UST-44 version 1 Requirements of the State Institute for Drug Control for the creation, content and distribution of a letter to the operator related to a quality defect of medicinal products

This guideline supersedes the guideline UST-44 with effect from 3 February 2025

The Instruction defines the terms, defines the content and regulates the conditions for providing information and documents to the State Institute for Drug Control (hereinafter referred to as "SÚKL") in the area of creation and distribution of letters addressed to operators concerning information related to quality defects of medicinal products.

Following the Guideline is recommended.

Related regulations:

Act No. 378/2007 Coll., the Act on Pharmaceuticals and on Amendments to Some Related Acts (the Act on Pharmaceuticals), as amended (hereinafter referred to as the "Act on Pharmaceuticals")

Act No. 372/2011 Coll., on Health Services and Conditions of their Provision (Health Services Act) (hereinafter referred to as the "Health Services Act")

Abbreviations:

EMA	European Medicines Agency
MAH	Marketing Authorization Holder
QD	Department of Quality Defects of the State Institute for Drug Control
MP	Medicinal product
API	Active pharmaceutical ingredient
Medicine	Medicinal product or active pharmaceutical ingredient
SÚKL	State Institute for Drug Control

1. Definition of terms

Information letter for operators related to a quality defect in a medicinal product - an information letter designed by the marketing authorization holder (MAH) and sent directly to operators due to the need to quickly transmit important information related to a quality defect of medicinal product.

Operator - in accordance with Article 6(1) of the Act on Pharmaceuticals (among others, a manufacturer or distributor of medicinal products, a person authorized to provide health services, a seller of reserved medicinal products...).

Health service provider - a natural or legal person authorized to provide health services under the Health Services Act.

Characteristics of the medicinal product - mainly includes terms such as the active pharmaceutical ingredient, dosage form, strength, method of administration, indication according to the approved summary of product characteristics (SmPC), and importance of the medicinal product in the provision of health services.

Quality defect - non-compliance with the quality defined in the registration dossier, pharmacopoeia, or other generally accepted standards. It is classified according to the severity of the impact on patient health as Class I, Class II, and Class III.

2. Content of the letter to operators related to a quality defect in medicinal products

The reason for creating and distributing the Information Letter for Operators Related to a Defect in the Quality of a MP (hereinafter referred to as the "Letter") is to provide operators with new, important information related to an MP quality defect that does not pose a direct safety risk to the patient. Letters are produced and distributed based on requirements of requests of the SÚKL, the EMA, or on the MAH's own initiative. A Letter can only be distributed after approval by SÚKL.

In general, all available data relating to a defect in the quality of MP distributed in the Czech Republic is considered relevant information. It is appropriate to distribute the letter especially in situations where a

quality defect has been identified in an MP that is unique and significant on the market for the provision of health services or where the MP is irreplaceable or difficult to replace by another equivalent MP, especially with regard to the therapeutic properties of the MP in question and the presence or absence of non-defective batches of this MP on the market in the Czech Republic. The withdrawal of such an MP could lead to serious health risks for patients in the provision of healthcare services. The distribution of a letter should also be considered in cases where it is necessary to share with the professional community a proposal for solving a quality defect by issuing a Letter. The available information must be forwarded directly to the affected operator groups and the communication must clearly state the reason for the preparation of the Letter, the name of the MP, the name supplement, the SÚKL code, information on the affected batches of the MP on the market, and information for both doctors and patients on what steps and with what time frame will be taken subsequently to ensure, for example, replacement with unaffected batches, or what equivalent MP the affected product can be replaced by.

3. Preparation of the Letter

The initiative is a request from SÚKL – the content and form of the Letter related to the quality defect is the result of cooperation between SÚKL and the MAH. SÚKL may request a letter from MAH related to the quality defect of MP in situations where it considers it necessary for the protection of public health.

The initiative is the EMA decision - the content and form of the Letter related to the MP quality defect is the result of the cooperation between the MAH and the EMA. The MAH always ensures the preparation of the Czech version of the Letter. The accuracy of the translation into the Czech language, the resulting graphic form of the document, and the method of distribution in the case of transnational procedures are subject to the approval of the SÚKL.

The initiative is a decision of another medicines agency - the content and form of the Letter related to the quality defect of the MP is the result of cooperation between the MAH and the regulatory authority of another EU Member State (RMS in MRP/DCP procedure). The MAH always ensures the preparation of the Czech version of the Letter. The accuracy of the translation into the Czech language, the resulting graphic form of the document, and the method of distribution in the case of transnational procedures are subject to the approval of the SÚKL.

At the proposal of the MAH – the MAH shall request the approval of the SÚKL to create the Letter related to the quality defect in MP. The content and form of the Letter related to the quality defect in MP is the result of cooperation between the SÚKL and the MAH.

4. Method of submitting a Letter related to MP availability for approval

Send a draft Letter relating to the MP quality defect prepared in accordance with point 2. by e-mail to the address: zavady@sukl.gov.cz, the subject should be 'Letter relating to the MP quality defect - name of the MP concerned'. In case of an API defect, the title and the text of the Letter should be adjusted accordingly. The email should be attached by a Risk Analysis document specifying the possible impact of the quality defect on patient safety and health. The draft letter is submitted in *Word format* to allow for comments and revisions. The Czech version of the Letter is also submitted with the English original, if available. The draft must be well translated into the Czech language. An essential part of the e-mail is also a draft distribution plan specifying the method, time schedule, and target groups for distribution of the Letter.

5. Approval of a Letter related to a defect in the quality of MP

Based on the submitted documents, the QD will comment on the content, form, scope, graphic design of the document and the method of distribution. If the documentation sent is not complete, the QD staff will ask for completion. The final form of the Letter depends on the agreement between the MAH and the SÚKL. After approving the content, the MAH sends the final draft of the graphic design of the material in PDF format. If the MAH finds out after the approval of the final draft that the document contains grammatical or stylistic errors, it is necessary to inform the QD about the correction of the Letter by e-mail. The Letter indicating the correction will be sent as an attachment to this email. The email will be sent to zavady@sukl.gov.cz. Such correction will be noted by the SÚKL and will no longer be subject to new approval by the SÚKL. If, after approval of the Letter, the MAH finds that it is necessary to revise the Letter and that

there are no grammatical or stylistic errors, it is necessary to inform the QD department. Such a change should be discussed again before the Letter is actually sent to ensure approval of the revised version. Note: If it is necessary to complete the documentation, the processing time will be extended proportionately to the delivery time of the requested documentation.

6. Distribution of a Letter relating to a quality defect of MP

The distribution of a Letter should primarily target the affected operators. Other forms of distribution may only be carried out with the consent of the SÚKL. The date of publication on the SÚKL's website or in electronic systems should be the same as the date of sending the Letter to the operators concerned and is always determined by agreement between the MAH and the SÚKL. The specific publication date must be clearly stated in the written communication. The MAH is responsible for the content and distribution of the Letter and should inform SÚKL about the progress of the distribution of the Letter, possibly about any serious problem that arises or may arise in connection with its production and distribution, as well as about the measures that it is taking or will take in this context. This information can be sent by e-mail to: zavady@sukl.gov.cz, with the subject line of the message 'Letter related to MP quality defect - MP name'.

7. Template for a letter relating to a quality defect

To distinguish it from many other printed and advertising brochures and also from letters carrying important new information on the safety of medicines (so-called DHPC), a Letter related to the quality defect of the MP should be marked in the upper left corner of the first page with a clearly visible inscription <DEFECT!> in red. The font size must be significantly larger than the font size of the rest of the text. It must be clearly and distinctly separated from the rest of the text, headings, and other graphic elements. If the Letter is also distributed via electronic communication, the subject of the e-mail should include "DEFECT!" in the first place. This designation may only be used for a Letter relating to a quality defect of the MP, the form, content, and method of distribution have been approved by the SÚKL.

Annex 1: Sample letter relating to a quality defect in MP

Sample letter relating to a quality defect of MP

DEFECT!

Notice to operators related to a defect in the quality of a medicinal product.

<Date>

<Name of the medicinal product, name supplement, SÚKL code, and main message>

(e.g., warning about the appearance of the LP that does not fully correspond to the description in the SPC, or a label that is peeling off ...)

<Addressing>

(e.g., Dear Doctor)

<Name of the marketing authorization holder> in cooperation with the State Institute for Drug Control (and the European Medicines Agency, if applicable), would like to inform you about ...

Summary of the issue

- Brief summary of the quality defect and recommended procedure to minimize risks
- Indication of batch numbers with the described quality defect

Further information on the MP quality defect and subsequent recommendations

- Detailed procedure for minimizing risks related to the MP quality defects
- Information on the possible supply of non-defective batches to the Czech market
- Other important information

Contact details of the marketing authorization holder

If you have any further questions or require additional information, please contact: Contact person's name, telephone number or email, or company website, company address within the Czech Republic

<electronic or handwritten signature, name, and position of the responsible person**>**