January 2024

# Submission of comments on Guideline on Specific Adverse Reaction Follow-up questionnaires (Specific AR FUQ) (EMA/PRAC/490455/2023)

## Comments from:

| Name of organisation or individual |
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| EFPIA |

*Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.*

*When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).*

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# 1. General comments

| Stakeholder number<br>*(To be completed by the Agency)* | General comment (if any) | Outcome (if applicable)<br>*(To be completed by the Agency)* |
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| | We are welcoming this guideline which provides recommendation on the way to manage Specific Adverse Reaction Follow-up questionnaires (Specific AR FUQ) in an efficient way and provide more public visibility of such questionnaire. | |
| | More and more FU activities are not using predefined hard coded template questionnaires but are rather based on algorithms that identify specific missing information from the ICSR. This should be considered in this guidance. | |
| | We propose a consultation with the stakeholders; EMA and reporters (HCPs) who would be answering the concerned questionnaires to better understand the user friendliness. | |
| | In general, the term Adverse Reaction is used in the document where it seems that 'Suspected Adverse Reaction' is meant.<br>**Proposed change**<br>Specify 'Suspected Adverse Reaction' where this is applicable or make a general statement in the introduction mentioning that whenever Adverse Reaction is mentioned, 'Suspected Adverse Reaction' is meant. | |
| | Should the term "Specific Adverse Reaction Follow-up Questionnaires" be amended to "Specific Adverse Event Follow-up Questionnaires" throughout?<br>As these questionnaires will apply to both important identified and important potential risks, they will be used to collect additional information on both adverse reactions and adverse events. In addition, they could be used to collect further information not only from spontaneous case reports | |

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| | but also from case reports arising from non-interventional studies – for the latter these would not necessarily be adverse reactions.<br>Of note, there is already a discrepancy in the terminology within GVP Guidance: GVP Module V Rev 2 titles Annex 4 of the RMP "Specific adverse event follow-up forms" whereas the Guidance on the Format of the RMP in the EU titles Annex 4 "Specific adverse drug reaction follow-up forms." | |
| | Is there any initiative led by the Agency to share this guidance with other non-EU competent authorities? | |
| | What is the planned timeline for the Guidance to become effective?<br>What is the Agency's expectation for MAH to implement the guideline when it becomes effective:<br>-What will be the trigger to use or replace the existing MAH questionnaires?<br>-How will MAH phase this initiative into existing RMPs? | |
| | Does the Agency plan to publish specific FUQs for all Designated Medical Events as per the EMA list?<br>Our understanding is that this guidance is just related to safety concerns from the RMP/PSUR where the MAH has been requested by the NCA to create a Specific AR FUQ. | |
| | General comments on Outcome Indicators (line 225 – 231)<br>"The majority of AR FUQs are in place at Marketing Authorisation. For those it will be impossible to distinguish what kind of information would have been received without the AR FUQs in place. Also, the data entry process will make it technically impossible within one ICSR to distinguish exactly which information came from which form.<br>In addition, the receipt of additional information for an initial report can occur due to different triggers: for example, the reporter answers the questions from the CIOMS list A, B and C, which were addressed to him/her by the MAH, the reporter fills out the specific AR FUQs, the reporter spontaneously reports additional information to MAH. It is therefore difficult to determine an outcome indicator for the follow-up | |

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| | questionnaire, and it is questionable how a meaningful conclusion can be drawn from this. Depending on the case volume and specific FUQ number of requested data, it may be technically challenging to extract and analyse these data and therefore to provide indicators.<br>It is close to impossible to substantiate the added value of the additional information that is collected as part of a specific AR FU questionnaire versus the content of the initial ICSR. Additional information that is received by the MAH, regardless of whether that was gathered via spontaneous follow-up, a standard FU questionnaire, or a specific AR FU, questionnaire, is just added to the existing case in the MAH Safety database and the new set of information is always assessed in its entirety (ie, considering all the information gathered until that point in time). It is therefore not realistic to expect to be able to identify how much added value on a case/ICSR level was provided by the specific AR FU questionnaire.<br>We recommend a more general approach to look at the totality of data received for a specific event and analyse the "usefulness of the AR FUQ" by comparing this to the data points collected via the AR FUQ.<br>**Proposed change for lines 226-231:**<br>"Competent authorities may request to the MAHs to provide a ~~detailed analysis of the additional information provided and to substantiate how it contributes both to increase the quality of the data collected when compared with the initial information and~~ general analysis how the AR FUQ contributes to a better characterisation of the safety concern with a potential impact on the benefit/risk balance of the medicine. ~~The outcome indicators should reflect the added value of the information collected 231 compared to what already existed in the initial ICSR.`~~<br><br>General Comments on the Tool throughout the document:<br>When will the Tool and its use be available to MAHs.<br>Is the plan to use the same Tool as the RMP publication Tool?<br>What exactly will the Tool accommodate? (special AR FUQ without detail or any detail, i.e. responses or potentially data that may be confidential).<br>Will there be training sessions provided for its use?<br>What expectations are there for use of the Tool. | |

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| | What if there are no paper documents (FUQs) but electronic formats or other such as web-based tools/portals, how will this be accommodated.<br>Is the Tool used to send out AR FUQs to reporters or is the Tool aimed only at capturing AR FUQ (the questionnaires themselves)?<br>Will MAH be expected to share AR FUQs outside of the Tool in parallel to the Tool?<br>Will completed or retired AR FUQs be housed in a special section of the Tool as well as the active AR FUQs? How will the difference between active vs retired FUQs be visible?<br>Who will be responsible for making clear in the Tool that an AR FUQ is retired? | |

**2. Specific comments on text**

| Line number(s) of the relevant text<br>*(e.g. Lines 20-23)* | Stakeholder number<br>*(To be completed by the Agency)* | Comment and rationale; proposed changes<br>*(If changes to the wording are suggested, they should be highlighted using 'track changes')* | Outcome<br>*(To be completed by the Agency)* |
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| Line 41<br>Exec Summary | | "…developed by the MAH at the request of NCAs…". Could EMA also request development of these specific FUQs? (i.e. in the course of an RMP assessment)<br>**Proposed change:**<br>Amend text to "...developed by the MAH at the request of NCAs or the EMA…". | |
| Lines 48-51 | | The wording used is not clear (i.e., "For important identified risks listed in the product information, FUQs should not be generally used, but in some special situations, a Specific AR FUQ may be necessary for further characterization of the risk.")<br>Proposed change: "For important identified risks listed in the product information, in some special situations, a Specific AR FUQ may be necessary**, instead of the standard FUQ**, for further characterization of the risk.' | |
| Lines 52-54<br>(and 144-145) | | It may be too complex to have the specific FUQs itself prefilled. Would it be acceptable to have a kind of limited database extraction to join to our specific FUQs instead, pointing only missing data should be provided?<br>**Proposed change:**<br>The content of a Specific AR FUQ should focus on collecting the missing data of main importance for assessing the safety concerns in question and **could** be prefilled with available information**, as much as possible,** to avoid requesting the primary source to repeat information." | |
| Line 57 and along the document | | "Dissemination" means distribute, so that it reaches many people.<br>Proposed change: "**way to contact the reporter**" | |
| Lines 59-61<br>Exec Summary | | "The MAHs are not expected to use Specific AR FUQ for case reports that are not initially and directly sent to them (e.g., cases reported to NCAs or other MAHs)."<br>When reading lines from the Scope, 89-90: "The MAH is not expected to collect further information about a case report that is not initially and directly sent to them (e.g., cases reported to NCAs or other MAHs)", it seems that there is no expectation for any type of FUQs, not only the Specific AR FUQs, so it would be clearer to state in the Executive summary lines 59-61 the same sentence as in the Scope, i.e., lines 89-90.<br>**Proposed change** | |

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| | | The MAH is not expected to collect further information about a case report that is not initially and directly sent to them (e.g., cases reported to NCAs or other MAHs) | |
| Line 64 | | "Overall, in addition to existing GVP guidelines…"<br>**Proposed change**<br>We recommend adding references to the existing GVP guidelines. | |
| Lines 87-88 | | "The scope of this guidance is limited to specific (or targeted) AR FUQs requested by the competent authorities."<br>The term "targeted" is stated in brackets in relation to the FUQs. However, it is unclear whether "targeted" and "specific" can be used interchangeably.<br>**Proposed change**<br>Please clarify what is meant by the distinction between the terms "targeted" and "specific" or whether they are intended to be used interchangeably. | |
| Lines 89-90 | | Should "Literature" cases fall under the scope of General Questionnaires (GQ)? These cases are not technically reported/sent to the MAH but detected by the MAH. Therefore, does that mean authors can be excluded from being sent a GQ? | |
| Lines 88-90 | | To distinguish between general and AR specific FUQs<br>Proposed change (if any):<br>from "… for FUQs."<br>To "… for general FUQs." | |
| Lines 116-140 | | Guidance on the use of the specific AR FUQ:<br>The guideline describes that the specific adverse reaction Follow-up questionnaires (AR FUQ) are related to safety concerns which could impact the benefit/risk balance.<br>Considering that, AR FUQ are designed for use by health care professional (HCP) and the completion needs detailed medical knowledge, guideline should clarify that follow-up with AR FUQ is not mandatory for non-HCP. | |
| Lines 118-121 | | "Adverse reactions for which Specific AR FUQs are considered can be defined as those referring to safety concerns[4] (from RMP and/or PSUR) for which the collection of information as detailed as possible and their better characterisation may have an impact on the B/R balance of the medicinal product."<br>This seems in contradiction with lines 49-51, which states that "for important identified risks listed in the product information, FUQs should not be generally used, but in some | |

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| | | special situations, a Specific AR FUQ may be necessary for further characterization of the risk."<br>We believe it would be helpful to repeat the details from lines 49-51 after line 121 to clarify that for important identified risks listed in the product information, FUQs should not be generally used.<br>**Proposed change**<br>"Adverse reactions for which Specific AR FUQs are considered can be defined as those referring to safety concerns[4] (from RMP and/or PSUR) for which the collection of information as detailed as possible and their better characterisation may have an impact on the B/R balance of the medicinal product. <u>For important identified risks listed in the product information, FUQs should not be generally used, but in some special situations, a Specific AR FUQ may be necessary for further characterization of the risk.</u>" | |
| Lines 121 and 127 | | In **line 127**, though it is described below that there are conditions to apply AR FUQ, the sentence from **line 118** and **119** might lead to overinterpretation that in general safety concerns from RMP and PSUR need a FUQ.<br>**Proposed change**<br>It might be from the beginning relevant to identify for the reader directly after **line 121** that "not all Safety Concerns (from RMP and/or PSUR) require a Specific AR FUQ, and considerations listed below shall be taken into the account for the decision on issuing a Specific AR FUQ." | |
| Lines 122-124<br>Section 4.1 | | The wording is not covering the situation when the list of safety concerns in the PSUR has additional risks compared to the RMP.<br>**Proposed change**<br>For medicinal products requiring a Specific AR FUQ but without an RMP in place (exceptional and/or for old products) or when the list of safety concerns in the PSUR has additional risks compared to the RMP, the Specific AR FUQ could be associated to the safety concern identified and/or followed- up in the PSUR. | |

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| Lines 122-124 | | "For medicinal products requiring a Specific AR FUQ but without an RMP in place (exceptional and/or for old products), the Specific AR FUQ could be associated to a safety concern identified and/or followed- up in the PSUR." The word "identified" here contradicts to line 49-51 ("For important identified risks listed in the product information, FUQs should not be generally used, but in some special situations, a Specific AR FUQ may be necessary for further characterization of the risk.)<br>**Proposed change**<br>"For medicinal products requiring a Specific AR FUQ but without an RMP in place (exceptional and/or for old products), the Specific AR FUQ could be associated to a safety concern ~~identified and/or~~ followed- up in the PSUR." | |
| Lines 125-126 | | If the Specific AR FUQ is for a safety concern not in the RMP as it is not considered important, could it be associated to a safety concern identified and/or followed-up in the PSUR similar to the medicinal products without an RMP in place? Safety concerns can be listed as identified risks, potential risks or missing information and are included in the PBRER but not in the RMP.<br>**Proposed change**<br>If there is an RMP already in place, the (new) Specific AR FU should be included into the RMP (annex 4) if the associated safety concern is in the RMP. <u>If the safety concern relevant to the Specific AR FU is not in the RMP or is not considered for addition to an updated RMP, the Specific AR FUQ could be associated to a safety concern followed-up in the PSUR.</u> | |
| Lines 125-126 (and 138-140) | | In addition to proactive exchange of the information between MAHs, are MAHs encouraged to proactively check the information on published concerned RMPs by EMA (including MAHs for generics) since the RMPs for the new products main body, including Annex 4 (part of which the Specific AR FUQ) and Annex 6 will be published by EMA (effective as of 20-Oct-2023)? | |

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| Lines 125-126 | | "If there is a RMP already in place, the (new) Specific AR FUQ referring to the relevant safety concern should be included into the RMP (annex 4)."<br>We recommend a minor editorial revision.<br>**Proposed change**<br>"If there is a RMP already in place, the (new) Specific AR FUQ referring to the relevant safety concern should be included in~~to~~ the RMP (annex 4)." | |
| Lines 125-127 | | The addition of the AR FUQ in Annex 4 of the RMP should only be applicable when the specific AR FUQ is related to a safety concern listed in the EU RMP. If the safety concern is only listed in the PBRER, the form should not be included in the Annex 4 of the EU RMP.<br>**Proposed change**<br>"If there is a RMP already in place, the (new) Specific AR FUQ referring to the relevant safety concern **(retained as a safety concern in the RMP)**, should be included into the RMP (annex 4)."<br><br>It is described that the specific AR FUQ should be included in the RMP (annex 4). If the MAH uses a tool (e.g., query library) to request the relevant queries from the reporter and does not use a FUQ, what should be included in the RMP? Could the form be replaced by the list of queries that will be asked by the system/tool?<br><br>The statement 'As Specific AR FUQs are related to safety concerns which could impact the benefit/risk balance of a medicinal product' may suggest that ALL important potential risks/missing information would need a FUQ, especially when no PASS is in place. In practice, this is not always be feasible or useful. Propose changing 127 to state, 'Not all safety concerns would benefit from a Specific AR FUQ. Specific AR FUQs should focus on safety concerns that would benefit from detailed collection of information. The number of situations requiring such questionnaire is expected to be | |

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| | | limited and an assessment should be made regarding the value of a FUQ to further characterise a specific safety concern'. | |
| Lines 137-138 | | Clarification should be made about classification.<br>**Proposed change**<br>"Specific AR FUQs are considered as routine pharmacovigilance **beyond adverse reaction reporting and signal detection.**"<br><br>"Specific AR FUQs used by different applicants/MAHs (including for generics) for the same adverse reaction should be kept as similar as possible."<br>Comment:<br>Propose "involving the same active substance" be added to current statement.<br>Rationale:<br>To clarify that intent of the statement is related to Ars of the same active substance, not that Specific AR FUQs should be kept as similar as possible based on the AR alone.<br>Proposed change:<br>"Specific AR FUQs used by different applicants/MAHs (including for generics) for the same adverse reaction (involving the same active substance) should be kept as similar as possible." | |
| Line 139 | | Since it is planned to publish the approved AR FUQ, MAH should share the content of the AR FUQ only if not available on the EMA website.<br><br>**Proposed change**<br>"MAHs are strongly encouraged to share the content of their questionnaire(s) upon request from other MAHs **if not published on the EMA website**."<br><br>Though it is not expected, this allows instances where an element of an MAH's process may be listed in the FUQ.<br>**Proposed change** | |

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| | | From "MAHs are strongly encouraged to share the content of their questionnaire(s) upon request from other MAHs …"<br>To "The MAH may redact information deemed to be commercially confidential from these requests." | |
| Lines 138-140 | | "Specific AR FUQs should be kept as similar as possible among the MAHs (also generics) who are encouraged to share the content of their questionnaires." This is a big challenge and a burden for companies to agree on a unified specific FUQ, mainly for the generic companies. The specific FUQs should be adapted from originators or innovators to generic companies. Originators are accountable to create the specific FUQs and share them with the generic companies.<br>**Proposed change**<br>For the generic/biosimilar medicinal products, it is the responsibility of the originators/innovators of the medicinal product for the creation of specific FUQs which will be adopted by other MAHs for the generic/biosimilar products. | |
| Lines 138-139 | | "Specific AR FUQs used by different applicants/MAHs (including for generics) for the same adverse reaction should be kept as similar as possible."<br>There is reference to generics but not biosimilars. To avoid ambiguity, we recommend also stating biosimilars.<br>**Proposed change**<br>"Specific AR FUQs used by different applicants/MAHs (including for generics and biosimilars) for the same adverse reaction should be kept as similar as possible." | |
| Lines 142-143<br>Section 4.2 | | "Specific AR FUQs should focus on the collection of missing data of particular importance which were not initially provided by the reporter."<br>We recommend describing what considerations should be included in the content of the Specific AR FUQ in accordance with lines 134-136. We believe that this is the type of guidance that will be especially useful from a practical perspective and is therefore worth emphasizing.<br>**Proposed change** | |

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| | | "Specific AR FUQs should focus on the collection of missing data of particular importance which were not initially provided by the reporter and are not being collected as part of other tools in place which collect more data on the same risk and will be of additional value to better characterize the risk." | |
| Lines 144-145 | | "The Specific AR FUQ should be prefilled by the MAH with all the available information collected at the time of the initial report, to limit the burden on the reporters." → From an operational standpoint, it appears difficult for the MAH to prefill for each individual Specific FUQ the already provided information.<br>Proposed change: "To limit the burden of the reporter, the Specific FUQ should be **limited to the most essential information requests if possible.**" (Prefilled or not with the available information, to leave flexibility to the MAHs).<br><br>It would be simpler (and easier for the reporter) if it was possible to send a list of questions for the missing information only instead of sending a questionnaire where information has partially been included already. | |
| Lines 151-158 | | A preface could also be provided in the cover letter that is used to send out the Specific AR FUQ.<br>**Proposed change**<br>"[…] This preface could also be included in the cover letter/email body that is sent to distribute the Specific AR FUQ. It is then not necessary to repeat this within the questionnaire itself." | |
| Line 153<br>Section 4.2 | | The suggested wording for the preface of the specific AR FUQ states: "You have reported an adverse reaction(s) of XXXX for "medicinal product name". Here it seems suspected adverse reaction is meant.<br>**Proposed change**<br>"You have reported a suspected adverse reaction(s) of XXXX for "medicinal product name". | |

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| Lines 174-180<br>Section 4.2 Content | | This section speaks to the approval of the content of the Specific AR FUQ but only reflects the review if the Specific AR FUQ is included in the RMP annex 4. For Specific AR FUQs that are associated to a safety concern identified and/or followed-up in the PSUR, will these be reviewed as part of the PSUR? | |
| Line 177 | | "Therefore, Specific AR FUQs within an RMP usually require a review of the exact content by the competent authorities. However, the depth of the review may differ depending on e.g., the type of procedure or pharmacological considerations and may be limited to a consistency check."<br><br>Requesting clarification on the role of the competent authority (CA) on the review of the FUQ. I.e. is there a role for the National CA in the scope of a Centralized procedure or MRP?<br>**Proposed change**<br>Otherwise, propose to simplify by removing and including that review of a specific AR FUQ (only) occurs within the RMP review.<br><br>It would be helpful to clarify that update to existing FUQ would not trigger specific RMP submission. It is proposed to add after line 180: 'In case Specific AR FUQ included in Annex 4 of RMP are modified, updated FUQ can be included within the next planned RMP updates, i.e. there is no need to submit an updated RMP just for FUQ update.' | |
| Lines 177-178 | | "Therefore, Specific AR FUQs within an RMP usually require a review of the exact content by the competent authorities." It is not clear if the MAH can implement the AR FUQ only after the FUQ has been reviewed by the competent authorities or not.<br>**Proposed change**<br>Could you please clarify if the MAH can implement the AR FUQ **only** after the FUQ has been reviewed by the competent authorities or not. | |
| Lines 181-184 | | Caution to avoid being too specific with the MedDRA terms as this may not be clear for the reporter, could increase complexity of the FUQ and may require an update with 6 monthly MedDRA up-versioning. | |

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| | | **Proposed change**<br>"medical concept as represented in EU-RMP", instead of "MedDRA terms". | |
| Line 191 | | Review of FUQ could involve representatives of the target recipients, who may or may not be panel experts.<br>**Proposed change**<br>"representatives of target recipients" instead of "panel experts…" | |
| Lines 193-194 | | Specific AR FUQs in local language:<br>AR FUQ are designed for use by health care professional (HCP). It may be assumed that HCP has command of the English language, understands the questionnaire in English and can complete it accordingly. Therefore, sending AR FUQs in English to reporters seems appropriate unless otherwise required.<br><br>"Specific AR FUQs should be sent by the MAHs to the reporters in the local language of the reporter. The translations in local languages are the responsibility of the MAHs."<br>Given the education level of the HCPs and their good level of English, it is not always necessary translate the Specific AR FUQ.<br>**Proposed change**<br>"Specific AR FUQs ~~should~~ could be sent by the MAHs to the reporters in the local language of the reporter. The translations in local languages are the responsibility of the MAHs."<br><br>"The content of a Specific AR FUQ should focus on collecting the missing data of main importance for assessing the safety concerns in question and should be prefilled with available information to avoid requesting the primary source to repeat information."<br>AND "Specific AR FUQs should be sent by the MAHs to the reporters in the local language of the reporter. The translations in local languages are the responsibility of the MAHs." → Database is filled in English and so generation of prefilled FUQ may be complex and would need local completion or translation. Also, each time a new version of FUQ is available, this one will need to be (re)configured in the system, etc. | |

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| | | Proposed change: To leave flexibility to the MAHs depending on their own process and tool capability (please, also refer to the comment on lines 149-150 above). Not always feasible for all MAHs. | |
| Lines 203-205<br>Section 5 Publishing | | Per the Section 5 of the Guideline, does the agency plan to share "the existing Specific AR FUQs in place" even if they are not titled with the name of the medicinal product and the MedDRA term reflecting the underlying safety concern in the currently approved annex 4/or full RMP?<br><br>Will annex 4 of the RMP need to be provided by the MAH in a different format so each Specific AR FUQs for a product can be posted?<br>For Specific AR FUQs that are associated to a safety concern identified and/or followed-up in the PSUR what is the format and mechanism for provision of these for publishing? | |
| Lines 203-207 | | To clarify the difference between the heading within the RMP needing to include the medicinal product name and name of the Specific AR FUQ not including the medicinal product name (line 182-3)<br>**Proposed change**<br>From "Heading of the Specific AR FUQ should"<br>To "Heading of the Specific AR FUQ within the RMP annex 4 should"<br><br>For AR FUQs that apply to multiple products (which is highly likely given the preference for a consistent FUQ at the level of the medical concept), would it be necessary to create copies of the same FUQ with each one reflecting a different medicinal product in the header? | |

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| Lines 212-216 | | "…and should be discontinued when the safety concern has been sufficiently characterised". To be further detailed. Who (MAH, EMA) / when / based on what will it be decided that the risk is characterized?<br>**Proposed change**: "(...) and should be discontinued when the safety concern **is considered to be** sufficiently characterised **either by the MAH or the EMA (refer to section 6)**". | |
| Lines 218-231 | | Effectiveness of specific RA FUQ, outcome indicators should be analysed for all MAHs if the form is the same.<br>**Proposed change**<br>The MAHs assessment of the effectiveness could be presented in the RMP assessment report or in the tool and shared to all MAHs. | |
| Lines 218-225 | | (See general comments)<br>As per the draft guidance, outcome indicators may be used to "…substantiate how it contributes both to increase the quality of the data collected when compared with the initial information and to a better characterisation of the safety concern with a potential impact on the benefit/risk balance of the medicine. The outcome indicators should reflect the added value of the information collected compared to what already existed in the initial ICSR." While in theory this may seem to provide additional information, there are several factors that may provide a false perception of the quality of information provided. Some of these factors include recall bias by the TQ assessor (especially for AEs that may be more descriptive in nature than driven by recordable clinical lab values), delays between initial AE report and FUQ issuance, differences between reporter and treating physician, and existing burden on healthcare system. Further guidance or definition is required for 'increase of data quality' and 'better characterisation'<br>**Proposed change**<br>Removal of outcome indicators section. | |

| Line number(s) of the relevant text<br>*(e.g. Lines 20-23)* | Stakeholder number<br>*(To be completed by the Agency)* | Comment and rationale; proposed changes<br>*(If changes to the wording are suggested, they should be highlighted using 'track changes')* | Outcome<br>*(To be completed by the Agency)* |
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| | | "Targeted recipients" will be determined by the reporters of the AR and cannot necessarily be predetermined by the MAH.<br>**Proposed change**<br>can be used to monitor whether the reporters ~~targeted recipients (to be detailed by the MAHs)~~ of the Specific AR FUQs respond to the request for more information. | |
| Lines 232-233<br>Section 6 | | Effectiveness results should be submitted upon request of the competent authorities in a procedural framework (e.g., PSUR, RMP update).<br>For the reasons indicated above, an effectiveness analysis is not supported by (the majority of?) the available software (e.g. ARGUS) and such analyses, if at all feasible, would cause an extraordinary burden and questionable value added. Therefore, such analyses may only be justified in exceptional instances after feasibility check.<br>**Proposed change**<br>Effectiveness results can be requested by competent authorities if e.g., considered feasible to support the decision to discontinue a specific AR FUQ | |
| Lines 232-233 | | Clarification on where the effectiveness results should be provided in the PBRER/RMP. Should we expect an update of the RMP template?<br>**Proposed change**<br>"Effectiveness results should be submitted upon request of the competent authorities in a procedural framework (e.g., PSUR **section XXX**, RMP **section XXX** update)."<br><br>Removal of a Specific AR FUQ "…when a Specific AR FUQ is assessed as successful". This could be understood that a Specific AR FUQ can ONLY be (proposed to be) removed after such a formal assessment.<br>Other sources of information could lead to better characterisation of a risk and make the FUQ no longer required/useful.<br>Proposed change (if any): delete this notion, eg "Discontinuation and removal of a Specific AR FUQ in light of the characterisation of the safety concerns over time can be considered when the safety concerns is sufficiently characterised, for example…" | |

| Line number(s) of the relevant text<br>*(e.g. Lines 20-23)* | Stakeholder number<br>*(To be completed by the Agency)* | Comment and rationale; proposed changes<br>*(If changes to the wording are suggested, they should be highlighted using 'track changes')* | Outcome<br>*(To be completed by the Agency)* |
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| | | | |
| | | The removal of a FUQ is not only when it has been successful but could also be when other PV activities have been completed that result in a reclassification of a risk such that a FUQ is no longer needed.<br>**Proposed change**<br>Discontinuation and removal of a Specific AR FUQ in light of the characterisation of the safety concerns over time can be considered following ~~when a Specific AR FUQ is assessed as successful, for example led to~~ reclassification of an important potential risk as an important identified risk or a as a non- important risk (i.e. that would not warrant to be followed up through a safety concern in the RMP) or following ~~led to~~ the conclusion that there is no causal association ~~based on the additional information reported~~ and the important potential risk can be removed from the RMP and/or PSUR. | |
| Lines 234-239 | | Discontinuation and removal of a specific AR FUQ should be aligned between different MAHs of the same product/same indication<br>**Proposed change**<br>The tool will be updated with removal of Specific AR FUQ and rationale for this discontinuation | |

Please add more rows if needed.