Medicine authorisation holders, manufacturers, wholesalers/importers of unauthorised medicines and clinical trial sponsors may report a medicine quality defect to CInMED on working days from 7:00 a.m. to 3:00 p.m., using *Form for reporting the medicine quality defect* avalible on CInMED portal in the section *Medicinse quality defects.* The original of the completed form and accompanying documentation, where applicable, is submitted to CInMED. In urgent cases, a quality defect may be reported outside of working hours to the e-mail address specified in the contact information for submitting a quality defect report of this Instruction as it is necessary to establish contact with a CInMED employee to receive advice regarding the quality defect report.

Marketing authorisation holder, manufacturer, wholesaler/importer of unauthorised medicine, sponsor of a clinical trial of a medicine are obliged to immediately inform CInMED whenever they become aware of a medicine quality defect.

In case of suspected or identified medicine quality defect, marketing authorisation holder, manufacturer, wholesaler/importer of the unauthorised medicine and the clinical trial sponsor are obliged to do the following:

* provide an efficient system for recording and investigating the causes of medicine quality defects;
* enable drawing conclusions and submitting detailed reports and supporting data to CInMED.
  + 1. **Data and documentation submitted to CInMED**

Marketing authorisation holders, manufacturers, wholesalers/importers of unauthorised medicines and clinical trial sponsors are required to provide CInMED with the following information about a quality defect (QD):

* Name of the medicine
* Pharmaceutical form;
* Strength;
* Type and size of the packaging;
* Batch number;
* Expiry date;
* Marketing authorisation holder;
* manufacturer;
* importer that does not have marketing authorisation;
* general information on QD or suspected QD;
* history of the incident (when it happened, and/or when it was noticed);
* possible main cause of deviation from quality standards;
* description of preventive and corrective actions (CAPA);
* activities carried out by the regulatory authorities of other countries where the medicine is on the market;
* data on the distribution of the affected batches of the medicine;
* asessment of QD classification;
* proposal of the recall level of the batch(es) of the medicine if necessary;
* an opinion on whether the recall applies to all packagings or to part of the batch(es) of the medicine that was/were the subject of dispute;
* conclusion.

In the event that all the specified data are not currently available, they shall be submitted subsequently without delaying the reporting of quality defects, i.e. without deviating from the deadlines for taking action in relation to the class of quality defects.

CInMED may request that marketing authorisation holder or the manufacturer carry out an investigation regarding the medicine quality defects. An investigation may include:

* review of the manufacture and analytical documentation and equipment logs in order to determine the cause of the defect;
* review of all related batches, packagings, testings, batch releases and review of irregularities during distribution, which may explain suspected deviations from quality standards;
* analysis of control samples;
* review of similar deviations or complaints recorded for the same or other batches;
* assessment of the impact of the defect on the efficacy and safety of the medicine administration;
* marketing authorisation holder's risk assessment, including clinical assessment, if necessary;
* description of CAPA that will be taken by the marketing authorisation holder to correct the deviation from the quality standards in future;
* determination of the quantity of medicine with quality defect.

When requesting the investigation report, CInMED shall set the deadline for the delivery of the report (minimum 30 days, and for justified reasons, longer).

Deadline for defects elimination are set depending on the nature of the deviation from quality standards, the consequent risk to human/animal health, as well as the complexity of the investigation.

The deadline may be imposed by CInMED in case that there is a special reason for it. When marketing authorisation holders face problems related to deadlines, they should discuss them with CInMED in order to find an acceptable solution.

Marketing authorisation holders shall inform CInMED in writing about all activities carried out and theconduct of risk management measures that were defined during the procedure related to quality defects.

1. **Role of CInMED in procedures related to medicine quality defects**

By assessing the report on defects and the documentation submitted by the reporter, the responsibility of CInMED is to do the following:

* propose to the administrative body responsible for inspection affairs the recall of batches from the retail sale, i.e. to the administrative body responsible for veterinary affairs the recall of batches from retail sale and wholesale, when the assessment determines that recall is necessary, and the marketing authorisation holder/manufacturer has not proposed the recall
* proposes to the Inspectorate of CInMED the recall of batches from the wholesale, when the assessment determines that the recall is necessary, as well as when marketing authorisation holder/manufacturer voluntarily proposes the recall of the batch of the medicine
* propose to the Inspectorate of CInMED the conduct of extraordinary inspection supervision of the manufacturer when it determines that it is necessary
* notify the administrative body responsible for inspection affairs or the administrative body responsible for veterinary affairs about suspicion of the existence of falsified medicine
* approve the conclusions of the manufacturer's investigation and guidelines on further investigation in the quality defect procedure, and propose the risk management measures, where necessary
* inform healthcare/veterinary professionals and the public about recalls or other warnings (medicine alert) via the CInMED portal, when it is determined that this is necessary.

If CInMED receives the information and a report of the suspected medicine quality defect through the WHO network (e.g. "Notices of concerns"), EDQM (e.g. suspension/recall of CEP), i.e. other competent international organizations, as well as competent national regulatory authorities of other countries (e.g. "Warning Letters" from the FDA), the marketing authorisation holder shall be informed about it and requested to provide the reasons for the identified medicine quality defect, data on all batches of the mentioned medicine that are marketed in Montenegro and which are potentially threatened by the specified deviation from quality standards, as well as the report on further activities and corrective measures to eliminate the identified issue.

* 1. **Making a decision to recall the batch of the medicine from the market**

When making a recall decision and assessing the risk-benefit ratio of a certain medicine, in addition to the consequences of using the medicine of inadequate quality, the following must also be taken into account:

* possibility of a shortage in case of the recall
* criticality of the product (treatment of diseases that are life-threatening or irreversibly progressive, or the patient would be seriously harmed if he/she does not receive the medicine)
* availability of alternative approved medicines/unauthorised medicines that are imported through an emergency import (other strengths/formulations/dosages of the same medicine, other medicines with the same active substance, other medicines from the same therapeutic group or other therapeutic groups)
* patient groups that will be affected by the recall
* possibility that the unavailability of the medicine is a worse option than the use of a medicine of inadequate quality.

The decision that the medicine is crucial and that it will not be recalled must be carefully considered from a risk-benefit perspective. The marketing authorisation holder shall submit to CInMED a risk report related to the suspected quality defect, which can explain the impact on safety and/or efficacy of the medicine under consideration.

CInMED, in cooperation with the marketing authorisation holder, manufacturer, wholesaler/importer of the unauthorised medicine, clinical trial sponsor, makes a decision on possible marketing of a batch of the medicine that is affected by a quality defect, i.e. on measures that reduce the risk (e.g. further monitoring, medicine alert - warning for use, letter to healthcare professionals).

Recall of the medicine may be limited to a certain batch of the medicine and allow the delivery and use of other batches of the medicine. In exceptional cases, the medicine that has been recalled from the market may be allowed only to patients with ongoing treatment, which the reporter must explain in detail and justify by attaching appropriate documentation (the opinion of a doctor of the appropriate specialty on the necessity of using the medicine in question with information on the number of patients).

Marketing authorisation holder, manufacturer, wholesalers/importers of unauthorised medicines and clinical trial sponsor are obliged to regularly inform CInMED about the recall of the medicine from the market, and after the recall is completed, they are obliged to submit a summary report on the recallof the medicine from the market, which should contain summary harmonized data between the quantity of the medicine that was on the market and quantity of the medicine that was recalled up to the reporting date, as well as specified locations from which the medicine was recalled.

1. **Activities (measures) taken in relation to the quality defect**
   1. **Recall of the medicine/batch of the medicine**

Notice on the recall may include all participants of all levels at which the recall is carried out (blanket recall), (e.g. all wholesalers, public and hospital pharmacies) or it may be targeted (targeted recall) when it includes only targeted groups (e.g. hospital pharmacies only).

Marketing authorisation holder/wholesaler that is carrying out the recall shall submit the recall notification proposal to CInMED for review and approval.

If it is necessary to urgently contact the institutions, the marketing authorisation holder/wholesaler may do so by telephone, with the obligation to confirm this information later in writing. Within 24 hours, the marketing authorisation holder/wholesaler shall submit a confirmation to CInMED that the notices have been distributed and that the recall has been initiated.

Marketing authorisation holder/wholesaler must submit a report on conducted measures to CInMED within 14 days.

* 1. **Temporary suspension of placing a medicine on the market**

Notice on the suspension may be comprehensive or it can be targeted where it only includes targeted groups (e.g. only certain wholesalers, only hospital pharmacies).

Marketing authorisation holder/wholesaler shall submit to CInMED to review and approve a proposal for a notice on suspension.

If it is necessary to urgently contact the institutions, the marketing authorisation holder/wholesale may do so by telephone, with the obligation to confirm this information later in writing. Within 24 hours, the marketing authorisation holder/wholesaler shall submit a confirmation to CInMED that the notices have been distributed and that the suspension has been initiated.

The suspension lasts until the end of the quality control, or the assessment of the risk-benefit ratio of the use of the medicine, and may result in returning the medicine to, or recalling it from the market. CInMED shall approve the decision to return the medicine/batch to, or recall it from the market. If the suspension results in returning the medicine to the market, the marketing authorisation holder/wholesaler shall send a notification about the end of the suspension. The procedure for review and approval by CInMED is identical to the one for sending a notification about the start of suspension.

* 1. **Limitation of use of the medicine/batch of the medicine**

Limitation of use notice may include all healthcare professionals, all pharmacies, or it can only include targeted groups, for example, hospital pharmacies only.

Marketing authorisation holder/wholesaler shall submit to CInMED to review and approve a notification proposal, as well as confirmation that the notifications have been distributed.

* 1. **Sending notifications to healthcare/veterinary professionals**

In cases where recall is not appropriate, but measures are required to minimize the risk, notifications to healthcare/veterinary professionals are used. By sending notifications, the attention of healthcare/veterinary professionals who prescribe, dispense and administer the medicine is drawn to the medicine quality defect and they are advised on the necessary precautions and activities.

The notification may include all healthcare professionals, or it can be targeted when it includes only specific groups of healthcare professionals.

Marketing authorisation holder/wholesaler shall submit to CInMED a notification proposal to review and approve, as well as confirmation that the notifications have been distributed.

1. **Falasified medicines**

In case of suspected falsified medicine, CInMED shall conduct an investigation and take preliminary actions by notifying the relevant inspections, in order to suspend marketing of the medicine in question until the official outcome of the investigation.

CInMED may carry out additional tests for the reported medicine that is suspected to be falsified.

The manufacturer may be required to submit the analytical results to CInMED to review as soon as possible.

In the event that a batch of medicine that has been confirmed to be falsified is marketed in Montenegro, the recall procedure shall be initiated.

**Contact information for submitting a report on quality defect**

* Address:

Institute for medicines and medical devices Bulevar Ivana Crnojevića 64a

81000 Podgorica Montenegro

* E-mail address: [defekti.kvaliteta@cinmed.me](mailto:defekti.kvaliteta@cinmed.me)
* Telephone number: +382 (20) 310 280 local 41 within the working hours)

**Glossary**

* **Medicine alert** - notification to healthcare professionalsi.e. the professional public, about the medicine/batch recall from the market, or to the general public, depending on the level of the recall
* **Caution in use notification** - notification to healthcare professionals, i.e. the professional public, about a minor deviation (e.g. a minor deviation in the labeling of the medicine) that does not affect the quality, safety and/or efficacy of the medicine
* **CEP (*Certificate of suitability*)** - Certificate of compliance with Ph.Eur monograph.
* **CAPA** - corrective and preventive actions
* **Quality defect; QD** - deviation from the quality standard (quality defect)

The definition does not apply to a medicine with unintended quality defects and does not address issues of infringement of intellectual property rights

* **EDQM&HealthCare -** European Directorate for the Quality of Medicines & Health Care
* **EMA -** European Medicines Agency
* **Falsified medicine** shall mean any medicine with a false representation of:
  + its identity, including its packaging and labelling, its name or its composition as regards any of the ingredients including excipients and the strength of those ingredients;
  + its source, including its manufacturer, its country of manufacturing, its country of origin or its marketing authorisation holder; or
  + its history, including the records and documents relating to the distribution channels used.
* **Incident** - an unforeseen event, accident or error in the manufacture or distribution of the medicine, or other situations that cause doubts about the quality, efficacy and safety of the medicine
* **Quality of the medicine** - characteristic which can be determined by examining the quality of all ingredients of the medicine and represents acceptable physical, chemical, biological, pharmaceutical-technological and other characteristics of the medicine, in accordance with the requirements from the marketing authorisation
* **Suspected defective medicine** - a medicine for which a report on suspected quality defect has been submitted stating that the quality of the medicine is not appropriate, i.e. a medicine is not of the quality defined by the marketing authorisation
* **Marketing authorisation holder; MAH** - natural or legal person established in the European Union that is in possession of a marketing authorisation issued by Institute or the European Commission and that is responsible for placing a medicine onto the market
* **NRA -** National Regulatory Authority
* **Adverse reaction** - response to a medicine which is noxious and unintended
* **Adverse event** - unwanted experience created in the period of medicine administration for which the cause-effect relationship with medicine does not have to be proven and represents any unwanted and unintended sign (e.g. an abnormal laboratory finding), symptom or disease, the timely associated with medicine administration
* **Suspension of marketing/batch release** - represents an administrative ban issued by CInMED and lasts until the end of the quality control, i.e. the evaluation of the risk-benefit ratio of the use of the medicine, and may result in returning the medicine to, or recalling it from the market
* **Marketing authorisation holder's responsible person; MAH RP** – person responsible for the communication with CInMED regarding quality defects of medicines
* **OMCL (Official Medicines Control Laboratory)** - a laboratory that conducts laboratory testing of medicines on behalf of a regulatory authority independently from the manufacturer and the marketing authorisation holder
* **OOS (Out of Specification)** – results out of specification limits
* **OOT (Out of Trend)** - a result that does not follow the expected trend, compared to other results from previous laboratory tests obtained by the same method. A result that is OOT is not necessarily OOS
* **OCABR - Official Control Authority Batch Release** – regulatory body responsible for the batch release (applies to the vaccines, products derived from blood and plasma)
* **Batch recall** - the action of recalling the batch from the distribution chain and from the user; it may be carried out partially, in case that the batch is being recalled only from certain wholesalers or users
* **Substandard medicines** – medicines that fail to meet either their quality standards or their specifications, or both;
* **Systematic control –** quality control of the medicine done by taking random samples of the medicine from the wholesale and retail sale
* **Clinical trial sponsor** - individual, company, institution or organisation which takes responsibility for the initiation, conducting and/or financing of a clinical trial
* **Extraordinary control** - quality control that is carried out in order to solve the identified issues in the quality of the medicine
* **WHO -** World Health Organization

**Notes important for the preparation and submission of the documentation:**

Documentation submitted in paper form must be prepared in A4 format file folders with hard covers, which contain the following information on the side (block letters - handwritten information is not accepted):

* name of the medicine, strength, pharmaceutical form, type and size of packaging;
* applicant;
* manufacturer.

Documentation has to be arranged according to the scheme and seequence from the Annex 3 of the *Rulebook on more detailed conditions for issuance of marketing authorisation for a medicine*.

If during the documentation evaluation procedure, corrections of SPC, PL, inner or outer packaging for Montenegro are required, each new corrected version of these documents has to be submitted in electronic form. Corrections to the previous version of SPC and PL has to be done with the "Track changes" option enabled (submit both the "Track Changes" and "Clear" versions of the corrected documents).

All documentation, except for the cover letter (which is submitted in paper form) and the application form (which is submitted in paper and electronic form), should preferably be submitted in electronic form, in the following formats: Word documents (docx), Excel Worksheets (xlsx) and PDF.

The application for marketing authorisation under the fast-track procedure in accordance with Article 62 of the Law on Medicines (which has already obtained the marketing authorisation in the European Union Member States, through the centralized procedure (CP), the mutual recognition procedure (MRP) or the decentralized procedure (DC)), shall be accompanied by the following:

* Assessment report issued by the EMA, or reference Member State, for medicine authorised through the centralized procedure (CP), the mutual recognition procedure (MRP) or the decentralized procedure (DC);
* information on other Member States that participated in the DC or MRP procedure;
* the applicant's statement that the documentation on the basis of which the marketing authorisation has been applied for in Montenegro is identical to the documentation on the basis of which the Assessment report was prepared and issued, including all changes that were approved by the date of submission of the application, i.e., that the submitted documentation is valid in the European Union Member Sates;
* the applicant's statement to notify the Institute without delay about permanent or temporary revocation of the marketing authorisation in the European Union, as well as about all urgent security measures.

If the applicant has assessment reports for certain parts of the documentation (quality, safety and efficacy, i.e. BE and PSUR studies) issued by the competent regulatory bodies in the country of origin (regulatory bodies from neighbouring countries with which CInMED has Cooperation Agreements or from authorisation procedures carried out in the EU), they may be submitted within the Part 1. In this case, it is necessary to submit a statement of the applicant/manufacturer that the documentation submitted to CInMED is identical to the documentation approved by the regulatory body of the country from which the assessment report was submitted. If there are differences in the documentation, they must be stated and explained.