22 January 2013
EMA/35763/2013
Patient Health Protection

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

GVP Module XV – Safety Communication

The draft of this module was released for public consultation between 26 July and 21 September 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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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21 September 2012

Submission of comments on 'GVP Module XV – Safety communication' (EMA/118465/2012)

Comments from:

Name of organisation or individual
AESGP

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	'timeliness' is mentioned several times in the document. Will further guidance be provided on the expectations for actions?
	It is not 100% clear in the document in which instances marketing authorisation holder should use this process. It is our understanding that we should use common sense on when to apply the safety communication process (e.g. if a product sold over the counter is out of stock, while another over the counter product delivering similar benefits is still available, it is our understanding that this situation would not require a specific safety communication).
	It is important to note (Press Communication section (XV.B.6.3) that media will rarely use the full extent of a press release sent to them. Also, in some cases especially with non-specialised media (e.g. magazines for HCP), it is highly possible that the journalist will misunderstand and/or misreport some of the information provided to him/her. We believe that it is the responsibility of the source of information to ensure that the messages are as clear and adapted to the audience as possible, but the source of information should not be held responsible for misreport by the journalist.
	Strict alignment and consent between the Agency / HAs and the MAH is missing (the rights of the MAH e.g. to agree to or comment on safety communications are extremely limited).

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')*
119-121		It does not feel realistic to pre-test messages with the audience on safety communication material, in the case of urgent safety communication. We recommend to ensure that the people with the right expertise work on creating the safety communication material (e.g. medical affairs on communication for HCP, PR for communication toward the media) to ensure that the messages can be understood by the target audience.
134-139		Communication by media is very sensitive. An agreement between competent authorities and Marketing Authorisation Holder on the safety information provided to the media has to be done whenever possible.
182-183		It should be clarified whether this point refers to situations where new information has become available which was not available before, or if it refers to existing information such as CHMP recommendations which, for historical reasons, may be missing from product information which have been identified as being required.
193-196		Please provide proposed extent and time periods of such observation. Will further guidance be provided on when an observation turns into a potential signal?
215-233		Although media relations are a good means to reach out to patients and health professionals, it is also a channel which is difficult to control. Journalists are free to interpret information and often communications through the media are altered, either non-intentionally (lack of scientific background leading to misunderstanding of the messages) or intentionally (intent to make the news more “sensational”). To minimise the risk of altered messages, which could confuse patients, it might be reasonable to narrow the type of target media to those who have a greater knowledge of safety communication material and may not alter safety messages.
270-285		Will there be further guidance as to what the expectations are for mechanisms to measure how appropriate and

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')*
		effective communication has been? What is the expectation as to the level of research required to make such conclusions on effectiveness? This could be very time and resource consuming.
392-395		This seems unrealistic if the definition of 'third party' includes scientific journals or media. Usually the MAH becomes aware of the communication after it has been issued. It is not everyday practice that authors, editors or journalist express to the MAHs their 'intention to issue a communication related to the benefit-risk balance of a medicinal product'.
409-414		Does this mean that the content and presentation of a DHPC should always be agreed with the competent authority?
419-422		What is the role of competent authorities where a DHPC is raised for products authorised in more than one member state? With the PRAC only meeting monthly in cases of urgent response will timelines for the PRAC be defined? Currently the interaction with competent authorities works well in ensuring aligned, appropriate and timely communication. What might be the role of the PRAC concerning this process and communication channel?

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21.09.2012

Submission of comments on 'good pharmacovigilance practices module XV – safety communication' (EMA/118465/2012)

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

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')*
273-276		**Comment**: The measurement of effectiveness of safety information is a well-intentioned. But the feasibility is questionable beside the pure measurement of the effectiveness of its dissemination. In case of involvement of physicians/patients during the preparation of safety communication then there is no need for measuring the effectiveness of safety communication. An amendment of this section would support the involvement of physicians and patients during the preparation of safety communication. **Proposed change (if any)**: In case of involvement of physicians/patients during the preparation of safety communication only the measurement of the effectiveness of its dissemination is required.
301 – 303		**Comment**: The MAH should also be involved . **Proposed change (if any):** Prior to the publication of a safety announcement, the Member States, the MAH and the Agency or the European Commission shall inform each other not less than 24 hours in advance, unless urgent public announcements are required for the protection of public health [DIR Art 106a(2)].
382 - 385		**Comment**: Why is it necessary the inform also the European Commission if a authorisation holder in the EU intends to make a public announcement relating to information on pharmacovigilance concerns in relation to the use of a medicinal product? **Proposed change (if any):**

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')*
		As soon as a marketing authorisation holder in the EU intends to make a public announcement relating to information on pharmacovigilance concerns in relation to the use of a medicinal product, and in any event at the same time or before the public announcement is made, he shall be required to inform the competent authorities in Member States and~~,~~ the Agency ~~and the European Commission~~ [DIR Art 106a].

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21 September 2012

Submission of comments on 'GVP Module XV – Safety communication' (EMA/118465/2012)

Comments from:

Name of organisation or individual
CBG-MEB (Medicines Evaluation Board – the Netherlands)

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	The scope of this GVP is not very clear. It would be helpful if the distinction is made between 'regular' (standard) safety communication and 'additional' safety communication.
	The all inclusive nature of the aims as described in this GVP is not in line with the limited information /communication tools described as such. Either the aims should be more realistic or the safety communication should be broader. The aims of the current tools are only to bring to the attention of HCP and patients the fact that there might be a new risk identified , or new information that may have an impact in the daily practice.
	The process of what triggers a DHPC, how the information reaches the PRAC, the role of EMA/NCA and decisionmaking is still not very clear. Some examples: according to the GVP "A draft DHPC and communication plan relating to medicinal products authorised in more than one Member State should be referred to the PRAC for its recommendation to CHMP and CMDh.". It is unclear who actually 'refers' here. Is this the MAH/the NCA? Also " The PRAC assessment of the draft DHPC and its communication plan should be part of any assessment report of the safety concern". Assuming the assessment report is prepared by the NCA, what will be the role of the EMA (considering that EMA plays a central role in the coordination)? And specifically: what will be the role of the EMA for DHPCs concerning nationally authorized products?

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 55		Comment: What is meant with “2-way communication”? Proposed change (if any): Please clarify or rephrase.
Line 62		Comment: The purpose of the following sentence is not clear: “It also adds to the information contained in the public assessment report for each medicine made available by competent authorities” Proposed change (if any): Please clarify or rephrase.
Line 82-84		Comment: It is stated that this GVP refers to ‘safety communication as the communication of new or emerging information….”. The difference between new and emerging is unclear. Proposed change (if any): Please clarify or rephrase. Please also add Please add “..and does not address the routine communication that is available to the regulators as described in GVP Module XVI Risk Minimisation Measures”
Line 85-93		Comment: The scope of this GVP refers to ‘safety communication as the communication of new or emerging information

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')*
		which may have impact on its benefit/risk balance and it conditions of use." However, the objectives described in lines 85-93 are quite broad. If these are indeed all the aims then why only focus on new/emerging that impacts the b/r?
Line 87		Comment: 'effective use' also has a financial dimension, which can not be addressed here. Proposed change (if any): Change to "providing timely evidence-based information on the risks and safe use'
Line 88		Comment: These aims do not allow the safety communication to be limited to new/emerging issues with impact on b/r. In order to live up to these aims communication should be a continuous process. Some aims are too broad for the described possibilities (specifically 'improving attitudes, decisions and behaviours in relation to the use of medicines' and 'facilitating informed decisions on the rational use of medicines')
Section XV.B.3. Principles of safety communication		Comment: This section should start with a better description of when the communication is warranted as described in Volume 9A. With the current text in the GVP everything should be communicated; a PSUR has been assessed, a RMP has been updated,...
Line 95-97		Comment: add 'whole' Proposed change (if any): The need for communication should be considered throughout the *whole* pharmacovigilance and risk management process,

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 95-97		Comment: This is a very doubtful statement to live up to. With this text, it is not also necessary then to communicate negative findings on risks.
Lines 111-112		Comment: This might not always be feasible. Proposed change (if any): change wording
Lines 119-120		Comment: This might not always be feasible. Proposed change (if any):allow flexibility change wording
Section XV.B.4. Target audiences		Comment: the 'Means of communication' as described in section XV.B.6 do not match with the target audiences here. Also: how do we envisage communicating with patients directly; via press release?
Line 144		Comment: To whom should the reason for initiating safety communication be clearly explained?
Line 145-146		Comment: This is practically not possible. Proposed change (if any): Change wording to reflect that the safety communication should deal with the **current** safety concern.
Line 147		Comment: DIR art 106a(1) states that "The marketing authorisation holder shall ensure that information to the public is presented objectively and is not misleading."

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): Change wording to reflect the MAHs responsibility, for example: "*the MAH* should ensure that the information is presented objectively and is not misleading."
Line 153		Comment: What about adding the SPC?
Lines 160-162		Comment: DIR Art 106a does not refer to " various channels". This text is not in line with the Directive. Proposed change (if any): Change text in line with the Directive, or rephrase.
Lines 166-167		Comment: The following is stated: "to inform them of need to take certain actions". However, not every DHPC informs about an 'action' . Proposed change (if any): Change to "to inform them and present *where appropriate* the need to take certain actions"
Lines 169-174		Comment: The Directive allows the MAH to communicate on their own, provided the Regulatory Authorities are informed. The way it is presented here is not in line with the legal requirements. Proposed change (if any): Bring text in line with text 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')*
		Comment: Another comment is that from research done in collaboration with Piening and Mol (to be published in Drug Safety, special edition on Drug Safety Nov 2012) Dutch healthcare professionals emphasized they trust information coming from an independent source such as the Dutch-MEB more than information coming from industry. In line with theories on communication messages are picked up better when sent by a source that is trusted. Also, in that survey HCP indicate they would prefer that regulators play a more direct role in communicating drug safety issues. Proposed change (if any): Address that the competent authority should play an active role in disseminating drug risk information.
Line 197-199		Comment: Should a reference to the communication plan be included here? The experience gained so far with the template and this way of working has been quite good
Lines 319-321		Comment: Who decides here? And what to do when there is only 1 Member State where there is media attention?
Section XV.B.6.1		Comment: It could be that a DHPC has been agreed at EU level, but that a product has not yet been marketed in some of the EU countries. In this situation it should be possible that a DHPC will not be distributed in these countries at the discretion of the NCA. Proposed change (if any): Address this situation in the GVP accordingly.
Section XV.B.6.2		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')*
Documents in lay language		Where are these documents made available to the lay public and when would this be necessary? Will there be criteria or will this be always required?
Lines 194 and 197		Comment: 2 typo's "DHCP" Proposed change (if any): Change to 'DHPC'
Lines 413-414		Comment: The Directive allows the MAH to communicate on their own, provided the Regulatory Authorities are *informed*. The way it is presented here is that the content should always be *agreed* ; this goes beyond the legal requirements. Proposed change (if any): Align text with legal obligations from the Directive.
Lines 429-433		Comment: "marketing authorisation holder should submit the draft DHPC and communication plan" There is no guidance what the content of the communicationplan should be (does this include a proposal for the target population, timing, means of communication such as DHPC, etc)? Also, as the practical use of the product can differ between Member States, the target audience can be different. Should this also be addressed in the communicationplan (different target audiences proposed if this would be appropriate)? Proposed change (if any): Provide some more guidance on what is expected from the communicationplan submitted by the MAH, and also if this would need to take into account Member State variability.
Annex (template		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')*
for DHPC)		It is recommended to mention the authorised indication in the DHPC.

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 September 2012

Submission of comments on 'GVP Annex I – Definitions' (EMA/876333/2011)

Comments from:

Name of organisation or individual
Standing Committee of European Doctors (CPME)

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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')*
Lines 45-48 (Module XV – safety communication)		**Comment:** CPME believes that trust between the patient and his physician should not be compromised because of pharmacovigilance problems. A good patient-doctor relationship is of utmost importance for quality healthcare. **Proposed change (if any):** Communicating safety information to patients and healthcare professionals is a public health responsibility. Safety communication ~~and~~ is essential to guarantee trust between the patient and his/her physician and to achieve the objectives of pharmacovigilance in terms of promoting the safe and rational use of medicines, preventing harm from adverse reactions and contributing to the protection of patients' and public health (see Module I).
Lines 130-132 (Module XV – safety communication)		**Comment:** CPME believes that trust between the patient and his physician should not be compromised because of pharmacovigilance problems. A good patient-doctor relationship is of utmost importance for quality healthcare. **Proposed change (if any):** Effective safety communication is indispensable for the doctor to ensure patient safety. It enables healthcare professionals to give clear and useful information to their patients, thereby promoting patient safety and confidence in the regulatory system.
Lines 234-240 (Module XV – safety communication)		**Comment:** **Proposed change (if any):** A website is a key tool for members of the public (including patients and healthcare professionals) actively searching the internet for specific information on medicinal products. In order to avoid the dissemination of incorrect or biased information on medicinal products on the internet, competent authorities as well as marketing authorisation holders should ensure that important safety information is easily accessible and understandable by the public. Documents on websites should be found easily via search engines as well as by navigating from the home page.

21. September 2012

Submission of comments on 'GVP Module XV – Safety communication' (EMA/118465/2012)

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')*
Line 147		Comment: “should” to be replaced with “shall” to reflect the text in DIR 106a, paragraph 1, subparagraph 2 – where “The marketing authorisation holder shall ensure that information to the public is presented objectively and is not misleading.” Proposed change (if any): The information shall not be misleading and shall be presented objectively.
Line 149		Comment: Title “VII” to be replaced by title “VIII” in the reference to the directive. Title VII of the directive is about wholesale distribution of medicinal products. Proposed change (if any):
Line 180		Comment: Is it a condition that the withdrawal for safety reasons shall include a direct recall of products from the market? Suspension, withdrawal and revocation of a marketing authorisation could be the trigger of a DHPC. Proposed change (if any): It could be considered to delete the condition and only write: suspension, withdrawal or revocation of a marketing authorisation for safety reasons. Furthermore, it could be considered to add a separate bullet point with the text “recall of a medicinal product from the market for safety reasons”.
Line 257-262		Comment: Reference suggested Proposed change (if any): A reference to the article 98(1) of DIR 2001/83 which is stating that “The marketing authorisation holder shall establish, within his undertaking, a scientific service in charge of information about the medicinal products which he places on the market.” could be inserted.

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 384		Comment: Proposed change (if any): The words “be required to” appears unnecessary and could be deleted from the sentence.
Line 450		Comment: reference missing Proposed change (if any): A reference to DIR 23(2) regarding non-centrally authorised medicinal products should be included as the current reference to REG 16(2) only concerns the centrally authorised medicinal products.

Please add more rows if needed.

21 September 2012

Submission of comments on 'GVP Module XV – Safety communication' (EMA/118465/2012)

Comments from:

Name of organisation or individual
EFPIA

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	Overall much needed guideline providing the principles on communicating safety information. Some ambiguity in terms of the scope of this module; whether this relates to emerging safety issues or whether it covers also more general principles of how to communicate safety information to HCPs and the public. The criteria or threshold for "emerging information" would benefit from further discussion. While the *types of issues* that should be communicated are addressed, in part, in lines 179-196, the relative level of evaluation or certainty around an emerging safety issue has not been. The possible unintended consequences of making information available that is not yet reliable, and thus potentially misleading should be considered in context of the potential usefulness of emerging, but unsubstantiated, safety information. Marketing Authorisation Holders are frequently not at all or very late associated / informed of the preparation / distribution of safety information within the EU regulatory network and beyond. As entities responsible for the marketing of their products, they should be informed as soon as possible and at least when a project of safety communication is distributed within the EU network. It is difficult to provide complete comments to this GVP module as several references are made to modules not published yet (XI/XII mainly, as well as XVI/XIV). From the content provided in this module, it would appear that there may be significant overlap between the content of this module and module XII on the processing of DHPCs. Ideally, the detail of the DHPC process should be provided in a single document, so further detail (e.g. the content of the proposed communication plan) should be provided in this module. Also we welcome the acknowledgment in the guideline that safety communication is different from the transparency initiatives. Communication implicitly holds a promise of a two-way interaction; however the current guideline remains very vague on how this two-way interaction between MAHs & Patients would look like and in particular the legislative framework in many countries imposes restrictions on direct MAH / patient interaction. The interaction is limited to review of certain communications. We would therefore welcome some more guidance on this or at least a commitment to study this further. Guidance should be provided in this module as to how safety communication should be managed for a product that has a marketing authorisation and is also under further development in clinical trials. Consideration should be given in this module as to the alignment of this guidance with the GCP requirements for informing investigators (and subjects) of new safety information in clinical trials To avoid confusion, it is imperative that prescribers of the marketed products and clinical trial investigators are provided appropriate information on a new safety concern at the same time. The requirement for a DHPC for safety-related changes to the product information could result in a high volume of DHPCs. Highly critical communications could therefore be diluted. The processes and procedures around this need to be carefully considered and standardized, otherwise there will be a high burden on MAHs and competent authorities to agree upon on each and every

Stakeholder number *(To be completed by the Agency)*	General comment
	communication plan, information and timetable. Please provide flow charts with associated time frames; one for processes related to communication to HCPs, and one for processes related to communication to the broader public (if different from HCPs). It would particularly allow a description of the recommended/standardised timelines which are not fully detailed in the guideline. In addition, it would be good to include a statement confirming that a DHPC should not normally be distributed until the related regulatory procedure (e.g. variation) is completed. A clear description of what should be included in the “Communication Plan” would be helpful (the provision of a template for this document would be beneficial). Consideration should be given to the implementation of single tracking system by the EMA for all safety communications regarding marketed drugs (new and/or emerging information, and subsequent follow-up information). Such a system would provide patients and health care professionals systematic access to the most current information on a given issue. It should be made sure that each time the wording "communication " or information " is used it is specified "safety communication " or safety information " as relevant (ex : lines 55,62,82,105,106,133,136,138,139,147,...)

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')*
47		**Comment:** add “appropriate” Proposed change (if any) :Communicating safety information to patients and healthcare professionals is a public health responsibility and is essential to achieve the objectives of pharmacovigilance in terms of promoting the **appropriate,** safe and rational use of medicines, preventing harm from adverse reactions and contributing to the
60-63		Comment: highlights the ambiguity which is mentioned in the introduction. How does this safety communication position itself and who is responsible for it? How does it fit with the risk management plan requirements? Proposed change (if any): Safety communication … packaging **which can be used by both competent authorities and MAHs**
87		**Comment :**add “appropriate” Proposed change (if any): Safety communication aims at: • providing timely evidence-based information on the **appropriate,** safe and effective use of medicines;
96-97		**Comment:** Revise text for clarity Proposed change: The need to appropriately communicate new and emerging safety information should be part of the ongoing pharmacovigilance and risk management processes, and considered as part of risk assessment (see Module XI).
108-110		This bullet ends with “…*time to onset and reversibility of adverse reactions*.” There is often a focus on time to onset but different ADRs may also have different times to recovery (TTR). MAHs should be encouraged to provide information on TTR, if available, as this may be valuable to patients and health care professionals. Proposed change: amend to “… time to onset, reversibility of adverse reactions and, if available, expected time to recovery.

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 109		Comment: It may be best to delete “appropriate” here since the information that must be provided is not influenced by being appropriate, since the risks presented in context of the benefits will always be dependent seriousness, severity...etc... Proposed Change: Delete “appropriate” “...include information on the seriousness...”
Lines 111-112		Comment: This should be further expanded to include the concept that outdated information should be removed/deleted to prevent confusion or miscommunication of outdated information. Proposed Change: “Safety communication should address....and should be updated as further evidence becomes available, with outdated information being deleted”.
Lines 113-114		Comment: Information on competing risks should be included. proposed change: “Information on competing risks, such as the risk of non-treatment **or the risk of jeopardizing Public Health / prevention campaign, e.g. for communication concerning vaccines**, should be included where **appropriate** and possible”
Line 115		Comment: Examples should be inserted to give the user of the guidance what “appropriate” means. Alternatively, simply the statement without “appropriate” implies that the MAH must use judgement to determine the measures to be used when describing and comparing risks since standard methodologies have not been finalized. Proposed Change: Delete “appropriate” “Quantitative measures should be used....”
119-121		Comment: While it may be ideal to consult patients and healthcare professionals in the preparation of safety communications, this may not always be practical where urgent communication is necessary. **Proposed change**: Patients and healthcare professionals should, if possible and if the urgency of the communication permits sufficient time, be consulted by the regulatory agency ~~**and**~~ **to** pre-test the messages early in the preparation of safety communication, particularly on complex safety concerns.
Lines 122-123		Comment: Repetition of safety communications is not necessarily optimal and it can introduce inconsistencies in the message over time. Proposed change: delete lines 122-123

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 127-128		*Comment:* It is unclear if this statement about the primary target audience is applicable to competent authorities and the MAH *Proposed change:* "The primary target audiences of safety communication **from competent authorities in Member States, the Agency or MAH** should be patients and healthcare professionals…"
Lines 129-130		Comment: "…safety information should always be brought to their attention so that they can take **adequate** and timely action." What is meant should be further specified or deleted. Proposed change: Delete "adequate" or specify with examples of what would be acceptable and "adequate." "…safety information should always be brought to their attention so that they can take timely action."
Lines 137-139		Comment: Media may receive information directly from marketing authorization holders. Proposed change (if any): "It is therefore important that the media, which may obtain information from other sources, receive also information directly from the competent authorities *and marketing authorization holders.*"
139		Comment: If media receive information from competent authorities it should also be stated that the MAH receives the same information prior to communication to the media or at the latest at the same time as to the media. Proposed change: Expand '…receive also information directly from the competent authorities.' To '…receive also information directly from the competent authorities. This information shall also be communicated to the MAH prior to communication to the media or at the latest at the same time as to the media.'
141-143		Safety communications can be necessary for highlighting certain risks in off-label indications; therefore it would be good to specify that these communications are not always relating to the authorised medicinal product Proposed change: …any new important information on an authorised medicinal product which has an impact on the medicine's risk-benefit balance under any ~~or~~ conditions of use.
147		It is legally binding for the MAH to present the information in such a way that is not misleading and that is presented objectively without including advertising.

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: Replace the word “should” by “shall”.
Line 151		Comment: “**When applicable**, a statement on the agreement...” A statement on agreement between the MAH and the competent authority would always seem to be applicable and important in such Safety Communications. Proposed Change: Delete “When applicable” “ A statement on the agreement...”
Lines 154-155		Comment: As above in Line 151. A statement on agreement between the MAH and the competent authority would always seem to be relevant and important in such Safety Communications. Proposed Change: Delete “Where relevant...” Statement could read, “ Reporting of suspected adverse reactions should occur in accordance with national spontaneous reporting systems.”
160-161		Comment: Also MAHs should make use of various tools and channels for communication. For specific topics it might be useful that authorities and MAH coordinate their communication to increase efficiency. Proposed change: Competent authorities **and marketing authorisation holders** should make use of various tools and channels to communicate on the benefit and risks of medicines and to issue safety announcements. **Where feasible, communication strategies should be aligned between authorities and MAH**.
164-168		Comment: More emphasis could be given to the definition of DHPC as communication intervention (vs. routine information) Proposed change: DHPCs are not replies to requests for information from individual health care professionals, **nor are they meant as educational material to make HCPs aware of routine risk minimisation activities.**
Line 172		Comment: “Whenever possible” implies that the competent authority may not engage in a full, two -way discussion with MAH prior to distribution of a DHPC. This should always be the case, to enable the MAH to provide their perspective & rationale for DHPC format & content.

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: Delete “whenever possible” “...when the DHPC is issued by the marketing authorisation holder, and also when issued by a competent authority.”
182-183		Comment: The examples given for changes to the product information appear to cover all safety-related changes. Furthermore use of the phrases “important change” and “major warning” are open to interpretation as to when a DHPC is needed or not. Proposed change: Amend to “~~an important~~ changes to the product information resulting in ~~particular~~ the restriction of an indication **for safety reasons**, new contraindication, change in the recommended dosing regimen due to safety reasons, ~~major~~ change to warnings or precautions for use”
184-185		Comment: Clarify this is for safety reasons Proposed change: “restriction in availability **secondary to safety reasons** which impacts on the medicinal product’s current use by patients and healthcare professionals.
186-192		Comment: The situations described in this part would all result in a change to the product information and therefore is already covered by the bullet on line 182/183 (or possibly 180/181). Proposed change (if any): delete lines 186-192
188-189		Comment: typo Proposed change: “ - new data identifying a previously unknown risk or a change in the frequency or severity ~~or~~ of a known risk;”
188-189		Comment: Not all changes in frequency or severity of known risks should result into a DHCP. Only clinically significant changes may need to communicate in a rapid manner. Unnecessary DHCPs should be avoided. Proposed change: “new data identifying a previously unknown **clinically significant** risk or a **significant** change in the frequency or severity o**f** a **serious or life threatening** known risk”
192		Comment: Not for all risk changes a DHCP is an appropriate measure. It should be limited to serious or life-

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')*
		threatening adverse events. Proposed change: "new recommendations for treating or preventing **of serious or life threatening** adverse reactions (relating specifically to the use of the product itself and not more generally to the practice of medicine);"
194		Comment: typo Proposed change: amend to "...the DHPC should encourage..."
197		Comment: typo Proposed change: amend to "...to disseminate a DHPC in any situation..."
197-199		*Proposed change:* A competent authority should **disseminate or** request the marketing authorisation holder to disseminate a DHCP in any situation where the authority considers it relevant to the safe and effective use of the medicinal product.
199		Recognizing the recommendations in section XV.B6.2 "Document in Lay Language" , we propose it would be helpful to append the Q & A lay "language version" and send out with the DHCP letter for physicians to use with their patients. Proposed change: Add at 199: 'The Q&A in lay language should accompany the DHCP letter for physicians to enable them to use it with their patients.'
200-201		*Proposed change to title of section and first line :* **Communication to general public** **Communications using** material in lay language (**simple, non-technical terms)** helps patients and the general public….
Line 212		Comment: "**Whenever possible** it is advised that patients and healthcare professionals are involved..." As described in Lines 119-120 Due to the importance of safety communication, it would be very important to have patients and healthcare professionals involved. Proposed Change: delete "Whenever possible" It is advised that patients and healthcare professionals are involved..."

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')*
216-217		<u>comment:</u> MAH should be informed before a press communication to journalists is decided and a copy of the communication should be addressed to the MAH. This would allow the MAH to get prepared. It is particularly relevant when referring to medicines under prescription and reimbursed for which the MAH is not allowed to communicate via press to Public.
Lines 218-219		Comment: Taking into account the collaboration and the transparency between Competent Authorities and Marketing Authorisation Holders, MAHs should be informed before any publishing in order to avoid discovering a press communication from Competent Authorities through journalists. Proposed Change: “Competent authorities may send press releases directly to journalists following discussion and awareness of the MAH in addition to publishing them on their websites.”
223		This paragraph is rather unclear in terms of reviews; is it meant to be a review by a regulatory authority in the framework of a referral; or also ongoing signal detection activities (as published)
225-230		Comment: It is difficult to ensure that assessments by competent authorities are mentioned in any communication, e.g. single country websites, facebook sites, local press releases, local sales force communication materials, product leaflets etc. It should also be considered that efficient communication needs to be as concise as possible. Where feasible, it would be better to add a reference to an information published on an authority webpage rather than repeating information. Proposed change: It is also recommended **to make reference to ~~that~~ relevant** ongoing **authority** reviews **~~be mentioned~~** in **~~any~~** communication by the marketing authorisation holder **(e.g. by adding a reference to a respective communication on an authority website)**. Although aimed at journalists, press releases will be read by other audiences such as healthcare professionals, patients and the general public. Reference should therefore be made to related communication materials on the topic **where feasible**.
228-233		Comment: It should be recommended that the HCP community is informed prior (whenever possible) or in close proximity of the press releases so that the HCPs can adequately respond to patient’s questions following the press release. Proposed change: … complex or public health-sensitive messages need to be conveyed to journalists. **If feasible, healthcare professionals should be informed prior or around the same time of the press release so that they are better prepared to respond to patient requests.**

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')*
234-240		Whilst the sentiment of this section is agreed with, acknowledgement should be made to the fact that the position of a website on a search engine such as Google is not easily controlled by the website owner. Also much health information on the intranet is not under the control of the MAH or Competent Authority Proposed change: Competent authorities as well as marketing authorisation holders should ensure that important safety information published on websites **under their control** is easily accessible to the public Documents on websites **under the control of competent authorities or marketing authorisation holders** should be found easily via search engines as well as by navigating e.g. via the search function on the website or easy navigation from the home page.
234-245		Comment: Section B.6.4 and B.6.5 allow websites/social media to be used e.g. the use of QR codes where relevant. However, this does not seem to be in line with Article 62 of Council Directive 2001/83/EC, whereby MAHs are not allowed to communicate such information to the public in this way. Proposed change (if any): delete lines 234-245, unless this can be verified against Article 62 of Council Directive 2001/83/EC.
Line s 236-238		Comment: Please see comment in regards to Lines 111-112 above. This should be further expanded to include the concept that outdated information should be removed/deleted to prevent confusion or miscommunication of outdated information. Proposed Change: "..should ensure that important safety information remains updated, is easily accessible by the public, with removal of outdated safety information to prevent confusion or miscommunication to the public"
250		comment: Inter-authority communication scope should be specified as it should be understood "within EU". Proposed change: add "within the EU" to the title
265		These means of communication are also applicable to MAH Proposed changes: Competent Authorities **and Marketing Authorisation Holders** should consider and make the best use of all available tools…
276-277		Comment: Safety communication tools and channels are numerous and varied. It is not possible to evaluate the effectiveness of all safety communications.

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): "*Safety communication tools and channels are numerous and varied. When possible and potentially as part of the RMP, a* research-based approach should be used in order to establish that safety communications have met the standard of XV.B.3."
281-285		Comment: If the intent of this paragraph relates to checking the actual distribution of the DHCP, this should be specified, without the ambiguity of the term "effectiveness" Proposed change: "in case of DHPCs, the MAH should at least be responsible **for evaluating its actual dissemination**, and should inform…" Comment: It would be helpful to clarify how the MAH will report back on the effectiveness of the dissemination of the DHPC. We propose that the MAH provides a simple 'tracker' or equivalent with the date of dissemination of DHPCs in each EU Member State to illustrate the outcome . This information could be provided to the Competent Authority or Agency after a period of at least one month and to be agreed with the Competent Authority or Agency. Proposed change: Add to 284: 'The MAH may fulfil the outcome by providing a simple 'tracker' or equivalent with the date of dissemination of DHPCs in each EU Member State to the Competent Authority or Agency after a period of at least one month and to be agreed with the Competent Authority or Agency.'
Lines 301 – 302; 323 and 366		*Comment:* The MA Holders should also be informed of the preparation of a safety announcement 24 hours before its publication. The Marketing Authorisation Holders should be in the loop as well to support other bodies for communication. The MAH should be a real partner of Competent Authority for safety communication rather than discovering a safety announcement once published. *Proposed change:* l. 301-302: "Prior to the publication of a safety announcement, the Member States, the agency or the European Commission shall inform each other **and the MAH of the concerned product(s)** not less than 24 hours in advance…" l.323: "A competent authority of a Member State or the Agency shall inform the EU regulatory network **and the MAH of the concerned product(s)** prior to the publication of a safety announcement that pertains to active substances…" l.366: "As part of the coordination of safety announcements, competent authorities in Member States**,** ~~and~~ the

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')*
		Agency **and the MAH of the concerned product(s)**…"
329		Comment: This implies that the messages can be different across EU depending on whether or not the competent authorities agree. This should be clarified. Proposed change: Amend to "Under the coordination of the agency, the Member States shall ~~make all reasonable efforts to~~ agree on a common message."
346		Not only coordination of safety announcements but also a scientific review of the data included in it should be done in cooperation with the MAH Proposed change: coordination *and review* of safety announcements
346-349		Comment: MAHs should have the opportunity to delete any personal or commercially confidential information prior to publication, in accordance with DIR article 106a(4). Proposed change: Amend to "Coordination of safety announcements should be done in cooperation with the concerned marketing authorisation holder(s). Whenever possible, the Agency and the competent authorities in Member States should provide any safety announcement prior to its publication to the concerned marketing authorisation holder(s), together with the timetable for the information being made public. <u>In agreement with the MAH, information of a personal or commercially confidential nature shall be deleted unless its public disclosure is necessary for the protection of public health."</u>
Lines 347-349		Comment: The competent authorities should be required to notify the marketing authorization holder of its publication and timetable before the information is made public. Proposed change (if any): "The Agency and the competent authorities in Member States *shall* provide any safety announcement *at least 24 hrs prior to* its publication to the concerned marketing authorisation holder(s), together with the timetable for the information being made public."
Lines 362-364		Comment: There are several places where the word "embargo" was used for "publication embargo of 24 hours" and there are other places where "embargo" was used by itself. See an example on lines 362-364. Please clarify if the embargo applies to publication and if the 24 hour timeline applies. Proposed change (if any): "Safety announcements from the EU regulatory network should be shared with international partners in accordance with the guidance provided in Module XIV, subject to *publication* embargo and the specific confidentiality arrangements in place."
371		This requirement should be expanded to include 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: Competent Authorities should bring to the attention of the EU regulatory network *and the relevant MAH* any such
383-384		Comment: It would be helpful to mention again that the policy concerns products authorized in more than one member state. Proposed change: … to information on pharmacovigilance concerns in relation to the use of a medicinal product **authorised in more than one Member State**, and in any event at the same time or before …
Line 386		*Comment:* In the sentence "This should relate to announcements intended for the EU as well as outside the EU", it should be clarified that the communication to EU competent authorities of planned public announcements outside the EU should be restricted to products authorised in the EU or having a positive Art 58 opinion. *Proposed change:* Add the following sentence after "This should relate to announcements intended for the EU as well as outside the EU": **"Communication to EU competent authorities of planned public announcements outside the EU should be restricted to products authorised in the EU or having a positive Art 58 opinion"**
386-387		Comment: Make it clearer that "informing the authorities at the same time" refers to informing the public and not to informing EU and non-EU authorities as mentioned in the sentence before. Proposed change: Informing the authorities at the same time **as the public** ~~however~~ should only occur exceptionally and under justified grounds.
392-395		comment: Scope, format and timing should be further defined for this MAH requirement : - Third-party should be defined as a regulatory authority in a third-country. Indeed "third party" could be an article for example which should not be within the scope of this requirement. - The timing for communication should also be better defined. The wordings "Becomes aware" / "intends to" are not specific enough. We propose to make explicit reference to art 23(2) of the Directive, where such situations requiring forthwith notification are well defined, as well as the situation for DHPC from other HAs, as clearly described lines 446-448.
413-414		Comment: This statement implies that the content and presentation of a DHPC could be different across competent authorities. The sentence should clarify that the message should be consistent where more than one competent authority is involved.

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: Amend to "The content and presentation of a DHPC disseminated by the marketing authorisation holder should be agreed with the competent authorities."
436-438		comment: "purely nationally authorised products" should be understood as a nationally authorised products in only one Member State. Otherwise this paragraph is contradicting what is described lines 419-422 (role of the PRAC for medicinal products authorised in more than one Member State). Proposed change: "purely nationally authorised products, **i.e. products nationally authorised in only one Member State**, ….
Lines 446-450		Comment: "In cases where an authority outside the EU requests the dissemination of a DHPC in their territory for a product also authorised in the EU, the marketing authorisation holder should notify the relevant competent authorities in the EU. This is a part of the legal requirement under which the marketing authorisation holder shall notify the competent authorities of any new information which may impact the risk-benefit balance of a medicinal product [REG Art 16(2)]." The word should be "shall" if it is part of the legal requirement that marketing authorization holder shall notify the competent authorities. Proposed change (if any): "In cases where an authority outside the EU requests the dissemination of a DHPC in their territory for a product also authorised in the EU, the marketing authorisation holder *shall* notify the relevant competent authorities in the EU."
Lines 458-459		Comment: "The draft translations should be submitted to the Member States for a language review within a reasonable timeframe (no more than two working days)." Should be either "reasonable timeframe" or stipulate "no more than two working days". As this is a guidance and not a legal requirement, perhaps "reasonable" is a better choice. Proposed change (if any): "The draft translations should be submitted to the Member States for a language review within a reasonable timeframe."
Line 494-495		*Proposed change:* An estimation of the frequency of the adverse reaction or reporting rates with estimated patient exposure**, if needed**

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21 September 2012

Submission of comments on 'GVP Module XV Safety communication' (EMA/118465/2012)

Comments from:

Name of organisation or individual
EGA - EUROPEAN GENERIC MEDICINES ASSOCIATION

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

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

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)
	The EGA welcomes this opportunity to comment on the GVP proposal incorporating new elements coming from the new pharmacovigilance legislation. Although we fully understand and support the intention of the proposed module, the EGA members have a few comments.
	Safety communication to healthcare professionals and patients or other members of the public is important and essential. It is recognised that some proposed actions might be useful within an ideal world but less practicable during daily work. It is mentioned in the introduction that communication is a two way process, between the MAH and the public. But the guidance is only relevant for the MAH (and competent authority) and neglects the fact that there is no obligation for the other party to even participate within the proposed communication. Any additional means and tasks which might be good for an ideal communication like involvement of laymen or external health care professionals during the preparation of communication materials goes far beyond practical work. In practical life competent authorities define the content and wording of the communication and not the target group. Measurement of the effectiveness of communication goes into the same direction. Ideal for an academic project but not feasible for the daily work for all types of communication. If mentioned in the guidance it will be a target for inspections of the MAH. An effective communication is defined as when the target group understood what was intended. There will be always groups within the public which will refuse any information from the industry (and this applies also for authorities). The target group can't be forced to get educated. This is against the right of self-determination of e.g. patients. The industry proposes that the effectiveness might be recommended only.

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 164-168		Comment: In the interest of patient safety it should be avoided that HCP do get direct healthcare professional communication (DHPC) from different MAH on the same topic. It should therefore be emphasized that the competent authorities should force the MAH in the interest of patient safety to send combined DHPC. Proposed change (if any): Add: In this paragraph MAH should be read as MAHs when more MAHs are marketing the same active substance for which a DHPC should be communicated. Competent authorities should cooperate with all MAH to make sure only one DHPC is distributed.
Line 187		Comment: there is no need to consider a DHPC when the risk benefit balance is changed in a positive way. Proposed change (if any): "a *negative* change in the risk-benefit…"
Lines 239 - 240		Comment: Some techniques may exist to influence search engines to get information from a website but it is beyond the capabilities of SMEs to have such IT experts. A guideline is written for all types of MAH. Proposed change (if any): ~~Documents on websites should be found easily via search engines as well as by navigating from the home page.~~
Lines 258 - 262		Comment: Responding to enquiries from the public should not be restricted to public domain or authority issued information. There is still information available at the MAH which might be important in the specific situation of the patient. This paragraph ignores the fact that physicians advice patients today to get into contact with the MAH to get further information. Proposed change (if any): Responses should take into account the information which is in the public domain

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')*
		and should include the recommendations to patients and healthcare professionals issued by competent authorities but are not restricted to this information. Where questions relate to individual treatment advice, the patient should be advised to contact a healthcare professional, if appropriate.
Lines 410-414		Comment: add the option of combined letters Proposed change (if any): " is usually disseminated by the MAH or group of MAH for the respective medicinal product or active, either at the …"
Lines 429 – 430; 460 - 462		Comment: Not every MAH is obliged to participate within an EU safety referral. Therefore it can't be the obligation of the MAH to submit a draft DHCP and communication plan to the Agency nor to provide translations of a DHPC into all EU languages. Proposed change (if any): for centrally authorised ~~products and for products subject to an EU referral procedure for safety reasons,~~ the marketing authorisation holder
Lines 346 – 349; 470 - 472		Comment: The EGA welcomes the intention of the Agency and competent authorities to inform the MAH before a safety announcement is published. But this is contradicting to any publication of PRAC minutes or press releases of the Agency of opinions of the CHMP within referrals. Currently any preliminary publication of opinions, recommendations etc. ignores the fact that an appeal, or the decision making process at the EU commission might change the final decision and sets standards in the market. Proposed change (if any): The Agency should inform the public not only about minutes of the PRAC or CHMP but also about the intended process and the timelines to implement measures in the market. Or any information to the public should be under publication embargo until the final decisions have been taken and the MAH is informed.

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 512-514		Comment: Product information and scientific information are in general huge documents which give a high environmental burden and huge additional costs to the MAH if the DHPC has to be distributed in the whole of EU to a large group of HCP. The option should be given to refer to the MAH or authorities' websites for this information. Proposed change (if any): Annexes: Should be attached or referred to in the public domain.

Please add more rows if needed.

<Date of submission>

Submission of comments on 'GVP Module XV – Safety communication' (EMA/118465/2012)

Comments from:

Name of organisation or individual
EIPG - European Industrial Pharmacists Group

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).

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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 173		Comment: Clarification of Section B.6.1 Proposed change (if any): Clarify whether marketing authorisation holders can publish agreed DHPC on their websites.
Line 219 Line 242		Comment: Clarification of Section B.6.3 Proposed change (if any): Clarify whether Press Releases prepared by the marketing authorisation holders can be published on their website (same as applicable to Competent Authorities)
		Comment: Proposed addition to Section B.6.5 Proposed change (if any): Better define in what circumstances and scope, safety information can be disseminated via web tool (both for marketing authorisation holders and competent authorities)

21 September 2012

Submission of comments on 'GVP Module XV – Safety communication' (EMA/118465/2012)

Comments from:

Name of organisation or individual
EuropaBio

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).

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)
	EuropaBio, the European Association of Biotechnology Industries, thanks the European Medicines Agency (EMA) for the opportunity to submit comments on 'GVP Module XV – Safety communication'. EuropaBio supports fast, well co-ordinated and clear safety communication. We are however disappointed that the current draft guideline only codifies the regulator's business practice while missing new options and communication tools which are evolving at a rapid pace. As all stakeholders have the common goal of protecting public health, it would be desirable to establish a working group including marketing authorisation holders to reflect and develop new models for fast, effective and co-ordinated communication within a global context. EuropaBio members would be interested in supporting such effort." From the content provided in this module, it would appear that there may be significant overlap between the content of this module and module XII on the processing of DHPCs. Ideally, the detail of the DHPC process should be provided in a single document, so further detail (e.g. the content of the proposed communication plan) should be provided in this module. Guidance should be provided in this module as to how safety communication should be managed for a product that has a marketing authorisation and is also under further development in clinical trials. Consideration should be given in this module as to the alignment of this guidance with the GCP requirements for informing investigators (and subjects) of new safety information in clinical trials. To avoid confusion, it is imperative that prescribers of the marketed products and clinical trial investigators are provided appropriate information on a new safety concern at the same time.

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 98		**Comment:** "For communication to be effective, **adequate coordination**...." "Adequate coordination" implies that one party feels that it is adequate, rather than having a mutual agreement on the parameters of what defines "adequate". **Proposed change (if any):** Suggest providing more context/example around what would constitute "adequate" coordination, including the amount of time that would be reasonably expected to coordinate communication on a safety issue [urgent versus non-critical, i.e. Benefit:Risk Assessment remains unchanged.
Line 109		**Comment:** "...include **appropriate** information on the seriousness..." It may be best to delete "appropriate" here since the information that must be provided is not influenced by being appropriate, since the risks presented in context of the benefits will always be dependent seriousness, severity...etc... **Proposed Change:** Delete "appropriate" "...include information on the seriousness..."
Lines 111-112		**Comment:** "Safety communication should address....and should be updated as further evidence becomes available." This should be further expanded to include the concept that outdated information should be removed or deleted to prevent confusion or miscommunication of outdated information. **Proposed Change:** "Safety communication should address....and should be updated as

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		further evidence becomes available.
Line 115		**Comment:** "**Appropriate** quantitative measures should be used...." Examples should be inserted to give the user of the guidance what "appropriate" means. Alternatively, simply the statement without "appropriate" implies that the MAH must use judgement to determine the measures to be used when describing and comparing risks since standard methodologies have not been finalized. **Proposed Change:** Delete "appropriate" "Quantitative measures should be used...."
Lines 137-139		**Comment:** "It is therefore important that the media, which may obtain information from other sources, receive also information directly from the competent authorities." Media may receive information directly from marketing authorization holders. **Proposed change (if any):** "It is therefore important that the media, which may obtain information from other sources, receive also information directly from the competent authorities *and marketing authorization holders.*"
Line 151		**Comment:** "**When applicable**, a statement on the agreement..." A statement on agreement between the MAH and the competent authority would always seem to be applicable and important in such Safety Communications. **Proposed Change:** Delete "When applicable" " A statement on the agreement..."
Lines 154-155		**Comment:** "**Where relevant**, the information should include a reminder of the need to report suspected adverse reactions in accordance with national spontaneous reporting

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		systems." As above in Line 151. A statement on agreement between the MAH and the competent authority would always seem to be relevant and important in such Safety Communications. **Proposed Change:** Delete "Where relevant..." Statement could read, "Reporting of suspected adverse reactions should occur in accordance with national spontaneous reporting systems."
Line 172		**Comment:** "...when the DHPC is issued by the marketing authorisation holder, and also, **whenever possible**, when issued by a competent authority." "Whenever possible" implies that the competent authority may not engage in a full, two -way discussion with MAH prior to distribution of a DHPC. This should always be the case, to enable the MAH to provide their perspective & rationale for DHPC format & content. **Proposed Change:** Delete "whenever possible" "...when the DHPC is issued by the marketing authorisation holder, and also when issued by a competent authority."
Lines 194 & 197		Amend "DHCP" to "DHPC".
Line 212		**Comment:** "**Whenever possible** it is advised that patients and healthcare professionals are involved..." As described in Lines 119-120 Due to the importance of safety communication, it would be very important to have patients and healthcare professionals involved.

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		Proposed Change: delete “Whenever possible” It is advised that patients and healthcare professionals are involved...”
Lines 218-219		**Comment:** “Competent authorities may send press releases directly to journalists in addition to publishing them on their websites.” This is problematic if no attempt is made to discuss and align with the MAH. **Proposed Change:** “Competent authorities may send press releases directly to journalists following discussion and awareness of the MAH in addition to publishing them on their websites.”
Line s 236-238		**Comment: “**Competent authorities as well as marketing authorisation holders should ensure that important safety information is easily accessible by the public.” Please see comment in regards to Lines 111-112 above. This should be further expanded to include the concept that outdated information should be removed to prevent confusion or miscommunication of outdated information. **Proposed Change:** “..should ensure that important safety information remains updated, is easily accessible by the public, with removal of outdated safety information to prevent confusion or miscommunication to the public”
276-277		**Comment:** “A research-based approach should be used in order to establish that safety communications have met the standard of XV.B.3.” Safety communication tools and channels are numerous and varied. It is not possible to evaluate the effectiveness of all safety communications. **Proposed change (if any):** “*Safety communication tools and channels are numerous*

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		and varied. When possible, a research-based approach should be used in order to establish that safety communications have met the standard of XV.B.3."
Line 290		**Comment:** "...**subject to procedures**...ensuring their accuracy and clarity" Clarification of "subject to procedures" is needed, as audit trail could be problematic for the MAH as this is currently written. **Proposed Change:** Clarification of "subject to procedures" – what type of procedures?
Lines 347-349		**Comment:** "Whenever possible, the Agency and the competent authorities in Member States should provide any safety announcement prior to its publication to the concerned marketing authorisation holder(s), together with the timetable for the information being made public." The competent authorities should be required to notify the marketing authorization holder of its publication and timetable before the information is made public. **Proposed change (if any):** "The Agency and the competent authorities in Member States *shall* provide any safety announcement *at least 24 hours prior to* its publication to the concerned marketing authorisation holder(s), together with the timetable for the information being made public."
Lines 362-364		**Comment:** "Safety announcements from the EU regulatory network should be shared with international partners in accordance with the guidance provided in Module XIV, subject to embargo and the specific confidentiality arrangements in place." There are several places where the word "embargo" was used for "publication embargo of 24 hours" and there are other places where "embargo" was used by itself. See an example on lines 362-364. Please clarify if the embargo applies to publication and if the

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		24 hour timeline applies. **Proposed change (if any):** "Safety announcements from the EU regulatory network should be shared with international partners in accordance with the guidance provided in Module XIV, subject to *publication* embargo and the specific confidentiality arrangements in place."
415-462		**Comment:** There is insufficient detail in these sections to provide MAHs with clear guidance as to the Agency's expectations of what shoud be provided to them and when, in relation to a DHPC. It would be helpful if the following were provided in these sections: • A statement confirming that a DHPC should not normally be distributed until the related regulatory procedure (e.g. variation) is completed. • A clear description of what should be included in the "Communication Plan" (the provision of a template for this document would be beneficial). • A flow-chart presenting a timetable and actions required by the MAH and competent authorities (as an Annex) to ensure the efficient processing of a DHPC (this is particularly relevant to DHPCs that relate to an ongoing variation procedure). See "The linguistic review process of product information in the centralised procedure" for good examples for this flow-chart.
Lines 446-450		**Comment:** "In cases where an authority outside the EU requests the dissemination of a DHPC in their territory for a product also authorised in the EU, the marketing authorisation holder should notify the relevant competent authorities in the EU. This is a part of the legal requirement under which the marketing authorisation holder shall notify the competent authorities of any new information which may impact the risk-benefit balance of a medicinal product [REG Art 16(2)]." The word should be "shall" if it is part of the legal requirement that marketing

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		authorization holder shall notify the competent authorities. **Proposed change (if any):** "In cases where an authority outside the EU requests the dissemination of a DHPC in their territory for a product also authorised in the EU, the marketing authorisation holder *shall* notify the relevant competent authorities in the EU."
Lines 458-459		**Comment:** "The draft translations should be submitted to the Member States for a language review within a reasonable timeframe (no more than two working days)." Should be either "reasonable timeframe" or stipulate "no more than two working days". As this is guidance and not a legal requirement, perhaps "reasonable" is a better choice. **Proposed change (if any):** "The draft translations should be submitted to the Member States for a language review within a reasonable timeframe."
Line 473		**Comment:** ANNEX Template for DHPC It is unclear if this is a mandated format, or simply an example. **Proposed Change:** Specify in the guidance that the Annex Template for the DHPC is an example.

17 September 2012

Submission of comments on 'GVP Module XV – Safety communication' (EMA/118465/2012)

Comments from:

Name of organisation or individual
European Organisation for Rare Diseases (EURORDIS)

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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')*
108-110		Comment: and also measures patients and their healthcare professionals can take to diminish the risk of occurrence or to manage the side effect once it has occurred. Proposed change: Information on risks should be presented in the context of the benefits of the medicine and should include appropriate information on the seriousness, severity, frequency, risk factors, time to onset and reversibility of adverse reactions, as well as measures to be taken by patients and healthcare professionals when the reaction occurs.
113-114		Comment: another type of information, often difficult to communicate about, is the distinction between an adverse event due to the medicine or its administration mode and one due to the disease evolution (e.g. blurred vision after injection of a medicine into the eye to treat vitreo-macular traction). Although it is not always possible to distinguish both, it would be important to improve this information in the package leaflet and other documents. When appropriate, patients should also be aware of the risks they could take by switching themselves to an alternative regimen that may induce side effects. Proposed change: Information on competing risks, such as the risk of non-treatment or the risk of a self-medicated alternative regimen, should be included where appropriate and possible. Information on the cause of the event when it may be due to the medicine itself, its administration or to the disease evolution should be included where appropriate and possible.

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119-121		Comment: patient/consumer and healthcare organisations can have an important contribution in pre-testing safety communication. Although pre-testing by individual patients and HCP is mentioned, the role of their organisations (who can offer a wider range of reviewers e.g. in the case of patient organisations often caregivers are involved as well) should be highlighted as well. Often those organisations are also ware of the background situation of the safety issue which can be of additional value. Proposed change: Patients and healthcare professionals and their respective organisations when appropriate should be consulted and, if possible, pre-test the messages early in the preparation of safety communication, particularly on complex safety concerns (see Module XII).
169-170		Comment: the role of learned societies and healthcare professionals' organisations in contributing to the DHCP letter review and dissemination was envisaged as some point. It was proposed that some letters should also involve such organisations. Proposed change: A DHPC is a specific tool which should involve both the marketing authorisation holder, ~~and~~ the competent authority and learned societies or healthcare professionals' organisations when appropriate, for the purpose of protecting public health
186-196		Proposed change: Other situations where dissemination of a DHPC should be considered are: • a change in the risk-benefit balance of a medicinal product following for example: – new data identifying a previously unknown risk or a change in the frequency or severity or a known risk; – substantiated knowledge that the medicinal product is not as effective as previously considered;

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		• new recommendations for treating or preventing adverse reactions or to avoid misuse/medication error with the medicinal product; • ongoing assessment of an important potential risk, for which data available at a particular point in time are insufficient to take regulatory action (in this case, the DHCP should encourage close monitoring of the safety concern in clinical practice and encourage reporting, and possibly provide information on how to minimise the potential risk).
209-211		Comment: we fully acknowledge the complexity this represents with 22 official languages, however we would like to stress the importance to also consider linguistic minorities who live in the EU, who use medicines authorised in the EU, and who may not necessarily understand one of the official languages. The Australian health authority web site proposes translation tools and interpretation resources for 27 linguistic minorities on their territory, see http://www.health.gov.au/internet/main/publishing.nsf/Content/Other+Languages-1 Proposed change: For lay language information to be effective, it should be made available in an official language or official languages of the Member State, as specified by the Member State where the communication is targeted. For other languages also used in the European Union, translation facilities should be proposed.
234-240		Comment: The European medicines web portal should be mentioned. Proposed change: A website is a key tool for members of the public (including patients and healthcare professionals) actively searching the internet for specific information on medicinal products. Competent authorities as well as marketing authorisation holders should ensure that important safety information is easily accessible by the public. The European medicines web portal will highlighting information on medicines, safety issues with medicines, promote patient reporting through linking to online forms, promote transparency on regulatory procedures associated with safety of medicines, announce public hearings on medicine safety issues. Documents on websites should be found easily via search engines as well as by navigating from the home page.

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236		Comment: *Competent authorities as well as marketing authorisation holders should ensure that important safety information is easily accessible by the public*. Is the information, apart from the statutory documents, on the MAHs website subject to any review by competent authorities prior to publication?
256-262		Comment: The information role of public hearings is missing. Still they have the potential to address safety concerns raised in the media/public opinion and this would be particularly useful when there is a discrepancy between actual risk and public fear, or when there is a major media interest but controversial coverage. For example a public hearing on the risks associated to hepatitis B vaccination could help disseminating the objective, scientific, rational information available. Proposed change: Competent authorities and marketing authorisation holders should have systems in place for responding to enquires about medicines from individual members of the public. Responses should take into account the information which is in the public domain and should include the recommendations to patients and healthcare professionals issued by competent authorities. Where questions relate to individual treatment advice, the patient should be advised to contact a healthcare professional. Public hearings could also be organised with the same aims. In this respect, Article 86(2) of Directive 2001/83/EC applies to marketing authorisation holders.
297-299		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')*
		The document mentions the European Commission, national competent authorities in the Member States, and the Agency. Maybe this could be further defined to include other health agencies with whom coordination is also desired: for example in February 2009 following the discovery of a prion protein agent associated to variant Creutzfeldt-Jakob disease in the spleen of a deceased British haemophilia patient, other agencies than agencies regulating medicines issued press-releases (e.g. the Health Protection Agency in the UK), in this case causing no harm as the information was consistent among agencies, and the Agency could have taken this opportunity to communicate on its actions to ensure highest safety in blood-derived products. Proposed change: A good level of coordination of safety communication within the EU regulatory network[3] is of particular importance so that healthcare professionals and patients receive consistent information on regulatory decisions in the EU. 3: i.e. the competent authorities in the Member States, the Agency, the European Commission and also other health authorities when appropriate
365-368		Comment: Patients', consumers' or healthcare professionals' organisations should not only be part of the dissemination but also of the readability/understandability check as it is already the case. In some situations communication might be urgent. Having up-to-date contact listings of relevant patient, consumer and healthcare professional organisations at hand will avoid losing time and missing important stakeholders and targets. Proposed change: As part of the coordination of safety announcements, competent authorities in Member States and the Agency should interact with concerned stakeholders in the EU (mainly patient, consumer and healthcare professional organisations), acknowledging their role in reviewing and disseminating key information on the safe and rationale

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		use of medicines to users (patients and healthcare professionals). For this purpose, it is advisable that competent authorities in Member States keep up-to-date listings of relevant patient, consumer and healthcare professional organisations and their contact details.
390		Comment: *The marketing authorisation holder shall ensure that information to the public is presented objectively and is not misleading [DIR Art 106a].* Is the information from MAHs to the public subject to review by the competent authority, prior to publication?
400-403		Comment: See above same as for line 209-211
463-468		Comment: The European Medicines Web Portal could serve as a depository of all DHCP letters in all EU languages. Proposed change: The competent authorities may publish the final DHPC, regardless of whether they are from a marketing authorisation holder or a competent authority. The timing for such publication should be aligned to that of the dissemination of DHPC in the Member States. The competent authorities may also issue an additional safety announcement, and disseminate the DHPC to relevant healthcare professionals' organisations as appropriate. All versions of DHCP letters will be posted on the European Medicines Web Portal to ensure ease of access.

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 September 2012

Submission of comments on 'GVP Module XV – Safety communication' (EMA/118465/2012)

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
	The nature and extent of safety communication covered by this module would be useful as in some circumstances it appears to be in the context of urgent safety information and yet in others reference is made to taking account of the views of patients and healthcare professionals (HCPs). Guidance on how to solicit views of patients and HCPs in this context would be useful. Reference is made to two-way communication, but it would necessitate three-way communication between MAH, Agencies and HCP/Patients if understood correctly. The module makes suggestions about use of many tools but the target audience for implementing such tools is unclear e.g. registered readers.

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')*
115		Comment: Examples would be useful as to appropriate quantitative measures, similarly absolute risks are difficult to portray – what is expected here? Proposed change (if any): Please provide examples.
119		Comment: Please confirm at which stage HCP and patients should be consulted. Would this occur during consultation with Agencies? Requirements and expectations can differ as discussions begin. How much time is anticipated to be made allowable for such consultation in the event of important issues? Is public consultation always to be required? Proposed change (if any): Please confirm.
122		Comment: Please clarify what is meant by repetition. Should a Direct Healthcare Professional Communication (DHPC) be repeated and, if so, at what frequency? How will repetition be balanced with not creating undue concern and what will be the role of Agencies in this repetition of messages? Proposed change (if any): Please clarify.
194 & 197		Comment: The term 'DHCP' has been incorrectly used instead of 'DHPC'. Proposed change (if any): Please replace 'DHCP' with 'DHPC'.
237, 241		Comment: Please clarify the expectation regarding important safety information on websites – is this through the SmPC? If other formats are anticipated please provide guidance – should DHPC and lay Q&A be posted?

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		Linkage to non-company website or social media platforms is not anticipated. Proposed change (if any): Please clarify.
247		Comment: To what does “Bulletins to registered readers” refer? Proposed change (if any): Please clarify and provide further detail.
Annex		Comment: Perhaps the DHPC should also make known if the product is already subject to additional monitoring. Proposed change (if any):

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21st September 2012

Submission of comments on 'GVP Module XV – Safety communication' (EMA/118465/2012)

Comments from:

Name of organisation or individual
Medicines and Healthcare Products Regulatory Agency (MHRA) Pharmacovigilance 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')*
Lines 83, 117, 143, 187, 450		Comment: "risk-benefit" should be "benefit-risk" to be consistent with other modules and the legislation. Proposed change (if any):
Various lines		Comment: Some of the bullet points are blue whereas others are black. Proposed change (if any):
Lines 122-123		Comment: Agree with this to some extent, although it is important to get a balance between repeating to reinforce the message versus too much repetition. Proposed change (if any):
Line 138		Comment:: "receive also" suggest changing to "also receive" for ease of reading. Proposed change (if any):
Line 158		Comment: "Safety communication should make use of an increasing" suggest changing to "… make use of the increasing" Proposed change (if any):

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 194 and 197		Comment: "DHCP" should be "DHPC" Proposed change (if any):
Line 198		Comment: "frequency or severity or a known..." should be frequency or severity of a known..." Proposed change (if any):
Line 218		Comment: This line mentions that NCAs may send press releases direct to journalists. At no point in the document does it state that safety communications should take account of relevant requirements relating to data protection and patient confidentiality e.g. patient identifying information should not be released.
Lines 234-240		Comment: Section on websites. Suggest adding something about ensuring websites are kept up to date and in the absence of up to date documents, inaccurate/out of date information should be removed. It is very easy to add information to a website but ongoing review and updating of websites is often overlooked. Proposed change (if any):
Line 242		Comment: This line mentions that safety communications may also be made available via web tools such as social media applications. NCAs should take steps to ensure that the messages transmitted via such means can, to the extent possible, be identified as a bona fide message from the NCA (as there is a danger that bogus alerts may cause public alarm).
Line 258		Comment: Typo "responding to enquires" should be "..enquiries" Proposed change (if any):

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 303		Comment: Does the Directive state that if communication to other NCAs/EMA/EC cannot be made at least 24 hours in advance it should be made at the same time as communication to the public? Proposed change (if any):
Lines 335, 336, 342, 374 and 378 (and elsewhere)		Comment: "lines-to-take" can be abbreviated to LTT as this abbreviation has been introduced earlier in the document (line 253). Alternatively, do not abbreviate at any point in the document and always use the term in full. Proposed change (if any):
Line 374		Comment: "Agency's safety…" should be "Agency…" ie singular Proposed change (if any):
Lines 423-425		Comment: Unclear on the purpose of doing this if the product is only authorised in one Member State. What will the other MSs do with it? Proposed change (if any):

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21 September 2012

Submission of comments on 'GVP Module XV – Safety communication' (EMA/118465/2012)

Comments from Novartis:

Name of organisation or individual
Novartis Pharma AG Novartis Vaccine & Diagnostics Novartis Consumer Health Alcon

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	Novartis is committed to the overall intention of the module to create more transparent and harmonised communication toward HCPs and patients. However, it is difficult to comment on this module in isolation, as, as stated in line 57, it 'supplements the specific guidance given in' two other modules, GVP Module XI on public participation, and GVP Module XII on communication planning, which have not been released. This means that it is not possible from this GVP to understand in which instances marketing authorisation holder should use this process. Other unreleased modules, e.g. Module XVI, are also referenced.
	This GVP refers to the involvement of the PRAC only in the context of a DHPC. This is inconsistent with the role of the PRAC, which is also expected to provide advice on MS safety announcement and communication. (http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/07/WC500129301.pdf, page 15)
	Section XV.8.6. is unclear: • It confuses means of communication and channels of communication; • It confuses proactive means of communication (e.g. DHPC) and reactive means of communication (e.g. answer to query); • It does not take into account that safety communications, which are defined as needed for 'new or emerging information', have a need for timeliness and therefore not all communication means or channels are appropriate. More specific comments are provided below on these points.
	Section XV.8.6. condones the use of social media in the context of safety communications. As social media are a relatively new platform, general guidance by EMA on using social media by marketing authorisation holders would be welcome.
	This document includes press communication such as press releases and briefings as part of safety communication. This implies that there is a way of controlling tightly the content and accuracy of the messages eventually released/disseminated by third parties, based on the releases and briefings. This seems optimistic, especially with non-specialised media when it is highly possible that the journalist will misunderstand and/or misreport some of the information provided to him/her. This is likely to be challenging to implement and enforce. It is also unclear if this is truly within the scope of a GVP or simply part of the way health authorities or MAHs deal with the press as part of their internal processes.

Stakeholder number *(To be completed by the Agency)*	General comment
	This GVP concentrate on single safety communication. For safety issues affecting a product that can be a class issue, it is not clear how MAHs should react and communicate on the safety of the class as a whole. There should be some guidance for other marketing authorisation holders with marketed products of the same class.
	This GVP concentrates on safety communication with emerging concerns. There is a need to also be able to communicate on the resolution of safety concerns
	Safety communications are complementary to the SmPC/PL. This GVP does not describe how the new or emerging information will be used to update/revise the SmPC or PL. It would be useful to have some clarification on how the safety information will be reflected/translated into the product information (update timelines, process, etc) and how it may affect a potential inclusion into the additional monitoring list.

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')*
92, 132 and 137		Should effective safety communication only promote confidence in the regulatory system? Proposed change: 'confidence in the regulatory system **and medicines manufacturers**'
98-100		MAHs have agreements with third parties for the distribution and marketing of their products. Proposed change: For the communication to be effective, adequate coordination and cooperation should be initiated between the different parties involved (e.g. competent authorities, public bodies, marketing authorisation holders **and third parties/distributors acting on behalf of MAHs**)
111-112		It is unclear how useful a safety communication on the uncertainties related to a safety concern can be, as there is a risk of confusing the recipients.
119-121		It does not feel realistic to pre-test messages with the audience, in the case of urgent safety communication, a process during which "quick" action will likely be expected. We recommend to ensure that the people with the right expertise work on creating the safety communication material (e.g. medical affairs on communication for HCP, PR for communication toward the media) to ensure that the messages can be understood by the target audience. Also it is unclear whose responsibility this would be (MAH or HA?)
122-123		Repeating messages carries the risk of overloading the recipients and of losing their attention. How communication is applied is as important as its content. In addition it is unclear what this may imply concretely – would this translate into needing to agree with PRAC/CHMP on a how frequently a message should be repeated?
134-139		This paragraph is about the interaction between HAs and the media – is this in scope of the present guideline? In case of safety communications, how disruptive may this be? How can this remain under control? If poorly or uncontrolled, it might carry the risk of misleading messages reaching HCP/public – potentially in contradiction of the information released in a more focused / traditional way.
137		The GVP promotes close collaboration between HAs and MAHs in safety communication. As a result, information is communicated by regulatory authorities but also MAHs.

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: 'It is therefore important that the media, which may obtain information from other sources, receive also **consistent** information directly from the competent authorities and **marketing authorisation holders.**'
142		To be consistent with the definition in XV.B.1. 'emerging' should be added. Proposed change: '…safety communication should describe in a clear and concise way any new **or emerging** information on an authorised medicinal product…'
155		While the template in the annex acknowledges that the product information may be updated as part of the safety communication (line 512), this is not mentioned in section XV.B.5. Clarification is needed on how this would be prepared.
170-172		"When" should be changed to "before" Proposed change: 'An agreement between these two parties should be reached ~~when~~ **before** the DHPC is issued by the marketing authorisation holder, and also, whenever possible, ~~when~~ **before** issued by a competent authority.
177		It is unclear why 'may' is used in this sentence. Proposed change: 'A DHPC **is** ~~may be~~ a risk minimisation measure'
178		The reference to the consistency principle should be XV.B.**3**
182-183		"Change in the recommended dose" may not be a suitable example as changes in dose might occur for new indications which would not qualify for a DHPC. If the example is maintained, it would need to be qualified to indicate that it applies only if such a change has an impact on safety.
193-196		A DHPC can be considered a regulatory action, so issuing a DHPC at a point in time when data are insufficient to take regulatory action, is contradictory. Also this seems rather broad in scope, encouraging the issuance of DHPC to communicate about risk and not about a safety concern, before full knowledge is at hand.
197-199		The statement that a competent authority should request a DHPC in any situation where it considers it relevant seems too strong, especially considering that all situations where a DHPC may be needed are described in lines 179 to 196. Should this be possible, some control from PRAC would be expected. Proposed change: A competent authority **may** request the MAH to disseminate […] **Any such request should be discussed at the PRAC prior to implementation.**

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')*
200-214		**Comment 1**: It is unclear: • which types of lay language documents this refers to, in particular from where these are issued, as both competent authorities and/or MAHs could be involved in writing such documents, • and who is responsible for the translation into other languages. **Comment 2**: In any case, this does not seem to be realistic given the timeframe MAHs would typically operate under in the context of a safety issue.
215-233		While media relations are indeed a good means to reach out to patients and health professionals, it is also a channel which cannot be controlled (see above general comment). Journalists are free to interpret information and often communication through the media are altered, either non-intentionally (lack of scientific background from the journalist, leading to misunderstanding of the messages) or intentionally (intent to make the news more "sensational"). To minimise the risk of altered messages, which would confuse patients, it might be good to narrow down the type of media to target. Maybe it should be called out here that media communication is more meant toward specialised press (press dedicated to the HCP target), which has a greater knowledge of safety communication material and will not alter messages.
223-227		This seems to imply that press releases prepared by MAHs will be checked more closely. Please clarify if this is so, and if yes by whom, and under which regulation.
241-245		This paragraph is worryingly vague. It should be amended to clearly identify: • if the use of social media channels such as e.g. Facebook or Twitter, is expected and allowed in the context of safety communication, for both competent authorities and MAHs, • how the accuracy of communication would be ensured, • and who would perform the review of communication practices (in particular to specify the meaning of 'regularly'). Social media are not a very secure means of communication and are subject to hacking and falsification of data, and it seems unwise to use this mode of communication in the context of safety.
246-249		Bulletins and newsletters are normally collation of information and may not meet the timeliness criterion needed for communicating on new or emerging safety concerns.

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')*
256-262		Responding to queries from individual members of the public is a reactive communication, and therefore not suitable in case of 'new or emerging information that may have an impact of the risk-benefit balance of a marketed product', when proactive communications should be used.
270-285		**Comment 1**: This paragraph on how to measure the effectiveness of safety communication makes reference to an unpublished GVP module, XVI, which makes commenting difficult. **Comment 2**: Measurement of the effectiveness of DHPCs across multiple countries, languages and cultures seems unrealistic and will be an enormous effort. EMA should clarify the type of measurement, measurement tools and sample sizes which would fulfil this requirement. The only measure proposed in the GVP is a purely mechanical measure of the effectiveness of the dissemination, and does not address the issue of the effectiveness of the communication itself. **Comment 3**: HAs would likely have a broader view of what works/what doesn't work based on the fact that they will have overview across several MAHs - would evaluation therefore not best be carried out by them? **Comment 4**: would the effectiveness of other means of communication, such as bulletins and newsletters sent by HAs also be measured?
339-341		There are in parallel two safety announcements, one from the Agency, and one from the Member State. It is unclear why this is necessary, and it is not consistent with the need for streamlined and consistent safety communication. Consideration should be given, in the interest of the public, to having a single, joint statement.
347-349		No coordination is possible if MAHs are not informed in advance of safety announcements concerning their products prior to publication. Proposed change: 'Coordination of safety announcements should be done in cooperation with the concerned marketing authorisation holder(s). ~~Whenever possible,~~ The Agency and the competent authorities in Member States should provide any safety announcement prior to its publication to the concerned marketing authorisation holder(s), together with the timetable for the information being made public.'
362-364		In the absence of Module XIV, it is difficult to comment fully, however, this sentence seems to state that the information circulated to the network is proactively shared with international partners. There should be some transparency to MAHs about what information is shared, and with whom, so that MAHs can prepare 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')*
		communications with these international partners. Proposed change (if any): if not already stated in Module XIV, state that MAHs will be copied in the communication for information.
392-395		The following requirement is too broad: "Whenever a marketing authorisation holder becomes aware that a third party intends to issue a communication related to the benefit-risk balance of a medicinal product which is authorised in the EU, the marketing authorisation holder should inform the relevant competent authorities and make all efforts so that the information is shared." The term "third party" should be replaced by a wording such as "public body". This would imply a communication by another health authority or other government-related agency. This is required because the next section (XV.C.1.4) states (line 397) "third party (e.g. scientific journals, learned societies, patients' organisations)". If the latter definition is followed, then the requirement in section XV.C.1.3 could be interpreted to mean that the MAH has to inform the EMA/NCAs of all review articles / editorials which may be sent to the MAH for comment prior to publication in any scientific journal worldwide. This seems unrealistic as it is not everyday practice that authors, editors or journalists express to the MAHs their 'intention to issue a communication related to the benefit-risk balance of a medicinal product'.
396-399		It is unclear how this can be enforced as, again, it is not everyday practice that authors, editors or journalists tell competent authorities prior to publication of 'relevant emerging safety information'. If this is enforced, the third parties should also be encouraged to inform the MAH alongside the competent authorities.
404-408		**Comment 1**: The information regarding translations is vague. There is a need to know which organisation will be responsible for the translation of each document used in communication on urgent safety matters and how consistency will be maintained across languages. Proposed change: clarify the process for translations by document (DHPC, lay language document, Press communications) and the means put in pace to ensure consistency of the messages. **Comment 2**: Clarify if and where these translations will be further processed (e.g. to create documents for publication to MS website or Safety webportal)
460-462		The MAH is expected to provide to the EMA a complete set of all final language versions of DHPCs and related safety communication documents for CAP and referrals. It is not clear why this is needed

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: delete paragraph.
466-468		It should be specified that any “additional safety announcement” by a NCA needs to be in line with the messages and actions included in the DHPC.

Please add more rows if needed.

21 September 2012

Submission of comments on 'GVP Module XV – Safety communication' (EMA/118465/2012)

Comments from:

Name of organisation or individual
Pfizer Inc

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	Overall, this draft module (GVP Module XV – Safety communication) is comprehensive and provides principles for MAHs and Competent Authorities to communicate safety information to various stakeholders. This guidance is very helpful. We thank the Agency for efforts to provide comprehensive guidance. Further, we appreciate the opportunity to review this document and we provide the following comments with the goal of improving, and thereby strengthening, the final guidance.
	Although this module seems to focus on “new and emerging information” (lines 82-84), the scope of the guidance is ambiguous, i.e., it is unclear whether this module is intended to address emerging safety issues only or whether it covers broader safety communication to HCPs and the public. Further, it is difficult to understand this guidance in context with referenced modules XI (Public participation), XII (Communication planning), XIV (International collaboration), and XVI (Tools, etc.) because these have not yet issued for public consultation. Module XIV, in particular, will be important for communication within the EEA, but also the interrelationships with the global healthcare community.
	The module indicates that safety communication is distinct from various transparency initiatives (line 64) and we strongly agree with this distinction. Communication between stakeholders, however, implies that MAHs and patients would enter into two-way interactions and legislation in many countries does not permit this.
	A second annex with a schematic flow diagram, including proposed timelines, would complement the explanatory text in section XV.C.2. on direct communication to HCPs.
	In common with other GVP modules, this module provides clarification as to the meaning of the words “shall” and “should” (lines 77-79). However, unlike other modules, this module makes use of the words “recommend” (line 226) and, in particular, “encourage” (line 406), without clarifying what either means. It is important to set expectations, as inspectors must have a clear understanding in this regard.

Stakeholder number *(To be completed by the Agency)*	General comment
	We reference the extensive comments made by the European Federation of Pharmaceutical Industry Associations (EFPIA), which we fully endorse, and we also offer the following additional suggestions to improve the Guideline. We would be glad to meet with representatives of the Agency to provide clarification on our comments.

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 55		Comment: Clarify focus on safety. Proposed change: Add "safety" to the sentence. "Communication of important new ***safety*** information …"
Line 60-63		Comment: While safety communication complements "statutory" information, it is not clear how safety communication is positioned with respect to these other documents. Who is responsible for it? What is the intended relationship with the risk management plan? Proposed change: Extend the first sentence. "Safety communication … packaging ***which can be used by both competent authorities and MAHs***"
Line 82		Comment: Add the word safety Proposed change: "...new or emerging ***safety*** information..."
Line 141-143		Comment: Safety communications can be necessary for highlighting certain risks in off-label indications. Thus, it would be desirable to specify that these communications do not always relate to the authorised uses of the medicinal product. Proposed change: "…any new important information on an authorised medicinal product which has an impact on the medicine's risk-benefit balance ***under any ~~or~~*** conditions of use."
Line 147		Comment: It is legally binding for the MAH to present the information in such a way that is not

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')*
		misleading and that is presented objectively without including advertising or promotional aspects. Proposed change: Replace the word "...should... " with "...***shall***..."
Line 216-217		Comment: Consistent with lines 346-349, the MAH should be informed before a CA holds a press briefing or issues a communication to journalists or media outlets; a copy of the planned communication should be provided to the MAH. This would allow the MAH to prepare additional contextual information. It is particularly relevant when referring to reimbursed prescription medicines for which the MAH is not allowed to communicate via press to the public. Proposed change: "...journalists. ***A copy of the planned press communication should be provided to the MAH by the competent authority in advance of its release to the press***."
Line 223-227		Comment: This paragraph is rather unclear in terms of reviews (line 226). Does the intended meaning refer to a review by a competent authority in the framework of a referral or does it also refer to ongoing signal management activities? Proposed change: Extend the paragraph (line 227). "... holder. ***Relevant ongoing reviews may include reviews by a competent authority in the framework of a referral or signal management activities being conducted by a marketing authorisation holder or competent authority***."
Line 234-240		Comment: Whilst the sentiment of this section is agreed with, acknowledgement should be made to the fact that the position of a website on a search engine such as Google is not easily controlled by the website owner. Also much health information on the Internet is not under the control of the

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')*
		MAH or competent authority Proposed change: Modify. “Competent authorities as well as marketing authorisation holders should ensure that important safety information published on websites ***under their control*** is easily accessible to the public.” “Documents on websites ***under the control of competent authorities or marketing authorisation holders*** should be found easily via search engines as well as by navigating e.g. via the search function on the website or easy navigation from the home page.”
Line 242-245		Comment: This paragraph contains no practical guidance with respect to the use of social media. The agency should commit to studying and providing recommendations on how to harness social media for safety communication purposes. Proposed change: Add to line 245. “...target audiences. ***The agency will publish more detailed recommendations on the use of social media and other emerging technologies for safety communication.***”
Line 250		Comment: Inter-authority communication should be specified as within the EU. Proposed changes: (a) Add “***within the EU***” to the title; (b) Modify line 251 to read “When one ***EU*** competent authority...”
Line 265		Comment: These means of communication are also applicable to MAHs.

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: Modify line 265 to read “Competent Authorities ***and Marketing Authorisation Holders*** should consider and make the best use of all available tools…”
Line 276-277		Comment: How does the agency envisage this requirement to be implemented in a practical manner? Would it be part of an RMP? Proposed change: Modify line 276 to read “ ***For example, as part of the RMP***, a research-based…”
Line 281-285		Comment: If the intent of this paragraph relates to checking the actual distribution of the DHCP, this should be specified, without the ambiguity of the term “effectiveness.” This section may eventually benefit from the report of the CIOMS Working Group IX. Proposed change: Modify line “In case of DHPCs, the marketing authorisation holder should at least be responsible for evaluating ~~***the effectiveness of***~~ its ***actual*** dissemination, and should inform…”
Line 346-347		Comment: A scientific review of the data that forms the basis for a safety communication should be conducted in cooperation with the MAH, in addition to coordination of safety announcement review. Proposed change: Modify line 346 to read “Coordination ***and review*** of safety announcements ***and the scientific evidence that forms the basis for the announcement*** should be done…”
Line 371		Comment: This requirement should be expanded to include 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: Modify line 372 to read “Competent Authorities should bring to the attention of the EU regulatory network ***and the relevant MAH*** any such...”
Line 392-395		Comment: Scope, format and timing should be further defined for this MAH requirement : - Third-party should be defined as a regulatory authority in a third-country. Indeed “third party” could be a published article, for example, which should not be within the scope of this requirement. - The timing for communication should also be better defined. The wordings “Becomes aware” / “intends to” are not specific enough. We propose to make explicit reference to art 23(2) of the Directive, where such situations requiring forthwith notification are well defined, as well as the situation for DHPC from other HAs, as clearly described lines 446-448. Proposed change: Extend line 395 to read “...is shared. ***For purposes of this section, third party refers to a regulatory authority outside the EU. Information sharing should be facilitated in a timeframe that is proportionate to the anticipated public health impact.***”
Line 436-438		Comment: “... purely nationally authorised products” should be understood as a nationally authorised products in only one Member State. Otherwise, this paragraph would be inconsistent with lines 419-422 (role of the PRAC for medicinal products authorised in more than one Member State). Proposed change: Modify line 436 to read “... purely nationally authorised products, ***i.e. products***

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')*
		authorised in only one Member State, the marketing authorisation holder ….”

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21 September 2012

Submission of comments on 'GVP Module XV – Safety communication' (EMA/118465/2012)

Comments from:

Name of organisation or individual
PHARMIG, the association of the Austrian pharmaceutical industry, has 120 members based in Austria and Germany and operating worldwide. The products of our members represent nearly 100 percent of the Austrian pharmaceutical market. Our members have ca. 10,000 employees.

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
	PHARMIG, the association of the Austrian pharmaceutical industry, would like to thank for the opportunity to comment on GVP Module XV – Safety communication.

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')*
83		Reference: risk-benefit balance Comment: Please change wording to benefit-risk balance and use this term throughout the whole GVP. Proposed change (if any): Benefit-risk balance
97		Reference: (see Module XI). Comment: We suppose that reference to Module XII is meant. Proposed change (if any): (see Module XII).
170 - 172		Reference: An agreement between these two parties should be reached when the DHPC is issued by the marketing authorisation holder, and also, whenever possible, when issued by a competent authority. Comment: Please delete “whenever possible”. The information in both directions should be mandatory.

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): An agreement between these two parties should be reached when the DHPC is issued by the marketing authorisation holder, and also, ~~whenever possible~~, when issued by a competent authority.
194		Reference: DHCP Comment: Please use “DHPC” consistently throughout the document. Proposed change (if any): DHPC
347 - 349		Reference: Whenever possible, the Agency and the competent authorities in Member States should provide any safety announcement prior to its publication to the concerned marketing authorisation holder(s), together with the timetable for the information being made public. Comment: Please delete “Whenever possible”. The information in both directions should be mandatory. Proposed change (if any): ~~Whenever possible~~, the Agency and the competent authorities in Member States should provide any safety announcement prior to its publication to the concerned marketing authorisation holder(s), together with the timetable for the information being made public.

Please add more rows if needed.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

13 August 2012

Submission of comments on Guideline on good pharmacovigilance practices (GVP) – Module XV – safety communication (EMA/118465/2012).

Comments from:

Name of organisation or individual
Zentiva

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment
	A flow chart on the process related to DHPC would be usefull as an appendix to this GVP module. Required/recommended timelines of the communication should be provided.
	This guideline does not deal with the topic of DHPC distribution when there are multiple MAHs in one country incl. generic companies. A section describing the procedure and coordination among MAHs and their interaction with the competent authority/ies should be added. As generic companies usually follow the originator, one possibility is to appoint the originator as the reposponsible MAH to organize the DHPC distribution for all MAHs in the Member State. However, the DHPC should be approved by all concerned MAHs.

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 55		Word “safety” should be added to the sentence *“Communication of important new* “safety*” information …”*
Line 89		This line should be rewritten as it is not clear how this point should be achieved without the safety communication looking like an advertisement.
Lines 147-148		It should be legally binding for the MAH to present the information in such a way that is not misleading and it is presented objectively without including advertising. Therefore the word “should” is proposed to be replaced by “shall”.
Line 182		“an important change to the product information” – the word important is not defined adequately, we propose to add the following wording “which might have a negative impact on safe use”.
Lines 218-222		Before a press communication is released, the MAH should be informed and provided a copy of the communication in advance in order to prepare for potential questions raised by the press.
Lines 392-395		Scope, format and timing should be further defined. Third-party should be defined as a regulatory authority in a third-country.