DOF [Official Gazette of the Federation by its Spanish acronym]: 03/29/2019

AGREEMENT through which the requested requirements and evaluation tests and procedures carried out through the Prequalification Program for Medicines and Vaccines of the World Health Organization are recognized as equivalent to the requirements established in Articles 161 Bis, 167, 169 and 170 of the Health Supplies Regulation and to the technical evaluation procedures carried out by the Federal Commission for the Protection against Health Risks for the purposes of granting a sanitary approval to health-related products referred to in Article 2, sections XIV, XV, subsections b and c, and Article 166, sections I, II and III of the Health Supplies Regulation, and in reference to Articles 222 and 229 of the General Health Law.

On the margin, a seal with the National Coat of Arms, which reads: United States of Mexico.- HEALTH.- Ministry of Health.

JORGE CARLOS ALCOCER VARELA, Ministry of Health, on the basis of Article 39, sections XV, XXI and XXVII of the Organic Law on Federal Public Administration; Article 3, section XXII, Article 4, section III, Article 13, part A, section II, Article 17 bis, sections IV and VI, Article 194, last paragraph, and Articles 222, 229 and 376 of the General Health Law; Article 84, sections II and IV of the General Law on Regulatory Improvement; Article 2, sections XIV and XV, subsections b and c, Articles 161 bis and 166, sections I, II and III, Articles 167, 167 bis, 168, 169 and 170 of the Health Supplies Regulation; and Article 7, section XVI of the Internal Regulation of the Ministry of Health, and

WHEREAS

Pursuant to Article 17 bis of the General Health Law, the powers of regulation, control and health promotion that correspond to the Ministry of Health, in accordance with the Organic Law on Federal Public Administration, the General Health Law and other applicable regulations, among which are the evaluation, issuance or revocation of the sanitary approval of health products, are exercised through the Federal Commission for the Protection Against Health Risks;

The last paragraph of Article 194 of the General Health Law, states that the sanitary control of the processing, import and export of medications, narcotic drugs and psychotropic substances and the raw materials involved in their preparation is the exclusive responsibility of the Ministry of Health, depending on the potential health risk that these products represent;

In accordance with the provisions of Articles 204 and 376 of the General Health Law, medications and other health products are required to have the corresponding health authorization, in the form of a sanitary approval, in order to be sold or supplied in the country;

Article 222 of the General Health Law establishes that the Ministry of Health will only grant the corresponding authorization to medications when it is proven that they, their production processes and the substances they contain meet the required characteristics of safety, efficacy and quality and that they comply with the provisions of said Law and other applicable general provisions, for which the Ministry of Health or its authorized third parties must previously verify compliance with good manufacturing practices and the production process of the medication as well as the certification of its active ingredients;

Article 161 Bis of the Health Supplies Regulation establishes that the Ministry of Health may issue general rules that aim to recognize that the

requirements, tests, evaluation procedures and other requirements requested by foreign health authorities to allow the sale, distribution and use of the supplies referred to in said Regulation in their respective countries are equivalent to those that the General Health Law, the Health Supplies Regulation and other applicable regulations require in order to guarantee the quality, safety and efficacy that these products must satisfy in order to obtain their sanitary approval in the country;

Article 166, sections I, II and III of the Health Supplies Regulation allows the issuance of a sanitary approval for allopathic medicines whose active ingredients are not registered in the United States of Mexico, but are registered and sold freely in their country of origin;

On the other hand, in accordance with Article 84 of the General Law on Regulatory Improvement, the heads of the agencies of the Federal Public Administration are empowered to simplify the procedures and services provided by law, regulation or any other provision that has been issued by the Head of the Federal Executive through general agreements published in the Official Gazette of the Federation which include, among others, response times that are less than the stipulated maximum, as well as to not demand the submission of data and documents;

On September 3, 2010, the following agreement was published in the Official Gazette of the Federation: "*Agreement that establishes the general provisions that must be met in order for the Ministry of Health to issue administrative agreements that recognize that the requirements, tests, evaluation procedures and other requirements requested by foreign health authorities to allow the sale, distribution and use of health products referred to in Article 194 Bis of the General Health Law in their respective countries, are equivalent to those required by the General Health Law, the Health Supplies Regulation and other related applicable legal and technical provisions in order to guarantee the quality, safety and efficacy that these products must evidence in order to obtain their sanitary approval, extension of their registration or any modification to the conditions in which they were registered in our country*" (General Provisions Agreement);

In accordance with the Amending Agreement to the General Provisions Agreement dated March 27 of the year in progress, which is duly published in the Official Gazette of the Federation, whose purpose was to establish the general rules that must be met in order for the Ministry of Health to issue administrative agreements that recognize that the requirements, tests, evaluation procedures and other requirements requested by the World Health Organization for the prequalification of health products referred to in Article 194 Bis of the General Health Law, are equivalent to those required by the General Health Law, the Health Supplies Regulation and other related applicable legal and technical provisions in order to ensure the quality, safety and efficacy that said products must evidence to obtain their sanitary approval, the extension of their registration or any modification to the conditions under which they were registered in our country;

The international standards of the World Health Organization, established in its Technical and Scientific Evaluation Procedure of its Health Supplies Prequalification System, are widely recognized at the international level, and the Federal Commission for the Protection Against Health Risks has carried out the necessary actions to verify that the requirements established in the aforementioned program are equivalent to the requested requirements and technical evaluation procedures in order to grant the corresponding sanitary approval in our country, in light of the foregoing I have decided to issue the following:

AGREEMENT

ONE. The evaluations and inspections carried out by the World Health Organization through its Program for the Prequalification of Medicines and

Vaccines, under the terms established in the Sole Appendix of this Agreement, are recognized as equivalent to the requirements established in Articles 161 Bis, 167, 169, and 170 of the Health Supplies Regulation and to the technical evaluation procedures carried out by the Federal Commission for the Protection Against Health Risks for the purposes of granting a sanitary approval to the health products referred to in Article 2, sections XIV, XV, subsections b and c, and Article 166, sections I, II and III of the Health Supplies Regulation, and in relation to Articles 222 and 229 of the General Health Law.

TWO. Applications for a sanitary approval that are processed before the Federal Commission for the Protection Against Health Risks under the terms of this Agreement must be submitted with the COFEPRIS-04-004-C and COFEPRIS-04-004-D identification codes, and it must be indicated in writing that they are being requested under this regulation.

PROVISIONAL ARTICLE

SOLE. This Agreement shall come into force on the day of its publication in the Official Gazette of the Federation.

Given in Mexico City, on the twenty-eighth day of the month of March of two thousand nineteen.- The Ministry of Health, Jorge Carlos Alcocer Varela.- Signature.

SOLE APPENDIX

CRITERIA AND PROCEDURES FOR THE RECOGNITION OF EQUIVALENCE OF THE REQUESTED REQUIREMENTS AND TESTS AND EVALUATION PROCEDURES CARRIED OUT THROUGH THE PRE-QUALIFICATION PROGRAM FOR MEDICINES AND VACCINES OF THE WORLD HEALTH ORGANIZATION

SECTION I

DEFINITIONS

ONE. For the purposes of this Appendix, it shall be understood:

Procedure Agreements: "Agreement through which the procedures and services are made known, as well as the forms that the Ministry of Health applies, through the Federal Commission for the Protection Against Health Risks, registered in the Federal Registry of Procedures and Services of the Federal Commission on Regulatory Improvement," published in the Official Gazette of the Federation on January 28, 2011 and its respective amending agreements, as well as the "Agreement through which the referenced forms of the procedures in charge of the Ministry of Health are made known," published in the Official Gazette of the Federation on September 2, 2015;

Demanding Regulatory Authority: To a member of the ICH; or an observer from the ICH, among which include the World Health Organization, or a regulatory agency associated with an ICH member through mutual recognition;

GMP: Good Manufacturing Practices;

COFEPRIS [by its Spanish initials]: Federal Commission for Protection Against Health Risks;

CTD: Common Technical Document;

ICH: International Conference on Harmonization;

Technical Information: The necessary tests, analyses, preclinical and clinical

trials, as appropriate, to demonstrate the safety, quality and efficacy required by the Ministry to grant a sanitary approval;

Law: General Health Law;

WHO: World Health Organization;

Biological Products: For the purposes of this Appendix, products of a biological origin shall be understood as those referenced in Article 229, sections I, II, V, VII and IX of the Law;

Regulation: Health Supplies Regulation;

Ministry: Ministry of Health, and

Series of Technical Reports: A series of technical documents issued by the World Health Organization;

SECTION II

GENERAL PROVISIONS

TWO. COFEPRIS will require the applicants for the sanitary approval of medicines and Biological Products that have WHO prequalification the following information and documentation:

Generic allopathic medicines: The application for a sanitary approval will be submitted in the official format issued by the Ministry through the Procedure Agreements, to which proof of payment of fees must be attached and the documents indicated in Article 167, sections I, II, III, IV, V and VI, and Articles 167 bis, 169 and 170 of the Regulation, which are listed in section III of this Appendix, and which must include the Technical and Scientific Information that demonstrates:

The identity and purity of its ingredients in accordance with the provisions of the Pharmacopoeia of the United Mexican States and its supplements;

The stability of the finished product according to the corresponding standards;

Therapeutic efficacy and safety according to the corresponding Technical Information;

Prescription information, in its long and abridged versions;

Corresponding label and instruction projects, as well as the specifications for the primary and secondary containers, in accordance with the Law, the Regulation and other applicable provisions;

GMP certificate of the drug and the medication issued by the Ministry or by the originating authority and, when applicable, that of the manufacturer of the diluent, issued by the Ministry or by the competent authority of the country of origin. In the event that the Ministry does not have executed GMP recognition agreements, the Ministry may verify, through COFEPRIS, compliance with the GMP;

In the case of a patent, documentation will be required to prove that the applicant is the patent holder of the active substance or active ingredient or that they hold the corresponding license, both registered with the Mexican Institute of Industrial Property;

For generic medicines that require a bioequivalence study as a test of interchangeability, such will be established by the General Health Council under the terms of the current Agreement that determines the type of test to demonstrate the interchangeability of generic medicines and that define the criteria that should be applied to them or in the related updates that are issued, and

Prequalification will be recognized for bioequivalent units that have the recognition of compliance in accordance with the requirements of technical reports issued by the WHO and/or of a Demanding Regulatory Authority, and

For Biological Products and new molecules: The application for a sanitary approval will be submitted in the official format issued by the Ministry through the Procedure Agreements, to which must be attached the proof of payment of fees and the documents indicated in Article 167, Sections I, II, III, IV and VI, and Articles 167 bis, 169 and 170 of the Regulations, which are listed in section III of this Appendix, and which must include the Technical Information that demonstrates:

The identity and purity of its ingredients in accordance with the provisions of the Pharmacopoeia of the United Mexican States and its supplements;

The stability of the finished product according to the corresponding standards;

The therapeutic efficacy and safety in accordance with the corresponding Technical Information;

The prescription information, in its long and abridged versions;

Corresponding label and instruction projects, as well as the specifications for the primary and secondary containers, in accordance with the Law, the Regulation and other applicable provisions;

GMP certificate of the drug and of the medication, issued by the Ministry or by the originating authority and, when applicable, that of the manufacturer of the diluent, issued by the Ministry or by the competent authority of the country of origin. In the event that the Ministry does not have executed GMP recognition agreements, the Ministry, through COFEPRIS, may verify compliance with the GMP, and

In the case of a patent, documentation will be required to prove that the applicant is the patent holder of the active substance or active ingredient or that they hold the corresponding license, both registered with the Mexican Institute of Industrial Property.

THREE. Vaccines and new molecules must obtain the favorable opinion of the New Molecules Committee in accordance with the provisions of Article 166, section III of the Regulations and Article 3, sections III and V of the Internal Regulations of the New Molecules Committee.

FOUR. It will be grounds for rejection of the application for a sanitary approval under this regulation, if there is evidence that the product to be registered has been flagged by the WHO or by some Demanding Regulatory Authority because the safety profile is not acceptable or the risk-benefit is not favorable.

FIVE. COFEPRIS will not require any additional documentation that may be applicable according to Article Two of this Appendix in order to process the application for a sanitary approval that is submitted on the basis of this regulation regardless of the country of origin of the medication.

SIX. COFEPRIS must decide on the application for a sanitary approval within a maximum period of 60 working days counted from the day following that in which the applicant delivers the applicable documentation according to Articles Two of this Annex. After the aforementioned deadline, if COFEPRIS has not responded, it will be understood that it has reached a negative decision.

In case the submitted documentation is not complete, COFEPRIS will inform the applicant within a period that will be equal to one third of the time granted to decide on the application, when it is of an administrative nature, and two thirds, when it is of a technical nature, under the terms of the provisions of Article 156 of the Regulation.

The deadline for responding to the request for missing documentation will be established by COFEPRIS in accordance with the provisions of Article 17-A of the Federal Law of Administrative Procedure.

SEVEN. The deadline for deciding on the application for a sanitary

approval, indicated in Article Seven of this Annex, will be suspended when COFEPRIS requires the applicant to submit, expressly and in writing, documents, clarifications or missing information and will resume the business day following the one in which the applicant delivers said information, documents or makes the pertinent clarifications. In case the applicant does not provide the documents, clarifications or missing information within the timeframe established for this purpose, the application shall be regarded as not having been submitted.

EIGHT. The holders and/or their legal representatives who obtain the sanitary approval under the terms established by this Regulation, will not be exempt from compliance with the requirements established in articles 43 and 131 of the Regulations or any other requirement or specification necessary to preserve said sanitary approval, in accordance with the applicable legal provisions, as well as any additional requirements the sanitary approval may be subjected to for commercialization in Mexican territory in accordance with the applicable provisions.

NINE. The holders of the sanitary approval granted under this Regulation, as well as the importers and vendors, shall inform COFEPRIS about the revocation, cancellation, or suspension of WHO prequalification, about which they have or should have knowledge; they must also notify COFEPRIS when there is any change in the safety profile or the risk-benefit of the medicines and vaccines that are registered under this Regulation, that occur during their commercialization or use, in terms of the provisions of Articles 38 and 81 Bis of the Regulation and the Official Mexican Standard NOM-220-SSA1-2016. Installation and operation of pharmacovigilance, as well as any other circumstance that must be reported to the competent authorities, in accordance with applicable legal provisions.

TEN. COFEPRIS, in addition to the cases established in Articles 376 and 380 of the Law, shall revoke the sanitary approval granted under this Regulation resulting from the loss of the prequalification granted by the WHO.

ELEVEN. The granting of a sanitary approval under the terms of this Regulation will not be prevent COFEPRIS from exercising its powers in matters of sanitary surveillance and sanitary control in accordance with applicable legal provisions.

TWELVE. No provision of this Regulation may be interpreted in such a way as to restrict the entry of products that obtain a sanitary approval before COFEPRIS in accordance with this Regulation for the sole reason of having obtained their registration through the recognition of established technical equivalence.

THIRTEEN. The documents accompanying the applications must be written in Spanish and, if not, they must have attached their respective translation to Spanish, endorsed with the signature of the responsible health manager.

Documents issued by authorities of other countries must be apostilled or certified and translated by a certified translator.

Technical documents accepted in English are indicated in section III of this Appendix.

FOURTEEN. Applications for extensions and modification to the conditions of the registration for health products granted under this Regulation must adhere to the provisions of the Law, the Regulation and other applicable legal provisions.

SECTION III

DOCUMENTS THAT MAKE UP THE REGISTRATION APPLICATION FILE

The applicant must submit the information in accordance with the CTD

and shall deliver it attached to the registration application with the updated information, printed and in electronic form via USB device in PDF format, according to the Electronic Common Technical Document Specification" (ICH M2 EWG).

The CTD shall be divided in five modules. Module 1 is specific for Mexico and modules 2, 3, 4 and 5 contain information common to all regions that use the CTD format. The content and information must conform to the applicable technical and legal requirements for each type of registration applied for, and the submission of some type of duly justified information may be excluded, for example, non-clinical trials in the case of applications for generic drug registrations.

The equivalence section indicated in the modules refers to the requirement that can be covered by what is indicated as equivalent.

Module 1: Administrative-legal information.

Module 1 contains specific documents for Mexico.

CTD Section	Description	Equivalence
1.1	Table of contents	NA
1.2	Free text letter (when applicable).	NA
1.3	Label proposals (printed in duplicate).	NA
1.4	Instructions, insert or leaflet (printed in duplicate).	NA
1.5	Prescription proposals, long and abridged versions (printed in duplicate).	NA
1.6	Prequalification certificate issued by the WHO, as well as the (electronic) link to verify the accuracy and validity of the prequalification.	NA
1.7	Patent information	NA
1.8	Distinctive denomination.	NA
1.9	Minutes with the conclusions of the meeting with the New Molecules Committee. Minutes with favorable technical opinion. Only applicable to Vaccines and New Molecules.	NA
1.10	Certificate of Good Manufacturing Practice (GMP) or Equivalent Document Drug manufacturer(s) Drug manufacturer (including primary and secondary packaging) Adjuvant Diluent	Certificate of Good Manufacturing Practices from the country of origin in accordance with the Series of Technical Report specified in the WHO Prequalification requirements
1.11	Information of the medical device. (When applicable)	NA
Holders with a Health License in National territory.		
1.12	Health License and Notice of Health Manager.	NA
1.13	Simple copy of the health license with the line of business and distribution of medicines or notice of operation, as the case may be, for the company that will serve as distributor of the medicine in national territory	NA

Holders abroad		
1.14	Documentation proving the legal representative has an address in national territory	NA
1.15	License, certificate or document proving that the holder has the permission to manufacture medicines, issued by the authority	The document issued by the authority of the country of origin of the holder of the registration is recognized.
1.16	Simple copy of the sanitary license with the line of business and distribution of medicines or notice of operation, as the case may be, for the company that will serve as distributor of the medicine in national territory	NA
1.17	Pharmacovigilance unit registered with the National Pharmacovigilance Center	NA
1.18	Agreement executed between the laboratory applying for registration and the auxiliary control laboratory for sanitary regulation that shall perform the corresponding analyzes of the medication for which the application has been submitted.	NA
For medicines of foreign manufacture, in addition to the above, you must submit		
1.19	Letter of representation/authorization (in not a subsidiary)	NA
1.20	Certificate of Free Sale	Pharmaceutical Product Certificate

Module 2: Summaries

The information must be submitted with its respective translation into Spanish and English.

The objective of this module is to summarize the quality data (chemical, pharmaceutical and biological) and the non-clinical and clinical data submitted in modules 3, 4 and 5 of the drug registration application file.

The experts who write these summaries should objectively address the decisive points of the quality of the vaccine, the non-clinical and clinical trials carried out, notify all relevant data for the evaluation and refer to the corresponding tables included in modules 3, 4 and 5. The information of module 2 must be submitted according to the following order:

CTD Section	Description	Equivalence
2.1	Table of Contents	NA
2.2	Introduction	NA
2.3	General quality summary	NA
2.4	Preclinical global analysis	NA
2.5	Clinical global analysis	NA
2.6	Preclinical written and tabulated summary	NA

2.7	Clinical summary	NA

Module 3. Quality

The summaries of the information in this section of the CTD must be submitted in Spanish, while the full report must be submitted in English.

CTD Section	Description	Equivalence
3.1	Table of Contents	NA
3.2	Contents	NA
3.2.S	Active principle(s)	NA
3.2.S.1	General information, starting materials and raw materials	NA
3.2.S.2	Manufacturing process of the active principle	NA
3.2.S.3	Characterization of the active principle	NA
3.2.S.4	Quality control performed on the active principle	NA
3.2.S.5	Container closure system	NA
3.2.S.6	Standards or reference materials	NA
3.2.S.7	Stability of the active principle	NA
3.2.S.8	Consistency of production of the active principle	NA
3.2.P	Finished product	NA
3.2.P.1	Description and composition of the finished product	NA
3.2.P.2	Pharmaceutical development	NA
3.2.P.3	Manufacture of the finished product	NA
3.2.P.4	Control of adjuvant, preservatives, stabilizers and excipients	NA
3.2.P.5	Control of the finished product	NA
3.2.P.6	Standards and reference materials	NA
3.2.P.7	Container closure system	NA
3.2.P.8	Stability	NA
3.2.A	Appendices	NA
3.2.A.1	Equipment and installations	NA
3.2.A.2	Evaluation of safety against adventitious agents	NA
3.2.R	Regional Information (Must be submitted in English and Spanish)	NA

3.2.R.1	Production documentation. Records of manufacturing lots/summarized manufacturing protocol.	You must submit the production orders of the lots used in the stability study.
3.2.R.2	Additives	Analytical certificates of origin and issued by the manufacturer of the medicine or establishment responsible for quality analysis.
3.2.R.3	Medical devices. Description and function of the medical device. (Indicate the manufacturer of the medical device).	NA
3.R.4.	Documentation for the release of the lots issued by the manufacturer of the drug and medication	For new molecules and generic drugs the analytical certificate of the lots used in the stability study issued by the manufacturer. For vaccines the certificate of release of the finished product issued by the regulatory authority of origin.
3.3	Bibliography	NA

In the subfolder of the 3.2.R Regional Information module, you must include the Product Summary File (PSF). In the PSF's Clinical Experience module, an analysis should be included with the global efficacy, safety and immunogenicity data, when applicable.

Module 4: Non-clinical evidence

The summaries of the information in this section of the CTD must be submitted in Spanish, while the full report must be submitted in English.

The agreed format for the organization of the reports of non-+trials for the applications of medicines that seek to obtain their registration in Mexico must be respected. The structure of this module is not intended to indicate which studies are required, it simply indicates the order and appropriate format for the non-clinical data.

The content of the CTD is listed as an example, however, the application must adhere to the ICH M2 EWG guide.

It should be noted that this section generally does not apply in the case of generic medicines.

CTD Section	Description	Equivalence
4.2	Study reports	NA
4.2.1	Pharmacology	NA
4.2.1.1	Primary pharmacodynamics	NA
4.2.1.2	Secondary pharmacodynamics	NA
4.2.1.3	Safety pharmacology	NA
4.2.1.4	Pharmacodynamic drug interactions	NA
4.2.2	Pharmacokinetics	NA

4.2.2.1	Analytical methods and validation reports (if separate reports are available)	NA
4.2.2.2	Absorption	NA
4.2.2.3	Distribution	NA
4.2.2.4	Metabolism	NA
4.2.2.5	Excretion	NA
4.2.2.6	Pharmacokinetic drug interactions (preclinical)	NA
4.2.2.7	Other pharmacokinetic studies	NA
4.2.3	Toxicology	NA
4.2.3.1	Single dose toxicity (in order per species, per route)	NA
4.2.3.2	Repeated dose toxicity (in order by species, by route, by duration, including supporting toxicokinetic evaluations)	NA
4.2.3.3	Genotoxicity	NA
4.2.3.3.1	In vitro	NA
4.2.3.3.2	In vivo (including supporting toxicokinetic evaluations)	NA
4.2.3.4	Carcinogenicity (including supporting toxicokinetic evaluations)	NA
4.2.3.4.1	Long-term studies (in order by species, including dose-ranging studies that cannot be appropriately included with repeated-dose or pharmacokinetic toxicity)	NA
4.2.3.4.2	Short-term or medium-term studies (including dose-ranging studies that cannot be appropriately included with repeated-dose or pharmacokinetic toxicity)	NA
4.2.3.4.3	Other studies	NA
4.2.3.5	Reproductive and developmental toxicity (including dose-ranging studies and supporting toxicokinetic evaluations)	NA
4.2.3.5.1	Fertility and early embryonic development	NA
4.2.3.5.2	Embryo-fetal development	NA
4.2.3.5.3	Prenatal and postnatal development, including maternal function	NA
4.2.3.5.4	Studies in which descendants (juvenile animals) are dosed and/or evaluated additionally	NA
4.2.3.6	Local tolerance	NA
4.2.3.7	Other toxicity studies (if available)	NA
4.2.3.7.1	Antigenicity	NA
4.2.3.7.2	Immunotoxicity	NA
4.2.3.7.3	Mechanistic studies (if they are not included elsewhere)	NA
4.2.3.7.4	Dependency	NA
4.2.3.7.5	Metabolites	NA
4.2.3.7.6	Impurities	NA
4.2.3.7.7	Others	NA

4.3	Bibliography	NA

Module 5: Clinical evidence

The summaries of the information in this section of the CTD must be submitted in Spanish, while the full report must be submitted in English.

For generic medicines the final report of the interchangeability study may be made in accordance with Appendix 6 of Pharmaceutical Products from multiple sources (generic): Guidelines on registration requirements in order to establish interchangeability for WHO prequalification TRS 1003, 2017.

The agreed format for the organization of the reports of clinical trials must be respected for the applications of medicines that seek to obtain their registration in Mexico. The structure of this module is not intended to indicate which studies are required, it simply indicates the order and appropriate format for the clinical information. The reports presented must adhere to the content and structure established in the ICH E3 guide.

The content of the CTD is listed as an example, however, the application must follow the ICH M2 EWG guide.

CTD Section	Description	Equivalence
5.1	Table of contents	NA
5.2	Tabulated list of all clinical trials	NA
5.3	Reports on clinical trials	NA
5.3.1	Reports on biopharmaceutical studies	NA
5.3.1.1	Reports on bioavailability studies (BA)	NA
5.3.1.2	Comparative reports of BA and bioequivalence (BE) studies	NA
5.3.1.3	Reports on In vitro-In vivo correlation studies	NA
5.3.1.4	Reports on bioanalytical and analytical methods for human studies	NA
5.3.2	Reports on studies relevant to pharmacokinetics that use human biomaterials	NA
5.3.2.1	Reports on plasma protein binding studies	NA
5.3.2.2	Reports on hepatic metabolism and drug interaction studies	NA
5.3.2.3	Reports on studies using other human biomaterials	NA
5.3.3	Reports on studies of human pharmacokinetics (PK)	NA
5.3.3.1	Reports on initial tolerability studies and PK of healthy subjects	NA
5.3.3.2	Reports on patient PK and Initial Tolerability	NA
5.3.3.3	Reports on intrinsic factor PK studies	NA
5.3.3.4	Reports on extrinsic factor PK studies	NA
5.3.3.5	Reports on population PK studies	NA
5.3.4	Reports on human pharmacodynamic studies (PD)	NA
5.3.4.1	Reports on PD and PK/PD studies on healthy subjects	NA
5.3.4.2	Reports on PD and PK/PD studies on patients	NA
5.3.5	Reports on Efficacy and Safety Studies	NA

5.3.5	Reports on Efficacy and Safety Studies – Indication name	NA
5.3.5.1	Reports on controlled clinical trials relevant to the claimed indication	NA
5.3.5.2	Reports on uncontrolled clinical trials	NA
5.3.5.3	Reports on data analysis from more than one study	NA
5.3.5.4	Other study reports	NA
5.3.6	After-market experience reports	NA
5.3.7	Case study report forms and individual patient lists	NA
5.4	Bibliography	NA