Submission of comments on Guideline on Specific Adverse Reaction Follow-up questionnaires

Fields marked with * are mandatory.

Introduction to the survey on draft Guideline on Specific Adverse Reaction Follow-up questionnaires (Specific AR FUQ)

Please click here to be redirected to the guideline text. The public consultation is launched on 6 December 2023 until 9 February 2024.

Those participating in the public consultation are asked to please submit comments via the EU Survey tool, by using the specific table for each section. Please note that login is not required to fill in the survey.

Before submission, a draft of the comments can be saved in the EU Survey tool. Once submitted, comments can be edited (by 9 February 2024) by clicking on "Edit contribution" in the link https://ec.europa.eu/eusurvey/ and entering your ID contribution that can be found on the pdf copy of your submission sent via email.

Data Protection Statement

You are invited to provide your organisation or name, country and email address below for the purpose of this public consultation (for further information, please see EMA's Data Protection Statement below).

EMA Privacy Statement
All personal data provided within this survey questionnaire will be processed in accordance with Regulation (EU) 2018/1725 on the protection of individuals regarding the processing of personal data by the Union institutions and bodies on the free movement of such data.
This data protection statement provides details on how the Agency, in its capacity as data controller, will process the information that you have given in your questionnaire.
Internally, an 'Internal Controller' has been appointed to ensure the lawful conduct of this processing operation. The contact details of the Internal Controller are the following: Datacontroller.HumanMedicines@ema.europa.eu

Collection of data

EMA will collect all the personal data in this questionnaire, such as your name, organisation, your view on the topics subject to the survey, country of residence and your contact details. Please do not reveal any other personal data in the free text fields. EMA does not directly intend to collect personal data but to use the aggregated data for the purpose of this survey.
For the collection of data in this survey, EMA relies on the EU Survey external system. For more information on how EU Survey processes personal data, please see: https://ec.europa.eu/eusurvey/home/privacystatement

The EU Survey external system uses:

- Session "cookies" to ensure communication between the client and the server. Therefore, user's browser must be configured to accept "cookies". The cookies disappear once the session has been terminated.
- Local storage to save copies of the inputs of a participant to a survey to have a backup if the server is not available during submission or the user's computer is switched off accidentally or any other cause.
- The local storage contains the IDs of the questions and the draft answers.
- IP of every connection is saved for security reasons for every server request.
- Once a participant has submitted one's answers successfully to the server or has successfully saved a draft on the server, the data is removed from the local storage.

Your consent to the processing of your data

When you submit this questionnaire, you consent that EMA will process your personal data provided in the questionnaire as explained in this data protection statement. You may also withdraw your consent later at any time. However, this will not affect the lawfulness of any data processing carried out before your consent is withdrawn.

Start of data processing

EMA will start processing your personal data as soon as the questionnaire response is received.

Purpose of data processing

The purpose of the present data processing activity is to collect the views of stakeholders and/or concerned individuals in relation to the subject-matter of the survey. Your personal data may be used to contact you in relation to the feedback you have provided in response to the survey. No further processing of your personal data for any other purposes outside the scope of this specific context is envisaged.

Location of data storage

All data is stored within a secure data centre at the EMA premises which is password protected and only available to EMA staff members.

Publication of data

The following data collected in this questionnaire will be published on the EMA website at the time of issuing the final guideline subject to this survey:

- organisation name (the entity on behalf you respond to this survey)
- or your name (only if you do not respond to the survey on behalf of an organisation)

- your view/comments on the topics concerned

Country information and your email address will not be published.

Retention period

If you complete and submit this survey, your personal data will be kept until the results have been completely analysed and utilised. Your personal data will be deleted by EMA at the latest 5 years after the questionnaire response was submitted. The file of the data as published will remain stored for archiving purposes beyond the maximum 5 years-retention time of the submitted questionnaire responses.

Your rights

You have the right to access and receive a copy of your personal data processed, as well as to request rectification or completion of these data. You may also request erasure of the data or restriction of the processing in accordance with the provisions of Regulation (EU) 2018/1725. You can exercise your rights by sending an e-mail to Datacontroller.HumanMedicines@ema.europa.eu.

Complaints

If you have any complaints or concerns about the processing of your personal data, you can contact EMA's Data Protection Officer at dataprotection@ema.europa.eu.

You may also lodge a complaint with the European Data Protection Supervisor: edps@edps.europa.eu.

* Please confirm that you have read and understood the Data Protection Statement above and that you consent to the processing of your personal data.
  - (●) Yes
  - ( ) No

* Please confirm that you consent to possibly be contacted by EMA in relation to your survey responses to support the finalisation of the document subject this EU Survey.
  - (●) Yes
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* Please confirm that you consent to the publication of your organisation name, your name (only if you do not respond to the EU Survey on behalf of an organisation) and your survey responses on the EMA website at the time of issuing the final guideline subject to this survey.
  - (●) Yes
  - ( ) No

Should you not want to give consent to publish, please send your objections to Datacontroller.HumanMedicines@ema.europa.eu.

Please be aware that the sender of the comments is responsible to not disclose any personal data of third parties in the comments.

When you have filled in the EU Survey, please use the submission button at the end of the form to submit

the comments to the European Medicines Agency.

For additional information, please consult EMA's privacy statement.

Your details

* Name of organisation or individual

EFPIA

* Country of organisation or individual

Belgium

* Email

katarina.nedog@efpia.eu

If you respond on behalf of an organization, please allocate yourself a name abbreviation to be used as "Stakeholder name" in the comment tables below. If you comment as an individual, please ignore this field and use your full name as your "Stakeholder name".

Katarina Nedog

1. General comments

1. General comments on the draft Guideline Specific AR FUQ

	Stakeholder name *(to be repeated in all rows)*	General comment
1	EFPIA	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.
2	EFPIA	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.
3	EFPIA	We propose a consultation with the stakeholders; EMA and reporters (HCPs) who would be answering the concerned questionnaires to better understand the user friendliness.
4	EFPIA	In general, the term Adverse Reaction is used in the document where it seems that 'Suspected Adverse Reaction' is meant. Proposed change 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? 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

5	EFPIA	used to collect further information not only from spontaneous case reports but also from case reports arising from non-interventional studies – for the latter these would not necessarily be adverse reactions. 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.”
6	EFPIA	Is there any initiative led by the Agency to share this guidance with other non-EU competent authorities?
7	EFPIA	What is the planned timeline for the Guidance to become effective? What is the Agency’s expectation for MAH to implement the guideline when it becomes effective: -What will be the trigger to use or replace the existing MAH questionnaires? -How will MAH phase this initiative into existing RMPs?
8	EFPIA	Does the Agency plan to publish specific FUQs for all Designated Medical Events as per the EMA list? 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) “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. 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

9	EFPIA	/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 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. 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. 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. Proposed change for lines 226-231: “Competent authorities may request to the MAHs to provide a 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. General Comments on the Tool throughout the document: When will the Tool and its use be available to MAHs. Is the plan to use the same Tool as the RMP publication Tool? What exactly will the Tool accommodate? (special AR FUQ without detail or any detail, i.e. responses or potentially data that may be confidential). Will there be training sessions provided for its use? What expectations are there for use of the Tool.

		What if there are no paper documents (FUQs) but electronic formats or other such as web-based tools/portals, how will this be accommodated. Is the Tool used to send out AR FUQs to reporters or is the Tool aimed only at capturing AR FUQ (the questionnaires themselves)? Will MAH be expected to share AR FUQs outside of the Tool in parallel to the Tool? 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? Who will be responsible for making clear in the Tool that an AR FUQ is retired?
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2. Specific comments

Executive summary

2. Specific comments on text

Executive summary

	Line number(s) of the relevant text *(e.g. 20-23)*	Stakeholder name *(to be repeated in all rows)*	Comment and rationale	Proposed guidance text
1	Line 41 Exec Summary	EFPIA	"…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)	Proposed change: Amend text to "...developed by the MAH at the request of NCAs or the EMA…".
2	Lines 48-51	EFPIA	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.”)	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.’
3	Lines 52-54 (and 144-145)	EFPIA	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?	Proposed change: 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.”
4	Line 57 and along the document	EFPIA	“Dissemination” means distribute, so that it reaches many people.	Proposed change: “way to contact the reporter”

5	Lines 59-61 Exec Summary	EFPIA	“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).” 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.	Proposed change 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)
6	Line 64	EFPIA	“Overall, in addition to existing GVP guidelines…”	Proposed change We recommend adding references to the existing GVP guidelines.
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2.1. Introduction (background)

2.1. Introduction (background)

	Line number(s) of the relevant text *(e.g. 20-23)*	Stakeholder name *(to be repeated in all rows)*	Comment and rationale	Proposed guidance text
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2.2. Scope

2.2 Scope

	Line number(s) of the relevant text *(e.g. 20-23)*	Stakeholder name *(to be repeated in all rows)*	Comment and rationale	Proposed guidance text
1	Lines 87-88	EFPIA	"The scope of this guidance is limited to specific (or targeted) AR FUQs requested by the competent authorities." The term "targeted" is stated in brackets in relation to the FUQs. However, it is unclear whether "targeted" and "specific" can be used interchangeably.	Proposed change Please clarify what is meant by the distinction between the terms "targeted" and "specific" or whether they are intended to be used interchangeably.
2	Lines 89-90	EFPIA	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?	
3	Lines 88-90	EFPIA	To distinguish between general and AR specific FUQs	Proposed change (if any): from "… for FUQs." To "… for general FUQs."
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2.3. Legal basis

2.3 Legal basis

	Description of the element of the figure	Stakeholder name *(to be repeated in all rows)*	Comment and rationale	Proposed guidance text
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2.4. Guidance on the use of the Specific AR FUQ

2.4.1. Requirements for a Specific AR FUQ

2.4. Guidance on the use of the Specific AR FUQ

2.4.1. Requirements for a Specific AR FUQ

	Line number(s) of the relevant text *(e.g. 20-23)*	Stakeholder name *(to be repeated in all rows)*	Comment and rationale	Proposed guidance text
1	Lines 116-140	EFPIA	Guidance on the use of the specific AR FUQ: 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. 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.	
2	Lines 118-121	EFPIA	“Adverse reactions for which Specific AR FUQs are considered can be defined as those referring to safety concerns4 (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.” 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 special situations, a Specific AR FUQ may be necessary for further characterization of the risk.”	Proposed change “Adverse reactions for which Specific AR FUQs are considered can be defined as those referring to safety concerns4 (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. 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

			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.	necessary for further characterization of the risk.”
3	Lines 121 and 127	EFPIA	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.	Proposed change 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.”
4	Lines 122-124 Section 4.1	EFPIA	The wording is not covering the situation when the list of safety concerns in the PSUR has additional risks compared to the RMP.	Proposed change 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.
5	Lines 122-124	EFPIA	“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	Proposed change “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

			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.)	to a safety concern followed-up in the PSUR."
6	Lines 125-126	EFPIA	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.	Proposed change 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. 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.
7	Lines 125-126 (and 138-140)	EFPIA	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)?	
8	Lines 125-126	EFPIA	"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)." We recommend a minor editorial revision.	Proposed change "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)."

9	Lines 125-127	EFPIA	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.	Proposed change “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).” 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? 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 limited and an assessment should be made regarding the value of a FUQ to

				further characterise a specific safety concern'.
10	Lines 137-138	EFPIA	Clarification should be made about classification.	Proposed change “Specific AR FUQs are considered as routine pharmacovigilance beyond adverse reaction reporting and signal detection.” “Specific AR FUQs used by different applicants/MAHs (including for generics) for the same adverse reaction should be kept as similar as possible.” Comment: Propose “involving the same active substance” be added to current statement. Rationale: 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. Proposed change: ”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.”
				Proposed change “MAHs are strongly encouraged to share the content of their questionnaire(s) upon request from other MAHs if not published on the EMA website.”

11	Line 139	EFPIA	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.	Though it is not expected, this allows instances where an element of an MAH's process may be listed in the FUQ. Proposed change From "MAHs are strongly encouraged to share the content of their questionnaire(s) upon request from other MAHs …" To "The MAH may redact information deemed to be commercially confidential from these requests."
12	Lines 138-139	EFPIA	"Specific AR FUQs used by different applicants/MAHs (including for generics) for the same adverse reaction should be kept as similar as possible." There is reference to generics but not biosimilars. To avoid ambiguity, we recommend also stating biosimilars.	Proposed change "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."
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2.4.2. Content of the Specific AR FUQ: aspects to be considered

2.4.2. Content of the Specific AR FUQ: aspects to be considered

	Line number(s) of the relevant text (e.g. 20-23)	Stakeholder name (to be repeated in all rows)	Comment and rationale	Proposed guidance text
1	Lines 142-143 Section 4.2	EFPIA	"Specific AR FUQs should focus on the collection of missing data of particular importance which were not initially provided by the reporter." 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.	Proposed change "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."
2	Lines 144-145	EFPIA	"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.	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). 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.
				Proposed change "[…] This preface could also be included in

3	Lines 151-158	EFPIA	A preface could also be provided in the cover letter that is used to send out the Specific AR FUQ.	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."
4	Line 153 Section 4.2	EFPIA	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.	Proposed change "You have reported a suspected adverse reaction(s) of XXXX for "medicinal product name".
5	Lines 174-180 Section 4.2 Content	EFPIA	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?	
6	Line 177	EFPIA	"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." 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	Proposed change Otherwise, propose to simplify by removing and including that review of a specific AR FUQ (only) occurs within the RMP review. 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

			CA in the scope of a Centralized procedure or MRP?	need to submit an updated RMP just for FUQ update.'
7	Lines 177-178	EFPIA	“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.	Proposed change 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.
8	Lines 181-184	EFPIA	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.	Proposed change “medical concept as represented in EU-RMP”, instead of “MedDRA terms”.
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2.4.3. Format of the Specific AR FUQ

2.4.3. Format of the Specific AR FUQ

	Line number(s) of the relevant text (e.g. 20-23)	Stakeholder name (to be repeated in all rows)	Comment and rationale	Proposed guidance text
1	Line 191	EFPIA	Review of FUQ could involve representatives of the target recipients, who may or may not be panel experts.	Proposed change “representatives of target recipients” instead of “panel experts…”
2	Lines 193-194	EFPIA	Specific AR FUQs in local language: 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. “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.” Given the education level of the HCPs and their good level of English, it is not always necessary translate the Specific AR FUQ.	Proposed change “Specific AR FUQs 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.” “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.” 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. 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.
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2.4.4. Dissemination of the Specific AR FUQ

2.4.4. Dissemination of the Specific AR FUQ

	Line number(s) of the relevant text (e.g. 20-23)	Stakeholder name (to be repeated in all rows)	Comment and rationale	Proposed guidance text
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2.5. Publishing of Specific AR FUQ

2.5. Publishing of Specific AR FUQ

	Line number(s) of the relevant text *(e.g. 20-23)*	Stakeholder name *(to be repeated in all rows)*	Comment and rationale	Proposed guidance text
1	Lines 203-205 Section 5 Publishing	EFPIA	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? 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? 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?	
2	Lines 203-207	EFPIA	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) Proposed change From “Heading of the Specific AR FUQ should” To “Heading of the Specific AR FUQ within the RMP annex 4 should”	

			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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2.6. Considerations on discontinuation and removal of Specific AR FUQ

2.6. Considerations on discontinuation and removal of Specific AR FUQ

	Line number(s) of the relevant text *(e.g. 20-23)*	Stakeholder name *(to be repeated in all rows)*	Comment and rationale	Proposed guidance text
1	Lines 218-231	EFPIA	Effectiveness of specific RA FUQ, outcome indicators should be analysed for all MAHs if the form is the same.	Proposed change The MAHs assessment of the effectiveness could be presented in the RMP assessment report or in the tool and shared to all MAHs.
2	Lines 218-225	EFPIA	(See general comments) 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	Proposed change Removal of outcome indicators section. Proposed change can be used to monitor whether the reporters of the Specific AR FUQs respond to the request for more information.

			and treating physician, and existing burden on healthcare system. Further guidance or definition is required for 'increase of data quality' and 'better characterisation' "Targeted recipients" will be determined by the reporters of the AR and cannot necessarily be predetermined by the MAH.	
3	Lines 232-233 Section 6	EFPIA	Effectiveness results should be submitted upon request of the competent authorities in a procedural framework (e.g., PSUR, RMP update). 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.	Proposed change Effectiveness results can be requested by competent authorities if e.g., considered feasible to support the decision to discontinue a specific AR FUQ
4	Lines 232-233	EFPIA	Clarification on where the effectiveness results should be provided in the PBRER /RMP. Should we expect an update of the RMP template?	Proposed change "Effectiveness results should be submitted upon request of the competent authorities in a procedural framework (e.g., PSUR section XXX, RMP section XXX update)."
			Removal of a Specific AR FUQ "…when a Specific AR FUQ is assessed as successful". This could be understood that a Specific	Proposed change (if any): delete this notion, e.g., "Discontinuation and removal of a Specific AR FUQ in light of the

5	Lines 232-233	EFPIA	AR FUQ can ONLY be (proposed to be) removed after such a formal assessment. Other sources of information could lead to better characterisation of a risk and make the FUQ no longer required/useful.	characterisation of the safety concerns over time can be considered when the safety concerns is sufficiently characterised, for example…"
6	Lines 232-233	EFPIA	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.	Proposed change Discontinuation and removal of a Specific AR FUQ in light of the characterisation of the safety concerns over time can be considered following 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 the conclusion that there is no causal association and the important potential risk can be removed from the RMP and/or PSUR.
7	Lines 234-239	EFPIA	Discontinuation and removal of a specific AR FUQ should be aligned between different MAHs of the same product/same indication	Proposed change The tool will be updated with removal of Specific AR FUQ and rationale for this discontinuation
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Other comments

Other comments

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Thank you

Thank you for your contribution.

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