

Annex 15
to the Procedure for Conducting Expert
Evaluation of Registration Materials Pertinent
to Medicinal Products Submitted for the State
Registration (Re-registration) and for Expert
Evaluation of Materials about Introduction of
Changes to Registration Materials during the
Validity Period of Registration Certificate
(item 10 of section IV)

LIST
of documents submitted for re-registration of medicinal product

1. Administrative data
 - 1.1. Cover letter.
 - 1.2. Comprehensive table of contents.
 - 1.3. Registration form (Annex 14 of the Procedure) with attachments to it.
 - 1.4. Information, which shall include details about qualification and experience of the authorized person of the applicant for pharmacovigilance and/or contact person in Ukraine of the authorized person of the applicant for pharmacovigilance (if different).
 - 1.5 Details of the contact person with the responsibility for product defects and recalls.
 - 1.6. List of countries where the medicinal product registered/marketed.*
 - 1.7. Chronological list of guarantees and obligations of the applicant, submitted since the registration indicating scope, status, date of submission and date when the issue has been solved (recommendations for post-registration investigation, elimination of any defects, specified by control and other agencies, etc.)*.
 - 1.8. Summary data of the manufacturer/applicant about safety of medical use of medicinal product in Ukraine during the validity period of registration certificate according to the form envisaged in the legislation.
 - 1.9. Updated SPC/instructions for medical use of medicinal product/other officially approved information about the use of medicinal product approved in the country of manufacturer/applicant; or country which regulatory authority follows high quality standards complying with WHO standards; valid in Ukraine instruction for medical use of medicinal product and SPC (if any); draft updated instruction for medical use of medicinal product to be approved in Ukraine (hard and electronic copy) (except for in bulk product).
 - 1.10. Approved labelling of medicinal product and updated labelling (except for in bulk product).
 - 1.11. Information about independent experts:
for quality issues (including signature and CV)*;
for preclinical issues (including signature and CV) - if applicable*;
for clinical issues (including signature and CV)*.
 - 1.12. Summary of pharmacovigilance system (if applicable).
 - 1.13. Risk management plan (if applicable)*.
2. Summary of dossier.

2.1. Addendum to quality overall summary

Addendum shall include a declaration of the registration certificate holder that he fulfils the obligation on taking account of technical and scientific progress and have timely introduced any changes that may be required to enable the medicinal product to be manufactured and checked by means of generally accepted scientific methods.

Addendum to quality overall summary shall also include:

Confirmation that all changes relating to the quality of medicinal product have been made according to the section VI of Procedure and the product conforms to current quality requirements.

Currently approved specifications for API and the finished medicinal product (with date and number of latest approval)

Qualitative and quantitative composition of medicinal product (API and the excipient(s)) (with date and number of latest approval)

2.2. Addendum to pre-clinical overview (if applicable)*.

An addendum to the pre-clinical overview is not required as part of re-registration.

When new data are submitted in the addendum to the pre-clinical overview, a critical discussion must be submitted as part of the re-registration procedure supporting the benefit/risk balance re-evaluation for the medicinal product taking into account any new pre-clinical data accumulated since the initial registration of medicinal product or the last re-registration, or any new information in the public domain.

2.3. Addendum to clinical overview*.

A critical discussion should be provided within the addendum to the clinical overview. It should address the benefit/risk balance for the medicinal product on the basis of the Periodic Safety Update Reports (PSUR) and safety/efficacy data accumulated since the first registration or since the last re-registration of medicinal product, making reference to relevant new information in the public domain.

The addendum to the clinical overview should contain the following information:

Data about pharmacovigilance inspections (date, regulatory authority performing the inspection, inspected object, type of inspection and, if a specific medicinal product has been inspected – the list of related medicinal products) and analysis of inspection results effect on benefit/risk ratio of medicinal product;

Registration status of medicinal product in the world: list of countries where the medicinal product is registered and marketed;

Actions taken for safety reasons during the period covered since registration/last re- registration until 90 days prior to submission of application for re-registration: description of significant actions related to safety that had a potential influence on the benefit/risk balance of the registered medicinal product (e.g. suspension, withdrawal, temporary halt or premature ending of clinical trial for safety reasons, safety issues requiring communication of information about medicinal product safety for public and/or healthcare professionals, etc).

List of significant changes made to the applicant's reference safety information during the period covered since the registration/last re-registration and the document identifying the changes included during the period covered since registration/last re- registration until 90 days prior to submission of documents for re-registration.

Draft of updated: summary of product characteristics, instruction for medical use and labelling;

Interpretation of significant differences between applicant's reference safety information and/or SPC/instruction for medical use of medicinal product/other officially approved information for use of medicinal product approved in the applicant's country and draft updated instruction for medical use of medicinal product submitted for approval in Ukraine;

Estimated exposure and used patterns: data on cumulative exposure of subjects in clinical trials as well as of patients in post-registration period. If the applicant becomes aware of a pattern of use of the medicinal product considered relevant for the implementation of the safety data, a brief description should be provided; such patterns may include in particular off-label use;

Summary tabulations of serious adverse events from clinical trials as well as summary tabulations of adverse reactions reported during the period covered since the date of registration/last re-registration until 90 days prior to the submission of re-registration documents.

Summaries of significant safety and efficacy findings from clinical trials and non-interventional studies with a description of any significant safety findings that had an impact on the conduct of clinical trials or non-interventional studies. It should also address whether milestones from post-registration safety or efficacy studies, studies from the RMP and studies conducted as condition of the registration certificate, have been reached in accordance with agreed timeframes.

Review of important literature references published during the period covered since the date of registration/last re-registration until 90 days prior to submission documents for re-registration: that had a potential impact on the benefit/risk balance of the medicinal product;

Risk evaluation: all summarized information related to important safety concerns, risk evaluation and characterization, and effectiveness of risk minimization activities during the period covered since registration/last re- registration until 90 days prior to submission of documents for re-registration.

Benefit evaluation: summarized important efficacy information (including information on lack of efficacy) for the period covered since the date of registration/last re- registration until 90 days prior to submission of documents for re-registration;

Benefit/risk balance: a discussion on the benefit/risk balance for the approved indication should be presented, based on the above information;

Late-breaking information: summarized the potentially important safety and efficacy findings that arise during the period of preparation of the addendum to the clinical overview (during 90 days prior to submission of documents for re-registration).

Together with the addendum to the clinical overview the clinical expert statement should confirm that:

No new clinical data are available which change or result in a new risk/benefit balance evaluation;

The medicinal product can be re-registered at the end of a 5-year period of registration for an unlimited period, or any action recommended or initiated should be specified and justified;

The authorities have been kept informed of any additional important data significant for the assessment of the benefit/risk balance of the medicinal product;

The product information given in draft updated instruction for medical use to be approved in Ukraine is up to date with the current scientific knowledge about the medicinal product.

* It shall not be submitted for traditional medicinal products, homeopathic medicinal products complying with the requirements of Annex 7 of the Procedure and medicinal products related to “Medical gases”.

Note. The risk management plan shall be obligatory submitted in 2 years after the Procedure has come into effect. Before this term, the RMP shall be submitted, if available. The RMP shall not be submitted for medicinal products originating from and having been re-registered in EC before June 2012, except for cases when RMP is required based on benefit/risk balance evaluation.

Addendum to the clinical overview shall be obligatory submitted in 2 years after the Procedure has come into effect. Before this term, it shall be submitted, if available. If it lacks, the latest periodic safety update report shall be submitted. If there is no addendum to the clinical overview at re-registration, the applicant shall prepare and submit it for expert evaluation to the Center within 2 years after the Procedure has come into effect.

(Annex 15 in wording of MoH Ukraine Order №460 as of 23.07.2015)