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Draft

HMA/EMA guidance document on the identification of personal data and commercially confidential information within the structure of the marketing authorisation application (MAA) dossier

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Comments should be provided using this EUSurvey form. For any technical issues, please contact the EUSurvey Support.

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Abbreviations

CCI	Commercially Confidential Information
CMO	Contract Manufacturing Organisation
CRO	Contract Research Organisation
CTD	Common Technical Document
EEA	European Economic Area
EMA	European Medicines Agency
HMA	Heads of Medicines Agencies
IEC	Independent Ethics Committee
INN	International Nonproprietary Name
IRB	Institutional Review Board
MA	Marketing Authorisation
MAA	Marketing Authorisation Application
MAH	Marketing Authorisation Holder
MCB	Master Cell Bank
NCA	National Competent Authority
PD	Personal Data
PI	Product Information
PIP	Paediatric Investigation Plan
PPD	Protected Personal Data
QP	Qualified Person
QPPV	Qualified Person Responsible for Pharmacovigilance
RMP	Risk Management Plan
WCB	Working Cell Bank

Definitions

For the purpose of this guidance the following definitions apply:

Anonymisation: shall mean the operation performed on personal data (e.g. redaction, masking, hiding) in such a manner that the recipient can no longer attribute the resulting information to a data subject and make it identifiable.

Applicant/Marketing Authorisation Holder (MAH): shall mean the natural or legal person(s) or organisation(s) that submitted documents to EMA/NCA in the context of applications in support of national, mutual recognition, decentralised or centralised marketing authorisations (MAs) and post-authorisation submissions for existing authorised medicinal products, as well as any person(s) or organisation(s) who own(s) copyright or other intellectual property rights in the submitted documents.

Commercially Confidential Information (CCI): shall mean any information which is not in the public domain or publicly available and where its disclosure may undermine the economic interest or competitive position of the owner of the information.

Contract Research Organisation (CRO): shall mean a person or an organisation (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's duties and functions.

Contract Manufacturing Organisation (CMO): shall mean an arrangement under which a manufacturer provides upstream manufacturing services under contract on behalf of third-party pharmaceutical companies.

Document: shall mean any content regardless of its medium (a written document stored electronically or on paper, or an audio, video or audio-visual recording) concerning a matter relating to the structure of the marketing authorisation application (MAA) dossier and documents containing data extracted from the MAA dossier for the purpose of this guidance and other documents related to finalised regulatory procedures.

Personal data (PD): shall mean any information relating to an identified or identifiable natural person ('data subject'); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person.

Protected Personal Data (PPD): shall mean any personal data which should be protected from disclosure.

Third party: shall mean any natural or legal person, or any entity outside EMA/NCA, including EU or non-EU institutions and bodies, applicants/MAH, sponsors and third countries.

This guidance document is intended to be applicable to information/documents pertaining to the initial and variation of **marketing authorisation application (MAA) dossiers of medicinal products for human use** for which the **regulatory procedure has been finalised**, under the national, mutual recognition, decentralised and centralised procedures. "Finalised" shall mean that the marketing authorisation (MA) has been granted or refused or that the MAA has been withdrawn.

By extension, the principles laid down in this guidance can be considered for other types of finalised procedures such as orphan designations, Paediatric Investigation Plans (PIPs)/waivers or scientific advice. The application of the general principles laid down in this guidance is without prejudice to national rules on transparency. The guidance should be read in conjunction with the relevant applicable legislation and case law on transparency and data protection.

1. Scope and purpose

In 2023, the Heads of Medicines Agencies (HMA) and the European Medicines Agency (EMA) agreed to update the guidance which had been adopted in 2012 defining the common approach on what should be considered as personal data (PD) and commercially confidential information (CCI) in the MAA dossier of medicinal products for human use. Based on the experience gained by applying the principles set out in the first version of the present guidance document in 2012, it became apparent that the guidance and its annex needed to be updated. The objective remains to continue to facilitate a common and consistent approach across the European Economic Area (EEA) to provide guidance on the identification of PD that must be protected and CCI included in the MAA dossier.

This guidance document is intended to apply to information/documents on medicinal products for human use, for which the procedure has been finalised under the national, mutual recognition, decentralised and centralised procedures.

By extension, it is also intended to cover documents concerning the variation of the MA or documents containing information pertaining to the MAA dossier or documents linked to the aforementioned applications.

When it comes to disclosure of information/documents, the decision lies with the EMA/NCA. Third parties shall be informed or consulted as needed depending on respective national and European legal frameworks.

This guidance addresses the shared approach to be taken as high-level principles when providing access to different information/documents in the MAA dossier and follows the structure of the Common Technical Document (CTD) according to Volume 2B Notice to Applicants Medicinal products for human use/ICH M8 Electronic common technical document (eCTD) v4.0 draft ICH implementation guide v2.0 – Scientific guideline (CHMP/ICH/143002/2015).

It is intended to be a consensus document agreed by the whole network of national competent authorities (NCAs) of the EEA for the disclosure of information/documents regarding medicinal products for human use (i.e., not applicable to medicinal products for veterinary use or medical devices) and lays down practical orientations for national and European authorities regarding the disclosure of the MAA dossier while providing adequate protection such as commercially confidential information and personal data. Notwithstanding this guidance document, it should be noted that EMA/NCA has to follow their European/national legislation on transparency and data protection (pursuant to Regulation (EU) 2016/679, Regulation (EU) 2018/1725 and any other relevant national data protection legislation applicable to NCAs, respectively).

In the following sections, the agreed principles on PD and CCI are presented, including guidance on whether such information can be disclosed.

Any information identified as PD or CCI must be subject to a preliminary review by the EMA/NCA prior to the possible disclosure of the information/documents.

2. Principles on the protection of personal data (PD)

The protection of PD is enshrined in EU legislation; it is a fundamental right of EU citizens. In compliance with the applicable European/national legislation, PD should be anonymised in order to avoid the disclosure of the document undermining the privacy and integrity of any individual.

Each assessment performed by EMA/NCA is carried out in compliance with Regulation (EU) 2018/1725, Regulation (EU) 2016/679 and national data protection provisions as applicable, in order to minimize the risk of re-identification of the individual by removing data elements which, in combination, could single out an individual. EMA/NCA applies a risk-based approach to assess which PD elements are to be removed from the information/documents in order to limit the risk of re-identification.

PD in the MAA dossier mainly falls into the following categories:

A. PD related to experts or designated personnel with legally defined responsibilities;

B. PD related to staff with no legally defined responsibilities;

C. PD related to subjects involved in clinical trials and clinical studies;

D. PD related to patients in the context of medicine safety.

A. PD related to experts or designated personnel with legally defined responsibilities

In general, it is considered that names of experts or designated personnel with legally defined responsibilities and roles with respect to aspects of the MAA dossier (e.g., qualified person (QP), qualified person responsible for pharmacovigilance (QPPV), clinical expert, investigator/principal investigator (PI), sponsor's signatory, etc.) are included in the MAA dossier because they have a legally defined role or responsibility and it is in the public interest to disclose this data. In addition, the names of experts or designated personnel with legally defined responsibilities involved in animal studies may be anonymised if it can be demonstrated that disclosure of such information may present a security risk to those individuals in the country concerned.

Applicants are advised that non-essential information (e.g., personal address, personal phone number) should not be included in the MAA dossier. If present in the MAA dossier, such PD should be anonymised.

B. PD related to staff with no legally defined responsibilities

HMA/EMA does not consider that the names or personal details of staff with no legally defined responsibilities need to be included in the MAA dossier. Applicants are therefore advised that such data should not be included in the MAA dossier. If present in the MAA dossier, such PD should be anonymised.

C. PD related to subjects involved in clinical trials and clinical studies

Information on subjects involved in clinical trials and clinical studies must be pseudo-anonymised when included in the MAA dossier submitted to competent authorities. Applicants should ensure that the dossier submitted meets the legislative requirements. When submitting the documentation related to clinical trials and clinical studies, the applicant is responsible and certifies that trials and studies have

been conducted in accordance with Good Clinical Practices (GCP), including the respect of patient confidentiality according to Principle 2.11 of the Guideline for good clinical practice E6(R2). The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).

The applicant remains responsible for compliance with the relevant legislation in cases where such data is inadvertently included in the MAA dossier. In these cases, this data should not be disclosed without being anonymised.

EMA/NCA applies a risk-based approach to assess which personal data elements need to be removed from the information/documents in order to limit the risk of re-identification.

D. PD related to patients in the context of medicine safety

In relation to PD related to patients in the context of medicine safety during the post-authorisation phase, the principles outlined in this guidance and in the HMA/EMA recommendations on the handling of requests for access to periodic safety update reports (EMEA/74133/2009) should be applied.

EMA/NCA applies a risk-based approach to assess which personal data elements need to be removed from the information/documents in order to limit the risk of re-identification.

3. Principles to be applied for the redaction of commercially confidential information (CCI)

Information/documents that may contain CCI should be subject to redaction prior to their disclosure. CCI relates to information that is not in the public domain or publicly available, and where its disclosure may undermine the economic interest or competitive position of the owner of the information.

Where the redaction of CCI is proposed by the owner of the information, an assessment of these proposed redactions should be performed by EMA/NCA, taking into account the justification provided by the owner of the information, in order to decide whether the definition of CCI applies.

Any proposal to consider information as commercially confidential should be properly justified by the owner of the information. This means that an explanation of how access to this proposed information could specifically and actually undermine the economic or competitive interest of the owner of the information should be provided. In this respect, any reference(s) to the risk of that interest being undermined should be foreseeable and not purely hypothetical.

Information that is already in the public domain is not considered to be commercially confidential. However, if information has been in the public domain through a breach of the law, it could still be considered confidential in accordance with the principles of this document. However, the owner of the information has to inform the respective EMA/NCA in writing about the breach of law.

The above principles do not prevent EMA or the NCA (as applicable) from satisfying themselves, by means of a concrete, individual examination of each document in the MAA dossier, whether the document is covered by the exception relating to the protection of CCI.

In the context of assessing a request for access to documents (policy on access to documents – Policy/0043 (EMA/729522/2016), the existence of an overriding public interest in disclosure may be assessed if the information concerned is found to be commercially confidential.

A statement expressing purely general considerations is not sufficient for the purpose of establishing that an overriding public interest prevails over the reasons justifying the refusal to disclose the

documents in question. Similarly, a statement expressing vague considerations is not sufficient for establishing that the principle of transparency is especially pressing and should prevail over the reasons justifying the non-disclosure of the information/documents concerned.

3.1. Information on the Quality and Manufacturing of medicines

A general principle regarding quality and manufacturing information is that detailed information could be considered commercially confidential but general information should be disclosed.

3.1.1. Composition and product development

In general, pharmaceutical development information is commercially confidential. This includes detailed data concerning the active substance, formulation, manufacturing, test procedures and validation (see Annex).

The final qualitative formulation (composition) of the authorised product is not commercially confidential.

In general, and if not in the public domain, the names of manufacturers or suppliers of the active substance or the excipients are considered commercially confidential.

3.1.2. Active substance

Information concerning the manufacturing of the active substance, including technical and industrial process parameters and in-process/intermediate specifications may be considered as CCI.

Detailed information on the synthesis or manufacture of the active substance, including details on the by-products and degradation products of active ingredients and validation of the manufacturing/synthesis process, is commercially confidential.

Information on the structure of the active substance is not commercially confidential. This will be known and published at the time of allocating the international non-proprietary name (INN) if relevant.

Detailed information concerning the particulars of studies regarding polymorphism and particle size should be treated as CCI.

Concerning impurities and degradation products, qualitative and quantitative information is regarded as CCI.

A general description of the type of test methods used and the appropriateness of the specification is not commercially confidential. However, detailed information on the test methods used and the specification and quantitative acceptance criteria established for the active substance is commercially confidential, unless the tests meet specific monographs in the European Pharmacopoeia or another national Pharmacopeia.

In addition, for biotechnology products, a general description of the active ingredient including the type of molecule and its general structural features (e.g., number of amino acids, general glycosylation details) or of the type of producer cell (e.g., *E. coli, S. cerevisiae*, Chinese hamster ovary cells, Madin Darby kidney cells) is not commercially confidential. A general statement on the establishment of the Master Cell Bank (MCB) or Working Cell Bank (WCB) and on the stability of the cell banks is also not considered commercially confidential. General information on the fermentation and purification process is not commercially confidential, although details including operating parameters and specific material requirements are commercially confidential.

Details on the process validation of the active substance manufacturing process are commercially confidential, although statements confirming that the manufacturing and control processes have been validated are not commercially confidential.

General information on the characterisation of the active substance such as the analytical technique(s) and statements confirming that the molecule is appropriately characterised are not considered commercially confidential. However, details of characterisation technique(s) are considered commercially confidential.

The above principles also apply to novel excipients.

3.1.3. Finished product

The detailed descriptions of the manufacturing and control processes for the product are commercially confidential.

Details of the validation of the manufacturing process are also considered commercially confidential.

A general description of the type of test methods used and the appropriateness of the specification is not commercially confidential. Detailed information on the test methods included in the specification of the finished product and the quantitative acceptance criteria is commercially confidential unless the tests are of Pharmacopoeial standard.

Concerning degradation products, qualitative and quantitative information is regarded as CCI.

3.2. Non-clinical and clinical information

Information encompassing non-clinical and clinical development of the medicinal product and the subsequent assessment by competent authorities is not *per se* commercially confidential. This includes information related to environmental risk assessments with related studies and risk management plans. In general, the data included in clinical trial study reports is considered to be data that can be disclosed once PD has been anonymised. In the case of exceptional and substantiated cases, particularly where innovative study designs and/or innovative analytical methods have been used, consideration will be given to the need for redaction of specific elements.

3.3. Information on inspections

Information on the outcome of inspections (e.g., conclusion on compliance/non-compliance/outstanding issues to be addressed) is already available in the public domain (e.g., EudraGMDP and EPAR) and therefore not considered commercially confidential.

3.4. Contractual agreements

Contractual agreements between companies are generally considered CCI, except contracts between companies and contract research organisations (CROs). With regard to information in modules 4 and 5 of the dossier, it is considered that contractual information with companies responsible for non-clinical and clinical studies, such as CROs, is not regarded as CCI as they may contribute to and be responsible for important information included in the dossier. The names of these CROs are therefore considered to be information which can be disclosed.

3.5. Scientific advice

The disclosure of information on an agreed therapeutical indication should not be regarded as CCI after the conclusion of the related regulatory procedure. However, all the information related to further developments and new formulations which have not yet received regulatory approval should be protected.

3.6. Handling of copyright information

The list of references of the publications included in the dossier is not considered to be CCI and can thus be disclosed. However, if the actual manuscripts are included, these may be subject to copyright of third parties. EMA/NCA expressly disclaims any liability with regard to possible infringements of third parties' copyrights.

References

This guidance should be read in conjunction with the documents listed below, as applicable:

- ICH guideline M4 (R4) on common technical document (CTD) for the registration of pharmaceuticals for human use - organisation of CTD (EMA/CPMP/ICH/2887/1999)
- European Medicines Agency policy on access to documents – Policy/0043 (EMA/729522/2016)
- European Medicines Agency policy on clinical data publication – Policy/0070 (EMA/144064/2019)
- HMA/EMA recommendations on transparency: Recommendations on release of information with regard to new applications for medicinal products before and after opinion or decision on granting of a marketing authorisation (EMA/484118/2010)
- Guidance document on how to approach the protection of personal data and commercially confidential information in documents uploaded and published in the Clinical Trial Information System (CTIS) (EMA/212507/2021)
- Guideline for good clinical practice E6(R2) (EMA/CHMP/ICH/135/1995)
- Principles to be applied for the implementation of the HMA/EMA Guidance on the identification of CCI and PPD in MA Applications. (adopted by written procedure on 9 March 2012)
- Recommendations on Transparency - Recommendations on the handling of requests for access to Periodic Safety Update Reports (PSURs) (EMEA/743133/2009)
- Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation)
- Regulation (EU) 2018/1725 of the European Parliament and of the Council of 23 October 2018 on the protection of natural persons with regard to the processing of personal data by the Union institutions, bodies, offices and agencies and on the free movement of such data, and repealing Regulation (EC) No 45/2001 and Decision No 1247/2002/EC

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Annex: Information that may be considered protected personal data (PPD) and/or commercially confidential information (CCI) in the structure of the marketing authorisation application dossier

This annex lists all the modules of the marketing authorisation application (MAA) dossier based on the agreed common format for applications that are submitted to EMA/NCA according to Volume 2B Notice to Applicants Medicinal products for human use/ICH M8 Electronic common technical document (eCTD) v4.0 draft ICH implementation guide v2.0 - Scientific guideline (CHMP/ICH/143002/2015).

In each module, a **non-exhaustive list of information** that **may be** considered protected personal data (PPD) or commercially confidential information (CCI) is included. In this list, reference is made to sub-sections A, B, C, D as mentioned in section 2 of this guidance in relation to personal data (PD). The term 'Not expected' shall mean that from the nature of the content of the section and based on the experience gained by applying the principles set out in the first version of the present guidance document in 2012, PPD or CCI are not likely to be found in the section. However, it is important to remember that any information identified as PD or CCI will need to be assessed according to the aforementioned principles laid down in the guidance. In addition, the assessment of information that may be considered PPD or CCI is without prejudice to national rules on transparency. The Annex should be read in conjunction with the relevant applicable legislation and case-law on transparency and data protection**.** In addition, in modules which may contain CCI, the third parties will need – if consulted – to provide appropriate justification to explain how the disclosure of the CCI would concretely undermine their commercial and economic interests.

In modules which may contain PPD, a risk-based approach should be applied to assess which PD is to be anonymised from the requested documents in order to limit the risk of re-identification of the individuals concerned, in accordance with applicable EU and national provisions, as well as relevant case-law.

350 ***Module 1 – Administrative information and prescribing information***

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
1.0	**Cover letter**	A. PD related to experts or designated personnel with legally defined responsibilities: • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature B. PD related to staff with no legally defined responsibilities: • Name of employee, consultant or contractor • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature C. PD related to subjects involved in clinical trials and clinical studies: Not expected D. PD related to patients in the context of medicine safety: Not expected	Not expected
1.1	**Comprehensive table of content**	Not expected	Not expected. However, if the table of content provides highly detailed information, in particular in relation to sub-module 2.3 and Module 3, CCI may be present. Please refer to the appropriate sub-modules hereafter for guidance.

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
1.2	**Application Form**	A. PD related to experts or designated personnel with legally defined responsibilities: • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature B. PD related to staff with no legally defined responsibilities: • Name of employee, consultant or contractor • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature C. PD related to subjects involved in clinical trials and clinical studies: Not expected D. PD related to patients in the context of medicine safety: Not expected	The application form reflects the various modules of the MA application and may contain CCI. Therefore, please refer to the appropriate sub-modules hereafter for guidance.
1.3	**Product Information**		
1.3.1	Summary of Product Characteristics, Labelling and Package Leaflet	Not expected	Not expected
1.3.2	Mock-up	A. PD related to experts or designated personnel with legally defined responsibilities: Not expected	Technical specifications of the packaging such as colour code, font, dimensions, etc.
1.3.3	Specimen		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		B. PD related to staff with no legally defined responsibilities: • Name of employee, consultant or contractor • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature C. PD related to subjects involved in clinical trials and clinical studies: Not expected D. PD related to patients in the context of medicine safety: Not expected	
1.4.1	Consultation with Target Patient Groups	Not expected	Not expected
1.4.2	Product Information already approved in the Member States	Not expected	Not expected
1.4.3	Braille	Not expected	Not expected
1.4	**Information about the Experts**	A. PD related to experts or designated personnel with legally defined responsibilities: • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature B. PD related to staff with no legally defined responsibilities:	Not expected

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		• Name of employee, consultant or contractor • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature <u>C. PD related to subjects involved in clinical trials and clinical studies:</u> Not expected <u>D. PD related to patients in the context of medicine safety:</u> Not expected	
1.5	**Specific Requirements for Different Types of Applications**		
1.5.1	Information for Bibliographical Applications	Not expected	Not expected
1.5.2	Information for Generic, 'Hybrid' or Bio-similar Applications	Not expected	Not expected
1.5.3	(Extended) Data/Market Exclusivity	Not expected	Not expected
1.5.4	Exceptional Circumstances	Not expected	Not expected
1.5.5	Conditional Marketing Authorisation	Not expected	Not expected
1.6	**Environmental Risk Assessment**		
1.6.1	Non-GMO	<u>A. PD related to experts or designated personnel with legally defined responsibilities:</u> • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc.	Not expected
1.6.2	GMO		This section includes quality data that may be considered CCI. Please refer to Module 3 hereafter for guidance.

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		• Signature B. PD related to staff with no legally defined responsibilities: • Name of employee, consultant or contractor • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature C. PD related to subjects involved in clinical trials and clinical studies: Not expected D. PD related to patients in the context of medicine safety: Not expected	
1.7	**Information relating to Orphan Market Exclusivity**		
1.7.1	Similarity	A. PD related to experts or designated personnel with legally defined responsibilities: • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature B. PD related to staff with no legally defined responsibilities: • Name of employee, consultant or contractor	This section includes quality data that may be considered CCI. Please refer to Module 3 hereafter for guidance.
1.7.2	Market Exclusivity		Not expected

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		• Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature <u>C. PD related to subjects involved in clinical trials and clinical studies:</u> Not expected <u>D. PD related to patients in the context of medicine safety:</u> Not expected	
1.8	**Information relating to Pharmacovigilance**		
1.8.1	Pharmacovigilance System	<u>A. PD related to experts or designated personnel with legally defined responsibilities:</u> • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature <u>B. PD related to staff with no legally defined responsibilities:</u> • Name of Deputy QPPV • Name of employee, consultant or contractor • Name of healthcare professional (HCP) • Name of (vice-)chair, members and alternate members of Institutional Review Board (IRB) and Independent Ethics Committee (IEC)	• Exposure data (patient exposure and sales volume) by country • Projected post-authorisation exposure data • Information on future development plans such as the evaluation of new formulation or exploration of the effect of the medicinal product in new indications or populations, studies which are part of ongoing Paediatric Investigation Plan (PIP), etc.
1.8.2	Risk-management System		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		• Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature <u>C. PD related to subjects involved in clinical trials and clinical studies:</u> • Direct identifiers such as name, signature, contact details, etc. • For indirect identifiers, the risk of re-identification of individuals needs to be defined. This may include taking into consideration the following criteria for instance: – The type of product such as orphan or non-orphan – The studied indication and prevalence such as rare or non-rare – The studied population such as paediatric, elderly, pregnant, etc. – The number of subjects enrolled – The number of sites and countries where the study was conducted – The duration of the study Once the risk of re-identification has been defined, the following identifiers may be considered for anonymisation:	

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		– Identification number (ID) such as subject number, patient number, case number, etc. – Age – Gender – Race – Country of origin, nationality, place of birth or information that can lead to it such as site number, language, etc. <u>D. PD related to patients in the context of medicine safety:</u> • Direct identifiers such as name, signature, contact details, etc. • For indirect identifiers, the risk of re-identification of individuals needs to be defined. This may include taking into consideration the following criteria, for instance: – The type of product such as orphan or non-orphan – The indication and prevalence such as rare or non-rare – The population covered by the indication such as adult, paediatric, elderly, pregnant, etc. – The post-marketing exposure – The number of countries where the product is marketed	

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		Once the risk of re-identification has been defined, the following identifiers may be considered for anonymisation: – Identification number (ID) such as subject number, patient number, case number, etc. – Age – Gender – Race – Country of origin, nationality, place of birth or information that can lead to it such as site numbers, language, etc.	
1.9	**Information relating to Clinical Trials**	<u>A. PD related to experts or designated personnel with legally defined responsibilities:</u> • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature <u>B. PD related to staff with no legally defined responsibilities:</u> • Name of clinical study director • Name of investigators other than the principal investigator • Name of employee or consultant and contractor • Name of healthcare professional (HCP) • Name of members of CT Safety Monitoring Board or Independent/External Data Monitoring Committee	• Innovative study designs and/or innovative analytical methods • Information on future development plans such as the evaluation of new formulation, innovative technology or exploration of the effect of the medicinal product in new indications or populations, studies which are part of ongoing Paediatric Development Plan (PIP) • Information that may reveal strategic (contractual) agreements

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		• Names of (vice-) chair, members and alternate members of Institutional Review Board (IRB) and Independent Ethics Committee (IEC) • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature <u>C. PD related to subjects involved in clinical trials and clinical studies:</u> • Direct identifiers such as name, signature, contact details, etc. • For indirect identifiers, the risk of re-identification of individuals needs to be defined. This may include taking into consideration the following criteria, for instance: – The type of product such as orphan or non-orphan – The studied indication and prevalence such as rare or non-rare – The studied population such as paediatric, elderly, pregnant, etc. – The number of subjects enrolled – The number of sites and countries where the study was conducted – The duration of the study	

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		Once the risk of re-identification has been defined, the following identifiers may be considered for anonymisation: – Identification number (ID) such as subject number, patient number, case number, etc. – Age – Gender – Race – Country of origin, nationality, place of birth or information that can lead to it such as site numbers, language, etc. <u>D. PD related to patients in the context of medicine safety:</u> • Direct identifiers such as name, signature, contact details, etc. • For indirect identifiers, the risk of re-identification of individuals needs to be defined. This may include taking into consideration the following criteria, for instance: – The type of product such as orphan or non-orphan – The indication and prevalence such as rare or non-rare – The population covered by the indication such as adult, paediatric, elderly, pregnant, etc. – The post-marketing exposure	

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		– The number of countries where the product is marketed Once the risk of re-identification has been defined, the following identifiers may be considered for anonymisation: – Identification number (ID) such as subject number, patient number, case number, etc. – Age – Gender – Race – Country of origin, nationality, place of birth or information that can lead to it such as site numbers, language, etc.	
1.10	**Information relating to Paediatrics**	<u>A. PD related to experts or designated personnel with legally defined responsibilities:</u> • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature <u>B. PD related to staff with no legally defined responsibilities:</u> • Name of employee, consultant or contractor • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature	• Information on future development plans such as the evaluation of new formulation, innovative technology or exploration of the effect of the medicinal product in new indications or populations, studies which are part of ongoing Paediatric Investigation Plan (PIP) • Detailed information concerning the quality and manufacturing of the medicinal product such as description of the manufacturing process, controls of materials and critical steps etc.

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		<u>C. PD related to subjects involved in clinical trials and clinical studies:</u> • Direct identifiers such as name, signature, contact details, etc. • For indirect identifiers, the risk of re-identification of individuals needs to be defined. This may include taking into consideration the following criteria, for instance: – The type of product such as orphan or non-orphan – The studied indication and prevalence such as rare or non-rare – The studied population such as paediatric, elderly, pregnant, etc. – The number of subjects enrolled – The number of sites and countries where the study was conducted – The duration of the study Once the risk of re-identification has been defined, the following identifiers may be considered for anonymisation: – Identification number (ID) such as subject number, patient number, case number, etc. – Age – Gender – Race	

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		– Country of origin, nationality, place of birth or information that can lead to it such as site numbers, language, etc. <u>D. PD related to patients in the context of medicine safety:</u> • Direct identifiers such as name, signature, contact details, etc. • For indirect identifiers, the risk of re-identification of individuals needs to be defined. This may include taking into consideration the following criteria, for instance: – The type of product such as orphan or non-orphan – The indication and prevalence such as rare or non-rare – The population covered by the indication such as adult, paediatric, elderly, pregnant, etc. – The post-marketing exposure – The number of countries where the product is marketed Once the risk of re-identification has been defined, the following identifiers may be considered for anonymisation: – Identification number (ID) such as subject number, patient number, case number, etc. – Age	

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		– Gender – Race – Country of origin, nationality, place of birth or information that can lead to it such as site numbers, language, etc.	
	Responses to Questions	Depending on the nature of the questions, the type of PD in the responses may vary: A. PD related to experts or designated personnel with legally defined responsibilities B. PD related to staff with no legally defined responsibilities C. PD related to subjects involved in clinical trials and clinical studies D. PD related to patients in the context of medicine safety Please refer to the appropriate sub-modules for guidance.	Depending on the nature of the questions, the type of information in the responses may vary (quality, non-clinical and/or clinical). Please refer to the appropriate module of this annex.
	Additional Data		

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CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
2.1	**CTD Table of Contents (Module 2 – 5)**	Not expected	Not expected. However, if the table of content provides highly detailed information, in particular in relation to sub-module 2.3 and Module 3, CCI may be present. Please refer to the appropriate sub-modules hereafter for guidance.
2.2	**CTD Introduction**	Not expected	Not expected

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
2.3	**Quality Overall Summary**	Not expected	Please refer to the appropriate sub-modules of this annex.
2.3.S	**DRUG SUBSTANCE (name, manufacturer)**		
2.3.S.1	General Information (name, manufacturer)	<u>A. PD related to experts or designated personnel with legally defined responsibilities:</u> • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature <u>B. PD related to staff with no legally defined responsibilities:</u> • Name of employee, consultant or contractor • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature <u>C. PD related to subjects involved in clinical trials and clinical studies:</u> Not expected <u>D. PD related to patients in the context of medicine safety:</u> Not expected	• Quantitative composition for the active substance and excipients (for formulated substances only) • Detailed information on: – Manufacturing process such as description of steps, reagents, equipment, parameters, instruments, materials, cell culture and harvest, etc. – Characterisation, controls – Approaches to pharmaceutical development such as Quality by Design – Analytical methods – Validation of the manufacturing process – In-process controls – Justification of specification – Amino acid sequence regarding new active substance – Cell clones used to express a protein/vector – Impurities and degradants • Quantitative acceptance criteria for intermediates and active substances • Batch size/production scale (commercial scale) • Detailed information on: – Manufacturing sites not listed in the Product Information (PI)
2.3.S.2	Manufacture (name, manufacturer)		
2.3.S.3	Characterisation (name, manufacturer)		
2.3.S.4	Control of Drug Substance (name, manufacturer)		
2.3.S.5	Reference Standards or Materials (name, manufacturer)		
2.3.S.6	Container Closure System (name, manufacturer)		
2.3.S.7	Stability (name, manufacturer)		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
			– Bulk manufacturers (except manufacturer of the biological active substance) – Excipients manufacturers – Packaging site(s) – Batch control/testing site(s) – Facilities – Partners/third parties such as suppliers, CMO, CROs, etc.
2.3.P	**DRUG PRODUCT (name, dosage form)**		
2.3.P.1	Description and Composition of the Drug Product (name, dosage form)	<u>A. PD related to experts or designated personnel with legally defined responsibilities:</u> • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature <u>B. PD related to staff with no legally defined responsibilities:</u> • Name of employee, consultant or contractor • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature <u>C. PD related to subjects involved in clinical trials and clinical studies:</u> Not expected	• Quantitative composition for finished product • Detailed information on: – Manufacturing process such as description of steps, reagents, equipment, parameters, instruments, materials, etc. – Characterisation, controls – Approaches to pharmaceutical development such as Quality by Design – Analytical methods – Validation of the manufacturing process – In-process controls – Justification of specification – Impurities and degradants – Adventitious agents safety information/virus removal validation – Post-approval Change Management Protocols (PACMPs) • Quantitative acceptance criteria for intermediates and finished product • Batch size/production scale (commercial scale)
2.3.P.2	Pharmaceutical Development (name, dosage form)		
2.3.P.3	Manufacture (name, dosage form)		
2.3.P.4	Control of Excipients (name, dosage form)		
2.3.P.5	Control of Drug Product (name, dosage form)		
2.3.P.6	Reference Standards or Materials (name, dosage form)		
2.3.P.7	Container Closure System (name, dosage form)		
2.3.P.8	Stability (name, dosage form)		
2.3.A	APPENDICES		
2.3.A.1	Facilities and Equipment (name, manufacturer)		
2.3.A.2	Adventitious Agents Safety Evaluation (name, dosage form, manufacturer)		
2.3.A.3	Excipients		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
2.3.R	REGIONAL INFORMATION	<u>D. PD related to patients in the context of medicine safety:</u> Not expected	• Novel excipients information • Detailed information on: – Manufacturing sites not listed in the PI – Bulk manufacturers (except manufacturer of the biological finished product) – Excipients manufacturers – Packaging site(s) – Batch control/testing site(s) – Facilities – Partners/third parties such as suppliers, CMOs, CROs, etc.
2.4	**Nonclinical Overview**	<u>A. PD related to experts or designated personnel with legally defined responsibilities:</u> • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature <u>B. PD related to staff with no legally defined responsibilities:</u> • Name of non-clinical study director • Name of a 'principal research scientist' in a non-clinical technical report • Name of employee such as toxicologist or consultant and contractor • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature	• Information on future development plans such as the evaluation of new formulation, innovative technology or exploration of the effect of the medicinal product in new indications or populations or exploration of the effect of the medicinal product in new indications or populations, studies, etc. • Detailed information on analytical methods such as reagents, equipment, instruments, materials, etc. • Reference to innovative methods and/or study design • Information on partners/third parties such as suppliers • Detailed information on the facilities

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		C. PD related to subjects involved in clinical trials and clinical studies: Not expected D. PD related to patients in the context of medicine safety: Not expected	
2.5	**Clinical Overview**		
2.5.1	Product Development Rationale	A. PD related to experts or designated personnel with legally defined responsibilities: • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature B. PD related to staff with no legally defined responsibilities: • Name of clinical study director • Name of investigators other than the principal investigator • Name of employee or consultant and contractor • Name of Healthcare professional (HCP) • Name of members of CT Safety Monitoring Board or Independent/External Data Monitoring Committee • Names of (vice-) chair, members and alternate members of Institutional Review Board (IRB) and Independent Ethics Committee (IEC)	• Innovative study designs and/or innovative analytical methods • Information on future development plans such as the evaluation of new formulation, innovative technology or exploration of the effect of the medicinal product in new indications or populations, studies which are part of ongoing Paediatric Investigation Plan (PIP) • Information that may reveal strategic (contractual) agreements
2.5.2	Overview of Biopharmaceutics		
2.5.3	Overview of Clinical Pharmacology		
2.5.4	Overview of Efficacy		
2.5.5	Overview of Safety		
2.5.6	Benefits and Risks Conclusions		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		• Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature <u>C. PD related to subjects involved in clinical trials and clinical studies:</u> • Direct identifiers such as name, signature, contact details, etc. • For indirect identifiers, the risk of re-identification of individuals needs to be defined. This may include taking into consideration the following criteria, for instance: – The type of product such as orphan or non-orphan – The studied indication and prevalence such as rare or non-rare – The studied population such as paediatric, elderly, pregnant, etc. – The number of subjects enrolled – The number of sites and countries where the study was conducted – The duration of the study Once the risk of re-identification has been defined, the following identifiers may be considered for anonymisation:	

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		– Identification number (ID) such as subject number, patient number, case number, etc. – Age – Gender – Race – Country of origin, nationality, place of birth or information that can lead to it such as site numbers, language, etc. <u>D. PD related to patients in the context of medicine safety:</u> • Direct identifiers such as name, signature, contact details, etc. • For indirect identifiers, the risk of re-identification of individuals needs to be defined. This may include taking into consideration the following criteria, for instance: – The type of product such as orphan or non-orphan – The indication and prevalence such as rare or non-rare – The population covered by the indication such as adult, paediatric, elderly, pregnant, etc. – The post-marketing exposure – The number of countries where the product is marketed	

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		Once the risk of re-identification has been defined, the following identifiers may be considered for anonymisation: – Identification number (ID) such as subject number, patient number, case number, etc. – Age – Gender – Race – Country of origin, nationality, place of birth or information that can lead to it such as site numbers, language, etc.	
2.5.7	Literature References	Name of author(s) of internal documents listed in the references	Not expected
2.6	**Nonclinical Summary**		
2.6.1	INTRODUCTION	<u>A. PD related to experts or designated personnel with legally defined responsibilities:</u> • Direct contact details such as telephone number, fax number, email, postal address, IP address etc. • Signature <u>B. PD related to staff with no legally defined responsibilities:</u> • Name of non-clinical study director • Name of a 'principal research scientist' in a non-clinical technical report • Name of employee such as toxicologist or consultant and contractor	• Information on future development plans such as the evaluation of new formulation, innovative technology or exploration of the effect of the medicinal product in new indications or populations, studies, etc. • Detailed information on analytical methods such as reagents, equipment, instruments, materials, etc. • Reference to innovative methods and/or study design • Information on partners/third parties such as suppliers • Detailed information on the facilities
2.6.2	PHARMACOLOGY WRITTEN SUMMARY		
2.6.2.1	Brief Summary		
2.6.2.2	Primary Pharmacodynamics		
2.6.2.3	Secondary Pharmacodynamics		
2.6.2.4	Safety Pharmacology		
2.6.2.5	Pharmacodynamic Drug Interactions		
2.6.2.6	Discussion and Conclusions		
2.6.2.7	Tables and Figures		
2.6.3	PHARMACOLOGY TABULATED SUMMARY (SEE APPENDIX B)		
2.6.4	PHARMACOKINETICS WRITTEN SUMMARY		
2.6.4.1	Brief Summary		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
2.6.4.2	Methods of Analysis	• Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service • Signature <u>C. PD related to subjects involved in clinical trials and clinical studies:</u> Not expected <u>D. PD related to patients in the context of medicine safety:</u> Not expected	
2.6.4.3	Absorption		
2.6.4.4	Distribution		
2.6.4.5	Metabolism (interspecies comparison)		
2.6.4.6	Excretion		
2.6.4.7	Pharmacokinetic Drug Interactions		
2.6.4.8	Other Pharmacokinetic Studies		
2.6.4.9	Discussion and Conclusions		
2.6.4.10	Tables and Figures		
2.6.5	PHARMACOKINETICS TABULATED SUMMARY (SEE APPENDIX B)		
2.6.6	TOXICOLOGY WRITTEN SUMMARY		
2.6.6.1	Brief Summary		
2.6.6.2	Single-Dose Toxicity		
2.6.6.3	Repeat-Dose Toxicity (including supportive toxicokinetics evaluation)		
2.6.6.4	Genotoxicity		
2.6.6.5	Carcinogenicity (including supportive toxicokinetics evaluations)		
2.6.6.6	Reproductive and Developmental Toxicity (including range-finding studies and supportive toxicokinetics evaluations)		
2.6.6.7	Local Tolerance		
2.6.6.8	Other Toxicity Studies (if available)		
2.6.6.9	Discussion and Conclusions		
2.6.6.10	Tables and Figures		
2.6.7	TOXICOLOGY TABULATED SUMMARY (SEE APPENDIX B)		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
APPENDIX A:	EXAMPLES OF TABLES AND FIGURES FOR WRITTEN SUMMARIES		
APPENDIX B:	THE NONCLINICAL TABULATED SUMMARIES – TEMPLATES		
2.7	**Clinical Summary**		
2.7.1	Summary of Biopharmaceutic Studies and Associated Analytical Methods	<u>A. PD related to experts or designated personnel with legally defined responsibilities:</u> • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature <u>B. PD related to staff with no legally defined responsibilities:</u> • Name of clinical study director • Name of investigators other than the principal investigator • Name of employee or consultant and contractor • Name of Healthcare professional (HCP) • Name of members of CT Safety Monitoring Board or Independent/External Data Monitoring Committee • Names of (vice-) chair, members and alternate members of Institutional Review Board (IRB) and Independent Ethics Committee (IEC) • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc.	• Innovative study designs and/or innovative analytical methods • Information on future development plans such as the evaluation of new formulation or exploring the effect of the medicinal product in new indications or populations, studies which are part of ongoing Paediatric Development Plan (PIP), etc. • Information that may reveal strategic (contractual) agreements • Any quality information on the clinical batches that might be included here (such as e.g. dissolution profiles of tablets, details on dissolution methods) may be considered CCI. Please refer to Module 3 hereafter for guidance.
2.7.1.1	Background and Overview		
2.7.1.2	Summary of Results of Individual Studies		
2.7.1.3	Comparison and Analyses of Results Across Studies		
2.7.1.4	Appendix		
2.7.2	Summary of Clinical Pharmacology Studies		
2.7.2.1	Background and Overview		
2.7.2.2	Summary of Results of Individual Studies		
2.7.2.3	Comparison and Analyses of Results Across Studies		
2.7.2.4	Special Studies		
2.7.2.5	Appendix		
2.7.3	Summary of Clinical Efficacy		
2.7.3.1	Background and Overview of Clinical Efficacy		
2.7.3.2	Summary of Results of Individual Studies		
2.7.3.3	Comparison and Analyses of Results Across Studies		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
2.7.3.4	Study Populations	• Function, position, organisational entity such as department, service, etc. • Signature <u>C. PD related to subjects involved in clinical trials and clinical studies:</u> • Direct identifiers such as name, signature, contact details, etc. • For indirect identifiers, the risk of re-identification of individuals needs to be defined. This may include taking into consideration the following criteria, for instance: – The type of product such as orphan or non-orphan – The studied indication and prevalence such as rare or non-rare – The studied population such as paediatric, elderly, pregnant, etc. – The number of subjects enrolled – The number of sites and countries where the study was conducted – The duration of the study Once the risk of re-identification has been defined, the following identifiers may be considered for anonymisation: – Identification number (ID) such as subject number, patient number, case number, etc.	
2.7.3.5	Comparison of Efficacy Results of all Studies		
2.7.3.6	Analysis of Clinical Information Relevant to Dosing Recommendations		
2.7.3.7	Persistence of Efficacy and/or Tolerance Effects		
2.7.3.	Appendix		
2.7.4	Summary of Clinical Safety		
2.7.4.1	Exposure to the Drug		
2.7.4.1.1	Overall Safety Evaluation Plan and Narratives of Safety Studies		
2.7.4.1.2	Overall Extent of Exposure		
2.7.4.1.3	Demographic and Other Characteristics of Study Population		
2.7.4.2	Adverse Events		
2.7.4.2.1	Analysis of Adverse Events		
2.7.4.2.1.1	Common Adverse Events		
2.7.4.2.1.2	Deaths		
2.7.4.2.1.3	Other Serious Adverse Events		
2.7.4.2.1.4	Other Significant Adverse Events		
2.7.4.2.1.5	Analysis of Adverse Events by Organ System or Syndrome		
2.7.4.2.2	Narratives		
2.7.4.3	Clinical Laboratory Evaluations		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
2.7.4.4	Vital Signs, Physical Findings, and Other Observations Related to Safety	– Age – Gender – Race – Country of origin, nationality, place of birth or information that can lead to it such as site numbers, language etc. <u>D. PD related to patients in the context of medicine safety:</u> • Direct identifiers such as name, signature, contact details, etc. • For indirect identifiers, the risk of re-identification of individuals needs to be defined. This may include taking into consideration the following criteria, for instance: – The type of product such as orphan or non-orphan – The indication and prevalence such as rare or non-rare – The population covered by the indication such as adult, paediatric, elderly, pregnant, etc. – The post-marketing exposure – The number of countries where the product is marketed Once the risk of re-identification has been defined, the following identifiers may be considered for anonymisation:	
2.7.4.5	Safety in Special Groups and Situations		
2.7.4.5.1	Intrinsic Factors		
2.7.4.5.2	Extrinsic Factors		
2.7.4.5.3	Drug Interactions		
2.7.4.5.4	Use in Pregnancy and Lactation		
2.7.4.5.5	Overdose		
2.7.4.5.6	Drug Abuse		
2.7.4.5.7	Withdrawal and Rebound		
2.7.4.5.8	Effects on Ability to Drive or Operate Machinery or Impairment of Mental Ability		
2.7.4.6	Post-marketing Data		
2.7.4.7	Appendix		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		– Identification number (ID) such as subject number, patient number, case number, etc. – Age – Gender – Race – Country of origin, nationality, place of birth or information that can lead to it such as site numbers, language, etc.	
2.7.5	Literature References	Name of author(s) of internal documents listed in the references	Not expected
2.7.6	Synopses of Individual Studies	Not expected	Not expected

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CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
3.1	**Table of Contents of Module 3**	Not expected	Not expected. However, if the table of content provides highly detailed information, CCI may be present. Please refer to the appropriate sub-modules hereafter for guidance.
3.2	**Body of Data**	Not expected	Not expected
3.2.S	**Drug substance (name, manufacturer)**		
3.2.S.1	General Information (name, manufacturer)	<u>A. PD related to experts or designated personnel with legally defined responsibilities:</u> • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature	• Quantitative composition for the active substance and excipients (for formulated substances only) • Detailed information on: – Manufacturing process such as description of steps, reagents, equipment,
3.2.S.1.1	Nomenclature (name, manufacturer)		
3.2.S.1.2	Structure (name, manufacturer)		
3.2.S.1.3	General Properties (name, manufacturer)		
3.2.S.2	Manufacture (name, manufacturer)		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
3.2.S.2.1	Manufacturer(s) (name, manufacturer)	<u>B. PD related to staff with no legally defined responsibilities:</u> • Name of employee, consultant or contractor • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature <u>C. PD related to subjects involved in clinical trials and clinical studies:</u> Not expected <u>D. PD related to patients in the context of medicine safety:</u> Not expected	parameters, instruments, materials, cell culture and harvest, etc. – Characterisation, controls – Approaches to pharmaceutical development such as Quality by Design – Analytical methods – Validation of the manufacturing process – In-process controls – Justification of specification – Amino acid sequence regarding new active substance – Cell clones used to express a protein/vector – Impurities and degradants • Quantitative acceptance criteria for intermediates and active substances • Batch size/production scale (commercial scale) • Detailed information on: – Manufacturing sites not listed in the PI – Bulk manufacturers (except manufacturer of the biological active substance) – Excipients manufacturers – Packaging site(s) – Batch control/testing site(s) – Facilities – Partners/third parties such as suppliers, CMOs, CROs, etc.
3.2.S.2.2	Description of Manufacturing Process and Process Controls (name, manufacturer)		
3.2.S.2.3	Control of Materials (name, manufacturer)		
3.2.S.2.4	Controls of Critical Steps and Intermediates (name, manufacturer)		
3.2.S.2.5	Process Validation and/or Evaluation (name, manufacturer)		
3.2.S.2.6	Manufacturing Process Development (name, manufacturer)		
3.2.S.3	Characterisation (name, manufacturer)		
3.2.S.3.1	Elucidation of Structure and other Characteristics (name, manufacturer)		
3.2.S.3.2	Impurities (name, manufacturer)		
3.2.S.4	Control of Drug Substance (name, manufacturer)		
3.2.S.4.1	Specification (name, manufacturer)		
3.2.S.4.2	Analytical Procedures (name, manufacturer)		
3.2.S.4.3	Validation of Analytical Procedures (name, manufacturer)		
3.2.S.4.4	Batch Analyses (name, manufacturer)		
3.2.S.4.5	Justification of Specification (name, manufacturer)		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
3.2.S.5	Reference Standards or Materials (name, manufacturer)		
3.2.S.6	Container Closure System (name, manufacturer)		
3.2.S.7	Stability (name, manufacturer)		
3.2.S.7.1	Stability Summary and Conclusions (name, manufacturer)		
3.2.S.7.2	Post-approval Stability Protocol and Stability Commitment (name, manufacturer)		
3.2.S.7.3	Stability Data (name, manufacturer)		
3.2.P	**DRUG PRODUCT (name, dosage form)**		
3.2.P.1	Description and Composition of the Drug Product (name, dosage form)	<u>A. PD related to experts or designated personnel with legally defined responsibilities:</u> • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature <u>B. PD related to staff with no legally defined responsibilities:</u> • Name of employee, consultant or contractor • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature	• Quantitative composition for finished product • Detailed information on: – Manufacturing process such as description of steps, reagents, equipment, parameters, instruments, materials, etc. – Characterisation, controls – Approaches to pharmaceutical development such as Quality by Design – Analytical methods – Validation of the manufacturing process – In-process controls – Justification of specification – Impurities and degradants – Adventitious agents safety information/virus removal validation – Post-approval Change Management Protocols (PACMPs)
3.2.P.2	Pharmaceutical Development (name, dosage form)		
3.2.P.2.1	Components of the Drug Product (name, dosage form)		
3.2.P.2.1.1	Drug Substance (name, dosage form)		
3.2.P.2.1.2	Excipients (name, dosage form)		
3.2.P.2.2	Drug Product (name, dosage form)		
3.2.P.2.2.1	Formulation Development (name, dosage form)		
3.2.P.2.2.2	Overages (name, dosage form)		
3.2.P.2.2.3	Physicochemical and Biological Properties (name, dosage form)		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
3.2.P.2.3	Manufacturing Process Development (name, dosage form)	<u>C. PD related to subjects involved in clinical trials and clinical studies:</u> Not expected <u>D. PD related to patients in the context of medicine safety:</u> Not expected	• Quantitative acceptance criteria for intermediates and finished product • Batch size/production scale (commercial scale) • Novel excipients information • Detailed information on: – Manufacturing sites not listed in the PI – Bulk manufacturers (except manufacturer of the biological finished product) – Excipients manufacturers – Packaging site(s) – Batch control/testing site(s) – Facilities – Partners/third parties such as suppliers, CMOs, CROs, etc.
3.2.P.2.4	Container Closure System (name, dosage form)		
3.2.P.2.5	Microbiological Attributes (name, dosage form)		
3.2.P.2.6	Compatibility (name, dosage form)		
3.2.P.3	Manufacture (name, dosage form)		
3.2.P.3.1	Manufacturer(s) (name, dosage form)		
3.2.P.3.2	Batch Formula (name, dosage form		
3.2.P.3.3	Description of Manufacturing Process and Process Controls (name, dosage form)		
3.2.P.3.4	Controls of Critical Steps and Intermediates (name, dosage form)		
3.2.P.3.5	Process Validation and/or Evaluation (name, dosage form)		
3.2.P.4	Control of Excipients (name, dosage form		
3.2.P.4.1	Specifications (name, dosage form)		
3.2.P.4.2	Analytical Procedures (name, dosage form)		
3.2.P.4.3	Validation of Analytical Procedures (name, dosage form		
3.2.P.4.4	Justification of Specifications (name, dosage form)		
3.2.P.4.5	Excipients of Human or Animal Origin (name, dosage form)		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
3.2.P.4.6	Novel Excipients (name, dosage form)		
3.2.P.5	Control of Drug Product (name, dosage form)		
3.2.P.5.1	Specification(s) (name, dosage form)		
3.2.P.5.2	Analytical Procedures (name, dosage form)		
3.2.P.5.3	Validation of Analytical Procedures (name, dosage form)		
3.2.P.5.4	Batch Analyses (name, dosage form)		
3.2.P.5.5	Characterisation of Impurities (name, dosage form)		
3.2.P.5.6	Justification of Specification(s) (name, dosage form)		
3.2.P.6	Reference Standards or Materials (name, dosage form)		
3.2.P.7	Container Closure System (name, dosage form		
3.2.P.8	Stability (name, dosage form)		
3.2.P.8.1	Stability Summary and Conclusion (name, dosage form)		
3.2.P.8.2	Post-approval Stability Protocol and Stability Commitment (name, dosage form)		
3.2.P.8.3	Stability Data (name, dosage form)		
3.2.A	**APPENDICES**		
3.2.A.1	Facilities and Equipment (name, manufacturer)		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
3.2.A.2	Adventitious Agents Safety Evaluation (name, dosage form, manufacturer)		
3.2.A.3	Excipients		
3.2.R	Regional Information		
3.3	**Literature References**	Name of author(s) of internal documents listed in the references	Not expected

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CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
4.1	**Table of contents of module 4**	Not expected	Not expected
4.2	**STUDY REPORTS**		
4.2.1	Pharmacology	<u>A. PD related to experts or designated personnel with legally defined responsibilities:</u> • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature <u>B. PD related to staff with no legally defined responsibilities:</u> • Name of non-clinical study director • Name of a 'principal research scientist' in a non-clinical technical report • Name of employee such as toxicologist or consultant and contractor	• Information on future development plans such as the evaluation of new formulation, innovative technology or exploration the effect of the medicinal product in new indications or populations, studies, etc. • Detailed information on analytical methods such as reagents, equipment, instruments, materials, etc. • Reference to innovative methods and/or study design • Information on partners/third parties such as suppliers • Detailed information on the facilities
4.2.1.1	Primary Pharmacodynamics		
4.2.1.2	Secondary Pharmacodynamics		
4.2.1.3	Safety Pharmacology		
4.2.1.4	Pharmacodynamic Drug Interactions		
4.2.2	Pharmacokinetics		
4.2.2.1	Analytical Methods and Validation Reports (if separate reports are available)		
4.2.2.2	Absorption		
4.2.2.3	Distribution		
4.2.2.4	Metabolism		
4.2.2.5	Excretion		
4.2.2.6	Pharmacokinetic Drug Interactions (nonclinical)		
4.2.2.7	Other Pharmacokinetic Studies		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
4.2.3	Toxicology	• Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature <u>C. PD related to subjects involved in clinical trials and clinical studies:</u> Not expected <u>D. PD related to patients in the context of medicine safety:</u> Not expected	
4.2.3.1	Single-Dose Toxicity (in order by species, by route)		
4.2.3.2	Repeat-Dose Toxicity (in order by species, by route, by duration; including supportive toxicokinetics evaluations)		
4.2.3.3	Genotoxicity		
4.2.3.3.1	In vitro		
4.2.3.3.2	In vivo (including supportive toxicokinetics evaluations)		
4.2.3.4	Carcinogenicity (including supportive toxicokinetics evaluations)		
4.2.3.4.1	Long-term studies (in order by species; including range finding studies that cannot appropriately be included under repeat-dose toxicity or pharmacokinetics)		
4.2.3.4.2	Short- or medium-term studies (including range-finding studies that cannot appropriately be included under repeat dose toxicity or pharmacokinetics		
4.2.3.4.3	Other studies		
4.2.3.5	Reproductive and Developmental Toxicity (including range-finding studies and supportive toxicokinetics evaluations) (If modified study designs are used, the following sub-headings should be modified accordingly.)		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
4.2.3.5.1	Fertility and early embryonic development		
4.2.3.5.2	Embryo-foetal development		
4.2.3.5.3	Prenatal and postnatal development, including maternal function		
4.2.3.5.4	Studies in which the offspring (juvenile animals) are dosed and/or further evaluated.		
4.2.3.6	Local Tolerance		
4.2.3.7	Other Toxicity Studies (if available)		
4.2.3.7.1	Antigenicity		
4.2.3.7.2	Immunotoxicity		
4.2.3.7.3	Mechanistic studies (if not included elsewhere)		
4.2.3.7.4	Dependence		
4.2.3.7.5	Metabolites		
4.2.3.7.6	Impurities		
4.2.3.7.7	Other		
4.3	**Literature references**	Name of author(s) of internal documents listed in the references	Not expected

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CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
5.1	**Table of Contents of Module 5**	Not expected	Not expected
5.2	**Tabular Listing of All Clinical Studies**	Not expected	Not expected
5.3	**Clinical Study Reports**		
5.3.1	Reports of Biopharmaceutic Studies		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
5.3.1.1	Bioavailability (BA) Study Reports	<u>A. PD related to experts or designated personnel with legally defined responsibilities:</u> • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Signature <u>B. PD related to staff with no legally defined responsibilities:</u> • Name of clinical study director • Name of investigators other than the principal investigator • Name of employee or consultant and contractor • Name of Healthcare professional (HCP) • Name of members of CT Safety Monitoring Board or Independent/External Data Monitoring Committee • Names of (vice-) chair, members and alternate members of Institutional Review Board (IRB) and Independent Ethics Committee (IEC) • Direct contact details such as telephone number, fax number, email, postal address, IP address, etc. • Function, position, organisational entity such as department, service, etc. • Signature	• Innovative study designs and/or innovative analytical methods • Information on future development plans such as the evaluation of new formulation, innovative technology or exploration the effect of the medicinal product in new indications or populations, studies which are part of ongoing Paediatric Development Plan (PIP), etc. • Information that may reveal strategic (contractual) agreements
5.3.1.2	Bioavailability (BA) Study Reports		
5.3.1.3	In vitro-In vivo Correlation Study Reports		
5.3.1.4	Reports of Bioanalytical and Analytical Methods for Human Studies		
5.3.2	Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials		
5.3.2.1	Plasma Protein Binding Study Reports		
5.3.2.2	Reports of Hepatic Metabolism and Drug Interaction Studies		
5.3.2.3	Reports of Studies Using Other Human Biomaterials		
5.3.3	Reports of Human Pharmacokinetic (PK) Studies		
5.3.3.1	Healthy Subject PK and Initial Tolerability Study Reports		
5.3.3.2	Patient PK and Initial Tolerability Study Reports		
5.3.3.3	Intrinsic Factor PK Study Reports		
5.3.3.4	Extrinsic Factor PK Study Reports		
5.3.3.5	Population PK Study Reports		
5.3.4	Reports of Human Pharmacodynamic (PD) Studies		
5.3.4.1	Healthy Subject PD and PK/PD Study Reports		
5.3.4.2	Patient PD and PK/PD Study Reports		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
5.3.5	Reports of Efficacy and Safety Studies	<u>C. PD related to subjects involved in clinical trials and clinical studies:</u> • Direct identifiers such as name, signature, contact details, etc. • For indirect identifiers, the risk of re-identification of individuals needs to be defined. This may include taking into consideration the following criteria, for instance: – The type of product such as orphan or non-orphan – The studied indication and prevalence such as rare or non-rare – The studied population such as paediatric, elderly, pregnant, etc. – The number of subjects enrolled – The number of sites and countries where the study was conducted – The duration of the study Once the risk of re-identification has been defined, the following identifiers may be considered for anonymisation: – Identification number (ID) such as subject number, patient number, case number, etc – Age – Gender – Race	
5.3.5.1	Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication		
5.3.5.2	Study Reports of Uncontrolled Clinical Studies		
5.3.5.3	Reports of Analyses of Data from More Than One Study		
5.3.5.4	Other Clinical Study Reports		
5.3.6	Reports of Post-Marketing Experience		
5.3.7	Case Report Forms and Individual Patient Listings		

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		– Country of origin, nationality, place of birth or information that can lead to it such as site numbers, language, etc. <u>D. PD related to patients in the context of medicine safety:</u> • Direct identifiers such as name, signature, contact details, etc. • For indirect identifiers, the risk of re-identification of individuals needs to be defined. This may include taking into consideration the following criteria, for instance: – The type of product such as orphan or non-orphan – The indication and prevalence such as rare or non-rare – The population covered by the indication such as adult, paediatric, elderly, pregnant, etc. – The post-marketing exposure – The number of countries where the product is marketed Once the risk of re-identification has been defined, the following identifiers may be considered for anonymisation: – Identification number (ID) such as subject number, patient number, case number, etc. – Age	

CTD	EU CTD	Information that may be considered PPD	Information that may be considered CCI
		– Gender – Race – Country of origin, nationality, place of birth or information that can lead to it such as site numbers, language, etc.	
5.4	**Literature References**	Name of author(s) of internal documents listed in the references	Not expected

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