



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Ms. Emily O'Reilly
European Ombudsman
1 avenue du President Robert Schuman
CS 30403
F-67001 Strasbourg Cedex

30 January 2015
EMA/55447/2015
Deputy Executive Director



Médiateur européen

02 FEV. 2015

Date d'arrivée

Dear Ms. O'Reilly

Subject: Your Own-Initiative Inquiry OI/3/2014/(BEH)FOR

I am writing to you with reference to your letter of 27 October 2014, in which you request the European Medicines Agency (hereinafter EMA) to answer your questions concerning the justifications for the redaction of certain information from the three clinical study reports (CSRs) of the medicinal product Humira, CSR M02-404, M04-691 and M05-769. These documents, which were requested under Regulation (EC) No 1049/2001, have been released to the initial applicant by EMA pursuant to Article 4(6) of Regulation (EC) No 1049/2001 on 11 April 2014.

The EMA would like to thank the European Ombudsman for its public campaign in fostering the case for transparency of clinical trial information and in particular for the support provided in the judicial proceedings instituted, and subsequently discontinued, by AbbVie in case T-44/13 related to the release of the concerned CSRs of Humira.

Preliminarily, it might be useful to restate briefly the unusual background of the EMA decision to release the concerned documents with some redactions carried out in order to protect the legitimate interests of the third-party originator of the document- i.e. the marketing authorisation holder of the medicinal product Humira, AbbVie, in accordance with Article 4(2) first indent of Regulation (EC) No 1049/2001.

In November 2012, the EMA received a request for access to documents for the three CSRs. This request followed very shortly a request submitted by a different applicant for access to documents, for access to other documents containing clinical information of the medicinal product Humira. Disputing the legality of all EMA decisions to release documents that AbbVie had submitted to EMA for the marketing authorisation of Humira under Regulation (EC) No 1049/2001, AbbVie lodged two applications for annulment of two similar decisions adopted by EMA to reject the requests by AbbVie to consider all information contained in the concerned CSRs as commercially confidential (Cases T-44/13 and T-29/13).

The European Ombudsman requested leave to intervene in support of the EMA in case T-44/13 *AbbVie v. EMA* submitting that in adopting the decision to disclose the concerned documents, EMA made a direct reference to the draft Recommendation made by the European Ombudsman in the course of his



inquiry into complaint 2560/2007/BEH with regard to the application of the exception under Article 4 (2) first indent of Regulation (EC) No 1049/2001. The European Ombudsman was granted leave to intervene in support of EMA, presenting the view that there is no general presumption of confidentiality applicable to CSRs but accepting that *"If such documents contain information which is commercially sensitive, that commercial sensitivity will be purely incidental and exceptional. [...] A view that Clinical Study Reports submitted to EMA are commercially sensitive could only be taken on the basis of a concrete individual examination of the document at issue determining if, exceptionally, there are **specific reasons relating to the specific nature of that specific document** which would justify such a view"* (emphasis added) (Cfr. Paragraph 15 of the European Ombudsman's Statement in Intervention in Case T-44/13).

In the course of the legal proceedings, EMA received a new proposal from AbbVie to accept the disclosure of the concerned documents, with a request to consider only a number of specific parts of the concerned documents as confidential information, and therefore to be redacted. It is on the basis of the interpretation of the limits of the exception of Article 4(2) first indent of Regulation (EC) No 1049/2001 to specific and clearly identified parts of Clinical Study Reports - which the European Ombudsman has indicated, in the Court proceedings, as the correct approach to the disclosure of CSRs -, that EMA considered the new proposal from AbbVie. By his letter dated 12.02.2014, the President of the General Court invited the parties to submit observations, *"stating in particular whether they have reached an agreement on the disclosure of the anonymised versions of the three reports on the clinical studies [...]"* (emphasis added). Both the applicant and the defendant took this invitation very seriously given the amount of time and financial resources devoted to the litigation in the past. Your services were duly informed about the invitation received.

In reviewing for the first time a set of specific requests for redactions on the basis of specific justifications by AbbVie, the EMA was able to examine extensively the set of redactions proposed. It rejected some of the redaction proposed but accepted some redactions of information closely related to the ongoing and confidential commercial development of the product Humira. EMA's behaviour is therefore in line not only with the rules laid down in Regulation (EC) No 1049/2001 and with its administrative practice stemming from the application of the *EMA Policy on Access to Documents of the 2010*, but also, we believe, with the European Ombudsman's position that, although CSRs could not be presumptively considered confidential, some specific parts of these documents could be legitimately and exceptionally redacted.

In this context, EMA would like to clarify an important element. In your letter of 16 April 2014, informing the EMA of the opening of the own-Initiative inquiry concerning the application of Regulation (EC) No 1049/2001 with regard to the redactions of the Humira documents CSR M02-404, M04-691 and M05-769, the European Ombudsman states that there have been *"additional redactions sought by AbbVie"* (emphasis added). The sequence of events demonstrates that no specific redactions of the concerned documents had been previously proposed to EMA as AbbVie, in seeking the annulment of the EMA decision to release redacted copies of the concerned documents, was claiming that no documents from the dossier submitted by a marketing authorisation holder could be disclosed to the public under Regulation (EC) No 1049/2001.

It should be highlighted that the redactions of the concerned documents proposed by AbbVie and accepted by EMA are in accordance with the *EMA Policy on access to documents (related to medicinal products for human and veterinary use)* of 2010¹ that the European Ombudsman has publicly supported².

¹ http://www.ema.europa.eu/docs/en_GB/document_library/Other/2010/11/WC500099473.pdf

² The Ombudsman applauds EMA's adoption of new transparency Policy <http://www.ombudsman.europa.eu/press/release.faces/en/5498/html.bookmark>

In the present case, it was in the context of an action for annulment and interim relief that the MAH provided a redacted version of the CSRs that the EMA – at the end – decided to release. Following the receipt of the redacted documents, neither the original requester, nor the subsequent requester of the same documents, did submit any confirmatory application under Article 8 of Regulation (EC) No 1049/2001 against the redaction of these three CSRs. Since the disclosure of these three documents to the initial requester in April 2014, the EMA received and satisfied several requests to access the following documents:

-“ *The original documents that the EMA initially intended to release but were not initially released due to the legal challenge by AbbVie*” (ASK-2669);

- “*Protocol and protocol amendments, sample informed consent forms, statistical analysis plan (SAP), narratives of serious adverse events for the same three CSRs*” (ASK-3516);

- “*A copy of the Humira CSR M02-404, CSR M04-691 and CSR M05-769*” (ASK-5967).

The redacted versions of these three CSRs were fully re-assessed in the frame of access to document (ATD) request (ASK-5967) as meanwhile information, previously redacted, could be found in the public domain. This shows that the redaction of a CSR is a dynamic process and evolves with time taking into consideration, amongst others, the stage of development of products and the availability of information in the public domain.

As a technical agency of the EU, responsible for providing opinions on medicinal products, EMA is aware of the importance of transparency and openness and to ensure the right of EU citizens to a good administration, a right enshrined in the Charter of Fundamental Rights of the EU. Data about adverse reactions of drugs are published from the Eudravigilance database. Minutes and agenda of meetings of scientific committees can now be found on the public website. Extensive records of declaration of interests of experts involved in the EMA decision-making are published on a user-friendly website. Furthermore, in accordance with the EMA Policy for access to documents adopted in 2010, the EMA started releasing documents submitted by pharmaceutical companies to applicants for access to documents. Our continuing commitment to transparency can be seen by the establishment in September 2013 of a dedicated multidisciplinary team of 13 full-time equivalent staff members working every day on ATD requests and requests for information. Only in 2014, the Agency dealt with 416 access to documents (ATD) requests; and released 1816 documents amounting to 167 309 pages.

The EMA would like to submit that in the application of the Regulation (EC) No 1049/2001 which foresees legitimate interests to be protected which include *inter alia* the legitimate economic interests of natural or legal persons. There are in fact specific exceptions to the principle that documents held by EU public administrations are publicly accessible. This means, in practice, that when EMA assesses the scientific information contained in CSRs, it has to balance the interest to have the information publicly accessible with the legitimate interest of those who submit it to have their commercially confidential information protected from disclosure in exceptional cases. The importance of appropriate technical competence in assessing these claims is therefore paramount.

The EMA would like to submit that any individual assessment of a request for ATD performed by an EU institution will have to rely on the technical competence of the assessors. To some extent, this is a discretionary analysis which, however, must comply with both the general transparency principles enshrined in Regulation (EC) No 1049/2001 and the internal rules/policy/guidelines of the institution, as well as with the principle of fair and equal treatment of all requesters. We would like to respectfully submit that the EMA enjoys a wide discretionary power in the scientific assessment underpinning claims of confidentiality for certain information contained in marketing authorisation dossiers submitted by pharmaceutical companies.

We would now like to comprehensively address your specific questions raised in the framework of this own-initiative inquiry. To ease your reading, we have attached an Annex to this letter with our answers to your questions. Many of the answers to your questions address substantially the same issue, which is often dealt with in different pages of the documents at stake. Therefore, we decided to group as many answers as we could, based on the nature of the question and your requests for a justification for our redactions.

Regarding these justifications, we agree that these are necessary in order to deviate from the general criterion of full transparency enshrined in Regulation (EC) No 1049/2001. That said, it has always been our understanding that a redaction could be acceptable if reference was made to the category of information protected by the relevant exception invoked, without necessarily describing at length the justification for the redaction of every single word. From our perspective, introducing the requirement of such a detailed justification at such granular level would impair a reasonable and efficient use of resources at the Agency and could even slow down dramatically the release of documents, which has been one of our strategic targets since 2011 onwards. In accordance with the principle of proportionality and good administration, we respectfully submit that there must be a reasonable balance between the level of details of such justifications and the efficiency of the service in disclosing documents. Such reasonable balance, we do believe, is in line with the spirit of Regulation (EC) No 1049/2001.

We intend to make public the present letter. If you have any comments in relation to this intention to make public the present letter, please provide us with such comments within 10 working days of the receipt of the present letter.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'A. Pott', with a large circular flourish above the name.

Andreas Pott

Deputy Executive Director

ANNEX

Reply to your questions concerning the redactions of the documents CSR M02-404, M04-691 and M05-769

The European Ombudsman has submitted a list of questions with progressive alphanumeric references. The EMA is pleased to provide all factual information in its possession related to the application of the relevant exceptions under Regulation (EC) No 1049/2001 to the disclosure of clinical study reports as they result from the application of these exceptions at the relevant point in time, i.e. February-March 2014. The EMA is however not in a position to provide comments or express opinions discussing the hypothetical assessment of the same information with regard to changed factual circumstances – for instance, some of the redacted information might have become in the meanwhile publicly available as a result of a voluntary disclosure of AbbVie or other legitimate third parties.

With regard to **Questions 1(a) and 1(b)**, the EMA would like to submit that the claim that the medicinal product Humira was undergoing “*a development programme*” was not, at the time of the redaction, unsubstantiated but perfectly reasonable for the product, as the marketing authorisation holder was involved in research activities concerning the testing of new dosing regimen and improved efficacy. This is confirmed by the fact that subsequent information concerning the new dosing regimen has eventually become publicly available³.

The EMA is therefore able to confirm that some of the information on the new induction dose being developed is now in the public domain. However, in accordance to the requisite legal standard, the claim made by AbbVie at the time of the review carried out by EMA, that the release of information about ongoing development of a commercial product could result in a reasonably foreseeable risk of undermining their legitimate economic interest could not have not been legitimately disregarded by EMA in when applying the exception under Article 4(2) first indent of Regulation (EC) No 1049/2001. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Question 1(c)**, the EMA confirms (as above stated) that the information in section 9.4.4 was redacted based on AbbVie’s claim that there was an ongoing development to improve the dosing regimen of Humira. In addition, we would like to submit that the redacted text in Section 9.4.4 describes the high level rationale for the dose selection strategy of the company, whilst on the other hand the information described in 9.4.5 gives factual information about protocol specific precise doses and the timing of administration. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Question 1(d)**, the EMA would like to submit that redacted text was not claimed to be linked to novel aspects of the process of selection of doses. The text was claimed to be linked to an on-going development to improve the dose regimen of Humira. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Questions 2(a), 2(b), 4, 8(g), 9, 10(a), (b), (c), (f), (g), (h), (k), (n), (o), 11(a) p.174, 12(a),14, and 15(f) and (g)**, the EMA accepts that the information redacted should not have been redacted. This has been overlooked in light of the massive amount of documents reviewed, the time pressure to release the documents. The EMA would like to confirm that this information was not redacted in subsequent access to documents requests (ASK-5967), where EMA performed the initial and the final redactions. The EMA would also like to recall that AbbVie did not

³ <http://www.abbvieinvestor.com/phoenix.zhtml?c=251551&p=irol-reportsannual>

raise any objection to release this information during the consultation phase concerning the subsequent requests for access to documents.

With regard to **Questions 3(a), 3(b), 3(c), 3(d) and 3(e)**, the EMA would like to clarify that the scope of the request covered the body of the CSRs, and the Appendix 16.1.1. (Protocol and Protocol Amendments) was not specifically requested. For this reason section 9.8.1 describing Protocol changes was not considered in the scope of this particular request. Should a confirmatory application have been received regarding the redaction of this section, the EMA would have considered the release of this information along with the corresponding Appendices (16.1.1, 16.1.2). In support of this statement, the EMA would also like to highlight that, these specific information and protocol Appendices have since been released to satisfy two subsequent requests to access these documents (ASK-3516 and ASK-5967).

With regard to **Question 3(f)**, the EMA would like to clarify that statistical analysis contained in CSRs are not, in principle, to be considered commercially confidential. The information on changes to the statistical analysis plan was redacted for the same reason as the changes to the protocol as not specifically requested (please see above answer). In support of this statement the EMA would also like to highlight that, these specific information and protocol Appendices have since been released to satisfy two subsequent requests to access these documents (ASK-3516 and ASK-5967).

With regard to **Question 5**, the EMA would like to confirm that the statistical methods referred to in the e-mail of 11 March 2014 have not been redacted in the CSR M02-404.

With regard to **Question 6**, the EMA would like to submit that the MAH claimed that exploratory and subgroup analyses on pages 127-130 were linked to an ongoing development to explore the dosing regimen of Humira in different populations, which could not be reasonably dismissed at that time (see *supra* the reply to questions 1(a) and 1(b)). On this basis, the detailed tables on pages 127-130 together with the corresponding titles of the tables on pages 25-28 and 40 were considered commercially confidential and redacted in line with the *EMA Policy on access to documents (related to medicines for human and veterinary use) of 2010*. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Questions 7(a), 7(b), 7(c), 7(d)**, the EMA would like to confirm that this is not a novel process. This specific information does not directly describe any details of the actual immunogenicity assays. However this section describes the collection, storage and the shipment of blood samples which were then used for immunogenicity analyses. The detailed description of the company's procedure for measuring adalimumab serum concentrations, anti-adalimumab antibodies and detailed technical methods was construed as commercially confidential information. It should also be noted that, in the context of a recent access to documents request (ASK-5967), most of the information has since been released as then found in the public domain.

With regard to **Questions 8 (a), (b)**, the EMA would like to confirm that the redacted text reveals the subgroup analyses performed by the MAH and is not directly linked to a sub-indication. The marketing authorisation holder claimed that the results of these sub-group analyses were used for an ongoing development aiming at exploring the dose adjustment of Humira in different sub-groups. The EMA accepted, on the basis of its 2010 Policy on access to documents, the justification submitted by AbbVie, i.e. that the release could undermine a reasonably foreseeable legitimate economic interest of the MAH. The EMA can confirm that, apart from the data concerned in this section, information has since been released in subsequent access to documents requests (ASK-5967).

With regard to **Question 8(c) and 8(d)**, the EMA can confirm that as of today it has not been made aware of any specific sub-indication linked to this redacted information. Therefore off-label use linked to this theoretical sub-indication does not apply.

With regard to **Question 8(e)**, the EMA confirms that the whole information was claimed by the MAH to refer to an ongoing development to explore the dose adjustment of Humira in different subgroups. Hence, the redaction of this information is in line with the 2010 EMA Policy on access to documents. The EMA can confirm that, apart from the data concerned in this section, information has since been released in subsequent access to documents requests (ASK-5967).

With regard to **Question 8(f)**, the EMA confirms that it is in the public domain that the MAH is running several ongoing development plans (<http://www.abbvieinvestor.com/phoenix.zhtml?c=251551&p=irol-reportsannual>). As of today no dose adjustment, corresponding to these sub-group analyses has been specifically approved. The EMA can confirm that apart from the data concerned in this section, information has since been released in subsequent access to documents requests (ASK-5967).

With regard to **Questions 8(h), 8(i) 8(j)**, the EMA confirms that this is not directly linked to a new sub-indications. The EMA could not legitimately dismiss the claim made by the MAH that the information to be redacted was to be used in an on-going development plan regarding improved dosing adjustments for Humira, thus constituting commercially confidential information. In any case, with regard to text redacted at page 129 and the sentence "*no clinically important differences*", EMA would like to submit that the value of this information for the understanding of the scientific information related to the approved indication of Humira is minimal and cannot reasonably generate any disadvantage to the requester. The EMA can confirm that apart from the data concerned in this section, information has since been released in subsequent access to documents requests (ASK-5967).

With regard to **Question 8(k)**, the EMA confirms that in this specific case, no overriding public interest was evident. Nor did the requester exercise their right to submit a Confirmatory Application by stating that there was an overriding public interest. Therefore we consider that the claim that there exists an overriding public interest in the disclosure of this information is speculative and theoretical, whilst the claim by the MAH that the information could be useful for the on-going development of the product is *prima facie* founded.

With regard to **Question 8(l)**, the EMA would like to submit that the redacted table reveals the results of subgroup analyses performed by the MAH. The MAH claimed that the information revealed by the redacted text was going to be used for an ongoing development aiming to explore the dose adjustment of Humira in different subgroups. Hence, the redaction of this information is in line with the 2010 EMA Policy on access to documents. The EMA can confirm that apart from the data concerned in this section, information has since been released in subsequent access to documents requests (ASK-5967).

With regard to **Question 8(m)**, in relation to the first part of your question, the EMA would like to submit that we cannot speculate if the currently ongoing developments of Humira are of clinical relevance, as the details of these development plans were not shared with us. Moreover, such conclusion of relevance to the present clinical use cannot be drawn before the development plan is completed and the full dataset supporting this label change/new indication is assessed. Such information is part of a dossier only submitted to us when the company applies for changes in the Product Information of a medicinal product. To reply to the second question we would like to emphasize that information on the overall benefit/risk of Humira in the approved indication is clearly

communicated in the EPAR of the product (Scientific discussion) and summarised in the product information. In addition, the overall benefit/risk is not based on the conclusions of a specific study but on the full data set that is submitted in a dossier. Therefore we think it is unlikely that these very specific results of exploratory analyses would make a difference in better understanding the overall risk/benefit of Humira in the approved indication. At the time of approval in the EU, the Applicant did not independently apply and did not bring evidence to consider dose adjustment in these sub-groups, which are therefore falling under the umbrella of the currently approved indication. The results redacted do not constitute enough evidence to use Humira *off-label*. The EMA can confirm that apart from the data concerned in this section, information has since been released in subsequent access to documents requests (ASK-5967).

With regard to **Question 10(d)**, the EMA would like to submit that the redacted text still leads to the conclusion that change from baseline in CDEIS score was higher in the adalimumab group compared to the placebo group at weeks 12 and 52, therefore the redaction does not alter the meaning of the text. Moreover, the EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Questions 10 (e)**, the EMA would like to submit that the 4th bullet point reveals the results of a secondary end-point which was measuring the change in "*Crohn's disease endoscopic index of severity*" (CDEIS) score from baseline. CDEIS is one of the most frequently used scores for quantifying the mucosal healing. In terms of the weight of the evidence, the results related to the above mentioned end-point can be considered at their best as an orientation trend and not a confirmatory efficacy result. In conclusion, the text in bullet point 4th reveals the positive efficacy trend of adalimumab as compared to the placebo group which can be used as supportive of the efficacy claim. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Questions 10 (g)**, the EMA would like to submit that 5th bullet point reveals the results of a secondary end-point which was measuring: change in total SES-CD (simple endoscopic score for Crohn's disease) score from baseline. SES-CD is one of the most frequently used scores for quantifying the mucosal healing. In terms of the weight of the evidence the results related to the above mentioned end-point can be considered at its best as an orientation trend and not a confirmatory efficacy result. We acknowledge that the text in bullet point 5th reveals interesting supportive data, but they reveal a trend therefore their redaction does not alter the conclusions reached on the efficacy results obtained for the primary endpoint. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Question 10 (i)**, the EMA would like to submit that the information redacted is part of the secondary efficacy analyses. We acknowledge that the text in bullet point 6 reveals interesting supportive data, but their redaction does not alter the conclusions reached on the efficacy results obtained for the primary endpoint. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Question 10(j)**, the EMA would like to confirm that the redaction does not lead to a misunderstanding of the text. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Question 10(l)**, the EMA would like to submit that the redacted text reflects the MAH's position which is based on the disclosed results. The redaction of the interpretation from the MAH does not alter the facts and data described above under the same bullet point.

With regard to **Question 10 (m)**, the EMA would like to concur with the European Ombudsman those facts and data have clinical value. The EMA submits that the facts and data have not been redacted but that the only part of information redacted in this page relates to the interpretation from the MAH which does not alter the facts and data described above under the same bullet point and therefore it does not alter the conclusion on overall efficacy aspects of Humira. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Question 10(p)**, the EMA submits that the relevant data have not been redacted but that only the interpretation from the MAH. This does not alter the understanding of the conclusion on the overall efficacy aspects of Humira. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Questions 10(q) and 10(r)**, the EMA submits that the method and design are not novel. The MAH claimed that releasing this information on these exploratory analyses would provide insight into their current development to explore the new dosing regimen that they were discussing with a non-EU regulatory body. The specific data were considered commercially confidential and redacted in line with the EMA Policy on access to documents (related to medicines for human and veterinary use) of 2010. No overriding public interest was found. Nor did the requester exercise their right to submit a confirmatory application by stating that there was an overriding public interest. Therefore we consider that the claim that there exists an overriding public interest in the disclosure of this information is speculative and theoretical, whilst the claim by the MAH that the information could be useful for the on-going development of the product is *prima facie* founded. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Questions 10(s) and 10(t)**, the EMA would like to submit that the MAH claimed that releasing this information on these exploratory analyses would provide insight into their current development to explore new endpoints in the context of the new dosing regimen that they were discussing with a non-EU regulatory body at that time. The specific data were considered commercially confidential and redacted in line with the EMA Policy on access to documents (related to medicines for human and veterinary use) of 2010. The EMA can confirm that apart from the data concerned in this section, information was released in subsequent access to documents requests (ASK-5967).

With regard to **Question 10 (u)**, the EMA would like to submit that the redaction on page 16 is about a likely explanation (hypothesis generating interpretation) provided by the MAH. It does not alter the facts and data mentioned in the rest of the paragraph and therefore not the understanding of the overall claimed efficacy of Humira. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Question 10 (v)**, EMA would like to submit that no overriding public interest was evident. Nor did the requester exercise their right to submit a confirmatory application by stating that there was an overriding public interest. Therefore we consider that the claim that there exists an overriding public interest in the disclosure of this information is speculative and theoretical, whilst the claim by the MAH that the information could be useful for the on-going development of the product is *prima facie* founded. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Question 11(a)**, p.175-177, the EMA would like to submit that the information redacted is part of the secondary efficacy variables and their redaction does not alter the broad understanding of the risk-benefit of Humira in the claimed indication. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Questions 11(b) and 11(c)**, the EMA would like to submit that the information redacted is predictive value within the additional secondary endpoints. The MAH claimed that the ongoing development was to investigate a new induction dose and discuss a new endpoint; the MAH did not mention any new indication and therefore we cannot comment on speculative *off-label* use in this context. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Question 11(d)**, the EMA would like to submit that such conclusion of relevance to the present clinical use cannot be drawn before the development plan is completed and the full dataset supporting this label change/new indication is assessed. Such information is part of a dossier only submitted to us when the company applies for changes in the Product Information of a medicinal product. As mentioned above, the MAH did not mention any new indication and therefore we cannot comment on speculative *off-label* use in this context. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Question 11(e)**, the EMA would like to submit that no overriding public interest was evident. Nor did the requester exercise their right to submit a confirmatory application by stating an overriding public interest. Therefore we consider that the claim that there exists an overriding public interest in the disclosure of this information is speculative and theoretical, whilst the claim by the MAH that the information could be useful for the on-going development of the product is *prima facie* founded. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Questions 12(b) and 13**, the EMA would like to submit that this information relates to on-going development plan of the MAH with regard to Humira and therefore it was deemed plausible that the release of these results could undermine a legitimate economic interest of AbbVie. The specific data were considered commercially confidential and redacted in line with the EMA Policy on access to documents (related to medicines for human and veterinary use) of 2010. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Questions 15 (a) and, 15 (d), 15 (i), and 15(j)**, the EMA would like to submit that the MAH claimed that information link to some of the secondary endpoints were being discussed with a non-EU regulatory body to discuss new endpoint for a study to explore a new induction dose. To be noted that according to the information available today in the public domain Abbvie is indeed running several on-going development plans for new indications and a new dosing regimen. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Question 15 (b)**, the EMA would like to submit that this redaction does not alter the overall meaning of text. It still leads to the conclusion that change from baseline in CDEIS score was greater from baseline to weeks 12 and 52. The MAH claimed that this information relates to an on-going development plan and therefore it was deemed plausible that the release of these results could undermine a legitimate economic interest of AbbVie. The specific data were considered commercially

confidential and redacted in line with the EMA Policy on access to documents (related to medicines for human and veterinary use) of 2010. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Questions 15 (c)** the EMA would like to submit that the MAH was involved in research activities concerning the testing of new dosing regimen and improved efficacy. This is confirmed by the fact that subsequent information concerning the new dosing regimen has eventually become publicly available (<http://www.abbvieinvestor.com/phoenix.zhtml?c=251551&p=irol-reportsannual>). The EMA is therefore able to confirm that some of the information on the new induction dose being developed is now in the public domain. However, in accordance to the requisite legal standard, the claim made by AbbVie at the time of the review carried out by EMA, that the release of information about ongoing development of a commercial product could result in a reasonably foreseeable risk of undermining their legitimate economic interest could not have not been legitimately disregarded by EMA in when applying the exception under Article 4 (2) first indent of Regulation (EC) No 1049/2001. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Questions 15 (e)**, the EMA confirms that the whole information redacted on pages 175-177 was claimed by the MAH to refer to secondary endpoint being discussed with a non-EU regulatory body to discuss new endpoint for a study to explore a new induction dose, which redaction was in line with the *EMA Policy on access to documents (related to medicines for human and veterinary use) of 2010*. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Questions 15 (h)**, the EMA would like to submit that this redaction does not alter the overall meaning of text. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Questions 15 (i)**, the EMA would like to submit that the 6th and 7th words refer to a scoring system SES-CD (simple endoscopic score for Crohn's disease). SES-CD is one of the most frequently used scores for quantifying the mucosal healing. The EMA can confirm that this information was not redacted in subsequent access to documents requests (ASK-5967).

With regard to **Questions 15 (j)**, the EMA would like to submit that the last two bullet points on page 175 describe the predictive value of clinical remission as oppose to the previous points describing the predictive value of mucosal healing. As in the meantime found in the public domain, this information was not redacted in subsequent access to documents requests (ASK-5967) where EMA performed the initial and the final redactions.

Finally with regard to **Question 16**, the EMA would like to submit that companies often formulate their batch numbers in such a way that it indicates manufacturing site, month of manufacture and number of the specific batch in the calendar year, which could possibly undermine their legitimate commercial interests.