EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 September 2017
EMA/14227/2017 Rev. 1
Documents Access and Publication Service
Office of the Deputy Executive Director

Questions and Answers (Q&As) on the External Guidance of Policy 0070 on Clinical Data Publication (CDP)

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Clinical data publication (CDP): questions and answers (Q&As)

This page lists some questions that applicants/Marketing Authorisation Holders (MAHs) may have on the procedure for the publication of clinical data. It provides an overview of the European Medicines Agency's position on issues that are typically addressed in discussions or meetings with applicants/MAHs. It will be updated regularly to reflect any new guidance updates during the implementation of Policy 0070. New or revised questions are marked with 'New' or 'Rev' together with the relevant date.

The external guidance of Policy 0070 on Clinical Data Publication is published: External guidance on the implementation of the policy on the publication of clinical data.

In case your question is not addressed here please contact the Agency in advance of your planned submission. The Agency's staff is available to address any questions Applicant/MAH(s) may have regarding a particular upcoming clinical data publication procedure.

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Procedural related questions

1. In which phase is the Agency in terms of Policy 0070 implementation?

The implementation of the Policy 0070 will be undertaken in a stepwise manner:

- ✓ In the first phase, the publication of clinical data relates only to clinical reports,
- ✓ In a second phase, the Agency will review various aspects in relation to individual patient data (IPD), including finding the most appropriate way to make IPD available in compliance with privacy and data protection laws.

Currently, the Agency is working on the implementation of the first phase of Policy 0070.

2. When shall I submit my Redaction Proposal Document Package? *Rev. September 2017*

There is currently a delay in publishing clinical data submitted in 2015 and 2016 as part of the regulatory procedures falling within the scope of this policy, due to extensive pilot phases for first publications under Policy 0070.

Applicants/MAH(s) will not receive notifications to submit the Redaction Proposal Document Package as per the published External Guidance. The timelines to provide the Agency with the Redaction Proposal Document Package set out in the external guidance are currently not applicable.

Regulatory procedures are being processed by the Agency in chronological order of their CHMP Opinion/withdrawal date, the first having been adopted in September 2015. As of September 2017 the Agency is processing applications adopted by the CHMP in the third quarter of 2016.

During the initial operational start–up phase of Policy 0070, MAHs of products that have already reached the CHMP Opinion stage will be contacted by the Agency to confirm the specific timelines for the submission. Applicants/MAHs should only submit their Redaction Proposal Document Packages once they have received an Invitation Letter from the Agency.

Regardless of the regulatory application type falling within the scope of Policy 0070, the first notification (validation letter) and second notification (CHMP Opinion letter or Acknowledgement letter of withdrawal) will not be sent out by the Agency. Instead, these automated notifications will be replaced by separate Invitation letter(s) to inform individual applicants/MAHs of the requested submission date giving at least 2 months' notice.

3. Will my clinical data package submission be eligible for a pilot phase?

As part of the initial operational start-up phase of the Policy, the Agency has set up a voluntary pilot phase to guide applicants/MAHs in the preparation of the Redaction Proposal Document Package. The aim is to provide support in addition to the published guidance. Eligible applicants/MAHs will receive an Invitation Letter with information on the preparation of Redaction Proposal Document Package submission, including a 2-month procedural timetable with the different milestones. The pilot phase only applies to the first procedure 'to be published' for each applicant/MAH.

The start of the 2-month pilot phase will be set out within the Invitation Letter sent to the applicant/MAH(s) by the Agency.

During the pilot phase, the Agency will respond to applicant/MAH questions on commercially confidential information (CCI), protected personal data (PPD), as well on the procedure itself. It is possible to arrange Teleconference(s) or a face-to-face meeting(s) to discuss any questions and to outline the steps in the process. The draft Anonymisation Report, or redacted clinical reports can be sent to the Agency within the pilot phase, for a preliminary consultation ahead of their official Redaction Proposal Document Package submission. There will be no pre-assessment of the CCI during the pilot phase.

The pilot phase is to provide guidance on the preparation of the package for submission and will not affect the timeline for the submission of the official Redaction Proposal Document Package.

For their second clinical data publication procedure(s), and provided that their first procedure had been through a pilot phase, applicants/MAHs will no longer be able to participate in a pilot phase. From the second clinical data publication procedure onwards MAHs should apply the principles learnt from their first submission. However, the Agency will still address questions (if any) posed by companies throughout the clinical data publication procedure.

4. Are clinical reports submitted as part of previous/other regulatory procedures subject to publication? *Rev. September 2017*

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, the Agency 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 pivotal clinical study reports as well as all 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 clinical study reports are cross-referred to within extension or modification of indication and line extension applications other than paediatric, only the pivotal clinical study reports submitted in the context of regulatory procedures not falling within the scope of Policy 0070 and considered the basis for that application will be subject to publication.

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).

5. How shall I submit my clinical data package to the Agency? Is there an acknowledgement of receipt provided?

The Redaction Proposal Document Package and Final Redacted Document Package should be submitted via the eSubmission Gateway. For general guidance on eCTD see eCTD Guidance Document (eSubmission) for the Centralised Procedure.

The applicant/MAH will receive two automated replies upon individual submission of the packages. An automated Gateway MDN (Message Delivery Notification) message will be sent to the applicant/MAH acknowledging receipt of the transmission.

The applicant/MAH will also receive a 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.

6. What do I need to do if my package(s) (Redaction Proposal/Final Redacted) is/are rejected upon submission?

The applicant/MAH is required to resubmit the entire package(s) within three working days to remain compliant with Policy 0070. Individual parts cannot be submitted separately to correct submission deficiencies.

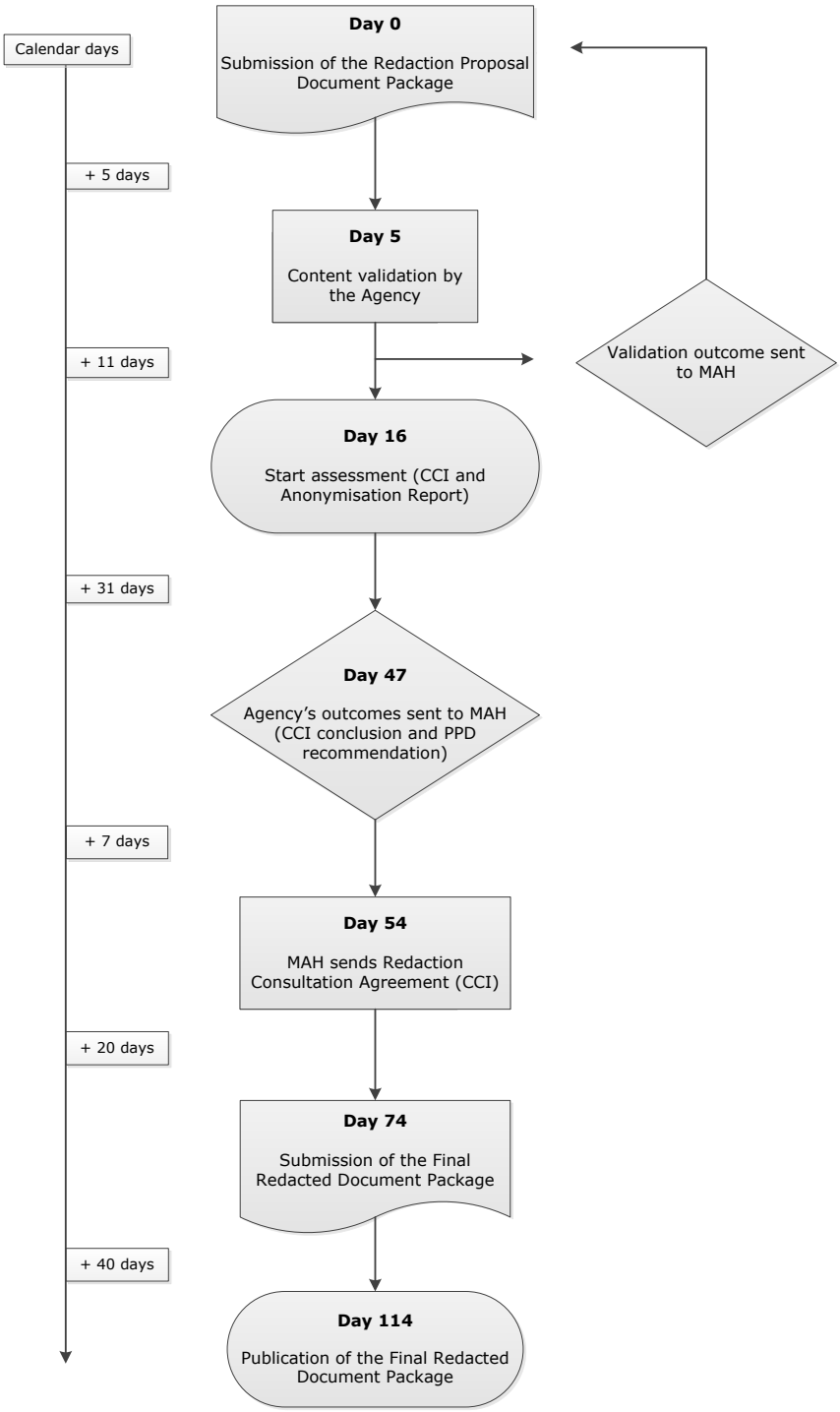
A submission will be rejected if any of the parts of the Redaction Proposal Document Package, and/or Final Redacted Document Package, as respectively set out in Table 1 and Table 2 of the External Guidance, including the required declaration text in the cover letter, are not submitted.

7. How will the submission of clinical reports be handled? Is there any procedural timetable available?

All the procedures for publication of clinical reports will follow the same procedural timetable from the moment the Redaction Proposal Document Package is submitted to the Agency, regardless of the type of application (i.e., marketing authorisation, line extension, extension of indication, withdrawn applications).

The timelines for the assessment of the Redaction Proposal Document Package submitted by applicants/MAHs are up to 114 days and the procedure terminates with the publication of the Final Redacted Document Package in the Clinical Data portal.

The detailed end-to-end process for the publication of clinical reports will take place as follows:



Upon receipt of a technically valid package submission through the gateway (**Day 0**), a dedicated Clinical Data Publication (CDP) team will be assigned to the procedure, and the consultation process starts.

The Agency will initiate the validation of the submission content. Supplementary information may be requested in order for the validation to be finalised e.g., request for clarification with regard to the CCI proposals (**Day 5**). This stage will ensure that clear and valid justifications are assessed in the next stage of the consultation process.

A validation outcome will be sent to the applicant/MAH, and in case of an unsuccessful (failed) validation, the Agency will reject the submitted package and the applicant/MAH will be asked to resubmit the revised Redaction Proposal Document package. Once the newly, resubmitted package is uploaded into the gateway (new eCTD sequence) the procedure will be restarted from **Day 0** and the revised package will be subject to a new content validation.

Following a successful validation, the Agency will start the assessment of the justifications submitted by the applicant/MAH regarding their proposed CCI redactions (**Day 16**). Therefore, all proposed CCI redactions should have a label, clearly indicating that the proposed redaction is requested on CCI grounds – please see *How shall I label CCI redactions on the clinical reports?*. During the assessment, initially, the Agency will review the justifications and if further clarifications are needed, the applicant/MAH will be contacted. Whenever clarification is requested, it will be clearly indicated in the justification table and sent to the applicant/MAH (via Eudralink). If the applicant/MAH fails to submit the requested clarifications, the Agency will consider the initial justifications irrelevant or insufficient and consequently reject the proposed redaction – please see *How should I complete the Justification Table(s) for my proposed CCI redaction(s)*. At the end of the assessment phase, the Agency will inform the applicant/MAH of its CCI conclusion for the entire set of clinical reports (**Day 47**). The outcome of the assessment (rejection, acceptance, or partial acceptance of the proposed CCI redactions) and its rationale will be clearly communicated and documented in the appropriate columns of the Justification Tables.

The Agency will also review the Anonymisation Report to check whether the applicant/MAH followed the anonymisation guidance and applied it consistently throughout the documents (**Day 16**). The submitted Anonymisation Report has to describe the methodology of the anonymisation applied in each of the clinical reports in the Final Redacted 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. A template Anonymisation Report can be found in the guidance document Annex 1.2. At the end of the assessment phase, the Agency will transmit its comments on the Anonymisation Report, if any, to the applicant/MAH but does not formally adopt the Anonymisation Report (**Day 47**). If applicable, the applicant/MAH will revise the Anonymisation Report, taking into account the Agency's comments. The final revised Anonymisation Report should then be submitted together with the Final Redacted versions of the clinical reports.

Once the outcome of the review of the CCI redactions is received by the applicant/MAH, they are required to submit, within 7 calendar days, their agreement or disagreement with the Agency's redaction conclusion on CCI (**Day 54**). In all cases, the applicant/MAH is required to submit the Final Redacted Document Package as a new sequence to the Agency for publication, within 27 calendar days from the date of the Agency's outcomes receipt (**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 the requirements of Phase 1 of Policy 0070, and thus a non-compliance notice to this effect will be published on the clinical data publication website.

The Final Redacted Document Package will be published by the Agency on its clinical data publication website (**Day 114**), within 40 calendar days after the submission by the applicant/MAH through the gateway. Prior to publication the Agency will watermark each page of the clinical reports in the Final Redacted Document Package submitted by the applicant/MAH to emphasise the prohibition of their use for commercial purposes.

8. If there were no comments from the Agency in the consultation phase do I have to re-submit the final redacted package?

Yes, the applicant/MAH is required to submit the Final Redacted Document Package as a new sequence to the Agency for publication. 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. In the cover letter submitted to the Agency for the Final Redacted Document Package, the applicant/MAH should check that it provided a declaration in the cover letter stating that the clinical reports submitted for publication are the same as those submitted for scientific review.

9. What do I need to know if I have duplicate marketing authorisation under the scope of Policy 0070? *New September 2017*

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[1]. 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 are needed.

10. What if I transfer a Marketing Authorisation to another company, which are my responsibilities under Policy 0070?

When a Marketing Authorisation Holder (the Transferor) submits an application to transfer a marketing authorisation to another company (the Transferee), responsibilities under Policy 0070 are transferred to 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 on Regulation (EC) No 2141/96 (the transfer date). These include responsibility for clinical reports that were redacted by the Transferor and published by the Agency before the transfer date.

Should a transfer application be submitted to the Agency 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 Agency will liaise with the Transferee for all remaining aspects of the Policy 0070 process for the product subject to the transfer.

[1] https://ec.europa.eu/health/sites/health/files/files/latest_news/2011_09_duplicates_note_upd_01.pdf

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

11. Who should I contact if I have a question?

The CDP team within the Agency can be contacted as follows:

If I have received an Invitation Letter for the start of my clinical data publication procedure

The *Clinical Data Publication Coordinator* (CDPC) and *Clinical Data Publication Manager* (CDPM) will be assigned at the procedure start. These will be the primary contact points during that specific clinical data publication procedure, and their contact details will be mentioned in the Invitation Letter.

If I have not received yet an Invitation Letter for my clinical data publication procedure

For any additional questions not addressed in the external guidance or in the Q&A please submit your request to the Agency using the web form (link) available on the corporate website. While filling in the field "What is the subject of your enquiry?*" please start by adding the reference "CDP –".

Commercially Confidential Information (CCI) related questions

1. I am preparing CCI justifications in the clinical reports; what does the Agency not consider to be CCI?

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, the Agency acknowledges that in limited circumstances clinical reports may contain information of a quality, non-clinical and general or administrative nature, some of which may potentially be considered CCI, and could, therefore, be subject to redaction prior to publication. Each individual CCI redaction proposed by the applicant/MAH will be scrutinised by the Agency in order to assess whether the definition of CCI applies.

Should the information proposed to be redacted be in the public domain or bear no innovative features, the Agency will not accept its redaction. In addition, if the applicant/MAH fails to provide sufficient and relevant justification, the proposed redactions will be rejected.

Section 3.2.3 of the External Guidance describes some additional examples of types 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 the Agency in the framework of Access to Documents in accordance with Regulation (EC) No 1049/2001.

In order to achieve a high level of consistency in the redaction of CCI in the final redacted documents (and to decrease the administrative burden) the Agency has grouped the types of information that the Agency does not consider CCI (please refer to Chapter 4 of the External Guidance). The Agency foresees the use of the following 5 rejection codes that would mirror the above considerations, and which at the end of the redaction consultation process, will be included in the justification table (if applicable), reflecting the Agency's final position:

- Information that is already in the public domain or publicly available – **Rejection code 01**
- Information that does not bear any innovative features – **Rejection code 02**
- Additional information the disclosure of which would be in the public interest – **Rejection code 03**
- Information lacking sufficient or relevant justification – **Rejection code 04 and 05**

2. How should I complete the Justification Table(s) for my proposed CCI redaction(s)?

For the Redaction Proposal Document Package of each of the clinical reports in which CCI redactions are proposed, Applicant(s)/MAH(s) must complete a separate justification table in Word format. Should there be no CCI identified in the document, no justification table is required, but this needs to be indicated in the Cover Letter. In such cases the Agency will understand that there are no proposed CCI redactions and therefore will not check those clinical reports. Consequently, the corresponding Final Redacted Document Package will be published as provided by the applicant/MAH.

As a general principle, the Agency expects that each of the justification tables corresponds to one submitted document. The applicant/MAH is also 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 (see section 3.2.1 of Chapter 4) 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.

Important note: The applicant/MAH should describe in detail the reasons why it considers the information proposed for redaction to be CCI. In Column 5 of the justification table (Justification of CCI), the Agency 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 as it will damage their legitimate commercial interest if released is not sufficiently specific for the Agency to reach an informed conclusion. Therefore unspecific, vague justifications will be rejected by the Agency.

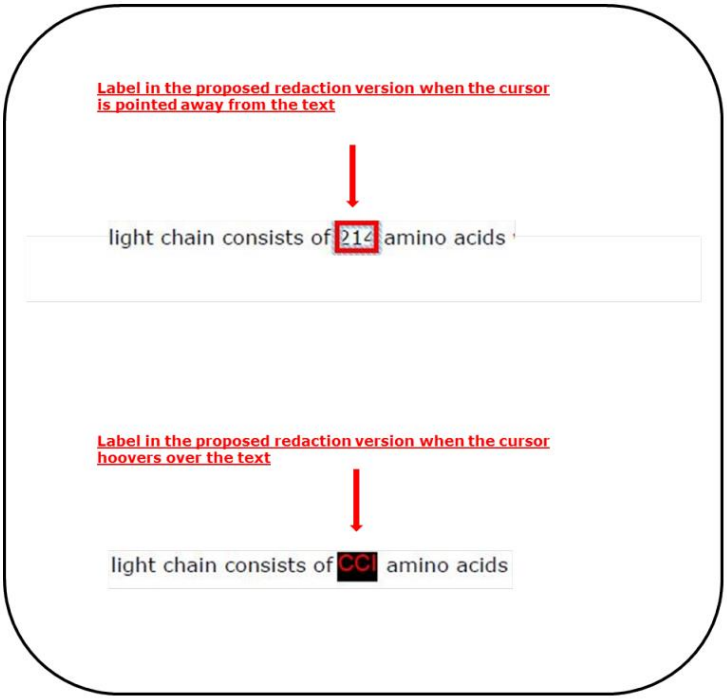
As an example, if the applicant/MAH has proposed information for redaction which falls within the scope of Annex 3 section of the Policy 'Biopharmaceutics - Detailed information on bioassays and analytical methods' (it will be in column 4 of the justification table) it is not sufficient to say that this 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.

For additional clarification on this topic please refer to section 4.2. Completing the justification table of the External Guidance.

3. How shall I label CCI redactions on the clinical reports?

In both the Proposal Redaction Document Package and the Final Redacted Document Package applicants/MAHs are required to colour code the redactions. CCI redactions should have a black background with red overlay text, as follows:

For the Redaction Proposal Document Package the text proposed for redaction should be clearly identified as such (i.e. marked) and the text itself should be legible (read-through) as per the following example:



Please note that redactions must be clearly visible. Any agreed CCI redaction labels should be visible and irremovable together with the final redacted text.

4. What if I disagree with the Agency's assessment outcome on the proposed CCI redactions?

A situation may arise where an agreement between the applicant/MAH and the Agency was not reached on the proposed CCI redaction(s), and the applicant/MAH decided to apply for interim relief against the Agency's 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 Document Package, whereby the clinical reports would be redacted according to the applicant/MAH's views. The applicant/MAH will confirm, in the text of the cover letter, which disputed redactions (page, line) have been made in the documents.

Please note that applications for annulment of the Agency's decisions and the related application for interim relief are filed with the General Court of the European Union in accordance with Article 263 of the Treaty 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 Agency's decision, the Agency 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 Document Package in accordance with the indications from the Court of Justice of the European Union. The Agency will withdraw from its corporate website the partial Final Redacted Document Package previously published. The Agency will then publish the Final Redacted Document Package.

In an exceptional situation where an applicant/MAH does not submit a complete Redaction Proposal Document Package or a complete Final Redacted Document Package, the Agency will publish a noncompliance notice.

5. Will the Agency's CCI assessment conclusions (if any) be published?

The Agency's assessment outcomes on the proposed CCI redaction are not published on the Clinical Data Publication website. Applicants/MAHs are advised not to include the assessed justification tables in the submission of the Final Redacted Document Package.

Anonymisation (PPD)/Anonymisation Report related questions

1. Who does the Agency consider to be the target audience for the anonymised reports?

The target audience should be considered to be the broadest possible spectrum (from patient, doctor, academic/researcher, curious/lay person, journalist, pharma industry etc.). It is assumed that all categories of users have one common requirement: to have access to data that is informative. Therefore the highest level of data utility is one of the aims that should be taken into account when deciding on the anonymisation strategy.

2. How many Anonymisation Reports do we have to submit? Do we have to prepare an Anonymisation Report for each clinical study report?

One overall Anonymisation Report has to be submitted describing the methodology of the anonymisation applied in the submitted clinical reports. A template Anonymisation Report is available setting out its content and structure requirements.

The Agency understands that in the same submission some CSRs present information from clinical trials where due to various factors (number of recruitment sites, number of subjects, rarity of the disease) the applied level of anonymisation will be different. In this case it has to be reflected in the Anonymisation Report, but under no circumstances should the applicant/MAH submit several different Anonymisation Reports.

3. If there are NO patient (direct or quasi) identifiers in the clinical reports do I need to submit an Anonymisation Report?

Yes, you do need to submit an Anonymisation Report and the Agency would advise you to use the abbreviated Anonymisation Report template, where appropriate. Please note that the following standard text should always be included in the Anonymisation Report: *The Marketing Authorisation Holder has not identified any patient (direct and quasi) identifiers. Therefore, no assessment of the risk of re-identification and no anonymisation process have been performed.*

There is a separate template for the Anonymisation Report published in annex 1.2 of the guidance for publication packages that contain clinical reports where patient identifiers are present.

4. How shall I label PPD redactions in the clinical reports?

In both the Redaction Proposal Document Package and the Final Redacted Document Package applicants/MAHs are required to highlight the proposed and final PPD redactions using the following colour code: blue (pantone 291 C - corresponding to RGB colours 115, 203 and 235) background with black overlay text reading "PPD". An example is provided below:

For the Redaction Proposal Document Package the proposed PPD redactions should be clearly identified as such (i.e. marked) and the text itself should be legible (read-through) as per the example shown in *How shall I label CCI redactions on the clinical reports?*.

For the Final Redacted Document Package the redactions must be clearly visible (using a blue rectangle as described above). Redacted text and the blue redaction box (that covers the redacted text) should neither be searchable nor subject to further editing.

5. Which are the required elements that need to be included in the Anonymisation Report?

The aim of the Anonymisation Report is to provide an overview of the anonymisation process followed, the methodology used, the rationale for data transformations/redactions required for the adequate anonymisation of the data and the impact of anonymisation on data utility.

The most important, required elements which applicants/MAHs should take into consideration while preparing their Anonymisation Reports, in view of their submission within the clinical data packages, are presented below and are identified as per the relevant Anonymisation Report core sections:

- **Anonymisation methodology** - Applicants/MAHs should provide information on the methodological approach chosen to protect personal information in their clinical reports, i.e. companies should clearly indicate whether the used methodology is analytical or non-analytical (qualitative risk-assessment);
- **Identification of data variables (direct and quasi identifiers)** - Applicants/MAHs should describe and list the direct and quasi identifiers identified in the clinical reports. The Anonymisation Report should also contain information on which anonymisation techniques were used to de-identify the data (e.g., redaction and/or recoding) and the rationale for choosing those anonymisation techniques;
- **Assessment of anonymisation** - According to the Opinion 05/2014 on anonymisation techniques of the Article 29 Data Protection Working Party, two options are available to establish if the data is anonymised. One option relates to the anonymisation based on three criteria, and the second option refers to the anonymisation based on the evaluation of the risk of re-identification. Only one of the options should be applied for the entire document package i.e. only one of the sections is to be completed in the Anonymisation Report:

  Fulfilment of the criteria for anonymisation (Option 1)

  Applicants/MAHs should demonstrate and confirm that, after anonymisation of the clinical reports, the three following criteria have been fulfilled:

  - No possibility to single out an individual (e.g. if no IPD line listings are present, and narratives have been adequately anonymised, this criterion is fulfilled);

  - No possibility to link records relating to an individual (e.g., if subject ID has been redacted this criterion is fulfilled);

  - Information cannot be inferred concerning an individual (if narratives are heavily redacted this criterion is fulfilled).

  Note: If this section has been completed and the three criteria have been met, there is no need to complete the section on *Risk-assessment (Option 2).*

Risk-assessment (Option 2)

Applicants/MAHs should determine how much de-identification/anonymisation is required in order to reduce the risk of re-identification to an acceptable level. In order to perform a risk assessment applicants/MAHs should be able to cover in detail the following key aspects:

- Possible adversaries and plausible attacks on the data should be duly identified;
- Risk of subjects/patients re-identification should be evaluated as follows:

1) The selected methodological approach (qualitative or quantitative) along with its justification for use should be described;

2) A threshold should be set (qualitative: *low*; quantitative: *numerical value*) and that selected threshold has to be justified;

3) The list of variables (quasi identifiers) that will be used for the risk calculation should be presented, and the risk of re-identification should be calculated:

- ✓ qualitative: calculate the level of risk (e.g. high, medium, low) based on the characteristics of the source data (e.g. prevalence of the disease, location of sites). As a practical example, if a qualitative approach is selected, applicants/MAHs should indicate that the risk threshold for the qualitative approach is set to "low" (or below), and should also explain which elements/variables need to be anonymized in order to reach the "low" threshold;
- ✓ quantitative: calculate the probability of uniquely identifying an individual. If a quantitative approach is selected, applicants/MAHs should describe the risk before and after the application of the anonymisation process, as well as mention whether the chosen threshold for the quantitative approach is 0.09 or below, and list the variables (quasi identifiers) that are used for the risk calculation and its results.

4) To check that the re-identification risk is lower than the pre-defined threshold;

5) If not, de-identify the data further in an iterative manner until the risk of re-identification is lower than the set threshold.

Note: Conversely, if the applicant/MAH decides to perform a risk assessment, there is no need to complete the section on the *Fulfilment of the criteria for anonymisation (Option 1).*

- **Data utility considerations -** Applicants/MAHs should state that they have carefully considered the impact of the anonymisation methodology used on data utility. Information should be given about the impact of the redaction or data modifications on the interpretation of the study results or patient narratives. General statements are discouraged; instead, this section should refer to data elements that have been redacted or modified in the submitted studies. This section should not contain any statements related to companies' data sharing agreement initiatives. The aim of phase I of policy 0070 goes beyond secondary analysis by researchers, and as such it is important to retain as much data utility as possible in the reports

for the benefit of the public. Therefore, the justification that there are alternative data sharing sources available does not seem appropriate to address the lack of data utility – please see *Can I make reference to my company's proactive data sharing initiatives in the Anonymisation Report?*

- **Conclusion -** applicants/MAHs should include a sentence/statement providing confirmation that the re-identification risk, after the data has been anonymised, is below the pre-defined threshold (Option 2), or that the three criteria (Option 1) have been fulfilled. Applicants/MAHs should include a statement declaring that the Anonymisation Report has been prepared following the guidance made available by the Agency, and the anonymisation techniques have been applied consistently (according to the Anonymisation Report template which can be found at Annex 1.2).

6. Can I make reference to my company's proactive data sharing initiatives in the Anonymisation Report?

During the initial operational start–up phase of Policy 0070 consent to link other data sharing portals in the Anonymisation Report was requested by several pharmaceutical companies. Whilst the Agency acknowledges that complimentary data sharing agreements undertaken by pharmaceutical companies exist, the aim of the Policy 0070 is to increase transparency on data underpinning the regulatory decision-making process and the scientific evaluation the CHMP based its opinion on. To avoid confusion resulting from disparities between the available platforms, such linking in the Anonymisation Report is not permitted.

7. Does the Agency issue a formal decision in relation to PPD redactions?

The Agency does not formally assess the proposed PPD redactions or the anonymisation approach. However, the Agency will review the Anonymisation Report to check whether the applicant/MAH followed the principles laid down in the anonymisation guidance and whether the anonymisation approach was applied consistently throughout the clinical reports.

The Agency will share its comments (which might include some points for clarification), if any, with the applicant/MAH but does not formally adopt the Anonymisation Report. The applicant/MAH is expected to revise the Anonymisation Report taken into account the Agency's comments. The revised version of the Anonymisation Report will have to be submitted as part of the Final Redacted Document Package along with the anonymised clinical reports. The Anonymisation Report and the clinical reports will subsequently be published.

8. Can patient narratives be removed from the clinical study reports?

It is the Agency's position that case narratives should not be removed nor redacted in full regardless of their location in the clinical study reports (body of the report or listings). Case narratives should be, instead, anonymised. The Agency cannot accept the redaction of the entire case narratives by default (as a rule). If, exceptionally, the entire case narrative needs to be redacted to ensure anonymisation, i.e. all identifiers (direct and indirect) need to be redacted in the clinical report(s), it has to be clearly justified in the Anonymisation Report (under "Data utility considerations" Section) why the applicant/MAH is currently compromising data utility in order to protect subject/patient re-identification. Hence, applicants/MAHs should discuss the impact on data utility, particularly, where case narratives have been extensively redacted.

Of note, there are additional elements that are present in the narratives but are not considered direct or quasi identifiers that could be released without increasing the risk of re-identification, such as

information on procedures as per protocol and/or standard of care. Additionally, other elements as laboratory values and/or common adverse events that do not fall into the category of directly identifying events could be also released with no strong impact on the risk of re-identification. In general, these are information that is likely to be unknown even for the patients.

Taking into account the fact that data collected during the study is considered to have high scientific value, it is the Agency's position that applicants/MAHs should inclusively re-consider the redaction of patient narratives, or provide more comprehensive explanations (possibly with examples) to highlight how the release of such information on patient narratives can lead to the identification of an individual if all direct and quasi identifiers are redacted as defined in the Anonymisation Report.

9. If I have individual patient data listings in the clinical reports (out of scope of phase I), how shall I remove these sections? *Rev. September 2017*

All sections of the CSR body (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. In particular, as per ICH E3, these individual patient data listings are most likely to be found in section 14.3.4 "Abnormal Laboratory Value Listing".

Therefore, individual patient data listings contained in CSR section 14.3.4 "Abnormal Laboratory Value Listing" can be considered out of scope of phase 1 of Policy 0070. Consequently, it is acceptable to have them removed from the clinical study reports prepared for publication. 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.

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.