EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 June 2016

Submission of comments on GVP Module V – Risk management systems (Rev 2) (EMA/838713/2011)

Comments from:

Name of organisation or individual
ACRO (Association of Clinical Research Organizations)

Please note that these comments and the identity of the sender will be published unless a specific justified objection is received (please see privacy statements: http://www.ema.europa.eu/ema/index.jsp?curl=pages/home/general/general_content_000516.jsp&mid *and* http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/02/WC500123144.pdf*).*

When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF) (see Introductory cover note for the public consultation of GVP under Practical advice for the public consultation: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/02/WC500123145.pdf).

1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment	Outcome *(To be completed by the Agency)*
	The Association of Clinical Research Organizations (ACRO) represents the world's leading, global clinical research organizations (CROs). Our member companies provide a wide range of specialized services across the entire spectrum of development for new drugs, biologics and medical devices – from discovery, pre-clinical, proof of concept and first-in-man studies through post-approval and pharmacovigilance research. With more than 110,000 employees engaged in research activities around the world (including more than 30,000 in Europe), ACRO advances clinical outsourcing to improve the quality, efficiency and safety of biomedical research. Each year, ACRO member companies conduct more than 9,000 clinical trials involving nearly two million research participants in 142 countries. On average, each of our member companies works with more than 500 research sponsors annually. ACRO welcomes and supports the draft Revision 2 of the GVP Module V – Risk Management Systems guideline. ACRO especially welcomes the focus on implementing the principles of the ICH E2C (R2) Question and Answer document on the Periodic Benefit-Risk Evaluation Report and the ICH E2E guideline on Pharmacovigilance Planning in recognising that risk management planning	

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	should be proportionate and targeted to adverse reactions that have an impact on the benefit-risk balance of the product when further characterised and/or if not managed appropriately in clinical practice. The consultation document requested feedback on four specific questions, and ACRO is pleased to answer these as follows: 1. *The updated risk definitions and guidance on Part II Module SVII of the RMP may lead, in the post-authorisation phase, to a list of safety concerns in the RMP that is a subset of the list of the product safety concerns as defined in the PSUR. What should be the priority of the GVP Module V: a focused RMP list of safety concerns or the full alignment with the PSUR content?* It is ACRO's view that the RMP should focus on risks that are important because of their medically significant outcomes for patients or public health. Not all adverse reactions pose important risks, and therefore ACRO considers that the RMP should address a focused list of safety concerns, which will be a sub-set of the product safety concerns defined in the PSUR. 2. *Should studies conducted by the MAH but neither*	

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	required nor imposed by the competent authority (previously classified as category 4 studies) be included, for information, in the RMP annex 2? ACRO recommends that these studies should be included, for information, in the RMP Annex 2 so that the tabulated information in Annex provides a complete summary of the pharmacoepidemiological study programme, whether or not individual studies are mandated. 3. *Should the additional risk minimisation materials as they were distributed in the Member States be included in the annexes of the RMP (i.e. RMP annex 6 – part B)?* 4. *Should section V.B.10 be maintained or deleted (i.e. in the light of the RMP terminology described in V.A.1.)?* ACRO considers section V.B.10 to be helpful in explaining the relationship between the RMP and the PSUR, and therefore recommends the section is maintained. ACRO further recommends that the section is strengthened by emphasising that not all adverse reactions pose important risks, and therefore the RMP should address a focused list of safety concerns, which will be a sub-set of	

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	the product safety concerns defined in the PSUR.	

2. Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
155 - 216		Comment: Rather than “Without prejudice to the definition of terminology provided in GVP Annex 1”, ACRO recommends that, to avoid confusion, the guideline should state clearly that the basic definition of terms is as stated in GVP Annex 1 and that the purpose of section V.A.1 is to further clarify the terminology within the context of risk management planning. Proposed change (if any): State clearly that GVP Annex 1 definitions apply and that the purpose of section V.A.1 is to further clarify the terminology within the context of risk management planning.	
251 - 269		Comment: The text correctly states that “The principal organisations directly involved in medicinal products’ risk management planning are applicants/marketing authorisation holders and the competent authorities”. However, the section describes only the relevant responsibilities of the marketing authorisation applicant/holder. ACRO recommends that the responsibilities of the competent authorities are also described. Proposed change (if any): Add text to explain the relevant responsibilities of the competent authorities.	
271 - 276		Comment: In explaining the advantages of the modular	

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		format of the RMP, ACRO recommends retaining the text of the current (R1) version of the guideline that allows for modules to be effectively “locked” until new data needs to be added. ACRO considers this an important point that is missing from the R2 draft. Proposed change (if any): Add the text of the current (R1) version of the guideline that allows for modules to be effectively “locked” until new data needs to be added.	
327		Comment: Given that the RMP should consider important risks associated with off-label use (line 186), ACRO recommends that it is made clear whether the term “indications” as used here means only those indications applied for/authorised or also potential off-label indications. Proposed change (if any): Make clear whether “indications” as used here means only those indications applied for/authorised or also potential off-label indications.	
410 - 416		Comment: ACRO recommends that the list of important non-clinical safety findings should also include a summary of any important drug interactions identified in non-clinical studies. Proposed change (if any): Add important drug interactions identified in non-clinical studies to the list of important non-clinical safety findings that should be summarised.	

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440 – 441 and 449		Comment: The text in line 449 refers to “age/gender/ethnic origin tables” but there is nothing otherwise to indicate that ethnic origin may be an important factor in risk management planning. ACRO recommends that the statement in lines 440 – 441 that “other stratifications should be provided where this adds meaningful information for risk management planning purposes” should be accompanied by appropriate examples (e.g., ethnic origin). Proposed change (if any): Add examples (including ethnic origin) to the statement “other stratifications should be provided where this adds meaningful information for risk management planning purposes”.	
454 - 468		Comment: The current (R1) version of the guideline includes the statement “Any experience of patients with different disease severities should be discussed, particularly if the proposed indication is restricted to those patients with a specific disease severity.” ACRO considers this an important point that should also be included in the new version of the guideline. Proposed change (if any): Add the statement “Any experience of patients with different disease severities should be discussed, particularly if the proposed indication is restricted to those patients with a specific disease severity.”	

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775		Comment: ACRO recommends adding “Non-imposed PASS” to table V.3 so that it provides a complete overview of additional pharmacovigilance activities, whether or not individual studies are mandated. Proposed change (if any): Add “Non-imposed PASS” to table V.3.	
824		Comment: There is an incorrect reference to “see V.B.7” within section V.B.7. Proposed change (if any): Correct the reference.	
1087 - 1100		Comment: ACRO recommends that this section, which explains the relationship between the RMP and the PSUR, is strengthened by emphasising that not all adverse reactions pose important risks, and therefore the RMP should address a focused list of safety concerns, which will be a sub-set of the product safety concerns defined in the PSUR. Proposed change (if any): Add a statement to explain that not all adverse reactions pose important risks and therefore the RMP should address a focused list of safety concerns, which will be a sub-set of the product safety concerns defined in the PSUR.	

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		ACRO thanks the Agency for this comment opportunity. Please do not hesitate to contact ACRO if we can provide additional information (knoonan@acrohealth.org)	

Please add more rows if needed.