1 26 July 2012
2 EMA/118465/2012

3 Guideline on good pharmacovigilance practices (GVP)

4 Module XV – Safety communication

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Draft finalised by the Agency in collaboration with Member States and submitted to ERMS FG	12 July 2012
Draft agreed by ERMS FG	20 July 2012
Draft adopted by Executive Director	25 July 2012
Start of public consultation	26 July 2012
End of consultation (deadline for comments)	21 September 2012
Anticipated date for coming into effect after finalisation	December 2012

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XV.A. Introduction

This Module provides guidance to marketing authorisation holders, competent authorities in Member States and the Agency on how to communicate and coordinate safety information in the EU.

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 safe and rational use of medicines, preventing harm from adverse reactions and contributing to the protection of patients' and public health (see Module I).

Experience so far has demonstrated the need for and the benefits of streamlining and coordinating communication processes effectively within the EU regulatory network. This is of particular relevance to safety communication. In these cases, higher levels of interest from the public are anticipated, and it is most important that clear and consistent messages are provided across the EU. The new legislation on pharmacovigilance therefore includes a number of provisions to strengthen safety communication and its coordination[1].

Communication of important new information on medicinal products should be a two-way process, taking into account the views and expectations of patients and healthcare professionals. This Module addresses some aspects of this two-way process and supplements the specific guidance given in Module XI on public participation, which takes into account views and needs of concerned parties, as well as the guidance on communication planning given in Module XII.

Safety communication complements the so-called statutory product information, i.e. the summary of product characteristics (SmPC), package leaflet (PL) and the labelling of the packaging. It also adds to the information contained in the public assessment report for each medicine made available by competent authorities.

Communication is distinct from transparency, which aims at providing public access to information on processes and outcomes related to data assessment, decision-making and safety monitoring performed by competent authorities. The new legislation on pharmacovigilance envisages an unprecedented level of transparency at EU level, and it is important that safety communication is coherent and consistent with all information which is made available through different means. Transparency provisions applicable to each pharmacovigilance process are provided in each relevant GVP Module.

Under XV.B., this Module describes principles and means of safety communication on authorised medicinal products. Among the various means described, particular consideration is given to direct healthcare professional communications (DHPCs), a specific tool which involves both marketing authorisation holders and competent authorities for the purpose of providing targeted information to healthcare professionals, who are crucial in ensuring the safe and rational use of medicines. XV.C. provides guidance on the operation of the EU network in relation to safety communication and its coordination.

In this Module, all applicable legal requirements are referenced in the way explained in the GVP Introductory Cover Note and are usually identifiable by the modal verb "shall". Guidance for the implementation of legal requirements is provided using the modal verb "should".

[1] Directive 2010/84/EU amending Directive 2001/83/EC (the latter is referenced as DIR), Regulation (EU) No 1235/2010 amending Regulation (EC) No 726/2004 (the latter is referenced as REG) and in the Commission Implementing Regulation (EU) No 520/2012 on the Performance of Pharmacovigilance Activities Provided for in Regulation (EC) No 726/2004 and Directive 2001/83/EC (the Implementing Regulation is referenced as IR).

XV.B. Structures and processes

XV.B.1. Safety communication

This Module refers to safety communication as the communication of new or emerging information on an authorised medicinal product, which may have an impact on its risk-benefit balance and its conditions of use.

XV.B.2. Objectives of safety communication

Safety communication aims at:

- providing timely evidence-based information on the safe and effective use of medicines;
- facilitating changes to healthcare practices (including self-medication practices) where necessary;
- improving attitudes, decisions and behaviours in relation to the use of medicines;
- supporting risk minimisation behaviour;
- facilitating informed decisions on the rational use of medicines.

Further, safety communication should support public confidence in the regulatory system.

XV.B.3. Principles of safety communication

The following principles should be considered when preparing safety communication on medicines:

- The need for communication should be considered throughout the pharmacovigilance and risk management process, and the planning of safety communication should be part of risk assessment (see Module XI).
- For the communication to be effective, adequate coordination and cooperation should be initiated between the different parties involved (e.g. competent authorities, public bodies and marketing authorisation holders).
- Safety communication should deliver relevant, clear, accurate and consistent messages and reach the right audiences at the right time.
- Safety communication should be tailored to the appropriate audiences (e.g. patients and healthcare professionals) by using appropriate terminology and taking account of the different levels of knowledge and needs. Communication may include specific recommendations for the different audiences, however the accuracy and consistency of the communication should always be maintained.
- Information on risks should be presented in the context of the benefits of the medicine and should include appropriate information on the seriousness, severity, risk factors, time to onset and reversibility of adverse reactions.
- Safety communication should address the uncertainties related to a safety concern and should be updated as further evidence becomes available.
- Information on competing risks, such as the risk of non-treatment, should be included where appropriate and possible.
- Appropriate quantitative measures should be used when describing and comparing risks, i.e. the use of absolute risks and not just relative risks; for risk comparisons, denominators should be the

same in size. The use of other tools such as graphical presentation of risk and/or the risk-benefit balance should also be considered.

- Patients and healthcare professionals 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).
- In order for safety communication to be effective, consideration should be given to strengthening messages by repetition, especially whenever a change in behaviour is sought over time.
- The effectiveness of safety communication should be evaluated where appropriate and possible (see XV.B.7.).

XV.B.4. Target audiences

The primary target audiences of safety communication should be patients and healthcare professionals who use (i.e. prescribe, handle, dispense, administer or take) medicinal products. The essential role of healthcare professionals is recognised, and safety information should always be brought to their attention so that they can take adequate and timely action. Effective safety communication enables healthcare professionals to give clear and useful information to their patients, thereby promoting patient safety and confidence in the regulatory system. Patient, consumer and healthcare professional organisations can play a role as multipliers in disseminating important information to target audiences.

The media should also be considered as a target audience of safety communication. The capacity of the media to reach out to patients, healthcare professionals and the general public is a critical element for amplifying new and important information on medicines. The way information is communicated through the media will influence the public perception and confidence in the regulatory system. It is therefore important that the media, which may obtain information from other sources, receive also information directly from the competent authorities.

XV.B.5. Content of safety communication

- Taking into account the principles in XV.B.3., safety communication should describe in a clear and concise way any new important information on an authorised medicinal product which has an impact on the medicine's risk-benefit balance or conditions of use.
- The reason for initiating safety communication should be clearly explained.
- Any related recommendations to healthcare professionals and patients on how to deal with any safety concern with the medicinal product should be provided if known.
- The information should not be misleading and should be presented objectively [DIR Art 106a(1),)]. Information should not include any material or statement which might constitute advertising within the scope of Title VII and VIIIa of Directive 2001/83/EC, or which is considered to be promotional or commercial by a competent authority.
- When applicable, a statement on the agreement between the marketing authorisation holder and the competent authority on the safety information provided should be included.
- A list of literature references should be annexed, when relevant.
- Where relevant, the information should include a reminder of the need to report suspected adverse reactions in accordance with national spontaneous reporting systems.

XV.B.6. Means of communication

Communication tools and channels[2] have become more numerous and varied over time, offering the public more information than was previously possible. Safety communication should make use of an increasing variety of means in order to reach the target audiences and meet their growing expectations. Competent authorities should make use of various tools and channels to communicate on the benefit and risks of medicines and to issue safety announcements [DIR Art 106a]. Examples of communication tools and channels are listed below.

XV.B.6.1. Direct healthcare professional communication (DHPC)

A direct healthcare professional communication (DHPC) is defined as a communication intervention by which important information is delivered directly to individual healthcare professionals by a marketing authorisation holder or by a competent authority, to inform them of the need to take certain actions or adapt their practices in relation to a medicinal product. DHPCs are not replies to requests for information from individual healthcare professionals.

A DHPC is a specific tool which should involve both the marketing authorisation holder and the competent authority for the purpose of protecting public health. 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. This will cover both the content of the information (see XV.B.5.) and the communication plan, including the intended recipients and the timetable for disseminating the DHPC (see Module XII).

A DHPC may be complemented by other communication tools and channels and the principle of consistent information should apply (XV.B.1.).

A DHPC may be a risk minimisation measure as part of a risk management plan (see Modules V and XV).

A DHPC should be disseminated in the following situations:

- suspension, withdrawal or revocation of a marketing authorisation with recall of the medicinal product from the market for safety reasons;
- an important change to the product information, in particular restriction of an indication, new contraindication, change in the recommended dose, major warnings or precautions for use;
- restriction in availability which impacts on the medicinal product's current use by patients and healthcare professionals.

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;
- new recommendations for treating or preventing adverse reactions;

[2] For the purpose of this section tools and channels are presented without distinction as they often overlap and there is no general agreement on their categorisation.

- 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).

A competent authority should 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.

XV.B.6.2. Documents in lay language

Communication material in lay language (e.g. using a questions & answers format) helps patients and the general public to understand the scientific evidence and regulatory actions relating to a safety topic. Lay language documents should contain the recommendations and advice for risk minimisation to patients and healthcare professionals issued by the competent authority in relation to the safety concern and should be accompanied by relevant background information.

Lay language documents are generally useful to members of the public who have an interest in the subject but do not have a scientific or regulatory background. Reference should be made to other communication materials on the topic to direct readers to where they can find further information.

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.

Whenever possible it is advised that patients and healthcare professionals are involved during the preparation of lay language documents to ensure, among others, that the information they deliver is useful and adapted to the target audience.

XV.B.6.3. Press communication

Press communication includes press releases and press briefings which are primarily intended for journalists.

Competent authorities may send press releases directly to journalists in addition to publishing them on their websites. This ensures that journalists, who may also obtain information from other sources, receive information that is consistent with the authority's scientific assessment. By targeting the media, it is expected that the message will reach out to a wider audience. Adequate use of press communication is also an important factor which contributes to building trust in the regulatory system.

Press releases may also be prepared by marketing authorisation holders. Their press releases may reflect the position of the marketing authorisation holder on a safety topic but should also contain information on any assessment and regulatory action taken by the competent authority. It is also recommended that relevant ongoing reviews be mentioned in any communication by the marketing authorisation holder.

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.

Press briefings with journalists should be considered by competent authorities for safety concerns or other matters relating to the safety of medicinal products that are of high media interest or when complex or public health-sensitive messages need to be conveyed to journalists.

XV.B.6.4. Website

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.

Documents on websites should be found easily via search engines as well as by navigating from the home page.

XV.B.6.5. Other web-based communications

Online safety information may also be disseminated via web tools, such as social media applications. When using newer, more rapid communication channels, the accuracy of the information should be ensured as for all communication. Communication practices should be reviewed regularly and kept up to date with emerging communication tools used by the various target audiences.

XV.B.6.6. Bulletins and newsletters

Bulletins and newsletters provide new information about medicines and their safety and effectiveness at regular intervals to registered readers. Competent authorities can reach a large audience with these tools by using web-based and other available means.

XV.B.6.7. Inter-authority communication

When one competent authority takes regulatory action on a particular safety concern, other authorities usually need to respond to enquiries or communicate on the same issue. The use of inter-authority communication material, such as lines-to-take (LTT) should be considered. LTTs are documents specifically prepared by a competent authority to assist its own staff and those of cooperating authorities in answering external enquires or communicating on a specific safety issue or concern.

XV.B.6.8. Responding to enquiries from the public

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.

In this respect, Article 86(2) of Directive 2001/83/EC applies to marketing authorisation holders.

XV.B.6.9. Other means of communication

Other tools and channels exist such as publications in scientific journals, journals of professional bodies and their websites. Competent authorities should consider and make the best use of all available tools and channels in order to properly target different audiences. Other tools and channels may be used in the context of risk management; risk minimisation measures often include specific programmes for risk communication. Tools used in such programmes such as patient alert cards or healthcare professional safety guidance are described in more detail in Module XVI.

XV.B.7. Effectiveness of safety communication

Safety communication is considered effective when the transmitted message is received and understood by the target audience in the way it was intended, and appropriate action is taken by the target audience. Adequate mechanisms should be in place in order to measure the effectiveness of the communication based on clear objectives. Measuring effectiveness allows lessons to be learned and helps in making decisions on prioritising and adapting tools and practices to meet the needs of the target audiences. A research-based approach should be used in order to establish that safety communications have met the standard of XV.B.3. This approach may measure different outcomes, including behaviour, attitudes, knowledge. When evaluating the effectiveness of a safety communication, the scope of the evaluation may be broadened to include factors other than the performance of the individual tools used in the safety communication (see Module XVI).

In case of DHPCs, the marketing authorisation holder should at least be responsible for evaluating the effectiveness of its dissemination and should inform the competent authorities of the outcome and of any difficulties identified (e.g. problems related to the list of recipients or the timing and mechanism of dissemination). Appropriate action should be taken as needed to correct the situation or prevent similar problems in the future.

XV.B.8. Quality system requirements for safety communication

In accordance with the quality system requirements in Module I, procedures should be in place to ensure that safety communications comply with the principles in XV.B.3. as appropriate for each intervention.

In particular, the communications should be subject to procedures ensuring their accuracy and clarity. For this purpose review processes with allocated responsibilities should be followed and documented.

XV.C. Operation of the EU regulatory network

XV.C.1. Coordination of safety announcements in the EU

In the EU, patients and healthcare professionals increasingly look at competent authorities as providers of important information on medicines. For safety communication to be effective, adequate coordination and cooperation is required between the different parties involved.

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.

When issuing safety announcements, competent authorities may make use of the different tools and channels described in XV.B.6.. Prior to the publication of a safety announcement, the Member States, 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)].

For active substances contained in medicinal products authorised in more than one Member State, the Agency shall be responsible for the coordination between national competent authorities of safety announcements [DIR Art 106a(3)].

For practical reasons and in order to focus on those topics of major health relevance, not all safety information made public by a Member State or the Agency will be subject to systematic exchange and coordination. Only safety announcements that relate to the following and that pertain to active

[3] i.e. the competent authorities in the Member States, the Agency and the European Commission.

substances contained in medicinal products authorised in more than one Member State should be exchanged and coordinated within the EU regulatory network:

- suspension, withdrawal or revocation of a marketing authorisation due to changes to its risk-benefit balance;
- start or finalisation of an EU referral procedure for safety reasons;
- restrictions of indications (i.e. changes to summary of product characteristics section 4.1);
- dissemination of a DHPC agreed by the Pharmacovigilance Risk Assessment Committee (PRAC) / Committee for Medicinal Products for Human Use (CHMP) or the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh) (see XV.C.2.1.);
- other emerging safety concerns that may give rise to public or media interest (e.g. a publication of important safety findings in a (scientific) journal, safety-related regulatory action taken in a Member State or in a country outside the EU).

XV.C.1.1. Process for exchange and coordination of safety announcements

A competent authority of a Member State or the Agency shall inform the EU regulatory network prior to the publication of a safety announcement that pertains to active substances contained in medicinal products authorised in more than one Member State and that refer to any of the situations identified in XV.C.1. It shall include a timetable for the information being made public [DIR Art 106a(3)]. Whenever possible a publication embargo of 24 hours shall be provided [DIR Art 106a (2)], in order to allow preparation and translation of communication plans and strategies in other EU Member States. Under the coordination of the Agency, the Member States shall make all reasonable efforts to agree on a common message [DIR Art 106a(3)].

The Agency should decide for each case, on the basis of the public health relevance and urgency of the safety concern, the population and number of Members States affected and the potential for media attention, whether action in addition to the dissemination of the safety announcement is needed to ensure an adequate level of coordination. This may be:

- preparation of lines-to-take (see XV.B.6.7.) which should be disseminated to the EU regulatory network. The lines-to-take document should help the EU regulatory network to respond more efficiently to any demand of information which may follow the publication of the safety announcement;
- preparation of an Agency's safety announcement in addition to that of the Member State, which should also be disseminated under embargo to the EU regulatory network together with a timetable for its publication.

The Agency should prepare both lines-to-take documents and any Agency's safety announcement together with the Member State(s) who originated the process and the PRAC Lead Member State or the PRAC Rapporteur, as appropriate. The PRAC, as well as the CHMP or CMDh, should also be consulted as necessary.

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.

The exchange and coordination of safety announcements within the EU regulatory network should make use of the early notification system. The early notification system was developed for use by the

Agency to provide advance notice to competent authorities in Member States and the European Commission of safety information on centrally authorised products. This system should also be used by competent authorities in Member States for the purpose of early exchange and coordination of safety announcements.

The early notification system includes the Heads of Medicines Agencies (HMA), the members of the PRAC, CHMP, CMDh and operational contact points for safety announcements at the competent authority in Member States, the European Commission and the Agency. Operational contact points should ensure that any information exchanged via the system reaches in a timely manner the relevant staff within each competent authority, including relevant staff working within the communications departments.

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.

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 disseminating key information on the safe and rationale use of medicines to users (patients and healthcare professionals).

XV.C.1.2. Exchange of safety information produced by third parties

There are situations where emerging safety information is to be published or has been published by a party other than a competent authority of a Member State or the Agency. Competent authorities should bring to the attention of the EU regulatory network any such safety information that they become aware of, together with the timing of the publication if known. Where necessary and after validation, the Agency should prepare and disseminate a lines-to-take document or an Agency's safety announcement to address the information from third parties (see XV.C.1.1.).

In the context of collaboration with authorities outside the EU, the Agency may become aware of safety announcements to be published by these authorities (see Module XIV). In these cases the Agency should, as necessary, prepare and disseminate lines-to-take or safety announcements within the EU regulatory network. In all cases, the terms of the relevant confidentiality agreements and the embargoes of the information received should be respected.

XV.C.1.3. Requirements for the marketing authorisation holder in the EU

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, the Agency and the European Commission [DIR Art 106a]. This should relate to announcements intended for the EU as well as outside the EU. Informing the authorities at the same time however should only occur exceptionally and under justified grounds. Whenever possible, the information should be provided under embargo at least 24 hours prior to its publication.

The marketing authorisation holder shall ensure that information to the public is presented objectively and is not misleading [DIR Art 106a].

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.

XV.C.1.4. Consideration for other third parties

Any other third party (e.g. scientific journals, learned societies, patients' organisations) is encouraged to inform the Agency and the competent authorities in Member States of any relevant emerging information on the safety of medicines authorised in the EU under embargo ahead of its publication.

XV.C.1.5. Languages and translations

Consistent messages should reach the public across the EU in a timely manner and in an official language or official languages of the Member State as specified by the Member State where the medicinal product is placed on the market.

For the purpose of coordination, the Agency shall use English to inform the EU regulatory network of any safety announcement. When informing the Agency, the competent authorities in Member States are encouraged to provide English translations of their safety announcements for the purpose of initiating the coordination process. In the absence of a full text translation, an English summary may be provided.

XV.C.2. Direct healthcare professional communications in the EU

In the EU, a direct healthcare professional communication (DHPC) (see XV.B.6.1.) is usually disseminated by the marketing authorisation holder for the respective medicinal product, either at the request of a competent authority in a Member State or the Agency, or at the marketing authorisation holder's own initiative. The content and presentation of a DHPC disseminated by the marketing authorisation holder should be agreed with the competent authority.

XV.C.2.1. Processing of DHPCs

The situations when a DHPC is necessary or should be considered are provided in XV.B.6.1. When drafting a DHPC, the template (see ANNEX TEMPLATE) and the guidance provided in the annotations in the template should be followed as appropriate.

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. The PRAC assessment of the draft DHPC and its communication plan should be part of any assessment report of the safety concern (see Module XII).

For DHPCs relating to medicinal products authorised only in one Member State, the competent authority in the Member State should inform the other competent authorities in the EU and the PRAC of the proposed DHPC.

The roles and responsibilities of the competent authorities in a Member State, the Agency and marketing authorisation holders in the preparation and processing of DHPCs differ depending on the route of authorisation of the medicinal products:

- for centrally authorised products and for products subject to an EU referral procedure for safety reasons, the marketing authorisation holder should submit the draft DHPC and communication plan to the Agency.
- for products authorised through the mutual recognition or decentralised procedure, the marketing authorisation holder should submit the draft DHPC and communication plan to the Reference

Member State, which should co-ordinate the process with the marketing authorisation holder, while keeping the Concerned Member States informed of any proposed action.

- for purely nationally authorised products, the marketing authorisation holder should submit the draft DHPC and any communication plan to the competent authorities of the Member States where the product is authorised.

The marketing authorisation holder should allow a minimum of two working days for comments. However, whenever possible more time should be allowed. The timing may be adapted according to the urgency of the situation.

Competent authorities in a Member State and the Agency should exchange final DHPCs and communication plans using the early notification system (see XV.C.1.1.), and the Agency should coordinate any subsequent safety announcement as appropriate using the process described in XV.C.1.1.

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 need for any subsequent communication, e.g. a DHPC, in the EU should be considered and agreed on a case-by-case basis.

XV.C.2.2. Translation of DHPCs

For centrally authorised products, products subject to an EU referral procedure for safety reasons and, in most cases, also for products authorised through the mutual recognition or decentralised procedure, the working language for preparing the DHPCs will normally be English.

Once the text of the DHPC is agreed, the marketing authorisation holder should prepare translations in an official language or official languages of the Member State as specified by the Member State(s) where the DHPC is to be distributed. The draft translations should be submitted to the Member States for a language review within a reasonable timeframe (no more than two working days).

For centrally authorised products and products subject to an EU referral procedure for safety reasons, the marketing authorisation holder should provide the Agency with a complete set of all final language versions and any related communication documents.

XV.C.2.3. Publication of the DHPCs

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.

XV.C.3. Transparency of safety communication processes in the EU

Transparency of the safety communication processes in place would help the public understand the decision-making by competent authorities. For example, initiation by the PRAC of a safety communication will be reflected in the PRAC minutes which are available to the public.

ANNEX Template for Direct Healthcare Professional Communications

<Date>

Heading with the main message, e.g introduction of warnings or contraindications

Dear Healthcare provider,

Company X would like to inform you of the following:

Summary

<A brief description of the safety concern, recommendations for risk minimisation (e.g. contraindications, warnings, precautions of use) and, if applicable, switch to alternative treatment>
<Recall information, if applicable (e.g. pharmacy or patient level, date of recall).>

Style guide: The Summary section should be in larger font size than the other sections of the DHPC and preferably in bullet points.

<A statement indicating that the information is being sent in agreement with the national Competent Authority or the European Medicines Agency, if applicable.>

Further information on the safety concern and the recommendations

<Important details about the safety concern (adverse reaction, seriousness, statement on the suspected causal relationship, e.g. the pharmacodynamic mechanism, temporal relationship, positive re-challenge or de-challenge, risk factors), also indicating the reason for disseminating the DHPC at this point in time>

<If needed, details on the recommendations for risk minimisation>

<Placing of the risk in the context of the benefit>

<An estimation of the frequency of the adverse reaction or reporting rates with estimated patient exposure>

<A statement indicating any association between the adverse reaction and off-label use, if applicable>

<A schedule for follow-up action(s) by the marketing authorisation holder/competent authority, if applicable>

Further information

<Link/ref to other available relevant information, such as information on the website of a competent authority>

Call for reporting

<A reminder of the need and how to report adverse reactions in accordance with the national spontaneous reporting system>

<Details (name, postal address, fax number, website address) on how to access the national spontaneous reporting system >

Company contact point

<Contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address>

Annexes:

512 <Text of the revised Product Information (with changes made visible), if applicable>

513 <Detailed scientific information, if necessary>

514 <List of literature references, if applicable>