13 December 2012
EMA/806339/2012
Patient Health Protection

Comments received from public consultation on good pharmacovigilance practices (GVP)

GVP Module III – Pharmacovigilance inspections

The draft of this module was released for public consultation between 27 June and 24 August 2012. The module has been revised, taking the comments received into account.

Those who participated in the public consultation were asked to submit comments using a specific template.

The comments received are published, identifying the sender's organisation (but not name). Where a sender has submitted comments as an individual, the sender's name is published.

The European Medicines Agency thanks all those who participated in the public consultation for their contributions.

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An agency of the European Union

<Date of submission>

Submission of comments on 'good pharmacovigilance practices module III – Pharmacovigilance inspections' (EMA/119871/2012)

Comments from:

Name of organisation or individual
AEFI (Spanish Association of Pharmaceuticals in Industry)

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*).*

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment

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')*
110-112 Information on the conduct and outcome of pharmacovigilance inspections and the follow-up and evaluation of the consequences may be made publicly available as part of the overall transparency of pharmacovigilance activities.		Comment: We consider that this information is useful for other regulatory authorities. Regarding the provision of this information to other MAHs it should be considered how this information should be provided. We consider that the information should be anonimised, of non commercially confidential nature, and focused in general inspection findings (eg: inadequacy in construction of literature searching), like the "Common inspections findings". Regarding the provision of this information to consumers and health professionals, neither Regulation (EU) Nº 1235/2010 nor Directive 2010/84/EU specify on trasparency on providing the inspections results as the minimal information to be made publicly available. Please confirm this term. Unless its public disclosure is necessary for the protection of public health (and therefore, a safety problem), we consider that information on inspection finding should not be made publicly available. Proposed change (if any): Information on the conduct and outcome of pharmacovigilance inspections and the follow-up and evaluation of the consequences may be made available between national competent authorities and the Agency. This information might made available to other MAHs as general information on common inspections findings.
Line 217-218		Comment: For announced inspections it is important to anticipate a minimum deadline for said announcement, harmonized within all the EU countries, so that companies can ensure the availability of their personnel with enough time and include the appropriate timelines and responsibilities in their internal SOPs to be prepared for an inspection.

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')*
		Proposed change (if any): It is anticipated that the majority of inspections will be announced i.e. notified **30 days** in advance to the inspected party, to ensure availability of relevant individuals for the inspection.
Line 328-329		Comment: According to Module VI (VI.B.3: follow-up of reports), MAH should follow-up events of special interest such as reports of pregnancy, death of a patient, or cases reporting new risks or changes in the known risks. This module does not consider the consumer reports as of special interest, the same way as it does not consider the health professional ones. Proposed change (if any): Follow-up and outcome recording, for example final outcome of cases of exposure in pregnancy ~~**and medical confirmation of consumer reported events.**~~
Line 575		Comment: The document should facilitate the reader's access to the mentioned paper via Internet. Proposed change (if any): The general role of the PRAC is detailed in the PRAC mandate and rules of procedures ***(include web page)***
Line 683-685		Comment: As commented above the information on inspections and outcome should only name individual MAH in exceptional circumstances. Further clarity on what information will be published how frequently and in what medium is requested. Proposed change (if any): III.C.6. Transparency Information on the conduct and outcome of pharmacovigilance inspections and their follow-up will be made publicly available without prejudice to Regulation 1049/2001.

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')*
		Information about inspection findings should be useful both as a learning tool for other MAH and for regulators. It is therefore important that data are analysed periodically and published in form of aggregated reports listing the most frequent and most important types of findings. Individual MAH should only be mentioned in connection with potential public impact.

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

17 August 2012

Submission of comments on 'good pharmacovigilance practices module III – Pharmacovigilance inspections' (EMA/119871/2012)

Comments from:

Name of organisation or individual
AESGP

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*).*

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	III.C.6 We are concerned about the information that could be released to the public. What type of information will be released and under which timeframe? This should be further explicated in that section and "full release" restricted to significant major findings or when there is an impact of public health.

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')*
95-97		Comment: Proposed change (if any): Please specify that information of other Member States, the Agency and the Commission will take place in case of critical and significant major findings as indicated in other parts of the document.
110-112		Comment: Proposed change (if any): "Information... may be made publicly available ~~as part of the overall transparency of pharmacovigilance activities~~ in case of critical and significant major findings; resolution of those should also be made publicly available"
140-141		Comment: A change in the risk-benefit balance is not a compliance issue that should trigger an inspection – only a change that has not been handled appropriately by the MAH should trigger an inspection Proposed change (if any): Clarify that it is not just a change to the risk-benefit balance that should act as a trigger
280		Comment: Proposed change (if any): Please use the same wording as in Module II, Section IIB.4.1., i.e. contact person, responsible for pharmacovigilance

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')*
287		Comment: How would the Agency know that the management of the PSMF has transferred? Would it be obvious from the document who is managing it? (Only the summary details of the PSMF are included in EVMPD per Article 57, ie. location of PSMF, not who is managing it). Also, is this sentence referring to transfer of management to a third party? Proposed change (if any):
329		Comment: "medical confirmation of consumer reported events" – in some cases, the consumer may not have sought medical attention so medical confirmation would not be applicable / not possible to obtain. Proposed change (if any): "medical confirmation of consumer reported events (where applicable"
349-355		Comment: References to GCP aspects should not be part of routine pharmacovigilance inspections. Proposed change (if any): Line 349: delete "interventional and" Lines 350 + 351: deleted both lines Lines 354-355: delete "annual safety reports, development safety update reports (DSURs) and"
440-445		Comment: Sharing of information also concerns the MAH.

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')*
		Proposed change (if any): "Sharing information and communication between MAHs, inspectors and assessors is important for the proper follow-up of inspections. Recommendations on follow-up actions will be provided in the pharmacovigilance inspection reports and others may arise from the interaction between MAHs, inspectors and assessors in line with the EU pharmacovigilance inspection procedure on inspection follow-up, which will be included in the compilation of community procedures on pharmacovigilance inspections mentioned in III.B.5."
460-461		Comment: In the event of non-compliance, possible regulatory options include the following, in accordance with guidance and, as applicable, rules set in legislation – this sentence is rather complex and very legal in language Proposed change (if any):

Please add more rows if needed.

<Date of submission>

Submission of comments on Module III – Pharmacovigilance inspections EMA/119871/2012

Comments from:

Name of organisation or individual
British Association of Quality Assurance

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*).*

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	Is there an opportunity for the MAH to comment on the inspection process by the authorities? We have experienced professionally run, well organized inspections and others, have not been so well organized.
	To ensure compliance with a MAH's PV obligations, Member State CAs conduct PV inspections in cooperation with the Agency. The objectives of PV inspections are: • to determine that the MAH has personnel, systems and facilities in place to meet their PV obligations • to identify, record and address non-compliance which may pose a risk to public health • to use the inspection results as a basis for enforcement action, where considered necessary The supervisory authority for PV shall be the CA of the Member State in which the PSMF is located either at the site in the Union where the main PV activities of the MAH are performed or at the site in the Union where the QPPV operates. PV inspection programmes will be implemented, which will include routine inspections scheduled according to a risk-based approach and will also incorporate "for cause" inspections. As a general approach, a MAH should be inspected on the basis of risk-based considerations, but at least once every 4 years. This routine inspection programme will be separate from any "for cause" inspections, but if a "for cause" inspection takes place it may replace the need for one under this programme, dependent on its scope. It is anticipated that the majority of inspections will be announced, but sometimes it may be appropriate to conduct unannounced inspections or to announce an inspection at short notice. Any party carrying out PV activities in whole or in part, on behalf of, or in conjunction with the MAH may be inspected. *Pre-authorisation PV inspections* are conducted with the intent of examining the existing or proposed PV system as it has been described by the applicant in support of the MAA. The following recommendations may be considered: • non approval of the MA, or re-inspection prior to approval of the MA • granting of the MA with the recommendation to perform an early post-authorisation PV inspection

Stakeholder number *(To be completed by the Agency)*	General comment
	• imposition of safety conditions to the MA *Post-authorisation PV inspections* are intended to examine whether the MAH complies with its PV obligations. *PV system inspections* are designed to review the procedures, systems, personnel, and facilities in place and determine their compliance with regulatory pharmacovigilance obligations. *Product-related PV inspections* are primarily focused on product-related PV issues, including product-specific activities and documentation, rather than a general system review. *Routine PV inspections* are inspections scheduled in advance as part of inspection programmes. There is no specific trigger to initiate these inspections, although a risk-based approach to optimize supervisory activities should be implemented. *For cause PV inspections* are undertaken when a trigger is recognised. For cause inspections are more likely to focus on specific PV processes or to include an examination of identified compliance issues and their impact for a specific product including but not limited to: • change in the risk-benefit balance, or delays or failure to identify or communicate the risk or change • delays or omissions in reporting, or poor quality or incomplete reports • inconsistencies between reports and other information sources • failure to provide the requested information or data within the deadline specified by the CAs • concerns about the status or fulfilment of RMP commitments • delays in the implementation or inappropriate implementation of CAPAs • inspection information received from other authorities (EU or non-EU) or other types of GXP inspections The results of an inspection will be routinely provided to the inspected entity, who will be given the opportunity to comment on any non-compliance identified. If the outcome of the inspection is that the MAH does not comply with the PV obligations, the Member State concerned shall inform the other Member States, the Agency and the Commission. Where appropriate, the Member State concerned shall take the necessary measures to ensure that a MAH is subject to effective, proportionate and dissuasive penalties. When non-compliance with PV obligations is identified during an inspection, follow-up will be required until a CAPA plan is completed. Recommendations on follow-up actions will be provided in the PV inspection reports and others may arise from the

Stakeholder number *(To be completed by the Agency)*	General comment
	interaction between inspectors and assessors. Necessary action will be judged on a case-by-case basis, and will depend on the potential negative public health impact of the non-compliance(s), but any instance of non-compliance may be considered for enforcement action, with possible regulatory options including but not limited to: • education and facilitation • provision of information to other CAs, the Agency or third country regulators • warning letter, non-compliance statement or infringement notice • CAs may consider making public a list of MAHs found to be seriously or persistently non-compliant • product recalls • action relating to marketing or advertising information • amendments or suspension of clinical trials due to product-specific safety issues • administrative penalties, and referral for criminal prosecution with the possibility of imprisonment The Agency and the Member States shall cooperate to facilitate the exchange of information. A common repository, accessible to all Member State CAs, the Agency and the Commission, should be created to facilitate this information sharing on PV inspections. Information on the conduct and outcome of PV inspections and their follow-up will be made publicly available without prejudice to Regulation 1049/2001. With regards to a comparison between this guidance and Vol 9a, this represents clarification on existing inspection guidance as opposed to new requirements.

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')*
74		Comment: Is it possible to have qualified person at one location and master file located at another location, if yes then How Inspection will be done? Proposed change (if any):
139		Comment: In general, this section frequently contains the same information in different sub sections, so to avoid such duplications the text may be clubbed or rearranged. Proposed change (if any):
521		Comment: Please mention something about how the data security will be catered. The Information should not be accessible to any unauthorized person. Proposed change (if any):
575		Comment: Please provide the section if it is a part of some other document.
103		Comment: How will the communication come to the MAH? Will it be through the lead inspector or through another source? Is there an expected timing of the communication to the MAH?
109		Comment: can the penalties be clarified .. if an MAH is inspected through more than one affiliate and is centrally inspected at a head office, would any penalty decisions be made by the commission, or will each national authority be able to identify penalties .. for monetary penalties, will this only come from the commission or will each national authority have the ability to impose penalties on the MAH?
112		Comment: Is there a timeline on making inspection results public? Is this intended through freedom of

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')*
		information where the results need to be requested?
413		Comment: typo "inspections"
436		Comment: if the inspection results are communicated to other authorities, will the MAH be informed of this?
477		Comment: The national competent authorities can have their own lists or will this be managed by the EMA or the commission? It may be reasonable to have this centrally controlled as being included on this list may have significant impact on the MAH and the MAH should have assurances that addition and removal from the list, is managed appropriately.
477		Comment: To be removed from the list .. how will this be managed? What are the triggers to be included, and removed?
521		Comment: Does this section mean that is a local authority identified critical findings in their inspection, would not be obligated to re-inspect the MAH if another authority performed and inspection and identified no critical findings in those areas?
521		Comment: Does this section imply that a separate competent authority can perform an inspection which would be recognized as a re-inspection on behalf of another authority?
635		Comment: How frequently will the risks be assessed? Will the MAH be required to complete a risk assessment, like the MHRA requires of MAHs? Will this be done centrally or by each local authority?
654		Comment: If I understand this section correctly, the national competent authorities will have a limited scope for their inspections. They will cover local activities and will not include, the Global PV system. Is that correct?
215		Comment: Shouldn't this include section III.B.1.5 and III.B.1.7 as well? Proposed change (if any):
264-265		Comment: Even though this is EMA Module, should it matter whether the large patient exposure is in EU or not? Proposed change (if any): Rephrase the sentence "with large patient exposure in the EU" to "with large patient exposure"

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')*
405, 409		Comment: What is the difference between these two? Proposed change (if any):
413		Comment: Typo Error - Isnpections Proposed change (if any): Change this to “Inspections”
402- 421		Comment: Consider including “Post-authorization Inspections” as well. Proposed change (if any):

Please add more rows if needed.

17. August 2012

Submission of comments on 'good pharmacovigilance practices module III – Pharmacovigilance inspections' (EMA/119871/2012)

Comments from:

Name of organisation or individual
Bundesverband der Pharmazeutischen Industrie e. V. (BPI) - German Pharmaceutical Industry Association

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	Explain all abbreviations (DIR, REG, IR)

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')*
Line 91		**Comment**: "the results of an inspection" **Proposed change (if any)**: "the draft results of an inspection"
Line 95		**Comment**: If the MAH "..does not comply with the pharmacovigilance obligations.." is a vague description and a further explanation/classification of non compliance is need. **Proposed change (if any)**: "… does not comply with the pharmacovigilance obligations e.g. there are critical or major findings …"
Lines 260-266		**Comment**: one of the factors applies to almost all drugs **Proposed change (if any)**: delete the chapter
Line 272		**Comment**: we do not understand the sentence, why only centrally? **Proposed change (if any)**: delete centrally
(Line 272)		**Comment**: spelling error - bracket not closed **Proposed change (if any)**: close bracket)
Line 279		**Comment**: "multiple contracting partners" has to be more specified

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')*
		Proposed change (if any): please specify
Lines 311-312		**Comment**: The "compliance data available from the Agency such as EudraVigilance reporting and data quality audits" contain not validated recommendations and even mistakes. Therefore they are under discussion yet. E.g. it was proposed to code "Folfiri" as drug, but this is an abbreviation of 3 drugs, which were coded already. Moreover other items were discussed in the report, which were advised by other authorities. Therefore this data is not sufficient for consideration without discussion with the MAH. **Proposed change (if any)**: delete the passus
Line 413		**Comment**: spelling error - inspections **Proposed change (if any)**: inspections
Line 524		**Comment**: it has to be feared, that multiple inspections from different authorities will follow, despite the plan to save resources. There are too many triggers, e.g. PV system, Product related. **Proposed change (if any)**: reduce the amount of inspections. Only the authority where the PSMF is localized should conduct inspections.
Lines 110-112 and 683-685		**Comment:** Full Transparency is described. It should be specified. **Proposed change (if any)**: "will be made publicly available without prejudice to Regulation 1049/2001, if there are consequences to the public health and if not otherwise communicated (e.g. Dear Health Care Professional Letter, amendment of PIL)."

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

27. August 2012

Submission of comments on 'good pharmacovigilance practices module III – Pharmacovigilance inspections' (EMA/119871/2012)

Comments from:

Name of organisation or individual
Danish Health and Medicines Authority

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment

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')*
441		Comment: It is stated that recommendations on follow-up actions will be provided in the pharmacovigilance inspection reports. This is usually not the case for inspection reports in Denmark. We point out deficiencies but do not make recommendations. Proposed change (if any): We propose to delete the sentence.
665		Comment: Proposed change (if any): It should be added that this also includes 3rd parties agreement and that MAHs should make sure that 3rd party availability for inspections should be specified in a contract.
		Comment: Proposed change (if any):

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 August 2012

Submission of comments on 'good pharmacovigilance practices module III – Pharmacovigilance inspections' (EMA/119871/2012)

Comments from:

Name of organisation or individual
Dr Reddy's Laboratories UK

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	References to a risk-based approach to scheduling inspections are made throughout the draft guidance. Will this approach be consistent/comparable across the different competent authorities? Will the PRAC have oversight of the risk-based algorithms used by all the competent authorities?

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')*
53		Comment: Please clarify if inspections of third parties are as part of an inspection of a MAH, or if third parties can be inspected in their own right Proposed change (if any):
91		Comment: "routinely" does not mean the same as always Proposed change (if any): delete "routinely" or indicate under what circumstances results of an inspection will not be provided to the inspected entity
167		Comment: Proposed change (if any): delete space before the semi-colon
394-421		Comment: no reference to the manner in which inspections are conducted Proposed change (if any): add sentence to note that they should be conducted in a professional and courteous manner
504-503		Comment: it is concerning that pharmacovigilance inspectors may not have adequate experience of pharmacovigilance processes Proposed change (if any): allow inspected entities to see inspector's cv and list of competencies related to pharmacovigilance

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')*
511-518		Comment: no reference that competent authorities should have an independent process for the receipt and investigation of complaints regarding the inspection of a MAH Proposed change (if any): add requirement that competent authorities should have an independent process for the receipt and investigation of complaints regarding the inspection of a MAH

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 August 2012

Submission of comments on 'good pharmacovigilance practices module III – Pharmacovigilance inspections' (EMA/119871/2012)

Comments from:

Name of organisation or individual
EFPIA – European Federation of Pharmaceutical Industries & Associations

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	EFPIA welcome the opportunity to provide comments on this draft GVP module. The module provides transparency to the inspection process and gives MAH and NCA alike guidance on the expectations during inspections. The module is well structured and therefore our comments are very few and focus on a small number of areas in the text were further clarity could be given.

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')*
Line 95		Comment: If the MAH "... does not comply with the pharmacovigilance obligations.." is open to interpretation and required further definition. In III.C.I a reference is made to sharing a summary of critical and significant major findings and follow up actions. This clarity could be added here by adding a cross reference to the section on Sharing of information. Proposed change (if any): "If the outcome of the inspection is the MAH does not comply with the pharmacovigilance obligations…." should be changed to "If the outcome of the inspection is the MAH does not comply with the pharmacovigilance obligations …and the Commission **in accordance with section III.C.1**"
Line 111		Comment: Whilst EFPIA welcomes a move towards further transparency there is a concern that making information on the outcome of inspections publically available without sufficient background information may reduce patients' confidence in their medicines. A recent high profile example led to some NCA having to reassure patients to continue taking the medicines produced by the MAH in question Proposed change (if any): Aggregate information on the conducts of inspections and their consequences should be more usual with individual MAH being named in exceptional circumstances where public health may be impacted if it were not
Line 148		Comment: the word "Little" is subjective and open to interpretation Proposed change (if any): suspension or product withdrawal with ~~little or~~ no advanced notice to the competent authorities
Line 150, 159		While it is acknowledged that the triggers mentioned may justify an inspection, low levels of late expedite cases should not result in an inspection; nor should a minor concern about the RMP commitments lead to an inspection.

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')*
		Proposed change (if any): Line 150: Substantive delays or omissions in reporting Line159: Significant concerns about the status or fulfilment of risk management plan (RMP) commitments
Lines 216-221		Comment: In this section it should be specified that an agenda of the inspection should be provided with the announcement of the inspection Proposed change (if any) : Line 221 In the conduct of inspections or inspections at short notice, an agenda of the inspection will be provided along with the announcement of the inspection
Line 239-240		Comment: Recommend that the principle of collaboration with the MAH is referenced, particularly for remote inspections. Proposed change (if any): Such approaches are taken at the discretion of the inspectors, in agreement with the body commissioning the inspection and in collaboration with the MAH.
Line 280		Comment: Reference is made to a change to QPPV or person responsible for pharmacovigilance at a national level being a factor taken in to account at inspection planning. Article 104 of the Directive refers to a 'contact person for pharmacovigilance issues at national level' rather than a national responsible person and consistency of terminology should be used. Proposed change (if any): change of QPPV or ~~person responsible~~ contact person for pharmacovigilance issues at national level since the last inspection
Line 399		Comment: We welcome the publication of community procedures as Annexes to this module. Reference is made in line 420 and 421 to updated or new procedures: publication of these updated or new procedures for

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')*
		example on the Agency website would seem appropriate Proposed change (if any): These community procedures will be published as annexes to this module and updated or new procedures will be made available on the EMA website
Line 410		Comment: Recommended that the principle of providing feedback to MAHs at the conclusion of an inspection should be included in the list of items that should be covered in community procedures. Proposed change (if any): conduct of pharmacovigilance inspections, including feedback to MAH at the conclusion of the inspection.
Line 440		Comment: It is appropriate that inspectors share information with assessors. However, where follow-up actions may impact an on-going assessment e.g. for a new MA application or variation, it should be clarified to the applicant what action if any they need to take with respect to that application or filing and what action will be initiated by the inspectors during their communication with the assessors Proposed change (if any):
Line 476-477		Comment: In line with the comments above, individual competent authorities making public a list of seriously or persistently non compliant MAHs without sufficient background information may also reduce patients' confidence in their medicines. Propose change (if any): Competent authorities may consider making public a list of MAHs found to be seriously or persistently non-compliant, in exceptional circumstances where public health may be impacted.
Line 558-561		Comment: In addition to the Agency cooperating with Member States when they identify the need for an inspection of a third country site, they should also cooperate with the regulatory authorities in the third country (e.g. to conduct an inspection without infringement of the law/regulations in the third country) Proposed change (if any): coordinating third country inspections: according to Article 111(1) of the Directive

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')*
		2001/83/EC, the Agency shall cooperate in the coordination of inspections in third countries. Member States should liaise with the Agency when the need for an inspection of a third country site is identified in order to ensure productive use of pharmacovigilance inspection resource in the interests of the Union. When the Agency or Member States conducts an inspection in a third country site, the Agency should liaise with or notify the competent authorities of the third county of the plan and reason of the inspection.
Line 673		Comment: The sentence refers to critical or significant findings. It is unclear what is meant by significant finding. Proposed change (if any): To ensure that if critical or ~~significant~~ major findings are observed during an inspection, appropriate and timely corrective action plans are implemented.
Line 683-5		Comment: As commented above the information on inspections and outcome should only name individual MAH in exceptional circumstances. Further clarity on what information will be published how frequently and in what medium is requested. Proposed change (if any):

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 August 2012

Submission of comments on 'GVP Module III – pharmacovigilance inspections' (EMA/119871/2012)

Comments from:

Name of organisation or individual
EGA - EUROPEAN GENERIC MEDICINES ASSOCIATION Rue D'Arlon 50 B-1000 Brussels Belgium

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
	The EGA welcomes this opportunity to comment on the GVP proposal regarding pharmacovigilance inspections incorporating new elements coming from the new pharmacovigilance legislation. Although we fully understand and support the intention of proposed module, the EGA members have a few comments.
	With the proposed increasing role of the competent authorities in collecting, collating and assessing adverse events it is not understandable that no reference is made in this GVP module to inspections of competent authorities. Concern on this is arising in view of the proposed increased reporting and the requirements for follow up, additional monitoring, RMPs etc. To increase the quality of cases in the EV database the quality of cases as reported to the competent authorities should increase and with that, inspections at those centres should be conducted.

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')*
Lines 58-60		Comment: To maintain consistency with other GVP modules, the MAH should provide the PSMF and not a description of the PhV system in a master file. Proposed change (if any): Amend to "In particular, marketing authorisation holders are required to provide, on request, ~~a description of the pharmacovigilance system in a master file~~ **the pharmacovigilance system master file**, which will be used to inform inspection conduct (…)"
Line 64		Comment: For the definition of "risk to public health" there should be a reference or it should be defined here. Proposed change (if any): add a reference to elsewhere where it is defined.
Lines 94, 164-165, 229, 384, 424, 426, 428, 465, 482-483, 531, 570 and 674		Comment: The wording "…corrective and preventative…" is incorrect. It should be "corrective and preventive". Proposed change (if any): Amend to "…corrective and **preventive**…" in the applicable lines.
Lines 110-112		Comment: There is a contradiction in the document as on lines 110-2 and 684-5. On lines 110-2 it is mentioned that "Information on the conduct and outcome of pharmacovigilance inspections and the follow-up and evaluation of the consequences **may be made publicly available** (…)"; while in the end of the module, it is stated that "Information on the conduct and outcome of pharmacovigilance inspections and their follow-up **will be made publicly available** (…)." Proposed change (if any): Consistency is required.

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')*
Line 148		Comment: suspension of a product to avoid harm to patients with maybe only little advance notice to CA is necessary. This should not be seen as a trigger for an inspection. Proposed change (if any): Suspension or product withdrawal with ~~little or~~ no advance notice…
Lines 216 - 221		Comment: To minimise the high costs related to rescheduling meetings for relevant people who need to be available in inspections it would be helpful if the announced, routine inspections would be notified at least 6 weeks in advance. Proposed change (if any): add: "Announced, routine inspections are notified to the MAH at least 6 weeks in advance and dates should be set in mutual agreement."
Line 272		Comment: The final parenthesis is missing. Proposed change (if any): Please amend to "applicant with no previous marketing authorisations in EU (centrally authorised products**)**;
Line 413		Comment: The word "…isnpections…" should be corrected. Proposed change (if any): Please amend to "…i**ns**pections…"
Lines 450 - 451		Comment: This sentence is surprising as the authorities will take regulatory actions and sanctions according to "potential negative public health impact…" This means authorities would follow more the pressure of journalists and the lay press than to follow a rational scientific evaluation on the risk to public health. Proposed change (if any): health authorities should decide on a scientific rationale. If the authorities fear that under public pressure the process gets out of control any public statement should be avoided.

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')*
Lines 683 - 685		Comment: It seems that the information on transparency is missing. Proposed change (if any): It should be clarified whether the FINAL full report (without confidential data) will be published or only the findings. Furthermore it should state that the information is either removed or further explained when the MAH has fully executed the CAPA.

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

22 August 2012

Submission of comments on 'good pharmacovigilance practices module III – Pharmacovigilance inspections' (EMA/119871/2012)

Comments from:

Name of organisation or individual
European Confederation of Pharmaceutical Entrepreneurs (EUCOPE)

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	It would be helpful to add a note explaining the abbreviations used in GVP Module III

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')*
Line 91		**Comment**: "the results of an inspection" **Proposed change (if any)**: "the draft results of an inspection"
Line 95		**Comment**: If the MAH "...does not comply with the pharmacovigilance obligations..." is a vague description. A clarification what constitutes non compliance is needed. **Proposed change (if any)**: "… does not comply with the pharmacovigilance obligations e.g. there are critical or major findings …"
Line 272		**Comment**: It is unclear why the limitation to centrally authorized medicinal products. **Proposed change (if any)**: delete "(centrally authorized products"
Line 279		**Comment**: the term "multiple contracting partners" should be clarified **Proposed change (if any)**: please specify
Lines 311-312		**Comment**: The "compliance data available from the Agency such as EudraVigilance reporting and data quality audits" contain not validated recommendations. These information are therefore are under discussion. As numerous examples show this data is not sufficient for consideration without discussion with the MAH. **Proposed change (if any)**: delete the passus

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')*
Line 524		**Comment**: It should be avoided that multiple inspections from different authorities are conducted, thus binding resources due to a vast amount of triggers, e.g. PV system, Product related issues. **Proposed change (if any)**: A way to reduce the number of inspections would be that only the authority where the PSMF is localized should conduct inspections.
Lines 110-112 and 683-685		**Comment:** The concept of 'Transparency' should be specified. **Proposed change (if any)**: "will be made publicly available without prejudice to Regulation 1049/2001, if there are consequences to the public health and if not otherwise communicated (e.g. Dear Health Care Professional Letter, amendment of PIL)."

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 July 2012

Submission of comments on 'good pharmacovigilance practices module III – Pharmacovigilance inspections' (EMA/119871/2012)

Comments from:

Name of organisation or individual
European Organisation for Rare Diseases (Eurordis) [redacted]

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment

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')*
170-174		Comment: another reason to inspect the marketing authorisation holder is when a product supply shortage occurs. There can be a manufacturing issue (defect, contamination) or sometimes the MAH is facing a higher demand than planned and cannot satisfy the demand. This can occur post-marketing authorisation, or prior the marketing authorisation. In the past, when running a compassionate use programme, a large pharmaceutical company had to take measures to "pace down" inclusions in the programme, explaining the manufacturing site needed to be closed down for a few weeks to install new facilities for the commercial large-scale production. In fact the company was piling stock, anticipating a positive opinion for the marketing authorisation and making sure all distributors had enough stock to satisfy the demand immediately after the MA. To verify the claims of the company, only an inspection of the manufacturing site and process could respond the questions patients and their organisations had to their national competent authorities. Another product shortage occurred for another product marketed by another company where the demand rapidly exceeded the manufacturing capacities. The medicine was again for a life-threatening condition (HIV) and the first HIV antiprotease inhibitor suitable for paediatric use. The shortage had potentially dramatic public health consequences. The manufacturer explained the product was difficult to manufacture. Others were suggesting the marketing authorisation holder was "organising" the supply shortage on purpose, to provoke a "hype" in the patients' and doctors' community. Here again, only an inspection could verify the difficulties in manufacturing the product, and this inspection was conducted by a national competent authority. The conclusion showed "objective difficulties in manufacturing the product" and this helped solving the crisis that had started. Proposed change: others: – concerns following review of the pharmacovigilance system master file; – non-inspection related information received from other authorities, which may highlight issues of non-compliance;

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')*
		- concerns following a product supply shortage; – other sources of information or complaints.
		Comment: Proposed change (if any):
		Comment: Proposed change (if any):

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 August 2012

Submission of comments on 'good pharmacovigilance practices module III – Pharmacovigilance inspections' (EMA/119871/2012)

Comments from:

Name of organisation or individual
Gilead Sciences International Limited

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment

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')*
53		Comment: Please provide examples of relevant third parties. Proposed change (if any): Please add a definition
73		Comment: If pre-authorisation inspections are possible to verify the accuracy of the PV system, this implies provision of the pharmacovigilance master file (PSMF) will be routine at MAA Proposed change (if any): Please clarify.
81		Comment: While there is much in the guidance about sharing scheduled and planned inspections, there is little reassurance about minimising duplication and EMA oversight of such activities. Proposed change (if any): Please provide further detail.
84, 128, 197, 395, 550, 635		Comment: There are multiple references to inspections having a risk-based approach with no reference to the methodology that will support this and what the expectation of the MAH will be in this regard, for example, MHRA annual compliance reports – are these to be standardised or will they be duplicated across member states? Proposed change (if any): Please clarify.
85		Comment: Regarding "for cause" inspections to examine suspected non-compliance, it is not clear based on what this non-compliance is being based?

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')*
		Proposed change (if any): Please clarify.
90		Comment: Agencies adapt scope or timing, but not reconsider the need for or collaborate? Proposed change (if any): Consider the possibility of agencies reconsidering the need to collaborate on inspections.
93		Comment: If the inspected party is a third party provider of the MAH, the timing of communication with the MAH is unclear. Proposed change (if any): Please clarify.
171		Comment: Inspections can be triggered by review of PSMF but the frequency and extent of such reviews is unclear. This also results in merger/acquisition activities. How will this be monitored by Agencies? Proposed change (if any):
249		Comment: How the sharing of data for inspection prioritisation will result in prioritisation or reprioritisation is unclear. Proposed change (if any): Please clarify.
281		Comment: Please confirm that changes to persons responsible at a national level are notifiable only at a national level and hence could trigger an inspection and confirm this is not the case for CAPs. Proposed change (if any): Please confirm.

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')*
314		Comment: Examples of additional data requests would be useful to understand the nature and extent of such requests. Proposed change (if any): Please provide examples.
350		Comment: Please clarify that the reference to 2001/20/EC is in relation to interventional post-authorisation studies. Proposed change (if any): Please clarify.
426		Comment: Please provide examples when progress reports are likely versus following up CAPA at next inspection. Proposed change (if any): Please provide examples.
539		Comment: What does this paragraph mean with respect to minimising duplication across member states? Proposed change (if any): Please clarify.
555		Comment: Can only CHMP confirm “for cause” inspections or can member states do this as well? Proposed change (if any): Please confirm.
612		Comment: Regarding the availability of repository, Please provide clarity as to reducing duplication, regarding prioritisation or accepting inspection findings of another member state. Proposed change (if any): Please clarify.

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')*
665		Comment: The requirement of the MAH sites to accept to be inspected is unclear. Proposed change (if any): Please clarify.

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24th August 2012

Submission of comments on 'good pharmacovigilance practices module III – Pharmacovigilance inspections' (EMA/119871/2012)

Comments from:

Name of organisation or individual
Medicines and Healthcare products Regulatory Agency (MHRA) – GPvP Inspectorate

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment

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')*
Line 166-167		Comment: The term GXP is not defined in GVP Annex I – definitions and is not always understood. For clarity and consistency with lines 256-257 of this Module it is recommended that the sentence is changed as indicated below. Proposed change (if any): "information such as non-compliance or product safety issues from other types of inspections **(GCP, GMP, GLP)**"
Line 272		Comment: As this section describes inspection planning performed by competent authorities in general (not limited to supervisory authority inspections), this bullet point is relevant to all authorisation procedures and not centrally authorised products. Therefore, it is suggested that the bracketed section is removed. Also, a missing word. Proposed change (if any): applicant with no previous marketing authorisations in **the** EU;
Line 272		Comment: A close-bracket is missing at the end of the sentence. If the previous comment is not implemented (i.e. the bracketed section removed) then the close-bracket should be added. Proposed change (if any): applicant with no previous marketing authorisations in EU (centrally authorised products**)**;
Line 274		Comment: Same issue as comment relating to line 166-167 – the term GXP is not defined and may not be fully understood.

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')*
		Proposed change (if any):
Line 283		Comment: Unnecessary comma at the end of the line Proposed change (if any): database itself or associated databases, the validation status of the database as well as information
Line 362		Comment: Missing words Proposed change (if any): QPPV roles and responsibilities, e.g. access to **the** quality system, **the** pharmacovigilance system master file, performance
Line 372		Comment: Missing pluralisation Proposed change (if any): contract**s** and agreements with all relevant parties appropriately
Line 413		Comment: Incorrect capitalisation of first work (inconsistent with other bullet points in this list), spelling mistake "isnpection" and grammatical errors. Proposed change (if any): "**i**nteraction with PRAC in relation to in**s**pection and **their** follow**-**up"
Line 673-674		Comment: This bullet point implies that an MAH does not have to implement appropriate and timely corrective and preventative actions for major and minor/other findings

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')*
		Proposed change (if any): To ensure that appropriate and timely corrective and preventative action plans are implemented to address findings observed during an inspection, with appropriate prioritisation of critical or significant findings.

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

5 July 2012

Submission of comments on 'good pharmacovigilance practices module III – Pharmacovigilance inspections' (EMA/119871/2012)

Comments from:

Name of organisation or individual
Nilesh Sheth MRPharmS, Regulatory Consultant

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	In common with the previous draft GVP modules, there is a general issue concerning the use of unnecessarily long sentences, poor grammar, sentence construction and punctuation in the document. All of these factors detract from the readability of the document. It would appear that the writer(s) do not have a thorough command of the English language to be able to convey the subject matter clearly and succinctly. More time and thought should be invested in delivering a well written document that engages the reader.

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)*
		Comment: Proposed change (if any):	
		Comment: Proposed change (if any):	
		Comment: Proposed change (if any):	

Please add more rows if needed.

<20 August 2012>

Submission of comments on 'good pharmacovigilance practices module III – Pharmacovigilance inspections' (EMA/119871/2012)

Comments from: Novartis AG

Name of organisation or individual
Novartis Pharma AG Novartis Vaccines and Diagnostics Novartis Consumer Health Alcon

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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
	Novartis welcome the opportunity to provide comments on this draft GVP module. The module is well structured and therefore our comments are very few and focus on a small number of areas in the text were further clarity could be given. The inclusion of timelines would facilitate the management of the inspection process by both MAHs and competent authorities, defining clear expectations that can be built into operating procedures. For example the minimum amount of timeframe for an announcement of a routine inspection is 3 months before the date of inspection, or draft agenda is for a routine inspection 6 weeks before the date of inspection and final agenda 3 weeks before, or inspection report is finalised 4 weeks after inspection, or MAH must respond to the inspection report within 4 weeks of receipt of the inspection report. Rather than making public individual MAHs findings, a regular inspection summary report (similar to what the MHRA publish) of findings and criticality would serve as a valuable vehicle for sharing areas of attention enabling an MAH access to information in order to proactively improve its own PV systems.

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')*
Line 58 and 662		**Comment:** It is specified that MAH should provide the PSMF within seven days of request, however the requirement of having the PSMF in place is, through transition arrangements, tied with the next renewal or registration but not later than July 2015. Because of this transition arrangement should also be put in place for the inspection process where an MAH has not yet compiled a PSMF. The MAH should be allowed to submit either a DDPS or SPS.
Line 110, 111, 112, 684-685		Information on the conduct and outcome of Pharmacovigilance inspections and the follow-up and evaluation of the consequences may be made publicly available as part of the overall transparency of Pharmacovigilance activities. **Comment:** Will the criteria, for the basis of the decision of what information on the outcome and consequences of an inspection that will be made public, be standardised? Will these criteria be made available to all involved parties for transparency?
Line 126		Routine Pharmacovigilance inspections are inspections scheduled in advance as part of inspection programmes. **Comment:** Please see general comment regarding advance announcement timelines of upcoming inspection.
Lines 216-221		**Comment**: In this section it should be specified that an agenda of the inspection should be provided with the announcement of the inspection **Proposed change** : L. 221 – Add the sentence: "In the conduct of an inspection at short notice, an agenda of the inspection will be provided along with the announcement of the inspection."
Line 296		The site to be inspected may be located in the EU (e.g. EU QPPV site) or outside the EU.

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')*
		Comment: Since this GVP Module III is also intended as a basis of inspection conduct for the EU CAs it is not always known by all inspectors that if an inspection is to be conducted outside of the EU the host CA should be contacted as a matter of courtesy but in some instances that inspection cannot be conducted unless the host CA has given permission for it to go ahead. Novartis had such an experience for an EU CA inspection in Switzerland. Language should be added to this paragraph to indicate the necessity for such protocol.
Line 332		Record keeping for ICSRs **Comment:** for the sake of clarity archiving of records should be spelt out as well. The text should be amended to read - Record keeping and archiving for ICSRs
Line 413		Spelling mistake – Inspections spelt incorrectly.
Line 453		As stated in Article 111 (8) of Directive 2001/83/EC, …….. **Comment:** Article 111 (8) of Directive 2001/83/EC seems to be associated with manufacturing. Should it read Article 104 (9) of Directive 2001/83/EC? We would suggest the Article number should be confirmed prior to finalisation.
Line 558		…coordinating third country inspections: according to Article 111 (1) of the Directive 2001/83/EC…. **Comment:** Article 111 of Directive 2001/83/EC does not refer to third country inspections but to inspections of third country manufacturers for GLP/GMP inspections. We would suggest the Article number should be confirmed prior to finalisation.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

<24th August 2012>

Submission of comments on 'good pharmacovigilance practices module III – Pharmacovigilance inspections' (EMA/119871/2012)

Comments from:

Name of organisation or individual
Pharmaceutical Information and Pharmacovigilance Association

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	Section III.B.1.3. How will the fee structure for pre-authorisation inspections be calculated? If the product is a generic in a start-up then the company may not have the capital available compared to larger organizations.
	Section III.B.1.6. What would be the expected re-inspection time frame on the assumption that the re-inspection is announced and has provided sufficient time considered realistic to allow the MAH to fulfil or put in place his PV obligations?
	Section III.B.1.7. If a remote inspection is performed will the expectation of the CA be for the MAH to provide such software to conduct the inspection?
	Section III.B.2. Line 270 How will this be confirmed? RBI Questionnaire? Line 275 If the MAH has not previously had MA in the EU, but has contracted services to a service provider who has recently been inspected on behalf of another company. Will the service provider be re-inspected for this MAH if the scope of work contracted is the same?
	Section III.B.3. Para 296 How would this work if the site Ex-Eu is another MAH, co-marketing the product? Whereby they are conforming to their local country legislation which may not fall in line with EU legislation. Will you inspect them according to EU Law?
	Section III.B.4.1. Line 362 This section is for Ex-EU. Would QPPV not be defined in an EU inspection and merely confirmed accordingly according to Ex-Eu understanding and establishment of processes to allow the QPPV oversight in these countries?
	Section III.B.9. Paragraph 502 How will this be measured?
	Section III.B.10. Who would audit the competent authority?

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')*
		Comment: Proposed change (if any):
		Comment: Proposed change (if any):
		Comment: Proposed change (if any):

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 August 2012

Submission of comments on 'good pharmacovigilance practices module III – Pharmacovigilance inspections' (EMA/119871/2012)

Comments from:

Name of organisation or individual
PHARMIG – Association of the Austrian pharmaceutical industry

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	PHARMIG, the association of the Austrian pharmaceutical industry, would like to thank for the opportunity to comment on GVP Module III – Pharmacovigilance inspections.

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')*
95		Reference: If the outcome of the inspection is that the marketing authorisation holder does not comply… Comment: Please define "not comply". (Should be restricted to significant major and critical findings) Proposed change (if any): If the ~~outcome of the~~ inspection ~~is that the marketing authorisation holder~~ results in significant major or critical findings…
110		Reference: Information on the conduct and outcome of pharmacovigilance inspections and the follow-up and evaluation of the consequences may be made publicly available… Comment: The information on the outcome shall not be shared with the public. Proposed change (if any): Information on the conduct ~~and outcome~~ of pharmacovigilance inspections and the follow-up and evaluation of the consequences may be made publicly available…
148		Reference: suspension or product withdrawal with little or no advance notice to the competent authorities Comment:

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')*
		A withdrawal for commercial reasons shall not trigger a PV inspection. Proposed change (if any): suspension or product withdrawal caused by safety reasons with little or no advance notice to the competent authorities
174		Reference: other sources of information or complaints Comment: Should be restricted to safety relevant information or complaints Proposed change (if any): other sources of safety relevant information or complaints
413		Reference: Interaction with PRAC in relation to isnpections and its follow up; Comment: Proposed change (if any): Interaction with PRAC in relation to ins~~n~~pections and its follow up;
466 - 467		Reference: provision of information to other competent authorities, the Agency or third country regulators under the framework of confidentiality arrangements; Comment: Sharing of information with third country regulators may be in conflict with local legislation. The legal basis

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')*
		should be double checked. Proposed change (if any): provision of information to other competent authorities or the Agency ~~or third country regulators~~ under the framework of confidentiality arrangements;
476 - 477		Reference: competent authorities may consider making public a list of marketing authorisation holders found to be seriously or persistently non-compliant; Comment: This measure is inequitable and does not reflect reality since potentially non-compliant companies not yet inspected are not considered in the list. Proposed change (if any): Please delete this sentence.
530		Reference: A summary of the critical and significant major findings and a summary of… Comment: Please define significant major findings Proposed change (if any):
673 - 674		Reference:

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')*
		To ensure that if critical or significant findings are observed during an inspection, appropriate and timely corrective and preventative action plans are implemented. Comment: Please define significant findings Proposed change (if any):
684 - 685		Reference: Information on the conduct and outcome of pharmacovigilance inspections and their follow-up will be made publicly available without prejudice to Regulation 1049/2001. Comment: Please see our comment regarding line 110. The information on the outcome shall not be shared with the public. Proposed change (if any): Information on the conduct ~~and outcome~~ of pharmacovigilance inspections and their follow-up will be made publicly available without prejudice to Regulation 1049/2001.

Please add more rows if needed.