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External guidance on the implementation of the European Medicines Agency Policy 0070 on the publication of clinical data for medicinal products for human use

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Chapter 1

General information

1.1. Introduction

The European Medicines Agency policy on the publication of clinical data for medicinal products for human use (hereafter referred to as 'Policy 0070') was developed by the European Medicines Agency (EMA), in accordance with Article 80 of Regulation (EC) No 726/2004. Policy 0070 was adopted by the EMA Management Board on 2nd October 2014 and subsequently published on the EMA website.

Policy 0070 entered into force on 1st January 2015. Phase 1 of the policy pertains to publication of clinical reports only. Clinical reports and IPD are collectively referred to as "clinical data". This guidance has been prepared to assist applicants in preparing packages for publication and the general principles applied.

1.2. Scope

The scope of this guidance document relates to phase 1 of Policy 0070 which excludes individual patient data (IPD). Article 17 of Regulation (EU) No 123/2022 provides for the publication of the clinical data submitted to the Agency in support of the application in a public health emergency, such as the Covid-19 pandemic.

Clinical reports will be published, under Policy 0070, following conclusion of the regulatory decision-making process (positive, negative European Commission Decision or withdrawn of the Marketing Authorisation Application) in the frame of centralised marketing authorisation procedures, as follows:

- as part of a marketing authorisation application (MAA) with the exception of informed consent applications; effective date 1 January 2015, or
- as part of a procedure under Article 58 of Regulation (EC) No 726/2004; effective date 1 January 2015, or
- submitted by a third party in the context of a MAA: effective date 1 January 2015, or
- as part of extension of indication – understood as variations related to the "*addition of a new therapeutic indication or modification of an approved one – classified as C.I.6 a)"* as per the *Guidelines on the details of the various categories of variations, on the operation of the procedures laid down in Chapters II, IIa, III and IV of Commission Regulation (EC) No 1234/2008 of 24 November 2008* - and line extension applications relating to existing centrally authorised medicinal products; effective date 1 July 2015, or
- requested by EMA/submitted by the applicant/Marketing Authorisation Holder (MAH) as additional clinical data in the context of the scientific assessment process for the aforementioned situations.
- Clinical data submitted during public health emergencies as outlined in article 17 of Regulation 123/2022.

Clinical reports contained in applications where the applicant has notified EMA of the withdrawal of the MAA are also published under Policy 0070. However, in case of withdrawn applications where there is a confirmed re-submission date (e.g. CHMP eligibility letter) or re-submission of the application has already taken place, it is possible to request a delay in publication under Policy 0070. The clinical data package will not then be published for the withdrawn product, provided there is an outcome of the decision making process for the re-submitted application. In such cases, following the conclusion of the re-submitted application, the applicant is expected to submit the clinical package for publication under Policy 0070.

Clinical reports submitted as part of regulatory procedures not falling within the scope of Policy 0070

As a general rule all clinical reports submitted as part of a regulatory application will be subject to publication.

Regulatory applications may include cross-references to clinical study reports which have been submitted in regulatory procedures not falling within the scope of Policy 0070. In such situations, EMA expects the MAH to resubmit cross-referred to clinical study reports for the purpose of publication only in the following cases:

- **Extension of indication to include paediatric population or modification of a paediatric indication**

Where clinical study reports are cross-referred to within paediatric extension or modification of indication applications, the MAH is required to submit for publication all pivotal clinical study reports as well as supportive studies conducted in the paediatric population that were submitted in the context of regulatory procedures not falling within the scope of Policy 0070 and considered the basis for that application.

For example, according to the submission requirements laid down in Article 46 of Regulation (EC) No 1901/2006, the results of studies involving the use of an authorised medicinal product in the paediatric population should be submitted to the competent authority within six months of completion of the clinical study. As a result, these same studies may not be resubmitted in a regulatory procedure to add or modify a paediatric indication, but instead be referenced to the data submitted in the context of an earlier Article 46 procedure. In such cases, the clinical data submitted in the context of Article 46 of Regulation (EC) No 1901/2006 to which reference is made in a regulatory procedure for the addition or modification of a paediatric indication is also subject to publication under Policy 0070.

- **Other extension or modification of indication and line extension applications**

Where other clinical study reports, not provided in the marketing authorisation application or procedure under assessment are cross-referred to within extension or modification of indication and line extension applications, other than paediatric, only the clinical study reports submitted in the context of regulatory procedures and considered the basis for that application will be subject to publication. Where a clinical study report included in an application dossier has been previously submitted in another procedure and published, then the clinical study report is to be provided again for publication under the new procedure.

Clinical reports will be published following the redaction of CCI and anonymisation of the clinical data. This publication is independent of who the author or party holding any rights to the documents may be. Any such rights remain a contractual issue between the applicant/MAH and any third party(ies).

Informed consent applications

For informed consent marketing authorisation applications where only a complete module 1 is submitted, the applicant/MAH is not expected to submit any document as Policy 0070 does not apply.

Duplicate marketing authorisations

When submitting duplicate marketing authorisation applications, the Agency understands that the clinical reports included in such submissions are identical to the ones submitted in the application of the original medicinal product.

However, duplicate submissions might contain **differences** in certain data, such as different salt, excipient or manufacturing sites. In case these changes affect the content of the clinical reports submitted for publication, the applicant/MAH is required to flag such differences at the beginning of the procedure which will then be assessed by the Agency on a case-by-case basis.

Where the clinical reports submitted for the original and duplicate medicinal products are **identical**, the Agency will only initiate one consultation process based on one Redaction Proposal Document package, submitted for the original product. At the end of this consultation the Agency will send out the conclusion which will be equally valid for the duplicate medicinal product. A statement should be included in the cover letter of the duplicate Final Redacted Document package confirming that the Final Redacted Document package submitted for the duplicate is identical to the Final Redacted Document package of the original medicinal product.

Therefore, for identical duplicate medicinal products the Agency accepts that the redaction proposal package is only submitted for the original product but still requires the submission of two stand-alone Final Redacted Document packages, one for the original and the other for the duplicate medicinal product, as separate publications for each procedure are needed.

1.3. Definitions

For the purposes of the implementation of Policy 0070 the following definitions will apply:

- **Aggregated data:**

  Statistical data about several individuals that has been combined to show general trends or values without identifying individuals within the data.

- **Anonymisation:**

  The process of rendering data into a form which does not identify individuals and where identification is not likely to take place.

- **Anonymised/de-identified data:**

  Data in a form that does not identify individuals and where identification through its combination with other data is not likely to take place.

- **Article 29 Data Protection Working Party (Art. 29 WP):**

  The Art. 29 WP was set up under Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data. It has advisory status and acts independently. It is composed of a representative of the supervisory authority(ies) designated by each EU country, a representative of the authority(ies) established for the EU institutions and bodies, and a representative of the European Commission.

- **Clinical reports:**

  Clinical reports shall mean the clinical overviews (submitted in module 2.5), clinical summaries (submitted in module 2.7) and the clinical study reports (submitted in module 5, "CSR") together with the following appendices to the CSRs: 16.1.1 (protocol and protocol amendments), 16.1.2 (sample case report form), and 16.1.9 (documentation of statistical methods).

- **Clinical data:**

  Clinical data shall mean the clinical reports and IPD.

- **Clinical study:**

  Clinical study shall mean any investigation in relation to humans intended to:

  - discover or verify the clinical, pharmacological or other pharmacodynamic effects of one or more medicinal products;
  - identify any adverse reactions to one or more medicinal products; or
  - study the absorption, distribution, metabolism and excretion of one or more medicinal products;

  with the objective of ascertaining the safety or efficacy of those medicinal products.

- **Commercially Confidential Information (CCI):**

  CCI shall mean any information contained in the clinical reports submitted to EMA by the applicant/MAH which is not in the public domain or publicly available and where disclosure may undermine the legitimate economic interest of the applicant/MAH.

- **Data:**

  Data shall mean characteristics or information, usually numerical, that are collected through observation. The word can also be used to describe statistics (i.e. aggregations or transformations of raw data).

- **Data controller:**

  A person who (either alone or jointly or in common with other persons) determines the purposes for which and the manner in which any personal data are, or are to be, processed.

- **Data linkage:**

  A technique that involves bringing together and analysing data from a variety of sources, typically data that relates to the same individual.

- **Data mining:**

  Activity of going through big data sets to look for relevant or pertinent information.

- **Data processor:**

  An organisation that processes personal data on behalf of a data controller.

- **Data subject:**

  An individual who is the subject of personal data.

- **Disclosure:**

  The act of making data available to one or more third parties.

- **Individual patient data (IPD):**

  IPD shall mean the individual data separately recorded for each participant in a clinical study.

- **Protected personal data (PPD):**

  For the purpose of this guidance document the definition from Directive 95/46/EC applies: "Personal data" shall mean any information relating to an identified or identifiable natural person ('data subject'); an identifiable person is one who can be identified, directly or indirectly, in

particular by reference to an identification number or to one or more factors specific to his physical, physiological, mental, economic, cultural or social identity.

- **Pseudonymisation:**

  Consists of replacing one attribute (typically a unique attribute) in a record by another. The natural person is still likely to be identified indirectly. Pseudonymisation reduces the linkability of a dataset with the original identity of a data subject.

- **Re-identification:**

  The process of analysing data or combining it with other data with the result that individuals become identifiable, sometimes also referred to as 'de-anonymisation'.

- **Residual risk:**

  The risk that remains after controls are taken into account (the net risk or risk after controls).

- **Risk:**

  The probability of re-identifying a trial participant.

- **Study subject:**

  For the purpose of Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, a 'subject' is defined as 'an individual who participates in a clinical trial, either as a recipient of an investigational medicinal product or as a control'.
  Use is made in the guidance of the term 'research participant' as an equivalent to 'subject', in order to avoid confusion with the aforementioned protected personal data (PPD) term 'data subject'.

- **Redaction Proposal Version:**

  This is the clinical report version containing the applicant's/MAH's proposed redactions on commercial confidential information (CCI) and personal data. These proposed redactions should be highlighted in a 'read-through' manner.

- **Redaction Proposal Document package:**

  The "Redaction Proposal Document" package shall contain the redaction proposal versions of all clinical reports related to one single finalised regulatory procedure that falls under the scope of Policy 0070, along with a number of additional documents listed in the "External guidance on the procedural aspects related to the submission of clinical reports for the purpose of publication in accordance with EMA Policy 0070".

- **Final Redacted Version:**

  This is the clinical report version, submitted by the applicant/MAH for publication, which should reflect the EMA review outcome (accepted/rejected redactions).

- **Final Redacted Document package:**

  A "Final Redacted Document" package shall contain the final redacted versions of all clinical reports related to one single finalised regulatory procedure that falls under the scope of Policy 0070.

Chapter 2

External guidance on the procedural aspects related to the submission of clinical reports for the purpose of publication in accordance with EMA Policy 0070

2.1 Introduction

This chapter provides guidance to applicants/MAHs in relation to procedural aspects on the submission of the clinical reports for publication by EMA under Policy 0070 as follows:

- Clinical report document types
- Process for the submission of clinical reports for publication
- Publication process

2.2 Clinical report document types

2.2.1. Types of documents that fall within the scope of Policy 0070

Policy 0070 defines the clinical reports within its scope and which are subject to publication. This information is included in Chapter 1 (see section 1.2 Scope).

2.2.2. Types of documents or sections of documents considered to be in or out of scope of phase 1 of Policy 0070

In the Common Technical Document (CTD) sections falling within the scope of Policy 0070 there may be additional documents submitted by an applicant/MAH other than clinical overviews, clinical summaries and clinical study reports (CSRs). Therefore, EMA would like to clarify the types of documents that are subject to publication as well as whether there are any sections within the clinical reports that may be considered as out of scope of phase 1 of Policy 0070. Annex 5.7 of this guidance document contains a comprehensive list of which documents are subject to publication.

In addition to this comprehensive list EMA would like to further clarify the following points:

- The reports describing the safety and efficacy findings of the main period/phase of a clinical study are subject to publication. This position is taken regardless of the timing of submission of the results of the extension/follow-up of the same main study. More specifically, if the main part of the study (meaning the study preceding the extension/follow-up) is completed the study is not considered on-going. The status of the study (on-going or completed) is always evaluated at the time point of the publication. Where the study is on-going at the time of the regulatory submission but has been completed by the publication date, justifications stating "on-going study" will be disregarded. These completed (main parts) studies are considered in scope even if their follow-ups have not yet been completed by the time of the publication. In cases where the main period/phase of a clinical study is still on-going at the time of publication, the clinical reports are also subject to publication. If needed, applicants/MAHs may propose additional redactions to protect the blinding of the study (blinding redactions), that will remain in place until the study is unblinded. Applicants/MAHs should inform their designated contact person(s) in the Clinical Data Publication team of the need to apply blinding redactions as soon as possible.
- Case narratives should not be removed nor redacted in full regardless of their location in the clinical reports (body of the report or listings). They should be, instead, anonymised. Regardless of the anonymisation technique used by the applicant/MAH, EMA cannot accept the redaction of the entire case narrative by default (as a rule).
- Retention of Adverse Event Terms is of outmost importance and should be given the highest priority, regardless of their sensitivity. Surrounding information (e.g., in narratives) should be anonymised in a way that allows for the retention of all Adverse Event Terms. If, exceptionally, the

entire case narrative needs to be redacted to ensure anonymisation, i.e. all identifiers (direct and indirect) need to be redacted, it must be clearly justified in the anonymisation report.

- All sections of the CSR body (sections 1 to 15 as per ICH E3) are subject to publication.

  EMA notes that CSRs may contain **individual** patient data listings within the body of the report. These listings may include a subset of listings extracted from 16.2. Patient Data listings and repurposed as part of CSR section 14 for the purpose set by the ICH E3 guidance. Individual patient data listings within the body of the report cannot be considered out of scope and should not be removed, except for Abnormal Laboratory Value Listings typically found in section 14.3.4.

  If ICH E3 format is not followed for a particular CSR, the individual patient data listings included in the corresponding section presenting "Abnormal Laboratory Values" may be considered out of scope and removed from the clinical study report. All other individual patient data listings should instead be anonymised (e.g. listings concerning laboratory values outside normal ranges, PK and immunogenicity, protocol deviations, Adverse Events).

- It is important to note that data presented as **aggregated** patient data listings within section 14.3.4 "Abnormal Laboratory Value Listing" should NOT be removed.

- **Documents** that are presented in a language other than English will not be published in the context of Policy 0070.

2.2.3. Removal of out-of-scope sections and pages in non-English language within documents

In documents containing information which is agreed to be removed as out of scope, the removed pages should be replaced by a single blank page with text in black indicating that pages have been removed and **the nature of the information** that has been removed, as follows:

1. Title of section removed;

2. Statement to reflect the above ("Page(s) removed- Out of Scope of phase 1 of Policy 0070 – <type of information/heading removed>").

The page numbers of the removed information are not required to be included in the overlay text when the overall pagination remains intact in the document (i.e. the pages preceding and following the removed pages should retain their original page numbers) and it would be therefore obvious which pages were removed.

For example, in case there are individual patient abnormal laboratory value listings removed as out of scope of Policy 0070, it should read:

"Page(s) removed - **Out of Scope of phase 1 of Policy 0070 - Individual Patient Abnormal Laboratory Value Listings**"

If a **section within a document** considered in scope of Policy 0070 is presented in a language other than English, it is acceptable to have it removed from the clinical reports prepared for publication. In this case, the MAH should follow the below labelling:

"Page(s) removed **– non-English text removed"**

2.3. Process for the submission, review and publication of clinical reports

2.3.1. High level summary of the process

The process for the publication of clinical reports encompasses the following main steps:

- Invitation email to applicants/MAHs.
- Agreement on list of expected documents (LED).
- Submission of Redaction Proposal Document package.
- Redaction proposal document package validation and review.
- Submission of the Final Redacted Document package.
- Final Redacted Document package check and Publication.

The timelines for the publication of redacted/anonymised clinical reports will vary depending on the regulatory procedure. For initial MAAs, line extension applications and extension of indication applications EMA will publish the redacted/anonymised clinical reports within 120 days after CHMP opinion. For withdrawn applications and applications under Article 58 of Regulation (EC) No 726/2004 the publication of the redacted/anonymised clinical reports will take place within 150 days after the receipt of the withdrawal letter or adoption of the CHMP opinion, respectively.

A high-level workflow outlines the key components of the process from the submission by an applicant/MAH to the publication (please see section 2.3.3 for process steps).

2.3.2. Invitation to Applicants and agreement on list of expected documents

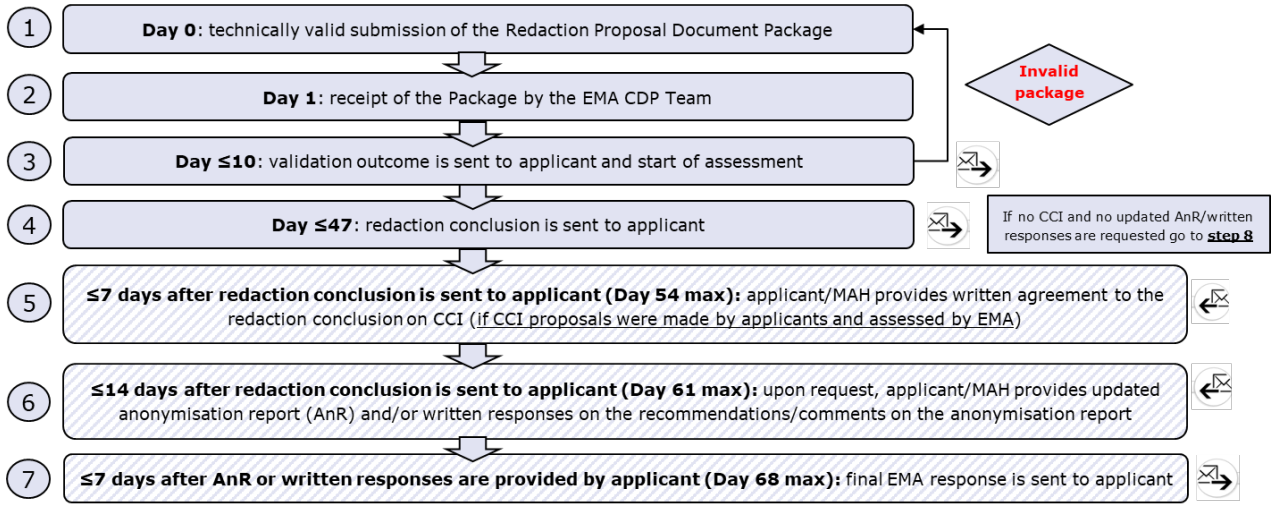
The applicant/MAH will receive an invitation email informing that they are expected to prepare and submit a Redaction Proposal Document package to comply with the requirements of Policy 0070. This invitation will be sent well in advance of the planned date of the CHMP outcome (e.g. by procedure Day 121 in the case of initial MAAs, or ≤90 days before the planned CHMP outcome in the case of post-authorisation procedures) and will include a preliminary list of expected documents (LED) for the applicant/MAH to review. Applicants/MAH will be given the opportunity to provide comments on the LED. Any proposals to exclude out-of-scope documents and/or sections within documents or to split and/or merge documents must be agreed during the pre-submission process at the time of the LED review. Amendments made by applicants/MAHs should be adequately justified and will be reviewed case-by-case before a final LED is agreed. Below are some examples of proposals to split and merge documents that are typically accepted:

- Splitting a lengthy CSR body or annex to the CSR in several documents (e.g. due to technical constraints arising when managing, anonymising or submitting documents).
- Merging versions (amendments) of the Clinical Study Protocol or the Statistical Analysis Plan in one single document.
- Merging several documents containing case narratives reported in the same clinical study.

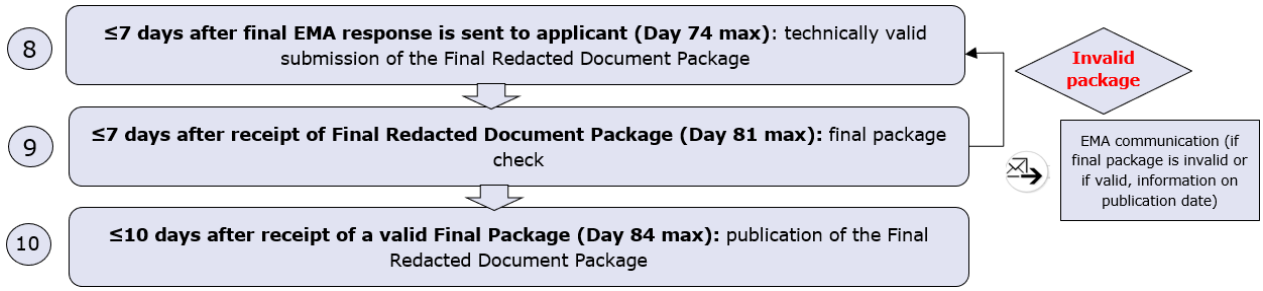
The LED may be updated if additional sequences including clinical data that fall within the scope of Policy 0070 are submitted later in the procedure (e.g. after procedure Day 121 or Day 181). The final LED will also serve as an agreed list of documents with out-of-scope sections. Any changes to the final LED should be agreed with EMA in advance of the submission of the redaction proposal.

2.3.3. Submission, validation, and review of document packages (end-to-end process)

Clinical data publication review process steps (1): Redaction Proposal Document Package



Clinical data publication review process steps (2): Final Redacted Document Package



The process steps are re-calculated based on the dates of the receipt of the packages by the CDP team and the communications to and from the applicant/MAH. Additionally, the holiday period from 23 December to 3 January is excluded from the calculation.

2.3.3.1. Submission of the Redaction Proposal Document package

2.3.3.1.1. Process to submit the Redaction Proposal Document package

A workflow for the submission of the Redaction Proposal Document package can be found in Annex 5.5 of this guidance document. This process requires the applicant/MAH to submit to EMA a redaction proposal version of the clinical reports for publication, in which proposed redactions are marked, in line with the CTD format of Modules 1, 2, and 5 or equivalent sections if the submission structure does not follow the ICH M4 guideline.

2.3.3.1.2. Submission timelines

The timeline for the submission of the Redaction Proposal Document package by the applicant/MAH varies depending on the regulatory procedure (CDP procedural timelines).

- For Initial MAAs, and line extension applications, applicants/MAHs must submit their Redaction Proposal Document package between day 181 and ≤30 days post-CHMP opinion.
- For Article 58 applications, applicants must submit their Redaction Proposal Document package ≤60 days post-CHMP opinion.
- For extension of indication applications, applicants/MAHs must submit their Redaction Proposal Document package ≤30 days pre-opinion and ≤30 days post-CHMP opinion.
- For withdrawn applications, applicants/MAHs must submit their Redaction Proposal Document package ≤60 days post-receipt of the withdrawal letter by EMA.

2.3.3.1.3. Content of the Redaction Proposal Document package

An exhaustive list of the documents to be submitted within the Redaction Proposal Document package is provided in Table 1 below, including the redaction proposal versions of all the listed clinical reports.

The required documents should be submitted within the relevant eCTD sections. For further reference please consult the eCTD Guidance Documents available on the eSubmission website.

All documents including the cover letter with the required declaration of the Redaction Proposal Document package must be uploaded via the gateway at the same time. Both, the proposed and the final redaction document packages should contain the same number of clinical reports. Therefore, even clinical reports where no CCI and/or PPD redactions are proposed, and no justification table is required have to be submitted as part of both packages. The eCTD submission of the Redaction Proposal Document package is a part of the product eCTD lifecycle and should be submitted as a subsequent sequence to the initial MAA, line extension application or extension of indication application as applicable.

Table 1: Content of the Redaction Proposal Document package, the corresponding eCTD location and the publication status

Redaction Proposal document package	eCTD Module/Section within the eCTD	Documents published
Cover letter including the declaration confirming that the clinical reports submitted for scientific evaluation are the same as those submitted for publication, except for the proposed redactions/anonymisation. The cover letter templates are at Annex 5.2 and 5.3	1.0	Not published
List of expected documents (LED), annexed to the cover letter in PDF format	1.0	Not published
eCTD Tracking table	1.0	Not published
Submission checklist	1.0	Not published
Anonymisation Report Form	1.9	Not published
Clinical overview supplement/amendment/appendix	2.5	Not published
Clinical summary supplement/amendment/appendix	2.7.1- 2.7.4	Not published
Clinical study report - body	5.3	Not published
Clinical study report - Appendices 16.1.1 (protocol and protocol amendments) 16.1.2 (sample case report form) 16.1.9 (documentation of statistical methods).	5.3	Not published
A complete set of justification tables (CCI redactions only) detailing all proposed redactions for each document. Downloadable templates are provided on Agency's corporate website under section Guidance and templates.	Working document	Not published

If any of the parts of the Redaction Proposal Document package, set out in Table 1 above, including the required declaration in the cover letter is not submitted, the whole package will be rejected. In that case, a corrected complete package must be re-submitted. Individual parts cannot be submitted separately to correct submission deficiencies.

2.3.3.1.4. Anonymisation Report Form

An anonymisation report detailing the methodology used for anonymising the clinical reports must be included in the submission. The report should also describe how the risk of re-identification has been measured and managed. The anonymisation report form template and instructions can be found in the 'Support for industry on clinical data publication' page in the EMA corporate website.

2.3.3.1.5. Issues with hyperlinks, bookmarks or external links

The applicant/MAH is not expected to provide/ensure that hyperlinks between and within documents are functional. This also applies to bookmarks. However, applicants/MAHs are encouraged to keep hyperlinks and bookmarks within clinical documents to the extent that is possible and avoid disabling all hyperlinks and removal of bookmarks by default. External links should be disabled.

2.3.3.1.6. Leaf title naming in index XML of eCTD submission and corresponding file names of the PDF documents

For submission of the Redaction Proposal version and the Final Redacted version of the clinical reports, EMA requires the applicant/MAH to follow a predefined naming convention. During the submission the documents will have an XML leaf title as well as a file name (pdf). The naming convention applies to both the XML leaf title as well as the file name.

EMA requires the applicant/MAH to apply the following naming convention for the leaf titles in the index.xml and the corresponding file names of the PDF documents:

Module 1 documents

Anonymisation report:

clinicaltrials-anonymisation-report-TradeName.pdf (where Trade Name is the name of the medicinal product).

Module 2 documents

m25-clinical-overview-var(.pdf)

m271-summary-biopharm-var(.pdf)

m272-summary-clin-pharm-var(.pdf)

m273-summary-clin-efficacy-var(.pdf)

m274-summary-clin-safety-var(.pdf)

Module 5 documents

m53xx-StudyReportNumber[9]-p (for PIVOTAL) or s (for SUPPORTIVE)-csr-body(.pdf)

m53xx-StudyReportNumber-p (for PIVOTAL) or s (for SUPPORTIVE)-app1611-protocol(.pdf)

m53xx-StudyReportNumber-p (for PIVOTAL) or s (for SUPPORTIVE)-app1612-crf(.pdf)

m53xx-StudyReportNumber-p (for PIVOTAL) or s (for SUPPORTIVE)-app1619-sap(.pdf)

Where the applicant/MAH submits the body of the CSR together with the 3 appendices (16.1.1, 16.1.2 and 16.1.9) as a single file, the leaf titles and file names should follow the below naming convention:

m53xx-StudyReportNumber-p-csr-with-app(.pdf)

m53xx-StudyReportNumber-s-csr-with-app(.pdf)

In case the applicant/MAH has included Integrated Summary of Safety (ISS) and Integrated Summary of Efficacy (ISE), the leaf titles and file names should follow the below naming convention:

m273-summary-clin-efficacy-ISE-var(.pdf)

m274-summary-clin-safety-ISS-var(.pdf)

m53xx-ISS-var(.pdf)

m53xx-ISE-var(.pdf)

In rare cases, or where more than one document is submitted in Module 2.5 or 2.7.1, 2.7.2, 2.7.3, 2.7.4 for the *same* indication/procedure, it should be indicated clearly in the var. part of the leaf title and the file name.

m25-clinical-overview-var(.pdf)

m271-summary-biopharm-var(.pdf)

m272-summary-clin-pharm-var(.pdf)

m273-summary-clin-efficacy-var(.pdf)

m274-summary-clin-safety-var(.pdf)

[9] For reports which present analysis of data collected from multiple studies, the applicant/MAH should include the report identification number (one identification number), instead of the study report numbers of each study from which the data was analysed (clinical trial or clinical study numbers). This information has to be included in the leaf titles and in the file names.

This var. part of the leaf title and file name should *only* be inserted where more than one document is submitted for that particular indication/procedure. If for one submission there is only one 2.5, 2.7.1., 2.7.2, 2.7.3, and 2.7.4 var. should be excluded from the leaf title and file name.

Regarding the technical requirements, please note that the leaf titles and PDF file names should be written in lower case and should not contain any special characters.

Example 1 naming of the leaf title and the PDF:

For example, if the applicant/MAH has submitted a clinical overview for monotherapy and combination therapy for the same product in the initial MAA the example below should be followed:

a. If they are two *separate* documents, the leaf title and the file names should include the following:

m25-clinical-overview-monotherapy(.pdf)

m25-clinical-overview-combination(.pdf)

m271-summary-biopharm-monotherapy(.pdf)

m271-summary-biopharm-combination(.pdf)

m272-summary-clin-pharm-monotherapy(.pdf)

m272-summary-clin-pharm-combination(.pdf)

m273-summary-clin-efficacy-monotherapy(.pdf)

m273-summary-clin-efficacy-combination(.pdf)

m274-summary-clin-safety-monotherapy(.pdf)

m274-summary-clin-safety-combination(.pdf)

b. If the two forms of therapies (mono and combination) or indications are discussed in one document, the leaf title and the file naming should follow the original proposal, in particular:

m25-clinical-overview(.pdf)

m271-summary-biopharm(.pdf)

m272-summary-clin-pharm(.pdf)

m273-summary-clin-efficacy(.pdf)

m274-summary-clin-safety(.pdf)

The same problem should not occur in the naming of the module 5.3 files, as *the study number* will clearly indicate the correct study.

Example 2 naming of the leaf titles and the PDF:

Another example is when during the scientific assessment additional information was included in the clinical overview or clinical summaries, which is reflected in a submission of an addendum. In this case the example below should be followed:

If an addendum was submitted *in addition* to the original document(s) the leaf title and the file names should include the following:

m25-clinical-overview(.pdf)

m25-clinical-overview-addendum(.pdf)

m271-summary-biopharm(.pdf)

m271-summary-biopharm-addendum(.pdf)

m272-summary-clin-pharm(.pdf)

m272-summary-clin-pharm-addendum(.pdf)

m273-summary-clin-efficacy(.pdf)

m273-summary-clin-efficacy-addendum(.pdf)

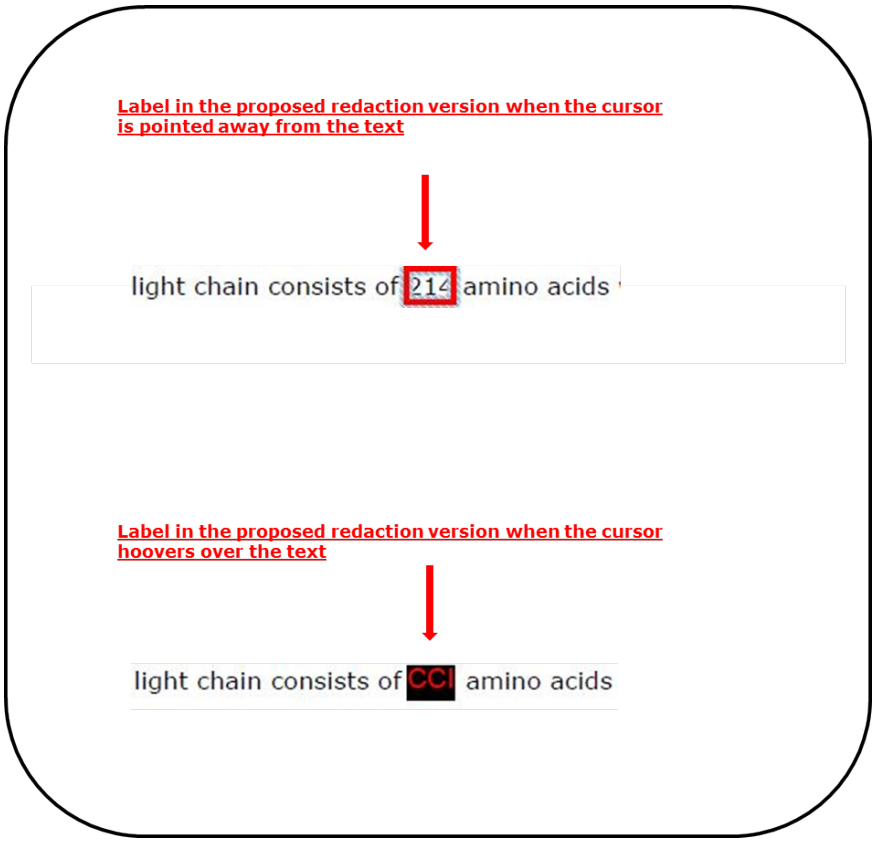
m274-summary-clin-safety(.pdf)

m274-summary-clin-safety-addendum(.pdf)

2.3.3.1.7. Technical requirements for the preparation of the Redaction Proposal version of the clinical reports

Applicants/MAHs must prepare the Redaction Proposal version of their clinical reports in line with the following requirements. These are the minimum requirements that the redaction tool used should fulfil. With regards to format of the PDF documents submitted within the eCTD, the current eCTD specification applies.

- The file format in which documents must be submitted is PDF format.
- The text proposed for redaction should be clearly identified as such (i.e. marked) and the text itself should be legible (read-through). Each proposed redaction of CCI and PPD should be labelled in the read-through documents using "CCI" or "PPD". For clarity, please see below an example of CCI labelling:



- In order to distinguish between CCI and the PPD redactions (when masking), the following labelling and colour coding is expected (i.e. the documents to be published):

  for CCI: black background with red overlay text;

  for PPD: blue (pantone 291 C - corresponding to RGB colours 115, 203 and 235) background with black overlay text;

- Redactions must be clearly visible (typically using a black rectangle).

The choice of the redaction tool is a decision to be taken by each applicant/MAH, EMA will make available to Micro, Small and Medium sized Enterprises (SMEs) a license for a redaction tool for a period of 12 months. SMEs are advised to contact the SME office five months prior to the CHMP opinion to apply for the redaction tool licence. The template of the letter can be found in Annex 5.1. SMEs will need to hold their SME status at the time of issuing the license for the product in question to qualify for the redaction tool licence.

EMA will assess the proposed CCI redactions. It is important that in the Redaction Proposal version of the submitted clinical reports the applicant/MAH clearly indicates each proposed CCI redaction. Therefore, all pieces of information proposed for CCI redaction should have a label, clearly indicating

that the proposed redaction is requested on CCI grounds. Justification for each proposed CCI redaction should be included in the justification table. Please refer to Chapter 4 for further details.

EMA will review the anonymisation report form to ensure that the applicant/MAH has followed the guidance and applied the chosen approach for anonymisation consistently in all clinical reports. For further information on anonymisation please see Chapter 3.

2.3.3.1.8. Cover letter including declaration

The applicant/MAH should use the template cover letter text provided in Annex 5.2 or 5.3 when preparing the submission.

2.3.3.1.9. Justification table

For each of the clinical reports in the Redaction Proposal version in which CCI redactions are proposed, the applicant/MAH must complete a separate justification table in Word format. Should no CCI be identified in the document, a justification table is not required.

If no CCI redactions are proposed in any of the clinical reports, the applicant/MAH should indicate this in the cover letter by including the following sentence:

<[Company name] points out that no commercial confidential information has been identified in the entire ''Redaction Proposal Document'' package and therefore, justification tables are not submitted.>

If CCI has been identified in some but not all clinical reports, the applicant/MAH is asked to include the following statement in the cover letter:

<[Company name] points out that commercially confidential information has only been identified in some documents for which [please insert the number of justification tables] justification tables were included in the "Redaction Proposal Document'' package and, confirms that in the documents for which with no corresponding justification table was submitted no CCI has been identified.>

Following the assessment of the justification table(s) the MAH/applicant will update the clinical report(s). Consequently, the corresponding Final Redacted version of the clinical reports will be published as provided by the applicant/MAH.

A sample justification table is available at Annex 5.6 and all templates can be downloaded from the 'Support for Industry on Clinical Data Publication' page.

The justification table for each document should be individually named so that its electronic name matches the name of the corresponding clinical report. Please see the detailed guidance in Section 2.3.3.1.6 of this guidance on the naming conventions that must be followed for individual documents. As a general principle EMA expects that each of the justification tables corresponds to one submitted file. For example, if during the regulatory procedure a clinical overview addendum is submitted in addition to the initial clinical overview, EMA expects the applicant/MAH to prepare two separate justification tables since both documents are subject to publication.

For CSRs in Module 5 the applicant/MAH should submit the justification tables taking into consideration the following principle:

If the CSR and the appendices are submitted for publication purposes as **one standalone file**, then **one justification table** is expected to be prepared. This justification table will have separate subheadings for each of the parts of the document (body, 16.1.1, 16.1.2, 16.1.9).

If the CSR and the appendices are submitted for publication purposes as **separate files**, then **four justification tables** are expected to be submitted: one for each of the files, e.g. body, 16.1.1, 16.1.2, 16.1.9.

The justification tables should be submitted only to EMA with the Redaction Proposal Document package, as part of a single ZIP package and outside the eCTD sequence structure in the separate folder named "Working Documents". The Working Documents are submitted together with the eCTD sequence as part of one ZIP package through the Gateway. EMA requires that within the "Working Documents'' folder the justification tables are placed in a separate folder entitled "Justification Tables". Applicants/MAHs must ensure that the sequence number folder (e.g. 0000) is a root folder in the ZIP package within the same gateway transmission. This sequence number is required to ensure that the submission passes the technical validation. It is important to ensure that the working documents package is correctly named as the technical eCTD validation will reject packages where the following naming has not been followed; sequence number, dash, working documents, for example '0025-workingdocuments' for sequence 0025.

2.3.3.1.10. Submitting the Redaction Proposal Document package through the Gateway

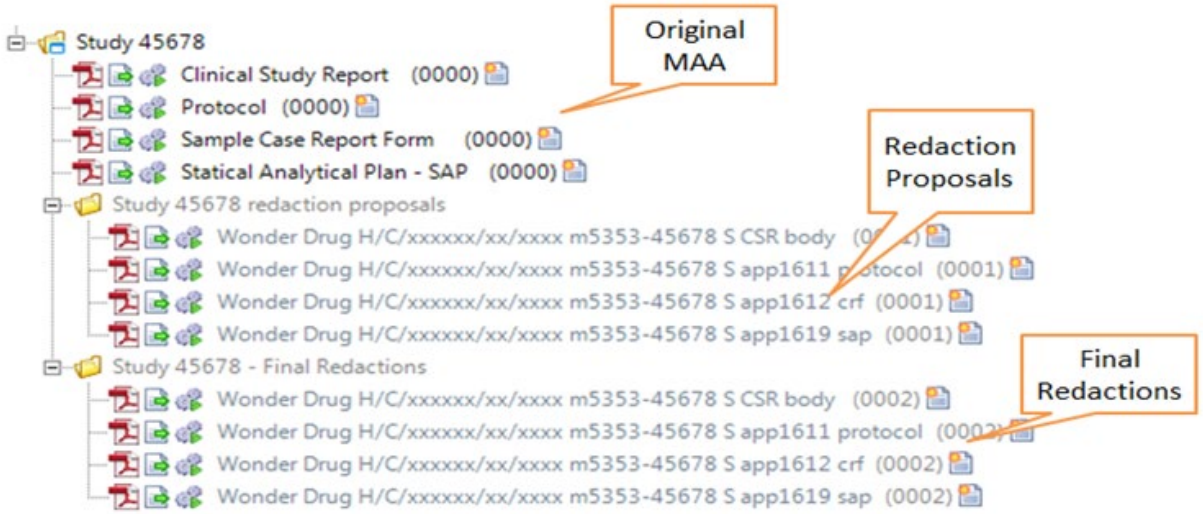
Table 1 is set out to demonstrate where each document of the Redaction Proposal Document package should be uploaded. The applicant/MAH must create a separate eCTD sequence with the relevant submission type, which will contain redacted/anonymised clinical reports as a separate data set (using eCTD operator 'new'). The related sequence field in the eCTD sequence should always be the same sequence number as stated in the EU Module 1 v3.1 specification. e.g. for Sequence 0010, related sequence field should be populated with value 0010.

The clinical reports submitted in the Redaction Proposal Document package must not be linked to any previously submitted documentation for the purpose of the scientific evaluation of a medicinal product.

In case of resubmission of the Redaction Proposal Document package due to content invalidation the applicant/MAH is expected to resubmit the **entire package in a new eCTD sequence**. The same eCTD requirements as outlined above apply, i.e. submitting it as a separate data set (using eCTD operator 'replace').

The EMA understands that in some cases the number of submitted documents in Module 5 can make it difficult to differentiate between the redaction proposal and final redacted document files as labelling them differently is not a requirement as per the naming convention. Therefore, to distinguish between the redaction proposal and final redacted files, and for a clearer structure of the submitted documents, the EMA recommends the use of two additional node extensions, as per the eCTD guidance[1], for submissions, for example:

[1] https://esubmission.ema.europa.eu/eumodule1/EU%20M1%20eCTD%20Spec%20v3.1%20-%20June%202024%20-%20final%20version.pdf



2.3.3.1.11. Automated replies following acknowledgement and notification

The applicant/MAH will receive two automated replies (messages are only visible in the eSubmission Gateway Syncplicity) following the eCTD sequence submission of their Redaction Proposal Document package. An automated Gateway MDN (Message Delivery Notification) message is sent to the sender of the package acknowledging receipt of the transmission. The MDN is equal to the signature upon delivery by the courier and only confirms that the package has been received by EMA. It does not confirm that a submission (eCTD) is technically valid, but only submission receipt. Users sending eCTD sequences containing the Redaction Proposal Document package will also receive an acknowledgement (ACK) confirming the receipt and pass/fail of the technical compliance check as per the current eCTD validation criteria for all submissions (the second automated reply). For failed submissions the error description can be found in the 'failure' acknowledgement (xml) and the submission has to be sent again.

2.3.3.1.12. Technical validation

Technical validation refers to the automated technical validation carried out on an eCTD submission by checking the document type definition (DTD) and technical components of the submission. EMA performs this technical eCTD validation upon receiving the eCTD sequence. On successful completion of this validation step, the applicant/MAH is informed through an automated acknowledgement (sent to the senders Syncplicity account).

Where an error is found during technical validation, the submission will not be loaded into the review system and a replacement sequence (sequence as appropriate) should be sent by the applicant/MAH.

2.3.3.1.13. Validation Stage

Following a successful technical validation of the package received via the eSubmission Gateway, the assigned Clinical Data Publication team will initiate the validation of the package (**Day 1**). The validation will ensure that the content of Redaction Proposal Document package, set out in Table 1 is submitted, the naming convention is followed, redaction labels (colour coding and overlay text) are correctly applied in documents (CCI/PPD) if applicable, out of scope sections (if applicable) are

correctly identified in documents, when CCI is proposed one justification table per relevant clinical report is submitted.

Further clarification on submitted justification tables will be required in cases such as:

- The text proposed for redaction is highlighted in the clinical report but missing from the justification table.
- All the proposed redactions are reflected in the justification table, but some columns/rows are incomplete.
- The same unspecific copy/paste justification is used throughout the entire justification table.

It is important to note here that validation covers more practical aspects of the completion of the justification tables and not the content of each justification. The assessment of the content of the justification comments is the subject of the review phase of the process.

Once the clinical data publication procedure has been validated by the Agency, a validation outcome letter will be sent to the applicant/MAH via Eudralink (**Day 10**). In case of an unsuccessful (invalid) validation, the Agency will reject the submitted package and the applicant/MAH is asked to resubmit the revised Redaction Proposal Document Package within 7 calendar days. At this stage recalculation of the timelines takes place.

The newly resubmitted package must be uploaded into the gateway (new eCTD sequence) and the revised package will be subject to a new content validation.

2.3.3.1.14. Review process of justifications of proposed CCI and anonymisation report form

Following a successful validation, the Agency will start the review of the justifications for the proposed redactions of commercially confidential information (CCI) and the review of the anonymisation report and associated redactions applied in the clinical study reports of the procedure (**Day 11**).

2.3.3.1.15. Review of justifications of proposed CCI

During the review the Agency will take into account the extent to which the company has followed/adhered to the principles regarding redaction of CCI as described in the CCI guidance (Chapter 4). This assessment extends mainly to the content of the reasoning/justification behind why particular information is considered CCI by the applicant/MAH. The applicant/MAH may be contacted if further clarifications are needed to assess their justifications. If the applicant/MAH fails to submit the requested clarifications, the Agency will consider the initial justifications irrelevant or insufficient and consequently will reject the proposed redaction(s).

At the end of the review process, a redaction conclusion letter is sent to the applicant/MAH via Eudralink indicating Agency's outcome on CCI (**Day 47**). The outcome of the CCI review (rejection, acceptance, or partial acceptance of the proposed CCI redactions) will be clearly communicated and documented in the appropriate columns of the justification tables.

2.3.3.1.16. Review of the anonymisation report form

The Agency will also review the Anonymisation Report to check whether the applicant/MAH has followed the anonymisation guidance and applied it consistently throughout the documents. The submitted Anonymisation Report must describe the methodology of the anonymisation applied in each of the clinical reports in the Redaction Proposal Document Package. The report should also describe how the risk of re-identification has been measured and managed, or if the three criteria for

anonymisation have been fulfilled. An anonymisation report form template and instructions can be found here. At the end of the review process, a redaction conclusion letter is sent to the applicant/MAH via Eudralink indicating the Agency's comments on the Anonymisation Report (**Day 47**). The Agency's comments, if any, will be indicated in the anonymisation comments (word document). If applicable, the applicant/MAH will revise the Anonymisation Report, taking into account these comments.

Once the redaction conclusion letter is received by applicant/MAH (**Day 47**). The applicant/MAH is required to submit their agreement or disagreement with the Agency's redaction conclusion on CCI (**Day 54**).

If required, the applicant/MAH may also be asked to send an updated anonymisation report and/or written responses to the comments raised by the Agency (**Day 61**). The Agency will review the responses and conclude whether the comments have been addressed in a satisfactory manner by the applicant/MAH. The final Agency response is sent to the applicant/MAH (**Day 68**).

2.4. Submission of the Final Redacted Document package

2.4.1. Process to submit the Final Redacted Document package

A workflow for the submission of the Final Redacted Document package can be found in Annex 5.5 of this guidance document. This process requires the applicant/MAH to submit to the Agency the final redacted version of the clinical reports for publication in which proposed redactions are applied.

2.4.2. Submission timeline

The applicant/MAH is required to submit the Final Redacted Document Package as a new sequence to the Agency for publication (**Day 74)**. Failure to submit written agreement, disagreement or to submit the Final Redacted Document Package will result in the applicant/MAH being deemed non-compliant with Policy 0070, and thus a non-compliance notice to this effect will be published on the clinical data publication website.

2.4.3. Content of the Final Redacted Document package

The applicant/MAH is required to prepare a separate sequence in eCTD format to submit the Final Redacted Document package. The eCTD submission of the Final Redacted Document package falls under the same eCTD life cycle of the initial MAA, line extension application or extension of indication application, as applicable. An exhaustive list of the documents to be submitted within the Final Redacted Document package is provided in Table 2 below, including the final redacted versions of all the listed clinical reports.

The applicant/MAH is required to submit the package of documents listed in Table 2 as part of a single Final Redacted Document package, all of which must be included in the same eCTD sequence.

Table 2: Content of the Final Redacted Document package, corresponding eCTD locations and the publication status

Final Redacted Document package	eCTD Module/Section within eCTD	Document published
Cover letter, see the template at Annex 5.9	1.0	Not published
List of expected documents (LED), annexed to the cover letter in PDF format	1.0	Not published
eCTD Tracking table	1.0	Not published
Submission checklist	1.0	Not published
Anonymisation report form	1.9	Published
Clinical overview supplement/amendment/appendix	2.5	Published
Clinical summary supplement/amendment/appendix	2.7.1 - 2.7.4	Published
Clinical study report – body	5.3	Published
Clinical study report – Appendices 16.1.1 (protocol and protocol amendments) 16.1.2 (sample case report form) 16.1.9 (documentation of statistical methods).	5.3	Published

If any of the parts of the Final Redacted Document package, set out in Table 2 above, including the cover letter is not submitted, the whole package will be rejected. In that case, a corrected complete package must be submitted. Individual parts cannot be submitted separately to correct submission deficiencies.

2.4.4. Anonymisation report form

The submitted anonymisation report form has to incorporate the feedback received from the Agency during the review process and describe the methodology of the anonymisation applied in each of the clinical reports in the Final Redacted version.

2.4.5. Technical requirements for the preparation of the final redacted version of clinical reports

The applicant/MAH must prepare a Final Redacted version of their clinical reports, as part of the Final Redacted Document package, using a redaction tool. In order to support the watermarking and publication process, the Final Redacted Version of the documents must fulfil a different set of technical requirements compared to the Redaction Proposal version as outlined below:

- With regard to PDF formats submitted within the eCTD, the current eCTD specification applies. The size of the PDF files should not exceed 200 Mbyte each as a best practice rule.

- The PDF files must not be password protected, as EMA will add a watermark to every page.
- **The un-redacted text only** must be text-searchable. Redacted text and the blackened redaction box (that covers the redacted text) should neither be searchable nor subject to further editing.
- In order to distinguish between CCI and the PPD redactions, correct labelling and colour coding is expected (see section 2.3.3.1.7.) in the ***Final Redaction Document Package*** (i.e. the documents to be published).
- Redactions must be clearly visible (typically using a black rectangle).
- Any (agreed) CCI or PPD redaction labels should be visible and irremovable together with the final redacted text.
- If the original clinical report contained text or figures in colour, the Final Redacted Version of documents in colour should also be in colour.

2.4.6. Cover letter including declaration

The applicant/MAH should submit the completed template cover letter provided in Annex 5.9, as a part of the Final Redacted Document package.

In the cover letter submitted to EMA for the Final Redacted Document package , an applicant/MAH should note that it provided a declaration in the cover letter with the Redaction Proposal Document package stating that the clinical reports submitted for publication are the same as those submitted for scientific review, with the exception of the agreed redactions and anonymisations.

2.4.7. Naming conventions for the clinical reports included in the Final Redacted Document package

The naming conventions of the clinical reports included in the Final Redacted Document package must be the same as those used for the Redaction Proposal Document package, see Section 2.3.3.1.6.

2.4.8. Submitting the Final Redacted Document package through the Gateway

The applicant/MAH is required to submit the Final Redacted Document package as a new sequence to the Agency for publication within 7 calendar days following the redaction conclusion letter or following the final EMA response. An applicant/MAH submitting multiple applications for the same medicinal product under different invented names is also required to provide a new sequence for the Final Redacted Document package for each of the products.

This separate sequence must have the relevant submission type and be separate (using eCTD operator 'new') to that created for the Redaction Proposal Document package.

2.4.9. Automated replies following acknowledgement and notification

Please refer to section 2.3.3.1.11.

2.4.10. Technical validation

Please refer to section 2.3.3.1.12.

2.4.11. Final Package Check

Once the Final Redacted Document Package has been submitted by the applicant/MAH, the Agency will perform the final package check to make sure the comments raised by the Agency when reviewing the Redaction Proposal Document Package have been addressed in the documents submitted. The Agency will send a communication to the applicant/MAH if package valid to inform the applicant/MAH of the publication date on the clinical data website or in case package invalid letter is sent to applicant/MAH via Eudralink (**Day 81**).

In case the final package is invalid, recalculation takes place and applicant/MAH has to submit the new Final Redacted Document Package within 7 calendar days. The same eCTD requirements as outlined above apply, i.e. submitting it as a separate data set (using eCTD operator 'replace').

2.4.12. Publication process

Redacted/anonymised clinical reports will be published by the Agency in EMA clinical data website within 10 calendar days after the receipt of a valid Final Redacted Document Package. Prior to publication EMA will watermark each page[2] of the clinical reports in the Final Redacted version submitted by the applicant/MAH. The applicant/MAH will receive an email from EMA once publication has taken place.

A situation may arise where an agreement between the applicant/MAH and EMA is not reached on the proposed redactions, and the applicant/MAH, in the context of a subsequent action for annulment, may decide to apply for interim relief against an EMA decision to publish the documents without accepting the redactions which are still controversial. In this case, the applicant/MAH will submit a partial Final Redacted version package, in which the clinical reports will be redacted according to the applicant/MAH's views. The applicant/MAH will confirm, in the text of the cover letter, which controversial redactions (page, line) have been made in the documents. Please note that applications for annulment of EMA decisions and related applications for interim relief are submitted before the General Court of the European Union in accordance with Article 263 of the Treaty on the functioning of the European Union and the Rules of Procedure of the General Court. The related deadlines and time limits are set therein.

In the event that interim relief is sought against the EMA decision, EMA will publish a partial Final Redacted Version of the clinical reports. When a final decision on the interim relief proceedings is issued, the applicant/MAH shall submit a Final Redacted Version in accordance with the indications from the Court of Justice of the European Union. EMA will withdraw from the EMA clinical data portal website the partial Final Redacted version previously published. EMA will then publish the Final Redacted version.

In an exceptional situation where an applicant/MAH does not submit a complete Redaction Proposal document package or a complete Final Redacted Document package, EMA will publish a non-compliance notice.

2.5. Marketing authorisation transfers

In cases where a marketing authorisation holder (the Transferor) submits an application to transfer a marketing authorisation to another company (the Transferee), as of the date of notification of the amendment of the Commission decision in relation to the transfer of the marketing authorisation based

[2] The watermark text is:'www.ema.europa.eu
This document cannot be used to support any marketing authorisation application and any extensions or variations thereof'

on Regulation (EC) No 2141/96 (the transfer date), the Transferee becomes the new marketing authorisation holder and takes over all responsibilities pertaining to a marketing authorisation holder under EU pharmaceutical legislation.

Responsibilities under Policy 0070 are also transferred to the Transferee, and include responsibility for clinical reports that were redacted by the Transferor and published by the EMA before the transfer date. Should an MA transfer application be sent to the EMA during the Policy 0070 process, the process will continue on the basis of the agreements, submissions and declarations made by the Transferor. From the transfer date onwards, the EMA will liaise with the Transferee for all remaining aspects of the Policy 0070 process for the product subject to the transfer.

In some cases the transfer date may occur after the EMA conclusion is issued (to the Transferor) but before the Final Redacted Document package is submitted. To remain compliant with Policy 0070 in these cases the Transferee must submit the Final Redacted Document package in line with the EMA conclusion issued to the Transferor. The EMA strongly encourages that the Transferor and Transferee exchange information on the agreements, submissions or declarations made between the Transferor and EMA under the scope of the Policy 0070 publication process.

Chapter 3

External guidance on the anonymisation of clinical reports for the purpose of publication in accordance with EMA Policy 0070

3.1. Introduction

Policy 0070 states that adequate personal data protection needs to be ensured and that full compliance with applicable EU legislation needs to be achieved. Furthermore, the processing of personal data and its publication on the website by EMA is subject to the provisions of Regulation (EU) 2018/1725 and in particular is limited only to information that is adequate, relevant and not excessive for the purpose of transparency. It is important to recall that no personal data of trial participants (i.e. individuals on whom information has been collected related to the scientific objectives of the trial, e.g. patients and healthy volunteers) should be published.

The objective of this chapter is to provide information to applicants/MAHs on the anonymisation of clinical reports in the context of EMA Policy 0070. The information contained in this guidance document should be considered as EMA recommendations on how best to achieve anonymisation.

The current guidance provides information on some of the anonymisation techniques that are available to applicants/MAHs. The field of anonymisation, i.e. the techniques used by controllers of personal data to anonymise data, is a field of active research and rapidly evolving. This guidance is not intended to provide an exhaustive list of the techniques available or to mandate a specific methodology but rather to highlight the anonymisation process to be followed to ensure that clinical reports submitted to EMA for publication are rendered anonymous prior to publication. The guidance document will be updated in light of new developments.

This guidance document is without prejudice to the obligations of applicants/MAHs as controllers of personal data under Regulation (EU) 2016/679 (General Data Protection Regulation – GDPR) and applicable national legislation on the protection of personal data.

3.2. Legal framework and available standards

This guidance has been developed based on the current available legislation in the EU as well as guidance and standards on the anonymisation of personal data (see below).

I. Legislation

- Regulation (EU) 2018/1725 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 of 23 October 2018.
- 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).

II. Guidance issued by data protection authorities

- Opinion 05/2014 on anonymisation techniques of the Article 29 Data Protection Working Party.
- Opinion 06/2013 on open data and public sector information reuse of the Article 29 Data Protection Working Party.
- Irish Data Protection Commission: Guidance on Anonymisation and Pseudonymisation
- Agencia Española de Protección de Datos:
  - K-anonymity as a privacy measure

  - Introduction to the Hash Function as a Personal Data Pseudonymisation Technique
  - 10 Misunderstandings related to anonymisation
- Information Commissioner's Office (ICO): Anonymisation guidance
- Information and Privacy Commissioner of Ontario: Deidentification Guidelines for Structured Data

III. Guidance issued by professional organisations active within data protection space

- Sharing Clinical Trial Data: Maximizing Benefits, Minimizing Risk | The National Academies Press. Institute of Medicine (IOM). 2015. Washington, DC: The National Academies Press.
- Pharmaceutical Users Software Exchange (PhUSE) De-identification Standard for SDTM 3.2.
- Transcelerate BioPharma Inc.
  - Clinical Study Reports Approach to Protection of Personal Data Version 2.0.
  - Protection of Personal Data in Clinical Documents – A Model Approach
  - Data De-identification and Anonymisation of Individual Patient Data in Clinical Studies– A Model Approach V2.0
- Scientific literature
  - K. El Emam, Kald Abdallah. "De-identifying Clinical Trials Data". Applied Clinical Trials, Mar 20, 2015
  - Khaled El Emam, Sam Rodgers, Bradley Malin. Anonymising and sharing individual patient data. *BMJ* 2015; 350: h1139.
  - David Carrell, Bradley Malin, John Aberdeen, et al. "Hiding in plain sight: use of realistic surrogates to reduce exposure of protected health information in *clinical text". J Am Med Inform Assoc 2013;20:342–348*.

3.3. General considerations

A number of general aspects need to be considered when providing recommendations on how best achieve anonymisation. These relate to:

3.3.1. Context of data disclosure

The risk of re-identification can vary depending on the context of disclosure. In the case of public data release (publication to the world at large) the risk of re-identification needs to be very low since there are no controls that can be put in place. However, for non-public data-sharing a higher risk could be acceptable because robust governance arrangements (security, privacy, and contractual controls) can be established. It means that the same data can be adequately anonymised in different ways depending on the context of the data release. Therefore, it is necessary to take into consideration the context of the data release when deciding on the anonymisation process.

3.3.2. Concept of anonymisation

According to Article 3(1) of 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: *'Personal data' 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.

Regulation (EU) 2016/679 (GDPR) refers to anonymisation in recital 26 and excludes anonymised data from the scope of data protection legislation. Hence, data protection law does not apply to data rendered anonymous in such a way that the data subject is no longer identifiable.

Anonymisation is the process of turning data into a form that does not identify individuals and where re-identification is not likely to take place. It allows for a much wider use of the information.

According to the Article 29 Data Protection Working Party (Art. 29 WP) data that have been altered using techniques to mitigate risks of re-identification of the individuals concerned, but have not attained the threshold required recital 26 of GDPR are not considered anonymised data. Therefore, such approach is only appropriate for limited disclosure for re-use by screened parties but not for public disclosure and re-use under open licence. Recital 26 signifies that to anonymise any data, the data must be stripped of sufficient elements such that the data subject can no longer be identified. More precisely, the data must be processed in such a way that it can no longer be used to identify a natural person by using "all the means likely reasonably to be used" by either the controller or a third party. The definition of personal data as described in Article 3(1) of Regulation (EU) 2018/1725 relates to a 'natural person'. The Article 29 Working Party opinion 4/2007 on the concept of personal data further clarifies that information relating to dead individuals is therefore in principle not to be considered as personal data to the rules of the Directive, as dead are no longer natural persons in civil law. However, the opinion also points out that data on the deceased may still be personal information since it may refer to living persons, e.g. it may indicate family diseases relevant to living children or siblings. In addition, it might be difficult for the data controller to establish whether the person to whom the data relates is still alive.

It must be emphasised that recital 26 of GDPR sets a high threshold, as described in the Opinion of Art. 29 WP. Unless data can be anonymised to meet this threshold, data protection law continues to apply.

The irreversibility of the anonymisation methodologies or techniques is also an important element as it can be used in order to differentiate from "pseudonymisation". Pseudonymisation consists of replacing one attribute (typically a unique attribute) in a record by another. When pseudonymisation is used alone, the natural person is still likely to be identified indirectly. Pseudonymisation reduces the linkability of a dataset with the original identity of a data subject but when used alone will not result in an anonymous dataset, therefore data protection rules still apply. It is, therefore, important to clarify that pseudonymisation is not an anonymisation method but a useful security measure. Consequently, additional measures should be considered in order to render the dataset anonymised, including removing and generalising attributes or deleting the original data or at least bringing them to a highly aggregated level.

3.3.2.1. Anonymisation criteria

According to the Opinion 05/2014 on anonymisation techniques of the Art. 29 WP, two options are available to establish if the data is anonymised. Either through the demonstration of effective anonymisation based on three criteria:

- Possibility to single out an individual.

- Possibility to link records relating to an individual**.**
- Whether information can be inferred concerning an individual.

or, whenever a proposal does not meet one of these criteria, through an evaluation of the identification risks.

An anonymisation solution preventing all three criteria is considered to be robust against re-identification performed by the most likely and reasonable means the data controller or any third party may employ and will render the data anonymous. However, the fulfilment of the three criteria sets a high bar in terms of achieving anonymisation and for many clinical reports this may translate into stripping them of the indirect identifiers bearing the highest data utility. Therefore, a risk assessment strategy is considered to strike a better balance between anonymisation and data utility.

3.3.2.2. Anonymisation techniques

There are several techniques that can be used in order to achieve anonymisation. Opinion 05/2014 on anonymisation techniques of the Art. 29 WP analyses the effectiveness and limits of existing anonymisation techniques against the EU legal background of data protection, and provides recommendations to handle these techniques by taking account of the residual risk of identification inherent in each of them.

3.3.2.3. Advances in technology

It is also important to take note of advances in technology (e.g. data mining, artificial intelligence) together with greater availability of data and the possibility of database linkage with the increased risk of re-identification. applicants/MAHs need to take into account (realistic) future developments in terms of availability of data and technologies that would allow re-identification. Art. 29 WP Opinion 05/2014 on anonymisation techniques emphasises that even where a data controller believes it has successfully anonymised personal data, the data controller must continuously follow the developments in re-identification techniques, and if necessary reassess the risk of re-identification.

3.4. Applying these general considerations in the context of clinical reports for publication in accordance with EMA policy

3.4.1. Context of data disclosure

This guidance document comes within the context of public data release since EMA has defined a process for publication of clinical reports where clinical reports are available on-screen for any user, with a simple registration process, and are available for downloading to identified users. Both situations are governed by dedicated Terms of Use that clarify that users of the data shall not, in any case, attempt to re-identify trial participants or other individuals.

3.4.2. Concept of anonymisation

Clinical reports submitted to EMA for applications for marketing authorisation or post authorisation procedures consist of pseudonymised data. They contain study results presented in an aggregated format and individual patient information within, e.g. case narratives, listings or tables of patient characteristics. Therefore, the reports cannot be considered anonymised and cannot be published as such. Applicants/MAHs, as data controllers of the personal information that might be contained in these documents, are required to submit clinical reports that have been rendered anonymous for the purpose of publication under Policy 0070. The anonymised clinical reports should be a copy of the clinical

reports submitted in the context of the scientific evaluation procedure, stripped of sufficient elements such that the participants can no longer be identified. The data in the clinical reports must be processed in such a way that it can no longer be used to identify a natural person by using "all the means reasonably likely to be used" by either the controller or a third party, as described in GDPR.

3.4.3. Data utility

Different anonymisation techniques will lead to different levels of data utility in the anonymised reports. Applicants/MAHs should take into consideration the impact of the data transformations/redactions on the scientific usefulness of the data. The aim of the anonymisation process should be to maximise the data utility while protecting the privacy of the study participants.

3.4.4. Advances in technology

As mentioned above, Art. 29 WP Opinion 05/2014 on anonymisation techniques emphasises that the data controller must continuously follow the developments in re-identification techniques, and if necessary reassess the risk of re-identification. Applicants/MAHs, in accordance with national legislation on data protection, will need to take this aspect into consideration and to monitor continuously the development of technologies in this area in order to assess novel risks of re-identification for any future clinical reports published.

3.4.5. Rare diseases and small populations

EMA understands the complexity involved in the anonymisation of clinical reports in the case of rare diseases and small populations, due to the very low number of trial participants and of overall patient population. Therefore, careful consideration should be taken in the anonymisation of the clinical reports in these instances.

In European Union the widely accepted prevalence threshold (EU rare diseases) for a disease to be considered rare is not more than 5 cases in 10,000 persons. There is no threshold or definition that can be applied to determine what could constitute a small population. For clinical trials the small populations could be the result of the study protocol inclusion/exclusion criteria which can focus the research on a limited number of individuals which share the same socio-economic characteristic and for example work in a specific environment or live in a small geographical location or are exposed to certain environmental hazards.

3.5. EMA recommendations to applicants/MAHs on how best to achieve anonymisation

3.5.1. Data utility

Taking into account the need to find the best balance between data utility and achieving a low risk of re-identification, the aim is to retain a maximum of scientifically useful information on medicinal products for the benefit of the public while adequately protecting the privacy of data subjects. Therefore, this guidance is to assist in achieving this objective by recommending methodologies and a process that could be applied to clinical reports.

The guidance is not intended to mandate any specific methodology but to highlight the available techniques and those that EMA considers most relevant in the context of the anonymisation of clinical reports prepared for publication under Policy 0070. However, the choice of anonymisation techniques to use, while retaining a maximum of scientifically useful information, is left up to the applicants/MAH.

EMA understands that redaction techniques are relatively easier to be applied in documents compared to transformation techniques. However, redaction alone is more likely to decrease the clinical utility of the data compared to other techniques. Therefore, EMA is of the view that applicants/MAH should prioritise the use of other anonymisation techniques that are more likely to preserve the clinical usefulness of the data published. Applicants/MAH are encouraged to use transformation anonymisation techniques over other anonymisation techniques, whilst ensuring data anonymisation is achieved.

3.5.2. Rare diseases, small populations and low frequency events

Clinical trials conducted on rare diseases and on small populations have a higher risk of re-identification. Therefore, specific attention should be given to them. Not only the small size of the recruitment pool but the knowability of the shared socio-economic or disease characteristics of the enrolled study subjects are equally important factors to be accounted for in the estimation of the initial risk of re-identification. In addition, a quantitative approach to the measurement of the risk of re-identification should be favoured (see Section 3.5.4). This approach is also applicable to genetic information and low frequency events (e.g. rare events, extreme values, unusual treatments, pregnancy outcomes).

3.5.3. Specific recommendations to applicants/MAHs for the anonymisation of personal data of trial participants

The anonymisation techniques described in this guidance are applicable only to trial participants. Personal data in relation to investigators, sponsors and applicants/MAHs should be redacted as described in section 3.6.

3.5.3.1. Anonymisation criteria

For clinical data, retaining the linkability of multiple records belonging to the same trial participant within the same document is important in order to understand the safety and efficacy profile of a medicinal product. In addition, inference is important in view of the scientific utility of the data, and emphasis should be made on the potential impact of inferred data on the trial participants. Therefore, in order to achieve a maximum usefulness of the data published, it is unlikely that for clinical reports all three criteria can be fulfilled by any anonymisation solution, it is EMA's view that a thorough evaluation of the risk of re-identification needs to be performed (see section 3.5.4).

3.5.3.2. Anonymisation techniques

It should be noted that each anonymisation technique has its own strengths and weaknesses. The robustness of each anonymisation technique is based upon the aforementioned anonymisation criteria and will help identify the most suitable technique (or combination of different techniques) to establish an adequate anonymisation process for a given clinical report. Ultimately, the aim is to preserve data utility as much as possible whilst ensuring adequate anonymisation of personal data in the clinical documents.

Not all anonymisation techniques described in Opinion 05/2014 of the Art. 29 WP may be suitable to anonymise personal data in clinical reports. The specificities of the clinical data should therefore be taken into consideration when selecting the most appropriate technique(s).

The simplest method of anonymisation is the masking of values for variables which allow direct or indirect identification of an individual from the data. This technique is sometimes called redaction. Technically, it can be achieved by using a redaction tool which ensures that the redacted information is

irreversibly blocked out. Redaction of pre-specified variables can be done manually and/or may include the use of software that can help identifying pre-specified variables that need redaction. Redacting entire sections of the report where redaction of pre-specified variables is possible is not considered appropriate, and is, therefore, not recommended by EMA.

Apart from redaction, the main anonymisation techniques are randomisation and generalisation.

Randomisation is a family of techniques that alters the veracity of the data in order to remove the strong link between the data and the individual. Recommended techniques include noise addition and permutation. Noise addition can consist of, for example, shifting dates randomly by a few days (forward or backwards), based on a uniform, or other type of, distribution. This anonymisation technique is known as offsetting and is described more in detail below. Permutation may have limitations as regards clinical utility as relationships between attributes can be destroyed. The differential privacy technique may not be applicable in the context of Policy 0070 since the same documents will be made available to all users.

The other main family of anonymisation techniques consists of generalising or diluting the attributes of the data by modifying the respective scale or order of magnitude. Recommended generalisation techniques include aggregation and k-anonymity. L-diversity and t-closeness may not be recommended as they limit inferences significantly. Aggregation involves the replacement of a value by a range, e.g. a trial participant's age is replaced with an age range (age of 56 replaced with range of 50 to 60). K-anonymity goes a step further by preventing a trial participant from being singled out since it is grouped with, at least, *k* other trial participants in that range.

EMA follows closely the developments in techniques that can be used to anonymise clinical data through mathematical models together with metrics of re-identification. These techniques can be directly applied to the anonymisation of electronic datasets and allow the anonymisation of the clinical reports for publication using the underlying clinical data which has already been anonymised. This may facilitate the anonymisation process and maximise the information included in the clinical reports anonymised for publication. It does not mean that anonymisation will take place before the scientific review of the data for the purposes of the clinical trial and marketing authorisation assessment. None of these processes should undermine the submission of the full, pseudonymised clinical reports and underlying data. Most importantly, it needs to be demonstrated that these techniques can ensure that the risk of re-identification is acceptably low and in line with requirements for public disclosure and that the data transformation resulting from the applied anonymisation techniques will not lead to a different interpretation of the study results.

3.5.3.2.1. Anonymisation of Direct Identifiers

Direct identifiers are elements that permit direct recognition or communication with the corresponding individuals.

Clinical reports submitted to EMA mostly consist of pseudonymised aggregated data and therefore it is unlikely that direct identifiers are present in the reports. Nonetheless, any direct identifiers still present should be redacted, e.g. name, email, phone number, signature and full home address. Patient ID numbers (including randomisation/treatment number or safety case ID) can be either redacted or recoded. Recoding or pseudonymising direct identifiers have been demonstrated to reduce the risk of re-identification. However, having a pseudonym means that information for the same individual can be linked which is likely to increase the risk of re-identification. On the other hand, the value of the data is significantly reduced where the ability to follow a patient across visits and events is broken. The risk of linking the information for the same individual can be measured and net effect on risk can be

determined. A decision on whether to redact or recode patient ID should be made on a case-by-case basis based on the impact on the risk. Moreover, it should also be considered that for any extension to the initial marketing authorisation application study, the same patients will be recoded differently from the initial marketing authorisation study. EMA recognises that in such situations data utility may be suboptimal since this creates a problem of linkability between the initial study and the extension study.

3.5.3.2.2. Anonymisation of Indirect Identifiers

Indirect identifiers are variables representing an individual's background information that can, in combination with other identifiers indirectly point to individuals. Information from indirect identifiers increases the scientific usefulness of the information published.

To render the clinical reports anonymised it is not always necessary to redact or transform all indirect identifiers. The decision to retain or to modify the indirect identifiers will depend on context and aspects such as:

- Number of indirect identifiers per trial participant
- Frequency of trial participants with same category/value on a set of the indirect identifiers (group size)
- Re-identification potential of specific identifiers
- Data utility of specific identifiers
- Size of reference population

It is up to the applicants/MAHs to propose which indirect identifiers need to be redacted or transformed and which ones could remain unchanged in the reports. The rationale for the decision should be included in the risk assessment section of the anonymisation report provided to EMA (see section 3.5.4).

The level of anonymisation is only partially determined by the data to be protected. The ability to identify a trial participant depends on both the personal data variables and the state of knowledge of the observer concerning the trial participants personal details present in the data. For instance, even though geographical location and calendar dates may not be the most specific identifiers of a trial participant, they are often the most easily obtainable from other sources, thus leading to a higher risk of re-identification. Therefore, clinical data containing information on geographical location and calendar dates should be carefully anonymised (see sections 3.5.3.2.2.3. and 3.5.3.2.2.2). In addition, the relative utility and/or confounding potential of patient-level information such as adverse events, medical history, concomitant medications and demographics (sex, age, race, ethnicity, height and weight) should be considered when defining the anonymisation strategy.

3.5.3.2.2.1. Adverse events, Medical History and Concomitant Medication

Adverse events are considered the variables with the highest data utility value, they are essential for the understanding of the safety profile of the medicinal product, therefore they should be retained at the expense of other indirect identifiers. Concomitant medications and medical history also play an important role in the adverse events causality assessment therefore transformation anonymisation techniques should be employed to preserve as much as possible the data utility of these variables. It is expected that all adverse event terms are retained in both summary-level (i.e., tables, descriptive summaries) and participant-level data (i.e., narratives). In exceptional cases where the (serious)/adverse event term poses a serious risk of re-identification or is unique, the term could be

generalised to the HLT (high level term), HLGT (high level group term) or SOC (system organ class) as classified by MedDRA. The same approach could be followed for medical history and for which the lowest-level term (LLT) could be disclosed. The concomitant medications' invented names could be replaced with the active substance in case the invented names are specific to certain regions or countries and if released would increase the risk of reidentification of individuals.

3.5.3.2.2.2. Dates

There are various dates that can be included in clinical reports, e.g. date of birth of trial participants, date of trial participant visits, dates of adverse events and study dates. Date of birth of trial participant, if possible, should be redacted (month and day) with the exception of the year in order to preserve the age of the trial participant. Other dates such as event or assessment dates can be offset as described below.

The most commonly used method to de-identify dates is to offset them. In this technique, dates are replaced with a new date generated using a random offset for each participant and this offset is applied to all dates in the study for that participant. By using one offset for all dates for a participant, the relative period between a participant's dates is maintained from their original dates to their de-identified dates.

It is not advisable to use only one random offset for an entire study, i.e. the same offset for all the trial participants since if the offset is identified for one participant, it is therefore identified for all participants in that study. For this reason, an algorithm that assigns different random offsets to each of the study participants is considered a more reliable approach when using this technique.

A date offset algorithm should be applied to offset dates. It can use the starting day of the trial as an anchor date and it must be ensured that the offset dates are within the range of dates for e.g. findings, events collected during the trial. The difference between the anchor date and the first event/finding will be set as the offset which will vary from trial participant to trial participant.

In case of partial dates the offset dates must also be partial. Partial dates after offsetting are less reliable in terms of date sequencing with a consequent negative impact on data utility. Special consideration should be made to adaptive design trials, e.g. if a new arm is added during the course of the trial.

An alternative to the method described above is to derive the relative study day method. If a variable containing relative study day is not already present in the datasets, it is calculated for each observation as the number of days relative to a reference date, e.g. date of study entry or date of randomisation. The same algorithm is applied to all dates across the study in order to maintain the relationship between events for each participant (e.g. their visit schedule).

Relative study days have high data utility due to their impact on the interpretation of the study results including the temporal causality assessment of the reported adverse events. Moreover, it is preferable, from a data utility perspective, to keep both types of dates, i.e. absolute (actual date) and relative.

3.5.3.2.2.3. Geographical location

While for some studies geographical location could have scientific value when for example the clinical practice varies from country to country directly impacting the outcome, the geographical location is an important element that can facilitate re-identification of the trial participant. It may be necessary to aggregate or generalise from country to region or continent unless this information is critical to the analysis. The need to aggregate or generalise should be considered when performing the

anonymisation risk assessment. The link between individual patient data and the identity of the site should be removed since this pinpoints the individual patient data to a geographical location much smaller than a country. In addition, a frequency analysis can most likely reveal the most recruiting site in a country, which will in turn include many of the trial participants. However, it may not be the case where the recruitment is uniform across all sites.

3.5.4. Anonymisation process

EMA recommends the anonymisation process described below:

1. *Determination of direct identifiers and indirect-identifiers*

   A person's identity can be disclosed from either direct identifiers or indirect identifiers. Direct identifiers are elements that permit direct recognition or communication with the corresponding individuals, such as personal names, email addresses, telephone numbers, and national insurance numbers. Direct identifiers are not often useful for clinical data analysis.

   Indirect identifiers are variables representing an individual's background information that can indirectly identify individuals, such as their date of birth, death, or clinic visit, residence postal code, sex and ethnicity. Indirect identifiers also include demographics, medical information and socioeconomic information. Both types of variables must be addressed during anonymisation. In recent cases of re-identification, attackers used indirect identifiers to successfully determine the identity of individuals. It is therefore important to protect the indirect identifiers as well as the direct identifiers.

   Classification of variables into categories of personal data

   There are three conditions for a variable to be considered an identifier (direct or indirect), i.e. replicability (the variable values must be sufficiently stable over time so that the values will occur consistently in relation to the data subject), distinguishability (the variable must have sufficient variability to distinguish among individuals in the data) and knowability (an adversary must know the identifiers about the data subject in order to re-identify them). If a variable is not knowable by an adversary, it cannot be used to launch a re-identification attack on the data (see below for further details on adversaries and attacks).

   Once a variable has been determined to be an identifier it is necessary to establish whether it should be classified as a direct identifier or a indirect-identifier. This is important because the anonymisation techniques used to protect direct identifiers are different from those used for indirect identifiers.

   PhUSE has defined a set of rules developed to facilitate the assessment of direct and indirect identifiers in the data. These rules help to establish the various categories of personal data that can be found in the clinical reports.

2. *Identification of possible adversaries and plausible attacks on the data*

   For public data release, adversaries are most likely to be interested in showing that an attack is possible (demonstration attack). The following potential scenarios of re-identification can be conceived in the context of the publication of clinical trial data:

- An organisation sees a financial interest in finding out who are the trial participants in the clinical trial. Usually, it would require some strategy to identify accurately a fair number of trial participants.

- One trial participant is of particular public interest and is focussed on by the press or other body.
- A group or individual, in order to embarrass the data controller, or to undermine the public support for release of data, wishes to identify just one trial participant without regard to which trial participant it might be.
- A random event in which an individual happens to examine a clinical report including data on a trial participant with whom they are well acquainted to the extent that they can accurately guess that certain information relates to that trial participant.

  Each of the scenarios described above reflect possible adversaries and plausible attacks, having different risk implications. Applicants/MAHs should identify possible adversaries and plausible attacks on the data and evaluate the impact on the risk of re-identification.

3. *Data utility considerations*

   This is an important requirement that needs to be considered carefully when selecting the anonymisation methodology. If anonymisation of the data results in clinical reports that are no longer useful for their intended secondary purposes, data utility is compromised. Furthermore, anonymisation of clinical reports results in the data being perturbed in some way. Ensuring that the analysis results produced after anonymisation are similar to the results that would be obtained from the original clinical reports is critical. Therefore, the amount of distortion should be minimised. Ultimately, a balance must be reached in order to obtain an acceptably low probability of re-identification and a high utility data.

4. *Determining the risk of re-identification threshold and evaluation of the actual risk of re-identification*

   Measuring the risk of re-identification involves selecting an appropriate risk metric, a suitable threshold and the actual measurement of the risk in the clinical data information to be disclosed. The choice of a metric depends on the context of data release. For public release it is advisable to use the maximum risk.

   Setting an acceptable threshold encompasses evaluation of the existing mitigation controls (none in the context of public disclosure), the extent to which a particular disclosure would be an invasion of privacy to the trial participant and the motives and the capacity of the attacker to re-identify the data. Once a threshold has been determined, the actual probability of re-identification can be measured. If the probability is higher than the threshold, anonymisation of the data needs to be performed. Otherwise, the data can be considered to have a very small risk of re-identification and to be fully anonymised.

   Based on the recommendations made in the IOM report and the available precedents for public release of health data, EMA believes that it is advisable to set the threshold to a conservative level of 0.09. However, it is up to the applicants/MAHs to decide on the most appropriate threshold for public disclosure of the clinical reports at stake, and if a different threshold is selected a justification must be provided.

   The most appropriate way to measure the risk of re-identification for an entire dataset, in the context of public disclosure, is through the maximum risk, which corresponds to the maximum probability of re-identification across all records.

   Further information about the methodology to calculate the risk of re-identification is available in the literature, such as for instance that the probability of re-identification of a record in a data set

is 1 divided by the frequency of trial participants with same category/value of a set of the indirect identifiers (group size).

It is acknowledged that initially the assessment of risk of re-identification may be mostly qualitative. The approach to be taken in the case of a qualitative risk assessment is very similar to that of a quantitative approach, the difference being that rather than having a probability and measure of the risk as numerical values there is instead a qualitative scale (e.g. high, medium, low risk).

Applicants/MAH are encouraged to use quantitative methods to measure the risk of re-identification as soon as they are in a position to do so.

Applicants/MAH may not follow, in an initial phase, an analytical approach, and therefore it will not be necessary to calculate the risk of re-identification. In such cases this anonymisation process step could be omitted.

5. *Anonymisation methodology*

   Applicants/MAH should identify the most suitable technique (or combination of different techniques) to establish an adequate anonymisation process and should describe how they reduce the risk of re-identification. In addition, justification should be provided for the data that is altered and the choice of anonymisation techniques used.

6. *Documenting the anonymisation methodology and process*

   Documenting the methodology used is an important step as it provides information not only on the techniques that have been used to anonymise the data but also the rationale for using them. It should also be described how the clinical reports have been rendered anonymous either by measuring and managing the risk of re-identification, or by demonstrating that the three criteria for anonymisation have been fulfilled.

3.5.5. Reporting on the anonymisation process

As recommended by the Art. 29 WP, data controllers should disclose the anonymisation technique(s) being implemented in the case of public release of the anonymised data. Therefore, an Anonymisation Report Form Template and instructions for completion have been developed jointly by EMA and the Health Canada Public Release of Clinical Information (PRCI) and are made available on the EMA clinical data publication landing page under support for industry section. The template is mandatory to be used and the MAHs are required to complete it and produce a specific Anonymisation Report for each individual data package submitted for publication.

The anonymisation methodology used must include a way of demonstrating adequate anonymisation of the clinical reports and have a replicable process to follow. Applicants/MAHs should therefore describe the anonymisation process followed in the anonymisation report. In addition, the report should describe how the risk of re-identification has been measured and managed, or if the three criteria for anonymisation have been fulfilled.

3.6. Redaction of personal data of investigators, sponsor staff and applicant/MAH staff

Personal data of individuals other than patients, i.e. investigators, sponsor staff and applicant/MAH staff will not be published with the following exceptions:

- The **sponsor** and coordinating **investigator signatories of the clinical study report** and the identities of the **principal or coordinating investigator**(s) who conducted the trial and their sites. The identities of these individuals should not be disclosed if the study roles are not clearly spelled out in the clinical reports.

However, their contact details and handwritten signature should be redacted. Personal data relating to all other clinical study personnel should also be redacted. Data pertaining to the above exceptions in other parts of the CSR will be redacted as they may give away geographical information (e.g. site number, site address, investigator names) that could be linked to patients and hence may enable their identification.

Handwritten text present in the clinical reports in the form of medical notes, annotations or even handwritten signatures and associated dates may lead to the identification of an individual and should be redacted.

3.7. Temporary redaction of interim results of ongoing blinded studies

The clinical studies may still be conducted in a blinded fashion at the time of publication of the interim clinical study report. In such scenarios the disclosure of some of the patient level data may lead to the premature unblinding of the study with a potential negative impact on the reliability of the final study results. When such cases are identified the applicants/MAHs may propose additional temporary redactions to prevent the data from being unblinded. These proposals are subject to the Agency's agreement. The implementation of additional redactions to protect from study from unmasking/unblinding should be explained in the deviation section of the Anonymisation Report.

The redaction boxes should display as white overlay text the acronym BLD on a black background to easily differentiate them from the redactions intended to protect personal data and commercially confidential information. Once the study is unblinded, the entire clinical data publication package without the previously applied blinding redactions should be resubmitted to the Agency for republication.

Chapter 4

External guidance on the identification and redaction of commercially confidential information in clinical reports submitted to EMA for the purpose of publication in accordance with EMA Policy 0070

4.1. Introduction

The guidance provided in this chapter has been developed as a reference document for applicants/MAH to identify and prepare their justifications of commercially confidential information (CCI) in documents that fall under the scope of Policy 0070.

Generally, the majority of the clinical information contained in clinical reports which fall under the scope of Policy 0070 should not be considered CCI.

However, EMA acknowledges that in limited circumstances clinical reports may contain CCI, and could, therefore, be subject to redaction prior to publication. Whenever redaction of CCI is proposed by the applicant/MAH, consultation with the third party in question will be undertaken. The justification for the redaction of CCI will be taken into consideration by EMA in order to assess whether the definition of CCI applies.

The ultimate goals of this chapter (guidance) are the following:

- To ensure a common understanding of what may potentially be considered CCI within clinical reports.
- To increase consistency in the proposed and accepted redactions across the range of clinical reports relating to various human medicinal products and regulatory procedures falling under Policy 0070.
- To ensure a good quality of the justifications for the proposed redactions, hereby reducing the administrative burden for all parties involved in the preparation and publication of the documents falling under Policy 0070.

It is anticipated that the preparation and publication of the documents covered by Policy 0070 will raise some practical questions, such as on how to apply the aforementioned redaction principles, and on the presentation and justification of the proposed redactions.

This guidance will enable the public to obtain a better understanding of the level and nature of redactions that are typically accepted within the published documents as well as a comprehensive overview on how the redaction of CCI is handled within the context of Policy 0070. The guidance focuses on:

- How to identify and highlight in the clinical report's pieces of text (proposed redactions) that may potentially qualify as CCI.
- The minimum level of detail expected in the justification that will allow EMA to perform an adequate and informed evaluation of the proposed redactions.
- Establishing a better-defined approach of the identification of CCI when applying the redaction principles laid out in policy 0070.

4.2. Existing guidance documents

While Policy 0070 applies without prejudice to EMA's activities conducted in accordance with Regulation (EC) No 1049/2001, EMA strives to ensure consistency between the approach for the redaction of documents published in accordance with Policy 0070 and similar documents released in response to requests for access to documents in accordance with Regulation (EC) No 1049/2001. This document should therefore be read in conjunction with the following policies and guidance documents which have been released in the past and provide relevant background:

- European Medicines Agency policy on publication of clinical data for medicinal products for human use (Policy 0070) Policy - Publication and access to clinical data (2019 revision).
- European Medicines Agency policy on access to documents (related to medicinal products for human and veterinary use) (Policy 0043) EMA policy on access to documents.
- HMA/EMA guidance document on the identification of commercially confidential information and personal data within the structure of the marketing authorisation application - release of information after the granting of a marketing authorisation HMA/EMA guidance document.

Over the past few years, EMA has worked in partnership with National Competent Authorities in establishing guidance which has contributed to a harmonised approach for access to documents across EU Member States.

4.3. Points to be taken into account for the preparation of the redaction proposal version of a clinical report

In view of the lack of a legal definition and for the purpose of this guidance, CCI shall mean any information contained in the clinical reports submitted to EMA by the applicant/MAH which is not in the public domain or publicly available, and where disclosure may undermine the legitimate economic interest of the applicant/MAH.

Prior to proposing any redactions, the applicant/MAH should be aware of the level of information already available in the public domain concerning their product's development (e.g. study design and results), scientific knowledge and advancements within the relevant (for the particular product) therapeutic area(s). Such preparatory work by the applicant/MAH is essential and will enable an expedited consultation process, thereby reducing the number of instances in which EMA will have to reject proposed redactions because the information is already in the public domain.

4.3.1. How to read and apply the redaction principles laid out in Policy 0070

EMA has identified in the HMA/EMA guidance document certain types of information that may potentially be considered CCI. These principles should not be perceived by the applicant/MAH as an open and unconditional invitation to propose, on a regular basis, the redaction of information falling within the types of information described in the aforementioned document. In other words, the applicant/MAH should not consider by default such types of information as being CCI. The redaction proposals based on grounds of CCI must be backed up by the applicant/MAH with a specific and clear justification which is subject to EMA's review.

If the applicant/MAH identifies a piece of information such as a word or figure, part of a sentence, part of a paragraph that they wish to include amongst the proposed redactions, the applicant/MAH has to ensure that the information in question does not fall under any of the data elements and types of information described in Section 4.3.2 of this guidance document.

Moreover, the applicant/MAH should ensure that a specific and relevant justification is included in the justification table corresponding to the piece of information that is proposed for redaction.

The applicant/MAH is advised to limit the extent of the proposed redactions to the word(s), figure, and pieces of text that, in their view, can be considered CCI. The applicant/MAH is discouraged from proposing the redaction of entire pages, sub-sections of a report or full tables, as in general, this information is not considered as CCI.

In order to achieve a high level of consistency in the redaction of CCI in the final redacted documents, EMA has grouped the types of information that it does not consider CCI. Should the information proposed to be redacted be in the public domain or bear no innovative features, EMA will not accept its redaction. In addition, if the applicant/MAH fails to provide sufficient and relevant justification, the proposed redactions will be rejected. Finally, section 4.3.2 describes some examples of the type of information which will not be accepted to be redacted as CCI. These examples reflect the most common redactions proposed by applicants/MAHs which are usually rejected by EMA in the framework of Access to Documents in accordance with Regulation (EC) No 1049/2001. The information covered by the above examples pertains to quality, non-clinical and clinical data which, in EMA's view, is necessary for the understanding of the rest of the clinical report, and therefore its disclosure is in the public interest. EMA foresees the use of 5 rejection codes that would mirror the above considerations. At the end of the redaction consultation process, these codes will be included in the justification table, reflecting EMA's final position.

4.3.1.1. Information that EMA does not consider CCI

Information that is already in the public domain or publicly available – Rejection code 01

CCI - Rejection 01 – Information already available in the public domain or publicly available

This code reads as follows:

> "*The information proposed to be redacted is already available in the public domain.*
>
> *In addition, EMA considers that it has not been demonstrated how the disclosure of this publicly available information would undermine your economic interest or competitive position.*
>
> *EMA therefore adopts the position that the information proposed to be redacted does not constitute commercially confidential information and it is not accepted by EMA as a valid redaction proposal.* "

EMA recommends that the applicant/MAH compiles a list of the most common websites/locations where information regarding their own medicinal product is usually made available. Applicants/MAHs should create and maintain their own specific list detailing the level of public information concerning their product(s). Based on EMA experience gained through handling Access to Documents Requests, EMA suggests that the following sources of information be included in the list (as a minimum):

- Applicants'/MAHs' own web-site(s).
- EMA web-site (product EPAR, scientific guidelines).
- Clinical trials registries (such as EU Clinical Trials Register, ClinicalTrials.gov).
- Web-sites of other regulatory authorities within the EU and outside the EU (such as FDA, PMDA, TGA, Health Canada) especially when the product (or another product containing the same active substance) is approved in those specific jurisdictions.
- Scientific literature and articles (such as Textbooks, PubMed, Medline).

The information sources suggested above by EMA are not intended to constitute an exhaustive list, but rather to serve as a starting point for the applicant/MAH in the creation of their own (more exhaustive, customised) list. The above-mentioned examples should be considered as the minimum number of information sources to be scrutinised by the applicant/MAH in order to reach a basic level of awareness on publicly available information related to the product concerned.

4.3.1.2. Information that does not bear any innovative features – Rejection code 02

CCI - Rejection 02 – Common knowledge

This code reads as follows:

> "*The information proposed to be redacted reflects approaches or decisions that were/are based on widely known practices/regulatory and scientific information.*
>
> *In addition, EMA considers that its innovative features have not been pointed out and it has not been demonstrated how its disclosure would undermine your economic interest or competitive position.*
>
> *EMA therefore adopts the position that the information proposed to be redacted does not constitute commercially confidential information and it is not accepted by EMA as a valid redaction proposal.* "

Information which has already been revealed to some extent, can be inferred from information available in the public domain, or has the content of textbooks or scientific guidelines as its scientific backbone, should not be included in the proposed redactions.

The fact that certain pieces of information are not in the public domain as such, (word for word) does not necessarily mean that they should be considered by default as CCI. The applicant/MAH is expected to duly justify why the piece of information in question should be considered CCI by EMA.

In many instances, particular pieces of text contained in clinical reports describe how the applicant/MAH complied with regulatory and scientific guidelines and how they applied the scientific knowledge available at that time to their own development programme. In essence, these pieces of text do not reveal any novel elements (of any regulatory or scientific nature) as the approach described in the text is in line with the content of publicly available documents such as:

- Scientific literature and articles (Textbooks, PubMed, Medline).
- Scientific and regulatory guidelines and guidance documents.
- Treatment/clinical practice/disease management guidelines.

4.3.1.3. Additional information the disclosure of which would be in the public interest – Rejection code 03

CCI - Rejection 03 – Disclosure due to public interest

This code reads as follows:

> "*The information proposed to be redacted is relevant for the understanding of:*
>
> - *the conduct of the clinical studies;*
> - *the reliability and validity of the data/research findings (data submitted for evaluation);*
> - *the safety and efficacy profile of the product;*
> - *the reasoning underpinning the company claims and the opinion adopted by the CHMP and the subsequent decision of the European Commission, if applicable.*
>
> *EMA therefore adopts the position that there is a genuine public interest in the disclosure of this information and consequently it should be released."*

4.3.1.4. Information lacking sufficient or relevant justification – Rejection code 04 and 05

CCI – Rejection 04 – Insufficient justification

This code reads as follows:

> *"EMA has concluded that the justification is not satisfactory as it does not clearly demonstrate how the disclosure of this particular information would undermine the economic interest or competitive position of your company."*

Whenever the justification provided by the applicant/MAH does not correspond to/match the (type of) information proposed for redaction, i.e. is not relevant to the information proposed to be redacted, the following rejection code will be used in the justification table:

The justification wording has to refer clearly to the information proposed to be redacted. It has to highlight the innovative features of the information in the context of the common knowledge within the specific scientific area. It has to indicate explicitly to which on-going development programme the proposed redaction relates. It also has to explain how the disclosure of the information concerned would undermine the applicant's/MAH's legitimate economic interest. If EMA considers that the level of justification is not sufficiently detailed, additional clarifications will be requested on an *ad-hoc* basis, whether formally or informally, e.g. via a telephone call. Failure to provide the requested clarifications within a reasonable time frame would render the available justification insufficient, as detailed below.

Whenever EMA considers that the level of justification provided by the applicant/MAH is not sufficiently specific or too vague, the following rejection code will be used in the justification table:

CCI - Rejection 05 – Irrelevant justification

This code reads as follows:

> "*EMA considers that the justification provided is not related to the information proposed to be redacted. Therefore, in the absence of an adequate justification EMA is unable to recognise how the disclosure of this particular information would undermine your economic interest or competitive position.*
>
> *EMA therefore adopts the position that the information proposed to be redacted does not constitute commercially confidential information and that is not accepted by EMA as a valid redaction proposal.* "

The following section of the guidance presents some examples of justifications that are considered by EMA to be insufficient.

4.3.2. Examples of elements not considered CCI

It is EMA's view that some data elements should not be redacted from clinical reports due to the fact that they are relevant for the understanding of the documents published in accordance with Policy 0070. The list is not intended to be exhaustive but details the most frequent data elements, considered CCI by applicants/MAHs, based on EMA's practice, and which are rejected by EMA.

The vast majority of information contained in clinical reports is of a clinical nature. However, these clinical reports may also contain information of a quality, non-clinical and general or administrative nature, some of which may potentially be considered CCI. Therefore, EMA has grouped the elements which are not considered CCI into four categories as follows:

General or administrative information

- Unit measurements, in such cases only the actual value may be considered CCI. [e.g.]2.5mL/kg → [redacted] mL/kg.
- Study identification number(s) (e.g. EudraCT, ClinicalTrials.gov Identifier (NCT…), sponsor's internal study number).
- Names and addresses of investigator sites and the names of the principal investigators at each study site (unless it is mentioned in the context of individual patient data/case narratives and is deemed to constitute personal data – see "External guidance on the anonymisation of clinical reports for the purpose of publication in accordance with EMA policy 0070").
- Names of the countries where the clinical study is/was conducted (unless it is mentioned in the context of individual patient data/case narratives and is deemed to constitute personal data – see "External guidance on the anonymisation of clinical reports for the purpose of publication in accordance with EMA policy 0070").
- Number (how many) of study sites/research facilities were involved in the research.
- Name of the applicant's/MAH's own research facility(ies) where clinical studies were conducted (e.g. phase I studies).
- Name of the trial sponsor or the legal entity (CRO) that acted as the clinical trial (CT) applicant on behalf of the sponsor.
- Names of all CROs and vendors involved in trial-related duties and functions (e.g. central laboratories, IVRS provider, image reading centres, conduct of assays).

Quality-related information

- Structural formula of active metabolite(s) and metabolic pathway(s).
- Lot/batch numbers of the investigational products understood as either test product, active comparator or placebo (excluding manufacturing site(s) IDs).
- Excipient names which usually constitute publicly available information detailed in SmPCs.
- Function of excipients as such information is widely available in the public domain.
- Excipient batch numbers.
- Even if a method of measurement is selected from several available methods, the name of the method or the combination of methods and their general description is not CCI.
- High level safety-related information such as a virus inactivation process, ultrafiltration (removal of pyrogen), and the name of a purification process or the operation of a specific material.
- The name of a cell line or strain with genetic recombination, when it is in commercial use or already published (e.g. CHO cell, *E. Coli* K-12).
- Standard storage and shipping conditions of blood or tissue samples such as storage temperature or duration, which are described in related scientific guidelines (e.g. bioanalytical methods).
- Temperature, humidity parameters, and storage duration as applied in stability tests.

Non-Clinical-related information

- Information concerning a generally-used/well-known immunohistochemistry method (e.g. ELISA/LC-MS).
- Drug concentration measurements including results.
- The quantification range (lower and upper quantification limits) of pharmacokinetic and pharmacology tests/methods.
- The name and high level description of test methods should not be redacted where a test is conducted based on a standard dissolution test/method referred to in scientific guidelines.
- Information on radio-labelled molecules including information on the tagging site (unless it constitutes a novelty feature of the method developed by a company, as its disclosure would undermine the applicant's/MAH's legitimate economic interest).
- Information on scientific advice received from any Regulatory Agency during the development of the product related to the approved indication. It includes but it is not limited to information on the design and conduct of completed studies for which the results were submitted within the marketing authorisation application, the timing of requesting/obtaining the scientific advice and the names of the Agencies that issued those scientific advice.

Clinical-related information

- Primary and secondary endpoints (including biomarkers and exploratory endpoints).
- The justification of planned sample size.
- Protocol and protocol amendments (including and not limited to: treatment arms, inclusion/exclusion criteria, allowed concomitant medication(s), reasons for withdrawal and reasons for protocol amendments).
- Statistical methods (including imputation methods used for missing data).
- Information on clinical data management (such as query resolution).
- Information on the purpose and outcome of audits and inspections carried out during the conduct of clinical trials, including the audit plans.
- Literature reviews, meta-analyses and pooled data analyses supporting certain study design elements or certain safety and efficacy claims.
- Bioanalytical methods: name of the methods and the general description together with the validation parameters.
- The fact that the formulation was changed during the development programme including the description of any relationships between the different formulations used in the various development programme phases, as well as the timing of such changes and the results of equivalence tests.
- Safety-related information such as adverse reactions (presented in various forms such as aggregated data or within case narratives) regardless of whether they are reflected in the approved product information or whether they were observed in clinical trials or reported after authorisation (unless certain elements/adverse reactions are deemed to constitute personal data –

see the "External guidance on the anonymisation of clinical reports for the purpose of publication in accordance with EMA policy 0070").

- Safety-related information/case narratives, even where the described case is related to "off label use" or reported from clinical studies conducted in other indications not yet applied for or approved.
- Plasma drug concentration values and pharmacokinetic and pharmacodynamic parameters.
- General information on PK/PD models, parameters and the results of the PK/PD model simulations, including NONMEM outputs.

Information on scientific advice received from any Regulatory Agency during the development of the product related to the approved indication. It includes but it is not limited to information on the design and conduct of completed studies for which the results were submitted within the marketing authorisation application, timing of requesting/obtaining the scientific advice and the names of the Agencies that issued those scientific advices.

4.4. How to prepare justifications in support of proposed redactions

4.4.1. The content of the justification table and its use

The purpose of the justification table is to enable targeted comments on the proposed CCI redactions for use by both EMA and the applicant/MAH. The justification table is essentially a living document and will be used as a communication tool throughout the redaction consultation process. It will contain the justifications from the applicant/MAH on the proposed CCI to redact and EMA's assessment. At the end of the redaction consultation process this table will be sent to the applicant/MAH as part of EMA's conclusion. The justification tables should contain justifications for all pieces of text considered CCI and proposed to be redacted. All the proposed redactions listed in the justification table should correspond to the text highlighted for redaction in the redaction proposal version of the corresponding clinical report. Should the applicants/MAHs highlight a piece of text proposed for redaction in the document, but fails to explain its redaction in the justification table, the proposal will be considered invalid and will be sent back for clarification. For further details on the redaction consultation process see the "External guidance on the procedural aspects related to the submission of clinical reports for the purpose of publication in accordance with EMA policy 0070".

4.4.2. Completing the justification table

For the Redaction Proposal Version of each of the clinical reports in which CCI redactions are proposed, applicants/MAHs must complete a separate justification table in word format. Should there be no CCI identified in the document, a separate justification table is not required to be submitted. In such cases EMA will understand that there are no proposed CCI redactions and therefore will not check the document. Consequently, the corresponding Final Redacted Version will be published in the CDP portal as provided by the applicant/MAH. Accordingly, the applicant/MAH is expected to indicate clearly which justification table corresponds to which clinical report. In addition, the justification tables should be individually named so that the electronic name of each table matches the name of the corresponding clinical report.

Please see a sample justification table below (Figure 1) and all templates can be downloaded from EMA corporate website and found in the following link in the 'Support for industry on clinical data publication' page.

As a general principle, EMA expects that each of the justification tables corresponds to one submitted file. For example, if during the regulatory procedure a clinical overview addendum is submitted in addition to the initial clinical overview, EMA expects the applicant/MAH to prepare two separate justification tables since both documents are subject to publication.

For CSRs in Module 5, the applicant/MAH should submit the justification tables taking into consideration the following principle:

- If the CSR and the appendices are submitted for publication purposes as **one standalone file**, then **one justification table** is expected to be prepared. This justification table will have separate subheadings for each of the parts of the document (body, 16.1.1, 16.1.2, 16.1.9).
- If the CSR and the appendices are submitted for publication purposes as **separate files**, then **four justification tables** are expected to be submitted: one for each of the files, e.g. body, 16.1.1, 16.1.2, 16.1.9.

Figure.1 Sample Justification table for CCI redactions

Justification Table: Invented Product name (INN) – procedure number

Applicant/MAH Consultation on <**Module 5.3.1** (Reports of Biopharmaceutical Studies), **Module 5.3.2** (Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials), **Module 5.3.3** (Reports of human pharmacokinetic (PK) studies), **Module 5.3.4** (Reports of human pharmacodynamic (PD) studies), **Module 5.3.5** (Reports of efficacy and safety studies), **Module 2.5** (Clinical Overview), **Module 2.7.1** (Summary of Biopharmaceutical Studies and Associated Analytical Methods), **Module 2.7.2** (Summary of Clinical Pharmacology Studies), **Module 2.7.3** (Summary of Clinical Efficacy), **Module 2.7.4** (Summary of Clinical Safety) - <Name of the document as per naming convention><Name of the Applicant consulted>

By submitting this justification table, you confirm that you have checked that the information you wish to redact is NOT in the public domain. Please ensure that the proposed redactions are in line with Annex 3 of POLICY/0070 and the Guidance on identification and redaction of commercially confidential information in clinical reports submitted to the European Medicines Agency for the purpose of publication.

Page number(s)	Title of Section(s)	Text proposed for redaction by the Applicant/MAH	Applicant/MAH to provide justification of CCI (Please explain how the release of this information will damage your company's commercial interest or competitive position)	Agency Assessment of the proposed redaction: Rejected/ Partially Accepted/ Accepted	Agency's rationale/redaction code

The applicant/MAH is not expected to propose information to be redacted that is already available in the public domain. Therefore, when completing the justification table, the applicant/MAH should confirm that all the necessary searches have been performed and the information proposed to be redacted as CCI is not in the public domain or publicly available, by ticking/checking the box at the top of the justification table. More details can be found in section 4.3.2 of this chapter on what EMA does not consider to be CCI.

The individual columns should contain the following information:

Column 1 (Page number(s)):

In column 1 the applicant/MAH should indicate the page number of the relevant clinical report, where the information that the applicant/MAH proposes to redact is located. If exactly the same information can be found throughout the document and the company has the same justification for the redaction of this information, EMA would advise the company to indicate all the page numbers in one row, instead of filling in a new line for each page.

Column 2 (Title of Section(s)):

In column 2, EMA expects the applicant/MAH to indicate the appropriate section of the document where the proposed redaction can be found. If exactly the same information can be found throughout the document and the company has the same justification for the redaction of this information, EMA would advise the company to indicate all relevant sections in one row, instead of filling in a new line for each page and section.

Column 3: (Text proposed for redaction by the applicant/MAH):

This column should include the exact proposed CCI redactions verbatim (to the extent that is feasible) from the clinical report. In case entire tables and figures are among the proposed redactions EMA would advise the applicants/MAHs to clearly identify in this column the table/figure number and its title. If for practical reasons the proposed redactions cannot be reflected verbatim in this column this should be pointed out in an understandable manner. Regardless of whether the proposed redactions are reflected verbatim in this column, the applicants/MAHs are reminded that in all cases these proposed redactions should be highlighted and easily identifiable in the corresponding clinical report.

Column 4 (Justification of CCI):

In column 4 the applicant/MAH should describe in detail the reasons why it considers the information proposed to be redacted to be commercially confidential.

For example, if the applicant/MAH has proposed information for redaction on 'bioassays and analytical methods' it is not sufficient to say that this section includes information about specifications on company assays and immunogenicity assays. Instead, details of which assay(s), and more importantly which part of the assay(s), the company considers CCI must be specified.

Another example is when the applicant/MAH proposes to redact information related to a future or an ongoing development programme for a new indication. In column 4 the applicant/MAH has to give details of this ongoing development programme and explain how it is related to the text proposed for redaction. From this explanation it should be clear to EMA which part of the text proposed for redaction is directly relevant and what the link is/how that particular piece of information would give insight to/inform the reader about a possible new indication.

In this column, EMA expects to see clear explanations as to how the release of the specific information proposed for redaction will damage the company's legitimate commercial interest. It is important to note that simply declaring that the information is considered CCI by a company because upon release it will damage their legitimate commercial interest is not sufficiently specific for EMA to reach an informed conclusion. Therefore, such unspecific, vague justifications will be rejected by EMA.

Finally, should any of the clinical reports contain data (results) pertaining to indications not applied for or not evaluated yet, it should be clearly explained in column 4. The applicants/MAHs are expected to justify every element proposed to be redacted. A justification based on the fact that the applicant/MAH has not yet applied for that particular indication would be deemed by EMA as insufficient. The applicant/MAH has to bear in mind that information related to future development plans is very likely to be available on their own web-sites and information related to on-going clinical trials is very likely to be available on clinical trials registries.

Columns 5 and 6 (EMA's review):

The last two columns will capture the conclusion of EMA's review and the rationale behind it. To the extent that the information proposed to be redacted falls within the scope of the information described in this guidance document (see section 4.3.2), EMA will include under the EMA rationale column the corresponding CCI codes (**CCI - Rejection 01 – Information already available in the public**

domain or publicly available, CCI - Rejection 02 – Common knowledge, **CCI - Rejection 03 – Disclosure due to public interest, CCI - Rejection 04 – Insufficient justification and CCI - Rejection 05 – Irrelevant justification.**)

The justification tables containing the outcome of EMA's review will be sent to the applicant/MAH once EMA has finalised the assessment and reached its conclusion.

Chapter 5

Annexes

5.1. Redaction tool application letter for SMEs

SME Request for Redaction Tool License

European Medicines Agency

Domenico Scarlattilaan 6

1083 HS Amsterdam

The Netherlands

Dear ,

RE:Product Invented Name; INN, EMEA/X/X/XXXXXX/XXXX (PROCEDURE NUMBER)

Request for Redaction Tool License ADOBE

[Company name] with EMA-SME NUMBER XXXXXX is writing to request an Adobe license for the purpose of creating the Redaction Proposal Version and Final Redacted Version of the clinical reports for the above-mentioned procedure.

The Redaction Proposal version and Final Redacted Version of the clinical reports will be submitted in line with the European Medicines Agency's policy on the publication of clinical data for medicinal products for human use, Policy 0070. It is understood that SME status will be checked by EMA at time of issuing the licence, with disclaimers to access rights to be removed if the SME status has expired at that time or in cases of merger/out licensing.

In addition, [Company name] undertakes not to transfer, redistribute, sublicense or otherwise make available the redaction tool license, as provided to [Company name] by EMA, to any third party, including to other EMA designated SMEs. [Company name] also confirms that by accepting a redaction tool license [Company name] also accepts the licence terms of use related to the redaction tool and all related liability for noncompliance or breach thereof. [Company name] acknowledges and agrees that EMA will not be liable or responsible in any way for any non-compliance with or breaches of these terms on behalf of [Company name].

Clinical Data Publication Policy:

Redaction Tool Application – SME

Please complete this form in capitals

Company name: _____

EMA-SME Number:_____ Expiry:_____

Product Invented Name: _____

INN: _____

EMA number: EMEA/H/C/_____

Contact person for interaction purpose with EMA
Name: ____

Position within the SME: ____

Address: ____

Post Code: | | | | | | | | | |

Country: ____

Telephone
Country Code: _____________ Area Code: _______________ Number:___________

Email Address: | | | | | | | | | | | | | | |

| | | | | | | | | | | | | | | | | | |

Email address specifically for software licence purposes. This email address will be used for all subscription purposes with the supporting company. This email address will be your company's identification reference with the supplier.

Identification

E-mail Address: | | | | | | | | | | | | | | |

| | | | | | | | | | | | | | | | | |

Name (in Capitals): ____________________________

Signed _____________________________________ Date:______________

5.2. Template cover letter text: "Redaction Proposal Document" package - For applications for which a CHMP opinion has been adopted

European Medicines Agency

Domenico Scarlatilaan 6

1083 HS Amsterdam

The Netherlands

XX XXXX XXXX

Dear ,

RE: EMEA/X/X/XXXXXX/XXXX

[Product INN, Company Name]

Redaction Proposal document package

Please find enclosed the "Redaction Proposal Document" package submitted at procedural Day xxx of the initial marketing authorisation application/line extension application/extension of indication application (delete as appropriate) for [product]. The "Redaction Proposal Document" package is submitted in line with the European Medicines Agency policy on the publication of clinical data for medicinal products for human use, Policy 0070. Comprising the "Redaction Proposal Document" package submitted to EMA are the following, with their respective locations in the eCTD:

- Cover letter - The agreed List of expected documents (LED) should be submitted as an attachment to the cover letter. This list should include all the documents falling in the scope for publication and all the information on the agreed out of scope sections if any. (Module 1.0)
- Clinical Overviews (Module 2.5)
- Clinical Summaries (Module 2.7, Sections 2.7.1 – 2.7.4)
- Clinical Study Reports – body and appendices 16.1.1, 16.1.2 and 16.1.9 (Module 5.0, Section 5.3)
- Justification table for each document (uploaded as a 'working document')
- Anonymisation Report (Module 1.9)
- eCTD tracking table
- Submission checklist (Module 1.0)

CCI – OPTIONAL TEXT AS APPLICABLE

<[Company name] points out that no commercial confidential information has been identified in the entire "Redaction Proposal Document'' package and, therefore, justification tables are not submitted.>

<[Company name] points out that commercially confidential information has only been identified in *some documents for which* [*please insert the number of justification tables*] justification tables were included in the "Redaction Proposal Document'' package and, confirms that in the documents for which no corresponding justification table was submitted no CCI has been identified and therefore no CCI redactions are proposed.>

OUT OF SCOPE SECTIONS- OPTOINAL TEXT AS APPLICABLE

<[Company name] points out that no sections containing information considered as out of scope of phase 1 of Policy 0070 have been identified in the entire ''Redaction Proposal Document'' package.>

<[Company name] points out that certain information is proposed to be removed as out of scope of Policy 0070. This information can be found in the List of Expected Documents (LED) attached to this cover letter.> [Optional text as applicable]

ANONYMISATION REPORT

[Company name] declares the anonymisation report has been prepared in accordance with the guidance made available by EMA and applied consistently in the preparation of the documents comprising the Redaction Proposal Version.

CLINICAL STUDIES

[In case some or all of the submitted studies have already been published under Policy 0070, the following text should be used, as applicable. In such cases, the Redaction Proposal version of the documents should be submitted as per the standard procedure described in section 2.3. Process for the submission, review and publication of clinical reports

<[Company name] points out that the following studies have already been published under Policy 0070 with procedure [Insert relevant procedure number]:

- Study title/number
- Study title/number

For those studies, [Company name] declares that the same level of anonymisation has been applied between the previous and the current procedure. [Optional text as applicable]

For those studies, [Company name] declares that a different level of anonymisation has been applied between the previous and the current procedure for the following reason(s): [Optional text as applicable]

COMPANY DECLARATIONS

In addition, [Company name] hereby declares that the documents submitted ("Original Submission") in accordance with European Medicines Agency's ("EMA") Policy on publication of clinical data for medicinal products for human use ("Policy 0070") are true and complete copies of the final version of [MODULES XX, XX, XX] submitted by the applicant/MAH in support of [DESCRIPTION OF THE RELEVANT REGULATORY APPLICATION] ("Clinical Reports Documentation") with the exception of (i)

omission of documents, or elements thereof, falling out of the scope of Policy 0070; and (ii) proposed redactions of commercially confidential information and any amendment aimed at ensuring anonymisation of the Clinical Reports Documentation. The proposed redactions of commercially confidential information and amendments pursuing anonymisation shall fully reflect the requirements of Policy 0070.

Finally, [FULL NAME AND POSITION] declares that [HE/SHE] is duly authorized to take this action and make this binding undertaking on behalf of [Company name].

Yours sincerely,

5.3. Template cover letter text: "Redaction Proposal Document" package -In case of withdrawal of applications

European Medicines Agency

Domenico Scarlatilaan 6

1083 HS Amsterdam

The Netherlands

XX XXXX XXXX

Dear ,

RE: EMEA/X/X/XXXXXX/XXXX

[Product INN, Company Name]

Redaction Proposal document package

Further to [Company name]'s written notification on [insert date] of the withdrawal of the initial marketing authorisation application/line extension application/extension of indication application (delete as appropriate) for [product INN], please find enclosed the "Redaction Proposal Document" package. The "Redaction Proposal Document" package is submitted in line with the European Medicines Agency policy on the publication of clinical data for medicinal products for human use, Policy 0070. Comprising the "Redaction Proposal Document" package submitted to EMA are the following, with their respective locations in the eCTD:

- Cover letter – The agreed List of expected documents (LED) should be submitted as an attachment to the cover letter. This list should include all the documents falling in the scope for publication and all the information on the agreed out of scope sections if any (Module 1.0)
- Clinical Overviews (Module 2.5)
- Clinical Summaries (Module 2.7, Sections 2.7.1 – 2.7.4)
- Clinical Study Reports – body and appendices 16.1.1, 16.1.2 and 16.1.9 (Module 5.0, Section 5.3)
- Justification table for each document (uploaded as a 'working document')
- Anonymisation Report (Module 1.9)
- eCTD tracking table
- Submission checklist (Module 1.0)

CCI -OPTIONAL TEXT AS APPLICABLE

<[Company name] points out that no commercial confidential information has been identified in the entire "Redaction Proposal Document'' package and therefore, justification tables are not submitted.>

<[Company name] points out that commercially confidential information has only been identified in *some documents for which* [*please insert the number of justification tables*] justification tables were included in the "Redaction Proposal Document'' package and, confirms that in the documents for which no corresponding justification table was submitted no CCI has been identified and therefore no CCI redactions are proposed.>

OUT OF SCOPE SECTIONS- OPTIONAL TEXT AS APPLICABLE

<[Company name] points out that no sections containing information considered as out of scope of phase 1 of Policy 0070 have been identified in the entire ''Redaction Proposal Document'' package.>

<[Company name] points out that certain information is proposed to be removed as out of scope of Policy 0070. This information can be found in the List of Expected Documents (LED) attached to this cover letter.>

ANOYMISATION REPORT

[Company name] declares the anonymisation report has been prepared in accordance with the guidance made available by EMA and applied consistently in the preparation of the documents comprising the Redaction Proposal Version.

CLINICAL STUDIES

[In case some or all of the submitted studies have already been published under Policy 0070, the following text should be used, as applicable. In such cases, the Redaction Proposal version of the documents should be submitted as per the standard procedure described in section 2.3. Process for the submission, review and publication of clinical reports"]

<[Company name] points out that the following studies have already been published under Policy 0070 with procedure [Insert relevant procedure number]:

- Study title/number
- Study title/number

For those studies, [Company name] declares that the same level of anonymisation has been applied between the previous and the current procedure. [Optional text as applicable]

For those studies, [Company name] declares that a different level of anonymisation has been applied between the previous and the current procedure for the following reason(s): [Optional text as applicable]

COMPANY DECLARATIONS

In addition, [Company name] hereby declares that the documents submitted ("Original Submission") in accordance with European Medicines Agency's ("EMA") Policy on publication of clinical data for medicinal products for human use ("Policy 0070") are true and complete copies of the final version of [MODULES XX, XX, XX] submitted by the applicant/MAH in support of [DESCRIPTION OF THE RELEVANT REGULATORY APPLICATION] ("Clinical Reports Documentation") with the exception of (i) omission of documents, or elements thereof, falling out of the scope of Policy 0070; and (ii) proposed

redactions of commercially confidential information and any amendment aimed at ensuring anonymisation of the Clinical Reports Documentation. The proposed redactions of commercially confidential information and amendments pursuing anonymisation shall fully reflect the requirements of Policy 0070.

Finally, [FULL NAME AND POSITION] declares that [HE/SHE] is duly authorized to take this action and make this binding undertaking on behalf of [Company name].

Yours sincerely,

5.4. Template cover letter text: "Final Redacted Document" package - For all applications covered by the policy, with the exception of duplicate applications

European Medicines Agency

Domenico Scarlatilaan 6

1083 HS Amsterdam

The Netherlands

XX XXXX XXXX

Dear ,

RE: EMEA/X/X/XXXXXX/XXXX

[Product INN, Company Name]

Final Redacted Document package

Further to the "Redaction Proposal Document" package submitted to EMA on XX XXXX XXXX and the written correspondence of XX XXXX XXXX confirming [company name]'s [partial/full] agreement with EMA's redaction conclusion of XX XXXX XXXX, please find enclosed the "Final Redacted Document" package for the [withdrawn]above mentioned procedure initial marketing authorisation application/line extension application/extension of indication application (delete as appropriate) for [product].

The "Final Redacted Document" package is submitted for the purpose of the European Medicines Agency policy on the publication of clinical data for medicinal products for human use, Policy 0070.

We hereby declare that that the clinical reports submitted for publication are the same as those submitted for scientific review, with the exception of anonymisations and redactions

In case of full agreement:

The "Final Redacted Document" package is submitted in line with the EMA redaction conclusion and to the extent these were agreed both by the Agency and [company name].

In case of partial agreement:

The "Final Redacted Document" package is submitted in line with the EMA redaction conclusion with the exception of those parts that are subject to interim relief proceedings.

[Company name] disagrees with the EMA's position concerning the rejection of the following redactions and these redactions were maintained in the "Final Redacted Document" package, contrary to EMA's redaction conclusion of XX XXXX XXXX:

- [The applicant/MAH will state which redactions (page, line) that were rejected in the EMA conclusion have been maintained in the Final Redaction version of the clinical reports to be published.]

The undisputed parts are in line with EMA's conclusion.

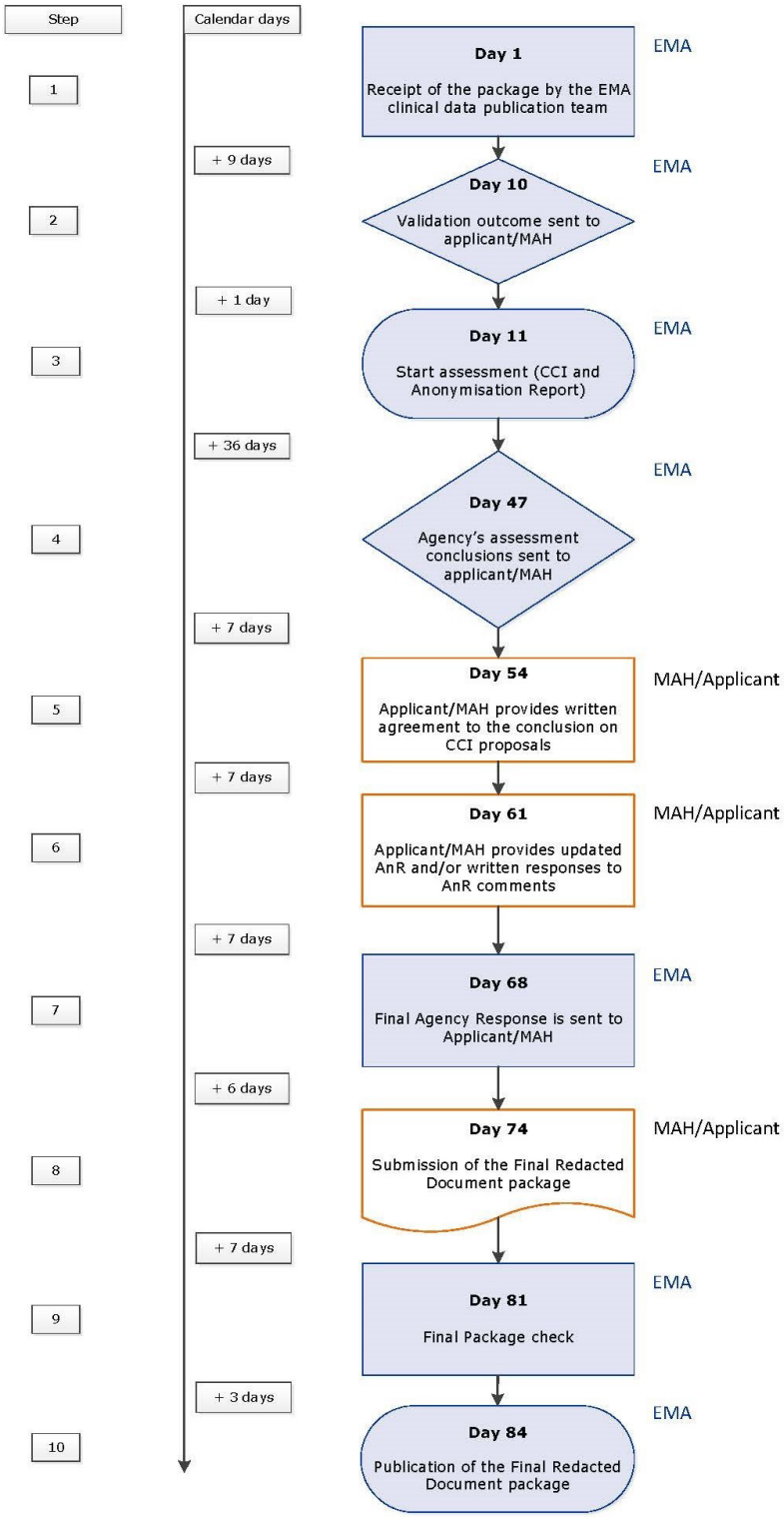
Comprising the "Final Redacted Document" package submitted to EMA are the following documents, with their respective locations in the eCTD:

- Cover letter [with reference to agreed list of documents (LED) is attached or indicate any changes/updates to agreed list of documents] The agreed List of expected documents (LED) should be submitted as an attachment to the cover letter. This list should include all the documents falling in the scope for publication and all the information on the agreed out of scope sections if any (Module 1.0)
- Clinical Overviews (Module 2.5)
- Clinical Summaries (Module 2.7, Sections 2.7.1 – 2.7.4)
- Clinical Study Reports – body and appendices 16.1.1, 16.1.2 and 16.1.9 (Module 5.0, Section 5.3)
- Anonymisation Report (Module 1.9)
- eCTD tracking table
- Submission Checklist (Module 1.0)

We look forward to the publication of the redacted clinical reports by EMA and to being notified by EMA of their publication.

Yours sincerely,

5.5. Workflow for the submission of clinical reports for publication



5.6. Sample of Justification table for CCI redactions

Justification Table: Invented Product name (INN) – procedure number

Applicant/MAH Consultation on <**Module 5.3.1** (Reports of Biopharmaceutical Studies), **Module 5.3.2** (Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials), **Module 5.3.3** (Reports of human pharmacokinetic (PK) studies), **Module 5.3.4** (Reports of human pharmacodynamic (PD) studies), **Module 5.3.5** (Reports of efficacy and safety studies), **Module 2.5** (Clinical Overview), **Module 2.7.1** (Summary of Biopharmaceutical Studies and Associated Analytical Methods), **Module 2.7.2** (Summary of Clinical Pharmacology Studies), **Module 2.7.3** (Summary of Clinical Efficacy), **Module 2.7.4** (Summary of Clinical Safety) - <Name of the document as per naming convention><Name of the Applicant consulted>

By submitting this justification table, you confirm that you have checked that the information you wish to redact is NOT in the public domain. Please ensure that the proposed redactions are in line with Annex 3 of POLICY/0070 and the Guidance on identification and redaction of commercially confidential information in clinical reports submitted to the European Medicines Agency for the purpose of publication.

Page number(s)	Title of Section(s)	Text proposed for redaction by the Applicant/MAH	Applicant/MAH to provide justification of CCI (Please explain how the release of this information will damage your company's commercial interest or competitive position)	Agency Assessment of the proposed redaction: Rejected/ Partially Accepted/ Accepted	Agency's rationale/redaction code

5.7. In and Out of scope of phase 1 of Policy 0070

- **Common Technical Document (CTD) structure**

CTD Module/ Section	Document	Scope	Explanation/Clarification
2.5 Clinical Overview			
2.5	Clinical Overview	In	All sections of the "**Clinical overview**" regardless whether they are submitted as separate standalone documents or all together in a single document are subject to publication. All documents included in CTD Module 2.5 such as "**Clinical overview supplement/amendment/appendix**" which were submitted during the evaluation procedure are subject to publication. Please note that only the **list of references** is subject to publication. If actual scientific papers and articles are included in CTD section 2.5.7 these documents are NOT subject to publication.
2.5.1	Product Development Rationale	In	
2.5.2	Overview of Biopharmaceutics	In	
2.5.3	Overview of Clinical Pharmacology	In	
2.5.4	Overview of Efficacy	In	
2.5.5	Overview of Safety	In	
2.5.6	Benefits and Risks Conclusions	In	
2.5.7	Literature References	In	

CTD Module/ Section	Document	Scope	Explanation/Clarification
2.5	Any other documents (not explicitly mentioned in ICH M4)	In	
2.7 Clinical Summary			
2.7.1 Summary of Biopharmaceutic Studies and Associated Analytical Methods			
2.7.1	Summary of Biopharmaceutic Studies and Associated Analytical Methods	In	All sections of the "**Summary of Biopharmaceutic Studies and Associated Analytical Methods**" regardless whether they are submitted as separate single documents or all together in a standalone document are subject to publication. All documents included in CTD section 2.7.1 such as "**Clinical summary supplement/amendment/appendix**"" which were submitted during the evaluation procedure are subject to publication.
2.7.1.1	Background and Overview	In	
2.7.1.2	Summary of Results of Individual Studies	In	
2.7.1.3	Comparison and Analyses of Results Across Studies	In	
2.7.1.4	Appendix	In	
2.7.1	Any other documents (not explicitly mentioned in ICH M4)	In	

2.7.2 Summary of Clinical Pharmacology Studies			
2.7.2	Summary of Clinical Pharmacology Studies	In	All sections of the "**Summary of Clinical Pharmacology Studies**" regardless whether they are submitted as separate standalone documents or all together in a single document are subject to publication. All documents included in CTD section 2.7.2 such as "**Clinical summary supplement/amendment/appendix**" which were submitted during the evaluation procedure are subject to publication.
2.7.2.1	Background and Overview	In	
2.7.2.2	Summary of Results of Individual Studies	In	
2.7.2.3	Comparison and Analyses of Results Across Studies	In	
2.7.2.4	Special Studies	In	
2.7.2.5	Appendix	In	
2.7.2	Any other documents (not explicitly mentioned in ICH M4)	In	
2.7.3 Summary of Clinical Efficacy			
2.7.3	Summary of Clinical Efficacy	In	All sections of the "**Summary of Clinical Efficacy**" regardless whether they are submitted as separate standalone documents or all together in a single document are subject to publication. All documents included in CTD section 2.7.3 such as "**Clinical summary supplement/amendment/appendix**" or **"Integrated Summary of Efficacy**
2.7.3.1	Background and Overview of Clinical Efficacy	In	
2.7.3.2	Summary of Results of Individual Studies	In	
2.7.3.3	Comparison and Analyses of Results Across Studies	In	

2.7.3.4	Analysis of Clinical Information Relevant to Dosing Recommendations	In	**(ISE)"** which were submitted during the evaluation procedure are subject to publication.
2.7.3.5	Persistence of Efficacy and/or Tolerance Effects	In	
2.7.3.6	Appendix	In	
2.7.3	Any other documents (not explicitly mentioned in ICH M4)	In	

2.7.4 Summary of Clinical Safety			
2.7.4	Summary of Clinical Safety	In	All sections of the "**Summary of Clinical Safety**" regardless whether they are submitted as separate standalone documents or all together in a single document are subject to publication. All additional documents included in CTD section 2.7.4 such as "**Clinical summary supplement/amendment/appendix**" or "**Integrated Summary of Safety (ISS)"** which were submitted during the evaluation procedure are subject to publication.
2.7.4.1	Exposure to the Drug	In	
2.7.4.2	Adverse Events	In	
2.7.4.3	Clinical Laboratory Evaluations	In	
2.7.4.4	Vital Signs, Physical Findings, and Other Observations Related to Safety	In	
2.7.4.5	Safety in Special Groups and Situations	In	
2.7.4.6	Post-marketing Data	In	
2.7.4.7	Appendix	In	
2.7.4	Any other documents (not explicitly mentioned in ICH M4)	In	
2.7.5 References			
2.7.5	(All) References	Out	These documents (the list of references or the literature references themselves) **are not clinical summaries** therefore are not subject to publication
2.7.6 Synopsis of Individual Studies			
2.7.6	(All) Synopsis of Individual Studies	Out	These documents **are not clinical summaries** therefore are not subject to publication
5 Clinical Study Reports			
5.1 Table of Contents of Module 5			

5.1	Table of Contents of Module 5	Out	This document **is not a clinical study report (CSR)** therefore is not subject to publication
5.2 Tabular Listing of All Clinical Studies			
5.2	Tabular Listing of All Clinical Studies	Out	This document **is not a clinical study report (CSR)** therefore is not subject to publication
5.3 Clinical Study Reports			
5.3.1 Reports of Biopharmaceutic Studies			
5.3.1.1 Bioavailability (BA) Study Reports			
5.3.1.1	(All) Bioavailability (BA) Study Reports	In	
5.3.1.2 Comparative BA and Bioequivalence (BE) Study Reports			
5.3.1.2	(All) Comparative BA and Bioequivalence (BE) Study Reports	In	
5.3.1.3 In vitro - In vivo Correlation Study Reports			
5.3.1.3	(All) In vitro - In vivo Correlation Study Reports	Out	These study reports contain information on predictive mathematical models describing the relationship between an in vitro property and a relevant in vivo response. These reports **are not expected to contain safety and efficacy results**. Therefore, EMA considers that these study reports are not subject to publication.
5.3.1.4 Reports of Bioanalytical and Analytical Methods for Human Studies			
5.3.1.4	(All) Reports of Bioanalytical and Analytical Methods for Human Studies	Out	These study reports contain information on the assays validation and analytical methods employed during the conduct of the clinical trials. These reports **are not expected to contain safety and efficacy results**. Therefore, EMA considers that these study reports are not subject to publication, regardless of their location within the Common Technical Document. However, references to, or summaries of, bioanalytical reports within an in-scope document (for instance, within Module 2.7.1.

			Summary of Biopharmaceutic Studies and Associated Analytical Methods) are subject to publication.
5.3.2 Reports of Studies Pertinent to Pharmacokinetics Using Human Biomaterials			
5.3.2.1 Plasma Protein Binding Study Reports			
5.3.2.1	(All) Plasma Protein Binding Study Reports	In	

5.3.2.2 Reports of Hepatic Metabolism and Drug Interaction Studies			
5.3.2.2	(All) Reports of Hepatic Metabolism and Drug Interaction Studies	In	
5.3.2.3 Reports of Studies Using Other Human Biomaterials			
5.3.2.3	(All) Reports of Studies Using Other Human Biomaterials	In	
5.3.3 Reports of Human Pharmacokinetic (PK) Studies			
5.3.3.1 Healthy Subject PK and Initial Tolerability Study Reports			
5.3.3.1	(All) Healthy Subject PK and Initial Tolerability Study Reports	In	
5.3.3.2 Patient PK and Initial Tolerability Study Reports			
5.3.3.2	(All) Patient PK and Initial Tolerability Study Reports	In	
5.3.3.3 Intrinsic Factor PK Study Reports			
5.3.3.3	(All) Intrinsic Factor PK Study Reports	In	
5.3.3.4 Extrinsic Factor PK Study Reports			
5.3.3.4	(All) Extrinsic Factor PK Study Reports	In	
5.3.3.5 Population PK Study Reports			

5.3.3.5	(All) Population PK Study Reports	In	The model and simulation report are in scope in their entirety including any available annexes. For example, the NONMEM outputs of the model(s) described in the report are also in scope. This includes output summaries and whole outputs of results.
5.3.4 Reports of Human Pharmacodynamic (PD) Studies			
5.3.4.1 Healthy Subject PD and PK/PD Study Reports			
5.3.4.1	(All) Healthy Subject PD and PK/PD Study Reports	In	
5.3.4.2 Patient PD and PK/PD Study Reports			
5.3.4.2	(All) Patient PD and PK/PD Study Reports	In	
5.3.5 Reports of Efficacy and Safety Studies			
5.3.5.1 Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication			
5.3.5.1	(All) Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication	In	
5.3.5.2 Study Reports of Uncontrolled Clinical Studies			
5.3.5.2	(All) Study Reports of Uncontrolled Clinical Studies	In	
5.3.5.3 Reports of Analyses of Data from More than One Study			
5.3.5.3	(All) Reports of Analyses of Data from More than One Study	In	All reports included in CTD section 5.3.5.3 including "**Integrated Summary of Safety (ISS)"** or **"Integrated Summary of Efficacy (ISE)"** which present the results of analyses of safety and efficacy data collected from more than one clinical study, and which were submitted during the evaluation procedure, are subject to publication. To be noted that for all reports presenting results of analyses of data from more than one study (e.g. meta-analyses and pooled analyses) the statistical plans are expected to be published. They are considered the equivalent of CSR section 16.1.9.
5.3.5.4 Other Study Reports			

5.3.5.4	(All) Other Study Reports	In	This CTD section may contain reports of **controlled or uncontrolled studies not related to the claimed indication or real-world evidence studies**. EMA would like to confirm that these reports are subject to publication. To the extent that for example only the safety findings reported in these documents were taken into account during the scientific review (e.g. included in the safety database) EMA foresees that the efficacy sections of the published reports would contain redactions. However, the applicants/MAHs are expected to justify these redactions and not to only provide as a justification that they have not yet applied for a particular indication. It is important to note that reports resulting from the evaluation of user comprehension of contents included in the Product Information (e.g. Label Comprehension Reports, Human Factors Study Reports) are also subject to publication.
5.3.6 Reports of Post-Marketing Experience			
5.3.6	(All) Reports of Post-Marketing Experience	Out	These reports (e.g. PSURs/PBERs) **are not Clinical Study Reports (CSRs)** therefore they are not subject to publication.
5.3.7 Case Report Forms and Individual Patient Listings			
5.3.7	(All) Case Report Forms and Individual Patient Listings	Out	These reports **are not Clinical Study Reports (CSRs)** therefore they are not subject to publication.
5.4 Literature References			
5.4	(All) Literature References	Out	These documents **are not clinical reports (understood as clinical overviews, clinical summaries or clinical study reports)** therefore are not subject to publication

- ## Clinical Study Report (CSR) structure

Clinical Study Report (CSR) components	Clinical Study Report (CSR) sections	Scope	Explanation/Clarification
A. CSR body			
	1. TITLE PAGE	In	If ICH E3 format is not followed for a particular CSR, the corresponding information/sections (1-15) and appendices (16.1.1, 16.1.2 and 16.1.9) will be subject to publication. To be noted that the same CCI, PPD and publication principles will apply to EU as well as non-EU studies in the context of Policy 0070.
	2. SYNOPSIS	In	
	3. TABLE OF CONTENTS FOR THE INDIVIDUAL CLINICAL STUDY REPORT	In	
	4. LIST OF ABBREVIATIONS AND DEFINITION OF TERMS	In	
	5. ETHICS	In	
	6. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE	In	
	7. INTRODUCTION	In	
	8. STUDY OBJECTIVES	In	
	9. INVESTIGATIONAL PLAN	In	
	10. STUDY PATIENTS	In	
	11. EFFICACY EVALUATION	In	
	12. SAFETY EVALUATION	In	
	13. DISCUSSION AND OVERALL CONCLUSIONS	In	
	14. TABLES, FIGURES AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT	In	
	14.3.1 Displays of Adverse Events	In	
	14.3.2 Listings of Deaths, Other Serious and Significant Adverse Events	In	

Clinical Study Report (CSR) components	Clinical Study Report (CSR) sections	Scope	Explanation/Clarification
14.3.3 Narratives of Deaths, Other Serious and Certain Other Significant Adverse Events		In	
14.3.4 Abnormal Laboratory Value Listing (Each Patient)		In	All sections of the body of the CSR (sections 1 to 15 as per ICH E3) are subject to publication. EMA notes that the CSRs may contain individual patient data listings within the body of the report. Individual patient data listings within the body of the report cannot be considered out of scope and should not be removed, with the exception of individual patient data listings of "Abnormal Laboratory Values" typically found in section 14.3.4. If ICH E3 format is not followed for a particular CSR, the individual patient data listings included in the corresponding section presenting "Abnormal Laboratory Values" may be considered out of scope and removed from the clinical study report. Nevertheless, individual patient data listings (other than abnormal laboratory value listings) presented in other sections of the body of the clinical study report (e.g. concerning PK and immunogenicity results, laboratory values, case narratives or protocol deviations) cannot be considered out of scope and should not be removed. They should instead be anonymised. This also applies to listings extracted from 16.2. Patient Data listings (and labelled as such) that have been repurposed as part of CSR section 14 as contemplated in the ICH E3 guidance. It is important to note that data presented as **aggregated** patient data listings within section 14.3.4 "Abnormal Laboratory Value Listing" should NOT be removed.

Clinical Study Report (CSR) components	Clinical Study Report (CSR) sections	Scope	Explanation/Clarification
			The pages/sections considered out of scope and therefore removed have to be replaced by a blank page containing the following overlay text: 1. title of the section removed; 2. statement that Individual Patient Abnormal Laboratory Value Listings are removed as out of scope of policy 0070, reading: "Page(s) removed- *Out of Scope of phase 1 of Policy 0070- Individual Patient Abnormal Laboratory Value Listings*".
15. REFERENCE LIST		In	
B. CSR Appendices			
16.1 STUDY INFORMATION			
16.1.1 Protocol and protocol amendments		In	The following CSR appendices ONLY are subject to publication: 16.1.1 Protocol and protocol amendments 16.1.2 Sample case report form (unique pages only) 16.1.9 Documentation of statistical methods If for a particular CSR the ICH E3 format is not followed, the corresponding information/sections (1-15) and appendices (16.1.1, 16.1.2, 16.1.9) will be subject to publication. Standalone study protocols or other CSR appendices submitted in the absence of a CSR are not subject to publication
16.1.2 Sample case report form (unique pages only)		In	

Clinical Study Report (CSR) components	Clinical Study Report (CSR) sections	Scope	Explanation/Clarification
16.1.3 List of IECs or IRBs (plus the name of the committee Chair if required by the regulatory authority) - Representative written information for patient and sample consent forms		Out	
16.1.4 List and description of investigators and other important participants in the study, including brief (1 page) CVs or equivalent summaries of training and experience relevant to the performance of the clinical study		Out	
16.1.5 Signatures of principal or coordinating investigator(s) or sponsor's responsible medical officer, depending on the regulatory authority's requirement		Out	
16.1.6 Listing of patients receiving test drug(s)/investigational product(s) from specific batches, where more than one batch was used		Out	
16.1.7 Randomisation scheme and codes (patient identification and treatment assigned)		Out	
16.1.8 Audit certificates (if available) (see Annex IVa and IVb of the guideline)		Out	
16.1.9 Documentation of statistical methods		In	Statistical Analysis Systems (SAS) shells, code scripts and outputs are also subject to publication
16.1.10 Documentation of inter-laboratory standardisation methods and quality assurance procedures if used		Out	
16.1.11 Publications based on the study		Out	
16.1.12 Important publications referenced in the report		Out	
16.2. PATIENT DATA LISTINGS			
All appendices located under **16.2. PATIENT DATA LISTINGS**		Out	

Clinical Study Report (CSR) components	Clinical Study Report (CSR) sections	Scope	Explanation/Clarification
16.3 CASE REPORT FORMS			
All appendices located under **16.3 CASE REPORT FORMS**		Out	
16.4. INDIVIDUAL PATIENT DATA LISTINGS (US ARCHIVAL LISTINGS)			
All appendices located under **16.4. INDIVIDUAL PATIENT DATA LISTINGS (US ARCHIVAL LISTINGS)**		Out	

Other reports included in the Common Technical Document (CTD)	Scope	Explanation/Clarification
1. Biomarker reports	In	Reports where the quantification of a specific biomarker is performed in samples obtained from study participants with the purpose of making inferences on the efficacy or safety of the investigational product are subject to publication
2. Patient Reported Outcomes (PROs) Evidence Dossier reports	In	These reports typically include information regarding the psychometric assessments used in the clinical trials and their analyses. Although the reports are subject to publication, certain sections included in the reports may be considered out of scope of scope of Policy 0070 (e.g. interview transcripts and/or filled questionnaires)
3. Reports resulting from analysis conducted on samples from participants enrolled in clinical studies (e.g. Pharmacogenomic/Genotyping reports, Virology reports, Micology reports)	In	
4. Safety Monitoring Committee Charters/Meeting Minutes	Out	
5. Unprocessed narrative-like reporting documents (e.g. CIOMS/SUSAR, MEDWATCH forms)	Out	

5.8. Checklist for "Redaction Proposal Document" and "Final Redacted Document" package

The checklist is to help applicants/MAHs when submitting clinical data to comply with Policy 0070 and are simply an aid to ensure that both the applicant/MAH and the Agency are able to identify validation non-compliance at an early stage.

Please note that the checklist is sent to the applicants/MAHs with the invitation letter and should be included in the submission.

Guidance for applicants/MAHs

The Agency strongly recommends that the checklist is used in advance of submitting the Redaction Proposal Document package or the Final Redacted Document package. You should be able to answer "Yes" to every item listed below unless a specific point is not applicable ("n/a") to the submission in question.

The checklist is published for transparency purposes and does not preclude that during the actual validation of the submitted package the Agency may identify other issues that could impact the validation outcome.

If the submitted package does not meet any part of this checklist, it may result in 'invalidation' and the entire eCTD package has to be resubmitted.

Submission checklist for: Redaction Proposal Document Package ☐
Final Redacted Document Package ☐

- To be annexed to the cover letter –

COVER LETTER CONTENT	YES	N/A
DECLARATION CONFIRMING THAT THE REDACTED/ANONYMISED CLINICAL REPORTS ARE TRUE AND COMPLETE COPIES OF THOSE SUBMITTED FOR SCIENTIFIC REVIEW IS INCLUDED	☐	
DECLARATION CONFIRMING FULL/PARTIAL AGREEMENT WITH THE AGENCY'S REDACTION CONCLUSION [1] (IF APPLICABLE)	☐	☐
LIST OF EXPECTED DOCUMENTS (LED) IS ANNEXED TO THE COVER LETTER IN PDF FORMAT	☐	
CCI HAS BEEN IDENTIFIED IN THE PACKAGE AND HOW MANY JUSTIFICATION TABLES WERE SUBMITTED (IF APPLICABLE)	☐	☐
OUT OF SCOPE SECTIONS MENTIONED (IF APPLICABLE)	☐	☐

[1] In case of full agreement: *The "Final Redacted Document" package is submitted in line with the EMA redaction conclusion and to the extent these were agreed both by the Agency and [company name].*

In case of partial agreement: *The "Final Redacted Document" package is submitted in line with the EMA redaction conclusion with the exception of those parts that are subject to interim relief proceedings.*

SPLIT OR MERGED DOCUMENTS MENTIONED (IF APPLICABLE)	☐	☐

JUSTIFICATION TABLES (IF APPLICABLE)	YES	N/A
		☐
THE JUSTIFICATION TABLES ARE SUBMITTED AS PART OF THE REDCATION PROPOSAL DOCUMENT PACKAGE (NOT TO BE INCLUDED AS PART OF THE FINAL REDACTED DOCUMENT PACKAGE)	☐	
THE SAME NUMBER OF JUSTIFICATION TABLES AS DECLARED IN THE COVER LETTER ARE ACTUALLY SUBMITTED	☐	
JUSTIFICATION TABLE(S) IS/ARE SUBMITTED AS WORD/WORKING DOCUMENT(S) (OUTSIDE ECTD)	☐	
ONE JUSTIFICATION TABLE PER RELEVANT CLINICAL REPORT IS SUBMITTED	☐	
THE JUSTIFICATION TABLE(S) IS/ARE CORRECTLY NAMED	☐	
THE TEXT LABELLED AS CCI IN THE CLINICAL REPORT(S) MATCHES THE CCI PROPOSALS DESCRIBED/LISTED IN THE CORRESPONDING JUSTIFICATION TABLE(S)	☐	
NONE OF THE CCI PROPOSALS CONCERN INFORMATION WHICH IS ALREADY AVAILABLE IN THE PUBLIC DOMAIN	☐	

OUT OF SCOPE SECTIONS WITHIN DOCUMENTS (IF APPLICABLE)	YES	N/A
		☐
OUT OF SCOPE SECTIONS ARE CORRECTLY IDENTIFIED/MARKED IN DOCUMENTS AND LABELLED AS REQUIRED (SEE SECTION 2.2.3[2])	☐	
NO PAGES HAVE BEEN REMOVED FROM THE DOCUMENTS OTHER THAN THOSE CONSIDERED OUT OF SCOPE	☐	

CLINICAL REPORTS	YES	N/A
ALL RELEVANT DOCUMENTS AND ONLY THOSE (SEE ANNEX 5.7[3]) FALLING IN THE SCOPE OF POLICY 0070 ARE SUBMITTED AS PER THE AGREED LIST OF DOCUMENTS	☐	
ALL DOCUMENTS ARE SUBMITTED IN THE CORRECT ECTD SECTION	☐	

[2] Available at https://www.ema.europa.eu/en/clinical-data-publication/support-industry-clinical-data-publication/external-guidance-implementation-european-medicines-agency-policy-publication-clinical-data-medicinal-products-human-use
[3] Available at https://www.ema.europa.eu/en/clinical-data-publication/support-industry-clinical-data-publication/external-guidance-implementation-european-medicines-agency-policy-publication-clinical-data-medicinal-products-human-use

THE REDACTED/ANONYMISED CLINICAL REPORTS BEAR THE SAME VERSIONS, HAVE THE SAME HEADINGS/FOOTERS, AND ARE TRUE AND COMPLETE COPIES OF THOSE SUBMITTED FOR SCIENTIFIC REVIEW	☐	[redacted]
CCI REDACTIONS ARE IN ACCORDANCE WITH THE CCI OUTCOME (IF APPLICABLE)	☐	☐
REDACTION LABELS (COLOUR CODING AND OVERLAY TEXT) ARE CORRECTLY APPLIED IN DOCUMENTS (CCI/PPD)	☐	[redacted]
REDACTIONS PROPOSED/APPLIED IN ORDER TO PROTECT THE BLINDING ARE LABELLED WITH THE OVERLAY TEXT BLD (IF APPLICABLE)	☐	☐
FINAL REDACTIONS AND ANONYMISATION ARE APPLIED CONSISTENTLY ACROSS ALL DOCUMENTS (APPLICABLE FOR FRDP SUBMISSION ONLY)	☐	☐

ANONYMISATION REPORT

	YES	N/A
ONLY ONE ANONYMISATION REPORT IS INCLUDED IN THE SUBMITTED PACKAGE UNDER eCTD MODULE 1.9	☐	[redacted]
ANONYMISATION REPORT DOES NOT CONTAIN COMMENTS AND IS THE FINAL PROPOSED/AGREED VERSION (APPLICABLE FOR FRDP SUBMISSION ONLY)	☐	☐
ANONYMISATION APPROACH FOR FRDP HAS NOT BEEN DRAMATICALLY REVISED WITHOUT INFORMING EMA BEFOREHAND (APPLICABLE FOR FRDP SUBMISSION ONLY)	☐	☐
SECTION 6 IN THE ANONYMISATION REPORT FORM (APPROVE HERE) CHECK BOX IS TICKED	☐	☐

NAMING CONVENTION

	YES	N/A
CORRECT NAMING CONVENTION IS FOLLOWED FOR ALL DOCUMENTS SUBMITTED (SEE SECTION 2.3.3.1.6[4])	☐	[redacted]
THE CTD MODULE IS REFLECTED IN THE ELECTRONIC NAMES OF ALL DOCUMENTS (E.G. M2.5, M5.3.5.3…)	☐	[redacted]
THE DOCUMENT TYPE IS REFLECTED IN THE ELECTRONIC NAME OF ALL DOCUMENTS (E.G. CLINICAL SUMMARY, SAP, CRF, CSR…)	☐	[redacted]
THE STUDY IDENTIFIER IS REFLECTED IN ALL DOCUMENTS SUBMITTED IN MODULE 5 (APPLICABLE FOR MODULE 5 DOCUMENTS)	☐	☐
CLINICAL STUDY REPORTS CONTAIN EITHER "S" OR "P" IN THE ELECTRONIC NAME OF THE DOCUMENT (APPLICABLE FOR MODULE 5 DOCUMENTS)	☐	☐

[4] Available at https://www.ema.europa.eu/en/clinical-data-publication/support-industry-clinical-data-publication/external-guidance-implementation-european-medicines-agency-policy-publication-clinical-data-medicinal-products-human-use

5.9. Template cover letter text: "Final Redacted Document" package

For duplicate applications

European Medicines Agency
Domenico Scarlatilaan 6
1083 HS Amsterdam
The Netherlands

XX XXXX XXXX

Dear ,

RE: EMEA/X/X/XXXXXX/XXXX

[Product INN, Company Name]

Final Redacted Document package

The "Final Redacted Document" package is submitted for the purpose of the European Medicines Agency policy on the publication of clinical data for medicinal products for human use, Policy 0070.

In case of full agreement with the EMA redaction conclusion on the original medicinal product:

The "Final Redacted Document" package is submitted in line with the EMA redaction conclusion for [name of original product/number of procedure] and to the extent these were agreed both by the Agency and [company name].

In case of partial agreement with the EMA redaction conclusion on the original medicinal product:

The "Final Redacted Document" package is submitted in line with the EMA redaction conclusion for [name of original product/number of procedure] with the exception of those parts that are subject to interim relief proceedings.

<[Company name] declares that the clinical reports submitted in the present package are identical to the clinical reports submitted in the Final Redacted document package of the original medicinal product [name of original product/number of procedure] with the exception of references to the product names.

Comprising the "Final Redacted Document" package submitted to EMA are the following documents, with their respective locations in the eCTD:

- Cover letter [with annexed list of documents covering the whole Final Redaction package of documents] (Module 1.0)
- Clinical Overviews (Module 2.5)
- Clinical Summaries (Module 2.7, Sections 2.7.1 – 2.7.4)
- Clinical Study Reports – body and appendices 16.1.1, 16.1.2 and 16.1.9 (Module 5.0, Section 5.3)
- Anonymisation Report (Module 1.9)

We look forward to the publication of the redacted clinical reports by EMA and to being notified by EMA of their publication.

Yours sincerely,