APPROVED

Order of the Ministry of Health of Ukraine

\_\_\_\_\_\_\_\_\_\_\_\_\_\_ №\_\_\_\_\_\_\_

**Requirements**

**to Module 1 electronic common technical document (eCTD) specification with recommendations for submitting registration dossier materials in electronic common technical document (eCTD)**

**І. General**

1. These Requirements are designed to make recommendations on the submission of registration dossier materials in the electronic Common Technical Document (eCTD) format (hereinafter – the dossier), which shall be used together with the eCTD Specification v3.2.2 developed by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), to provide an eCTD submission to the State Expert Center of the Ministry of Health of Ukraine (hereinafter – the SEC).

2. In these Requirements, the terms used have the following meaning:

baseline submission - a resubmission of documents that have already been submitted to and recommended for approval by the SEC but in a non-eCTD format;

node extensions - a way of providing extra organisational information to the eCTD. The node extension should be visualised as an extra heading in the CTD structure and should be displayed as such when the XML backbone is viewed;

regulatory activity - a single sequence or a collection of sequences covering the start to the end of a specific registration procedure;

sequence - a single set of information and/or electronic documents submitted at one particular time by the applicant as a part of or the complete dossier. Sequences may be related to one another within one regulatory activity. The related sequence number should always be stated. In case of activities with only one sequence the same sequence number shall be used;

submission type - the submission describing the regulatory activity, in relation to which the documents specified in Appendix 1 to these Requirements are submitted;

submission unit type - the submission unit type element of the envelope metadata set describes the content at a lower level (a “sub-activity”) which is submitted in relation to a defined regulatory activity such as the initial submission, the applicant response to questions or any other additional information.

Other terms used herein shall have the meanings ascribed to such terms in the Laws of Ukraine “On Medicinal Products”, “On Electronic Identification and Electronic Trust Services”, “On Information Security in Communications and Information Systems”, the Procedure for State Registration (Re-registration) of Medicinal Products and Amounts of Fees for Their State Registration (Re-Registration) approved by the Decree of the Cabinet of Ministers of Ukraine of May 26, 2005 № 376, the Procedure for Conducting Expert Evaluation of Registration Materials Pertinent to Medicinal Products, which are Submitted for State Registration (Re-Registration) and Expert Evaluation of Materials about Introduction of Changes to the Registration Materials during the Validity Period of Registration Certificate, approved by the Order of the Ministry of Health of Ukraine of August 26, 2005 № 426, registered at the Ministry of Justice of Ukraine on September 19, 2005 under № 1069/11349 (in wording of the Order of the Ministry of Health of Ukraine of July 23, 2015 № 460) (hereinafter – the Procedure № 426) and other regulatory documents.

3. The abbreviations, which are defined as follows, are used in these Requirements:

API - active pharmaceutical ingredient;

CTD - common technical document;

MP - medicinal product;

QCM - quality control methods;

MOH - Ministry of Health of Ukraine;

SEC - the State Expert Center of the Ministry of Health of Ukraine;

ICH eCTD specification - ICH eCTD version 3.2.2 specification;

DTD - document type definition;

eCTD - electronic Common Technical Document;

UUID - universally unique identifier;

XML - extensible markup language;

OCR - optical character recognition;

ICH M2 EWG - ICH M2 Expert Working Group.

4. Factors that could affect the content of the Requirements and serve to justify introduction of changes:

change in the content of the CTD, either through the amendment of information, at the same level of detail, or by provision of more detailed definition of content and structure;

change to the national requirements for dossiers that are outside the scope of the CTD;

updating standards that are already in use within the eCTD;

availability of new standards that improve conditions for the creation and/or usage of the eCTD;

availability of new functional requirements;

experience of use of the eCTD by all parties of the process.

**ІІ. Electronic Common Technical Document (eCTD)**

1. The electronic submission of registration dossier materials for medicinal products (hereinafter – MP) for human use during registration (marketing authorization), re-registration (renewal) and introduction of changes (variation) procedures in eCTD will cover all dosage forms and strengths of a medicinal product with any one name. In case of a formation of one eCTD per strength or dosage form, it is expected that each of these eCTDs will be maintained individually, such that submission of a single sequence that covers more than one strength or dosage form will not be possible.

At the time of switching to eCTD a baseline submission is recommended to give the SEC access to all or at least part of the previously submitted documentation within the eCTD lifecycle.

1. Document granularity at the submission is a collection of documents, each of them is provided as a separate file. The detailed structure of the eCTD is based on the specification developed by the ICH M2 EWG and these Requirements.
2. The eCTD file naming conventions described in these Requirements are based on those developed by the ICH M2 EWG, and are recommendatory.

In case of multiple files in one section, where only one highly recommended name is available, splitting the files can be achieved by adding a suffix to the filename or using a variable component in file name.

File names in eCTD shall contain fixed and variable components. Components are separated by a hyphen. No hyphens or spaces shall be used within each component.

Fixed components should be used for naming files in eCTD. The variable component should be used as appropriate to further define separate files or their components. The variable component is a meaningful concatenation of words without separation and should be kept as brief and descriptive as possible. File extensions in line with these Requirements should be applied as applicable.

The first component in a file name should be the country code, if applicable.

The second component in a file name should be the document type code.

The third component should be a variable one (if used). There are no recommendations for variable components in these Requirements. The format of the file is indicated by the file extension. File names should always be in lowercase, in line with the ICH eCTD specification.

Examples:

ua-cover.pdf;

ua-form-annex17.pdf.

In m1-responses/, the use of cc-responses{-var}.pdf with the -var component of the filename is preferable to define the content. It is recommended to use the variable component of the filename and the leaf title, to present the information clearly during the review.

The letters included in the registration dossier shall contain the word “letter” in the title.

File names are indicated in Latin letters.

1. The correspondence is designed to allow a view of the current status of the review of information submitted in the appropriate place of the eCTD dossier. A structure of eCTD format ensures that any correspondence relates directly to the content of the dossier submitted in such format except for requests sent outside the eCTD or consultations with the SEC.
2. Universally unique identifier of eCTD sequence, which is built in accordance with this specification, must contain a Universally Unique Identifier (UUID), linking the sequence to the eCTD dossier to which it belongs.

The UUID is used to facilitate archiving the sequence with the correct eCTD lifecycle, and also for automated sorting of incoming eCTD submissions to the correct eCTD lifecycle.

The UUID for each eCTD lifecycle is unique and it should be system generated, i.e. be created by the eCTD building tool or, if not possible, by using an online UUID generator.

The generation of a UUID complies with ISO/IEC 11578:1996 and ITU-T Rec X.667 | ISO/IEC 9834-8:2005. It is a hexadecimal number in the form of xxxxxxxx-xxxx-xxxx-xxxx-xxxxxxxxxxxx, consisting of 32 digits and 4 hyphens. The ‘x’ will be replaced by a number or a letter.

There are no upper or lower case restrictions. It is recommended to use UUID version 4. UUID version 4 is a universally unique identifier that is generated using a set of random numbers, for example: “f0d11e14-f076-4639-b5d7-1a8b72a54597”.

The 8-4-4-4-12 format is used.

This structure guarantees uniqueness across applicants and registration dossier materials.

The UUID will be generated for the first time when creating the first sequence following this version of the specification and will be provided in the eCTD envelope.

All subsequent sequences for that same dossier (lifecycle of MP) shall contain the same UUID that sequences are identified and allocated automatically to the correct eCTD dossier.

When the dossier is transferred (for example, during the procedure of transfer of ownership of the registered medicinal product from the approved applicant (the holder of registration certificate) to another legal entity/natural person as a new applicant (an successor) in accordance with Order No. 426), the UUID remains unchanged. During this process, sequence numbering should continue for this UUID and should not start with “0000”.

The only exceptions to the above are when the eCTD is split or merged or the eCTD is fully re-baselined by submitting a new 0000 sequence for that eCTD.

Any dossier with its own life cycle of MP should have its own UUID.

Beside the technical validation checking the correct UUID, the SEC can also check that the UUID is not the same as in another already existing eCTD lifecycle of MP in the SEC eCTD repository.

1. All PDF files included in the eCTD (regardless of the module) must be version 1.4, v1.5, v1.6 or v1.7, unless there is a requirement for a later version.

Before downloading an eCTD it is recommended to ensure that all submissions contain the maximum amount of text searchable content to facilitate the assessment of the eCTD content. PDF documents should therefore be produced from a text source (e.g. from docx/). If scanning is unavoidable, the use of an optical character recognition (OCR) is recommended. However, there are some documents where the scanned document would not be expected to include OCR (i.e., manufacturer’s license for MP; GMP certificate; certificate of analysis; document written in a foreign language where a translation is provided in English (the translation should be text searchable); literature references sourced from journals, periodicals and books (except when these are used to support the main claims included in the dossier).

1. Working documents are recommended to be submitted in separate Working documents folder outside of eCTD structure in docx/.

The materials (documents) in other formats differing from PDF are recommended to be submitted after agreeing upon with the SEC:

|  |  |
| --- | --- |
| Document | File name |
| 1.0 |  |
| Approved quality control methods | approved-quality |
| Changes to quality control methods | changes-quality |
| Proposed quality control methods | proposed-quality |
| 1.3.2 |  |
| Approved labeling text | approved-labeling |
| Proposed labeling text | proposed-labeling |
| 1.3.3 |  |
| Approved instructions for medical use | approved-instructions |
| Changes to instructions for medical use | changes-instructions |
| Proposed instructions for medical use | proposed-instructions |
| 1.3.4 |  |
| Approved Summary of Product Characteristics | approved-spc |
| Proposed Summary of Product Characteristics | proposed-spc |
| 1.8.2 |  |
| Approved Risk Management Plan (RMP)  | approved-risk |
| Proposed RMP | proposed-risk |

These documents, if requested, should not be referenced in the eCTD backbone, but should always be provided in addition to the PDF versions, but in a separate folder outside of the eCTD sequence folder (“working documents” folder).

The folder should be named: <sequence>-workingdocuments, for example “0002-workingdocuments”. The sequence number in the folder name must match the sequence number inside the eCTD submission. The folder should be placed in the root of the archive.

File naming conventions should be applied according to the current eCTD specification and validation criteria.

1. Sequence numbers are used to differentiate between different submissions of the same dossier over the life cycle of MP. It is recommended that sequence numbers follow the order of submission of the sequences. A sequence tracking table should always be included in section 1.0 in every submission for all procedures. If applicable, the next sequence number may be skipped over, specifying the reasons for skipping in the cover letter, this is recommended to agree upon with the SEC.

The initial eCTD lifecycle submission should normally have the sequence number of “0000”. If there are good reasons to use another number, they should be stated in the cover letter, this is recommended to agree upon with the SEC.

When additional information is submitted in response to questions or when information in a previously submitted sequence is modified in any way, the sequence number of the submission will advance accordingly, e.g. 0001, 0002, etc.

Only in the case of a technically invalid submission, at request from or after agreeing upon with the SEC, a sequence can be replaced with another one using the same number (e.g. the initial sequence “0000” will be replaced by another “0000”). No new documents may be included in this case, but technical problems should be fixed.

1. The related sequence element is used to identify sequences belonging to the same “regulatory activity”.

All submissions shall have a “related sequence” value. If submission unit type is “initial” or “reformat”, then related sequence attribute shall have a value equal to the current sequence.

If the submission unit type is not equal to ‘initial’ or ‘reformat' then the entry for related sequence must be equal to the sequence number of the initial sequence for the regulatory activity.

1. Bookmarks and hypertext links shall be used for navigation through an electronic submission.

Navigation through an electronic submission is greatly enhanced by the appropriate use of bookmarks and hypertext links.

Unreasonably frequent use of hyperlinks may cause problems in the MP lifecycle management, due to the large volume of links that must be processed.

1. The technical validation of eCTD submission is a separate activity to the content validation of a submission according to technical validation criteria against which all eCTDs can be verified irrespective of the type of the submission.
2. To ensure compliance of the eCTD dossier with the requirements of annexes to the Procedure № 426, for each section that does not correspond to the structure given in annexes to the Procedure № 426, or if the section in the submitted dossier is missing explanatory letters shall be kept in section 1.0. Detailed reasons for missing information in specific sections or missing specific sections of the CTD shall be provided in the Quality overall summary and/or Non-clinical /Clinical overviews.

It should be noted that a formation of placeholder documents highlighting 'no relevant content' should be avoided in the eCTD structure, as these would create a document lifecycle for non-existent documents, and complication and maintenance of the eCTD.

1. eCTD submission shall be made in accordance with the MOH Order of April 8, 2024 № 588 “On Amendments to the Order of the Ministry of Health of Ukraine of October 13, 2023 № 1789”, registered in the Ministry of Justice of Ukraine on April 22, 2024 under № 581/41926 using the software complex “Unified Information and Analytical System”.

The external interface for submitting eCTD in the software complex “Unified Information and Analytical System” is displayed through the Applicant Account of the system (hereinafter - Applicant Account).

You can familiarize yourself with the User Guide for the Applicant Account, the guide for downloading the registration dossier documents, and information on the user support on the official website of the SEC.

1. For eCTD submission qualified electronic signatures should be used.

Qualified electronic signatures should be embedded in PDF files using electronic keys from the accredited certification centers according to the Ukrainian legislation. It should be noted that embedding of signatures in PDF files should be done using container standard “PDF Advanced Electronic Signatures (PAdES)” in order to avoid affecting structure of such documents.

Letters signed using the QES shall be included in sections 1.0 and 1.2 of Module 1.

It should be noted, that the use of passwords, certificates, security policy settings, except for files in Modules 1.0, 1.2, 3.3, 4.3 and 5.4 makes the technical use and, accordingly, review of eCTD and/or submitted individual documents in the eCTD structure impossible. This means that security settings in for example Adobe Acrobat, all “restrictions” should normally be “allowed” when viewing the Document Preferences > Security settings. If for some reasons this is not possible for some documents, for example, for documents with a qualified electronic signature, it is advisable to allow printing and copying of the content for the possibility of its further processing.

1. An important element of eCTD submission is pre-submission checking of dossier files for malware such as computer viruses.

Checking for malware should be performed with licensed antivirus software (antivirus database signatures updated to the latest version), and specified in a cover letter.

In order to avoid the risks of malicious influence, the detection of any file with malware is blocked by the software complex “Unified Information and Analytical System” and makes it impossible for any viewing by the SEC.

**ІІІ. Baseline eCTD submission**

1. To support the reformatting of an existing submission dossier from any format (e.g. paper) to eCTD, a baseline eCTD submission containing no content change may be prepared.

The baseline submission is not subject to expert evaluation and the submission unit type “reformat” should be used in the envelope. This submission unit type will always be used together with the submission type “none”. After eCTD submission, returning to non-eCTD format disrupts the life cycle of the MP.

1. A baseline submission is recommended before starting a new registration procedure (for example, re-registration (renewal) and introduction of changes to registration materials (variations)).
2. A baseline submission shall consist of currently valid registration materials for medicinal products in eCTD format that were reviewed by the SEC on which basis the decision on state registration (marketing authorization), re-registration (renewal), introduction of changes (variations) was taken.
3. When preparing a baseline submission, it is necessary to consider requirements specified in these Requirements, validation criteria according to which the eCTD is prepared.
4. During a baseline submission, it shall be confirmed that all information uploaded to the eCTD represents currently valid documents with all approved changes, and does not contain new or unapproved information included in the baseline sequence.

While a baseline submission it is important to ensure that:

all information provided is a resubmission of currently valid documents and no new or unapproved information is included in the baseline sequence;

formatting is the only change and does not contain corrections to the materials of the registration dossier;

any missing information in the baseline submission does not cause the content to be misleading.

6.At the baseline, an eCTD dossier shall be submitted for each strength, dosage form.

7. If there is a need for re-baselining in the case of a broken eCTD lifecycle for the MP, or due to other reasons, consultations with the SEC are recommended.

8. The baseline, which contains all reviewed by the SEC currently valid Module 2-5 documents of the dossier of the previously registered medicinal product, is used in the case of changes requiring new registration (extension) (as a new sequence to the original dossier) according to the Procedure № 426.

The baseline would preferably consist of high quality documents, but good quality scanned images would also be acceptable in these cases, preferably with Optical Character Recognition (OCR) to allow text searching. The use of OCR allows the correction of all possible errors that may appear in the recognized text, and be responsible for the complete identity of the original and recognized text. At the same time, the lack of hyperlinks between modules is acceptable if establishing hyperlinks is not possible.

**ІV. Module information**

1. The ICH CTD specifies that Module 1 should contain national specific administrative information and registration information about the MP.

The documents that shall be provided during the procedure for state registration (marketing authorisation), re-registration (renewal) and introduction of changes to registration materials (variations) in Ukraine, are specified by the Procedure 426 and other regulatory documents.

It should be noted that for subsequent submission of sequences in the lifecycle of MP, not all of the above mentioned types of documents need be included in registration dossier. It is necessary to refer to the Procedure 426 and other regulatory documents regarding the relevant requirements in each specific case.

No additional file formats are defined for Modules 2-5 other than those mentioned in these Requirements and provided for by ICH.

Module 3.2.R may contain additional information on the API and/or medicinal product specific to Ukraine.

If the submission contains other information, it is necessary to seek advice from the SEC before submitting the materials.

1. Module 1 architecture is similar to that of Modules 2 to 5 of the eCTD, comprising a directory structure and a backbone with leaves.

The backbone is a XML document according to the UA National Document Type Definition (DTD). The backbone instance (the “ua-regional.xml” file) contains meta-data for the leaves, including pointers to the files in the directory structure. In addition, the UA national DTD defines meta-data at the submission level in the form of an envelope. The root element is “ua-backbone” and contains two elements: “ua-envelope” and “m1-ua”.

The UA national DTD is modularised i.e. the envelope and leaves are referenced from the main part of the DTD as external entities called respectively “ua-envelope.mod” and “ua-leaf.mod”. The UA “leaf” is identical to the leaf element described in the ICH eCTD DTD; reference is made to Table 6-8 of the ICH eCTD Specification. The description of ua-leaf.mod is given in Appendix 2 to these Requirements.

Files can be referred to across modules (e.g. from Module 1 to Module 2) or across sequences within the same eCTD dossier; it should be noted however that it is not possible to refer to files in sequences in other eCTD dossiers. When referring to files across modules or across sequences, the reference must always be relative, starting from the location of the XML file. For instance, a reference from within Module 1 of Sequence 0003 (e.g. 0003/m1/ua/ua-regional.xml) to a file located in Module 2 of Sequence 0000 (e.g. file “introduction.pdf” in folder 0000/m2/22-intro), would be encoded in the UA Module 1 as “../../../0000/m2/22-intro/introduction.pdf”.

The identical documents should not be submitted multiple times, but they should be referenced within the same sequence or the content of identical documents already been submitted in previous sequences should be referenced.

A complete description of the UA national DTD is given in Appendix 3 to these Requirements.

1. The “ua-envelope” element designed to be used for all types of submissions (registration (marketing authorisation), re-registration (renewal), changes (variations)) for a given medicinal product and will mainly be used for the first simple processing at the competent authority level. The envelope provides meta-data at the eCTD dossier and sequence level.

The envelope element submission ‘mode’ should only be used in the case of introduction of changes, and the value can be set to: “single”, “grouping”.

A description of each “envelope” element is provided in Appendix 1 to these Requirements.

A description of ua-envelope.mod is given in Appendix 4 to these Requirements.

1. Catalogue of meta-data at the leaf level including pointers to the location of files in a directory structure is provided by using a XML catalogue.

The “m1-ua” element of the UA national DTD is based on the same conceptual approach as the common part of the ICH eCTD DTD.

As for the ICH eCTD DTD, the “m1-ua” element maps to the directory structure (there may at times be what is seen to be an apparently 'redundant' directory structure, but this is necessary in order to be able to use the same file/directory structure for all procedures). Furthermore, as the same structure will be used during the lifecycle of the medicinal product, the use of country directories even to place a single file in one submission is justified because it could be used to house several files in a subsequent submission, and in doing so the structure would not change. The country code is implemented intentionally for future compatibility with EU recommendations.

A tabular overview of the directory structure explaining where to place all files is provided in Appendix 5 to these Requirements.

1. The UA Module 1 Specification provides a directory and file structure that is recommended and given in Appendix 5 to these Requirements.

The same high-level directory structure is used for all procedures.

1. It is not possible to update XML backbone attributes such as ‘manufacturer’ during the eCTD lifecycle, nor is it necessary to attempt workarounds such as deleting existing documents and resubmitting them with new attributes. The recommendation is to retain the initially made entry and to rely on the document content to explain the current details.
2. . Node extension

The use of node extensions should be limited to those areas where it is critical. The inconsistent use of node extensions can complicate the work during the review of the submission.

In Ukraine the use of node extensions corresponds to the following:

node extensions must not be used where ICH-specified sub-headings already exist (e.g. indication, manufacturer, active substance and medicinal product are all-ICH specified node extensions);

node extensions must only be used at the lowest level of the eCTD structure (e.g. a node extension can be used at the level 5.3.5.1 but must not be used at the level 5.3);

node extensions are mainly to be used to group together documents made up of multiple leaf elements (e.g. a clinical study made up of separate files for the synopsis, main body and individual appendices could be grouped together under a node extension with the Study Identifier as its Title attribute);

node extensions must be maintained over the entire life of the eCTD lifecycle of medicinal product (e.g. if a node extension is used in Sequence 0000 to group files for a study report in Module 5.3.5.1, then any files submitted in a later sequence must also be placed under a node extension, even if only one file is submitted);

node extensions may be nested as this is allowed by the eCTD DTD. However, as noted in bullet two of this item, the first node extension must be at the lowest level in the eCTD structure;

the content associated with a node extension can be placed in a separate subfolder in the submission (this is recommended for studies in Module 5 where study reports are provided as multiple files). However, there is no specific requirement for an additional subfolder. For example, if node extensions are used to further define ‘m1-responses’, additional folders under ‘m1/ua/responses/’ are not recommended. Instead, for navigational support the variable part of the file name can be used as outlined in Section V of these Requirements.

1. Up-to-date checksums of util files are placed on SEC official website in the section “To applicants”.
2. In the Applicant's Account, a cover letter with the registration materials can be downloaded, which contains the "new" document operation attribute, the template of which is published on the SEC official website.

In order to identify each cover letter leaf and the submission it is in, descriptive text is added in the title so as not to include the title repeatedly in each sequence.

1. A tracking table shall be included as an annex to the cover letter for submissions within all procedures. The file should be named ua-tracking-var.pdf (-var (variable) part can be changed or missing) and be placed in /XXXX/m1/ua/10-cover/.
2. According to Procedure No. 426, the registration form is submitted in section 1.2 of module 1, contains the document operation attribute "new" (the requirements as in item 9 of this section apply to the form), unless an error has been made in the form, and the updated form is provided in a new sequence, in which case the operation attribute must be "replace".
3. Supportive documents, which are not part of any section of Modules 2-5 or “Responses to Questions” document should be placed in section 1.2 of Module 1 of the eCTD as separate files and not as appended to the form itself.

Responses in the electronic eCTD format to comments on the registration dossier materials, generated in accordance with Procedure No. 426, are grouped under the extension of the m1-responses node, which reflects a certain regulatory activity. In the first leaf of the relevant section of the registration dossier materials, which reflects a certain regulatory action, it is recommended to have a copy of the full list of questions received from the SEC.

The responses are divided into separate files for each major section of the submission (e.g. Quality, Non-clinical and Clinical). Leaf titles should be used to identify the particular set of responses. If responses to more than one question are submitted in a single PDF file bookmarks should be used within to clearly identify each response.

**V. Submission instructions for procedure types**

1. The recommended start for an MP eCTD lifecycle is the initial state registration application (MA application). It should normally be specified as sequence 0000. If start with another sequence of numbers is justified, such a procedure is recommended to be carried out after prior consultation with the SEC. All documents included should have the “new” operation attribute and be placed in the relevant sections in line with the regulatory documents.

The submission type shall be «registration» («maa»).

Location of supportive documents during the state registration procedure (MA).

This is a list of locations of individual national documents during the submission of documents for registration (MA).

The list includes only files according to the Procedure № 426.

|  |  |
| --- | --- |
| Module 1 | Name in Ukrainian |
| 1.0 | Cover letter |
|  | Cover letter |
|  | Explanatory letter for empty or non-compliant dossier sections considering the requirements of Annex 5 to the Procedure № 426 |
|  | Quality control methods (QCM) |
|  | Letter from the applicant with recommendations regarding the publication of reports (Annexes 29, 30 to the Procedure № 426) |
|  | Report according to the Annex 29 to the Procedure № 426 |
|  | Report according to the Annex 30 to the Procedure № 426 (if there are several reports, indicate as 30.1, 30.2 of the Procedure № 426) |
|  | Public assessment report for medicinal product drawn up by another regulatory authority (Procedure № 426, Section V, item 9)  |
|  | Official assessment report for medicinal product (Procedure № 426, section V, item 10.1) |
|  | Applicant’s written confirmation (Procedure № 426, section V, item 10.1) |
|  | WHO Public Assessment Report for medicinal product (Procedure № 426, section V, item 10.2) |
|  | WHO Public Inspection Report for manufacturers (Procedure № 426, section V, item 10.2) |
|  | Official letter from the applicant (using the WHO approved template) (Procedure № 426, section V, item 10.2) |
|  | Applicant’s written confirmation (Procedure № 426, section V, item 10.2) |
|  | Batch control certificate (Procedure № 426, section V, item 10.3) |
|  | Protocol of manufacturer for three consecutive final batches (Procedure № 426, section V, item 10.3) |
|  | Information about Vaccine Vial Monitor (Procedure№ 426, section V, item 10.3) |
|  | Applicant’s written confirmation (Procedure № 426, section V, item 10.3) |
|  | A letter confirming that the composition, production and control of the medicinal product comply with the specification included in the List of medicinal products produced according to the approved specifications, approved by the MOH Ukraine Order of November 26, 2012 № 949 |

Location of registration dossier materials for state registration of API must comply with a List of documents required for conducting expert evaluation of registration materials for state registration of API specified by appendix 12 to Procedure № 426, taking into account requirements of appropriate regulatory documents and relevant recommendations for submitting eCTD. Submission type must be "registration" («maa»).

Location of registration dossier materials for the state registration of medicinal products belonging to the "Medical gases" group must comply with a List of documents required for conducting expert evaluation of registration materials for state registration of API specified by appendix 12 to the Procedure № 426 (including the instructions for medical use, the text of the labeling of the primary, secondary (if available) packages of the finished medicinal product, reports in accordance with annexes 29, 30 to the Procedure № 426 and a letter with recommendations for publishing these reports), taking into account the requirements of the relevant regulatory documents, as well as these Requirements. If the materials of the registration dossier are available in the format of Modules 1-5, it is possible to provide them in the relevant sections of the eCTD. Submission type must be "registration" («maa»).

Location of supporting documents during the procedure of state registration of a medicinal product, which is produced according to the approved specification in compliance with the MOH Ukraine Order of November 26, 2012 № 949 “On Approval of specifications for traditional medicinal products and a list of medicinal products produced according to the approved specifications”

|  |  |
| --- | --- |
| Module 1 | Name in Ukrainian |
| 1.0 | Cover letter |
| List of documents | Cover letter |
|  | Quality control methods (QCM) |
|  | A letter confirming that the composition, production and control of the medicinal product comply with the specification included in the List of medicinal products produced according to the approved specifications, approved by the MOH Ukraine Order of November 26, 2012 № 949.  |
|  | Letter from the applicant with recommendations regarding the publication of reports (Annexes 29, 30 to the Procedure № 426) |
|  | Report according to the Annex 29 to the Procedure № 426  |
|  | Report according to the Annex 30 to the Procedure 426 (if there are several reports, indicate as 30.1, 30.2 of the Procedure 426)  |
| 1.2 | Registration form |
| List of documents | Registration form (Annex 3 of the Procedure № 426) with its Annexes |
|  | Copy of registration certificate or other licensing document (Marketing Authorization, Certificate of a Pharmaceutical Product, Free Sale Certificate, etc.) issued by the competent authority of country of registration certificate holder (applicant) and/or manufacturer, or other country which regulatory authority follows high quality standards complying with WHO standards at the market where the medicinal product is placed. The list of countries, where the medicinal product concerned has been registered/re-registered shall be provided; |
|  | Copy of license to manufacture (if according to manufacturer’s country legislation the license to manufacture is available in electronic form only (e.g. USA), the printout with reference to appropriate official site certified by applicant’s signature/stamp (if any) shall be provided) or other licensing document to manufacture the applied pharmaceutical form in manufacturer’s country; |
|  | Certified copy of document confirming the compliance of manufacture of medicinal product with GMP issued by the State Service of Ukraine on Medicines and Drugs Control (Derzhliksluzhba) according to requirements of the Procedure for confirming compliance of manufacture of medicinal products with good manufacturing practice approved by the MoH Ukraine Order of December 27, 2012 № 1130, registered with the Ministry of Justice of Ukraine of January 21, 2013 under №133/22665 (as amended) or applicant’s letter of guarantee to submit such document during the specialized expert evaluation; |

Module 3 is provided taking into account the requirements of the MOH Ukraine Order of November 26, 2012 № 949 “On Approval of specifications for traditional medicinal products and a list of medicinal products produced according to the approved specifications” and Annex 8 to the Procedure № 426. Submission type must be "registration" («maa»).

2. Re-registration (renewal) can be used as the first eCTD in the MP life cycle, in a similar manner to changes (variations).

The submission type shall be “re-registration” (renewal).

Location of supportive documents during the re-registration procedure (renewal)

This is a list of locations of individual documents during the submission of documents for re-registration (renewal).

The list includes only files according to Annex 15 to the Procedure № 426.

|  |  |
| --- | --- |
| Module 1 | Name in Ukrainian |
| 1.0 | Cover letter |
| List of documents | 1.1. Cover letter |
| 1.2 | Registration form |
| List of documents  | 1.3. Registration form (Annex 14 to the Procedure № 426) with attachments to it1.4. 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 |
|  | 1.6. List of countries where the medicinal product is 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 resolved (recommendations for post-registration study, elimination of any defects, specified by control and other agencies, etc.) |
|  | 1.8. Summary data of the manufacturer/applicant on the safety of medical use of medicinal product in Ukraine during the validity period of the registration certificate according to the form provided for by the legislation |
| 1.3.1 | Copy of summary of product characteristics of medicinal product approved in the country of manufacturer/applicant |
| List of documents | 1.9. Updated summary of product characteristics/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 |
| 1.3.2 | Labeling  |
| List of documents | Approved text of the package labeling of the medicinal product and updated text of the package labeling (except for in bulk products)  |
| 1.3.3 | Instructions for medical use |
| List of documents | 1.9. Valid in Ukraine instructions for medical use of medicinal product and a summary of product characteristics (if any); draft updated instructions for medical use of medicinal product to be approved in Ukraine (except for in bulk products)  |
| 1.3.4 | Summary of product characteristics  |
| 1.4.1 | Information about the quality expert |
| List of documents | 1.11. Information about independent quality experts (including signature and CV) |
| 1.4.2 | Information about the non-clinical expert |
| List of documents | 1.11. Information about independent non-clinical expert (including signature and CV) – if applicable |
| 1.4.3 | Information about the clinical expert |
| List of documents | 1.11. Information about independent clinical expert (including signature and CV) |
| 1.8.1 | Pharmacovigilance system |
| List of documents | 1.12. Summary of pharmacovigilance system (if applicable) |
| 1.8.2 | Risk management system |
| List of documents | 1.13. Risk management plan (if applicable) |

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| --- | --- |
| Module 2 | Name in Ukrainian |
| 2.3 | Quality overall summary |
| List of documents | 2.1. 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 (Annex 15 to the Procedure № 426)Confirmation that all changes relating to the quality of medicinal product have been made according to the section VI of Procedure № 426 and the product conforms to current quality requirements Currently approved specifications for API (with date and number of latest approval)Currently approved specifications for 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)  |
| 2.4 | Non-clinical overview |
| List of documents | 2.2. Addendum to non-clinical overview (if applicable) |
| 2.5 | Clinical overview |
| List of documents | 2.3. Addendum to clinical overview |

The list includes only files according to Annex 16 to the Procedure № 426

|  |  |
| --- | --- |
| Module 1 | Name in Ukrainian |
| 1.0 | Cover letter |
| List of documents | Cover letter |
| 1.2 | Registration form |
| List of documents | 1. Registration form (Annex 14 to the Procedure № 426) with attachments to it  |
|  | 3. A letter confirming that the composition, production and control of the medicinal product comply with the specification included in the List of medicinal products produced according to the approved specifications, approved by the MOH Ukraine Order of November 26, 2012 № 949 |
| 1.3.2 | Labeling |
| List of documents | The approved text of the package labeling of the medicinal product and the updated text of the labeling |
| 1.3.3 | Instructions for medical use |
| List of documents | 2. Valid in Ukraine instructions for medical use of medicinal product and draft instructions for medical use of medicinal product |
| 1.3.4 | Summary of product characteristics |

1. All types of variations should be submitted to eCTD as new sequences under the Procedure for introduction of changes to the registration materials during the validity period of registration certificate (variations).

The type of submission should be variations of type IA (var-type1a), variations of type IAin (var-type1ain), variations of type IB (var-type1b), variations of type of II (var-type2), variations of type of I and II (var-type1-2), change of applicant (transfer-ma).

Documents related to the variation shall be included in the relevant sections or be deleted or replaced by use of the appropriate document operation attribute. Where documents cannot be assigned to specific CTD defined locations, then they should be provided as annexes to the m1.2 registration form. QCM, reports according to Annexes 29, 30 to the Procedure № 426, a letter from the applicant with recommendations regarding the publication of reports shall be placed in m1.0.

A list of locations of supportive documents in eCTD structure during the change of applicant (transfer-ma) is provided for placing supportive documents in eCTD structure during the change of applicant.

The list includes only files according to Annex 27 to the Procedure № 426.

|  |  |
| --- | --- |
| Module 1 | Name in Ukrainian |
| 1.0 | Cover letter |
| List of documents | Cover letter |
|  | Changes to QCM |
| 1.2 | Registration form |
| List of documents | Registration form (Annex 25 to the Procedure № 426) with attachments to it  |
|  | Documents in accordance with items 1-2.5, 2.7-2.10 |
| 1.3.2 | Proposals to the text of package labeling, which relate to the name and address of the new applicant (transferee) |
| 1.3.3 | Instructions for medical use |
| 1.3.4 | Summary of product characteristics  |
| 1.8.1 | Pharmacovigilance system |
| List of documents | 2.6. Documents showing the capacity of the new applicant (the transferee) to perform all the responsibilities required from a registration certificate holder under the country's pharmaceutical legislation |

1. Changes requiring new registration (extension) should be submitted within an existing eCTD, as a new sequence (continuous sequence numbering), or as a new eCTD (sequence 0000), if a separate lifecycle management for medicinal product is preferred.

Changes requiring new registration (extension) may be submitted as a new sequence within the original eCTD, submitting a new Module 1, an updated Module 2 and new or updated 3.2.P section. If m32p is combined for all previous existing strengths/dosage form(s), an updated section should be provided, replacing existing documents where necessary. If a separate m32p is provided for the additional strength/dosage form to describe the extension, then all documents should have the operation attribute of "new". For changes requiring a new registration and type of dossier, additional data in module 4 and/or 5 are provided, where necessary.

1. To ensure the relevance of registration materials documents downloaded in the Applicant's Account, in case of a decision according to the Procedure No. 426 regarding non-recommendation or rejection in the procedure for introduction of changes to the registration materials during the validity period of the registration certificate (variations), state re-registration (renewal), the corresponding sequence that restores the status of the registration dossier is downloaded immediately after the decision on the rejected procedure has been made to ensure the current display of the status of the dossier in the eСТD format.

When updating documents in eCTD format, it should be noted that, certain administrative information (cover letter, application, registration form, tracking table) and some scientific or regulatory information (e.g. a clinical trial report for a non-recommended new indication) shall be retained in the current view, to track the information submitted within the rejected procedure.

The consolidation sequence is part of the registration procedure, so it should have a "related-sequence" value that matches to the sequence number of the procedure's initial sequence.

1. Adjusting dossier materials in case of withdrawal of a strength, a dosage form or an entire withdrawal of a medicinal product

The type of submission "withdrawal" or the corresponding category of changes shall be used depending on the regulatory procedure.

If the withdrawal procedure does not include all strengths and/or dosage forms covered by the same eCTD, the sequence should be displayed with an operation attribute "delete" for documents that are no longer relevant. In addition, it may also include updated documents with a "replace" operation attribute for documents, which covered several other strengths and/or dosage forms and that now should be revised to remove the withdrawn strengths and/or dosage forms from the document.

An entire withdrawal of a medicinal product (all dosage forms and strengths) covered by the eCTD should preferably be displayed as a new sequence only, including a cover letter requesting the withdrawal. The "delete" operation attribute shall not be used for documents. The entire withdrawal submission for a medicinal product shall be made after it is agreed upon with the SEC.

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| --- | --- | --- |
| **Acting Director for Digital Transformation In Healthcare** | **/**signature/ | **Dmytro LUKIANOV** |