27 April 2021

Submission of comments on 'GVP Module XVI Addendum II – Methods for effectiveness of evaluation' (EMA/419982/2019)

Comments from:

| Name of organisation or individual |
| --- |
| 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).*

1. General comments

| # | Stakeholder number*(To be completed by the Agency)* | General comment (if any) | Outcome (if applicable)*(To be completed by the Agency)* |
| --- | --- | --- | --- |
|  |  | Comment: Please consider further recommendations from ISPE Whitepaper 2016: ‘Evaluating the Effectiveness of additional Risk Minimisation Measures via Surveys in Europe: Challenges and Recommendations’. <https://pharmacoepi.org/pub/?id=f46953df-de69-31e7-8f74-725bd7fa685f> |  |
|  |  | **Comment:** Measuring effectiveness is a joint effort between EMA/NCAs and MAHs, therefore, guidance on the agreement process for defining success metrics would be welcome, e.g. on threshold for determining whether intervention is successful.For most situations agreeing on standards should be possible. It can be added that if these standards cannot be met that this is to be justified. Without pre-defined expectations, databases might not evolve to accommodate effectiveness assessment. There also might be a risk of different interpretation and application during the assessment by the member states’. |  |
|  |  | **Comment**:The considerations for the data sources are not specific to the investigation of the effectiveness of risk management procedures – they could also apply to PASS or PAES. It is noted that the PAES guidance also contains scientific guidance around the use of health care databases, yet slightly different. It is proposed to create a separate scientific guidance on data sources to which the current guidance and PASS and PAES guidance can refer, preferably taking into account the feedback from the current review for its content.  |  |

1. Specific comments on text

| # | Line number(s) *(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)* |
| --- | --- | --- | --- | --- |
|  | 55-60 |  | Comment: we assume this will also be impacted with the operation of the EU DARWIN network in timeProposed change (if any): Suggest referring to DARWIN network in addition to ENCePP. |  |
|  | 62 |  | Comment: (Please see also comment on GVP Module XVI Draft revision 3: Line 615, Lines 648-654, and Lines 673-685) What about the use of PROMs/PREMs and patient-orientated outcomes? We would suggest considering these as well as examples of outputs of qualitative research into knowledge adoption.Proposed change (if any): Please consider adding language about the potential role of PROMs/PREMs and patient-orientated outcomes. |  |
|  | 62 |  | Comment: It might be beneficial to add examples of how qualitative methods contribute to evaluation; e.g. support of in-depth understanding ‘why’ RMM may demonstrate less effectiveness than hypothesised. Proposed change (if any): |  |
|  | 62-88 |  | Comment: From the perspective of non-prescription drugs (eg OTC medications), social media listening might have deserved being specifically addressed in this section. Data mining of social media conversations regarding medication use allows a better understanding of individuals’ perceptions and knowledge about medications, often uncovering conversations that are not conducted within the healthcare setting. These findings may be used to improve healthcare by pre-emptively addressing areas of concern, and also demonstrate that more easily accessible healthcare information for the general public would be beneficial. It may be interesting to repeat those studies to determine if any changes in how drugs are discussed on social media platforms since the introduction of risk minimization measures. The advantage of using web-based information collection includes the ability to gather information from individuals who might not otherwise take part in studies, as well as the ability to conduct global analyses with real-time collection from a broad sociodemographic range. While this method has advantages over traditional information-gathering, there are also limitations, including the fact that this is based on the web user’s declaration and can be heavily driven by advocacy groups.Proposed change (if any): propose some guidance on web-based information collection regarding use of social media listening and web based information to monitor impact of Risk MM plan |  |
|  | 72 |  | **Comment:** Consider highlighting the need for diverse viewpoints collated via methodologically robust tools versus “saturation of data” (of which the meaning here might be unclear) when referencing information gleaned from focus groups/interviews.**Proposed change (if any):** |  |
|  | 82 |  | **Comment:** The underlying epidemiology of the patient or healthcare population of interest should inform the choice of sample strategy; representativeness may require oversampling specific subpopulations due to possible participation barriers.**Proposed change (if any):**  |  |
|  | 87-88 |  | **Comment:** Response bias or recall bias? If response bias, consider adding that basic demographics/characteristics for responders and non-responders should be compared to assess the possible introduction of systematic error. If recall bias, consider specifying it as such and update “expected” to “potential”.**Proposed change (if any):**  |  |
|  | Lines 90-95 |  | Comment: We would like the Agency to clarify whether the use of an application would be appropriate here and if yes to add language accordingly.Proposed change (if any): add language accordingly. |  |
|  | 101-104 |  | **Comment:** Flaws in the study design, data collection or analyses could lead to deviations from the “truth”. Proposed change (if any): Consider broadening the paragraph to highlight the need to consider bias throughout the development, administration & interpretation of the surveys. Highlighting the need for non-leading questions within the survey instrument as well. |  |
|  | 106 |  | **Comment: Missing “are”...** **Proposed change (if any):** “Patient registries are...” |  |
|  | 120 |  | **Comment:** Consider adding the voluntary nature of registries as a potential limitation.**Proposed change (if any):** |  |
|  | 131-132 |  | Comment: In section XVI.Add.II.2.1.4. Medical records it is stated that *“Where relevant outcome variables are not routinely collected, complementary primary data collection may be considered.”* The collection of solicited data to compensate for unavailable routinely collected data may introduce bias. Proposed change (if any): add statement to indicate that a limitation of this approach is the introduction of possible bias. |  |
|  | 133-135:  |  | Comment: We would like to clarify that this is not a universal issue and some datasets are able to include both prescribing and dispensing information. However, no dataset includes actual adherence, i.e., did a patient take the therapy as prescribed.Proposed change (if any): Suggest amending the wording to reflect the above. |  |
|  | 145-149 |  | Comment: Another limitation is the periodicity of refresh in the data over time.Proposed change (if any): Suggest amending the wording to include the above: “Furthermore, information on inpatient medication and diagnoses made in hospitals may not be available. Another limitation is the periodicity of refresh in the data over time” |  |
|  | 151-154 |  | Comment: We would like to comment that data linkage is currently impossible in many Members States and that it should be reflected/acknowledged in this GVP Module.Proposed change (if any): suggest adding after the first paragraph: ‘Unfortunately in many Member States data linkage is prohibitively difficult under local and regional privacy restrictions’ |  |
|  | 156 - 161 |  | Comment: Readability may benefit from structuring the “i - iv integrated listing to a bullet format. Proposed change (if any): insert bullets “i – iv” |  |
|  | 156-168  |  | Comment: We would like to comment that also the resourcing, emphasis and infrastructure for spontaneous reporting in each Member State is heterogenous and ought to be addressed.Proposed change (if any): Suggest amending the wording to reflect the above. |  |
|  | 169 |  | Comment: if we have a factor influencing for data sources, do we need one for methods? And if we do, do we need anything in between intro (36) and data collection (50) that refers to the overall objective of in the context of the underlying risk i.e. start with the end in mind type of approach (please see also our comment on the need for an overview table).Proposed change (if any): Please amend the wording to reflect the above. |  |
|  | Lines 178-179 |  | Comment: it is likely to be extremely difficult for the MAH to realistically verify the reliability of data from secondary data sources.Proposed change (if any): Suggest to re-phrase to reflect the above. |  |
|  | 194\_196 |  | Comment: “In case of evaluating non-targeted effects, the study population should preferably not be limited to the population targeted by the product-specific regulatory action” It is unclear what is meant by this statement, especially the expected study populationProposed change (if any): please clarify  |  |
|  | Line 207 |  | Comment: when would it be appropriate to monitor non-targeted effects?Proposed change (if any): |  |
|  | Line 203 figure |  | Comment: Case study is listed as a method for evaluating effectiveness of RRM. It is unclear how to evaluate effectiveness with a case study? (Are case series meant?) Chart review is not an effectiveness method on its own. A cross-sectional study or a drug utilization study can include chart review, for example.Proposed change (if any): |  |
|  | 295 - 296 |  | Comment: Only the demonstration kit for the management of Important Identified Risk should be considered as Educational Material. Proposed change (if any): A demonstration kit for the management of Important Identified Risk is an educational material and is a tool that trains healthcare professionals or supports healthcare professionals intraining the patient for administering the medicinal product safely. |  |
|  | 327-331 & 353-357: same as 327-331 |  | Comment: We would like to make the wording about control group clearer as it appears to be unfeasible while required to establish such group as per proposed wording.Proposed change (if any): we suggest swapping the paragraph around and start with saying it is generally not possible to include a control group, but on the occasion where it is feasible a control group should be included. |  |
|  | 414-425 |  | Comment: Reporting items derived from the RIMES Statement for reporting results of effectiveness studies is incorporated in the Table XVI.Add.II.1.: Additional PASS reporting items for effectiveness study reports. It is not clear whether these reporting items are mandatory to be utilised by the MAHs for reporting results of effectiveness studies. Proposed change (if any): |  |
|  | Lines 414-425 |  | Comment: Consideration should be given to inhibitors of RMMs implementation in the marketplace (i.e., not directly in control of the Marketing Authorisation Holder). We suggest that EMA needs to consider how to include Member State active participation in a RMM implementationProposed change (if any):  | x |
|  | 425 |  | Comment“Table XVI.Add.II.1.: Additional PASS reporting items for effectiveness study reports”. This table is very helpful and the guidance would be strengthened considerably if elements of this table are further elaborated on.  |  |

Please add more rows if needed.