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Guideline on good pharmacovigilance practices (GVP)

Module XV – Safety communication

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This track-change version identifies the majority of changes introduced to the public consultation version of this document as the Agency's response to the comments received from the public consultation. This track-change version is published for transparency purposes and must not be taken or quoted as the final version.

* For this reason, the timetable above, and in particular the date of coming into effect, apply only the clean version published as final.

For the final version of this module and any future updates, please see the GVP webpage of the Agency's website.

Please note that in final GVP Modules, templates will appear in the GVP Annex.

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XV.A. Introduction

This Module provides guidance to marketing authorisation holders, competent authorities in Member States and the [European Medicines 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 for achieving~~ 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 protection of patients' and public health (see [Module I](#)).

~~Safety information, and safety communication in particular, is a broad term concept which covers different types of information on medicines, including statutory information on safety as contained in the product information (i.e. the summary of product characteristics (SmPC), package leaflet (PL) and the labelling of the packaging) and public assessment reports. Despite~~ Although some principles in this Module (i.e. [Section XV.B.1 and B.2](#).) apply to all types of safety communication, ~~the~~ ~~this~~ ~~module~~ provides general principles on safety communication which may apply to all circumstances, its scope focuses on communication ~~o~~ itself focuses on the communication of 'new or important emerging safety information'. ~~Therefore when using the term safety communication in this module we refer to, which means~~ new information ~~(about a previously known or unknown risk of a medicine)~~ which has or may have an impact on ~~the~~ medicines' risk-benefit balance and its condition of use, ~~and would therefore affect decisions and practices about prescribing or taking a medicine.. Unless otherwise stated, the term 'safety communication' in this module should be read as referring to emerging safety information.~~

~~Other ways to provide safety information are not covered in this module such as the safety information provided through the so-called statutory product information (i.e. the summary of product characteristics (SmPC), package leaflet (PL) and the labelling of the packaging), nor the safety information contained in the public assessment report for each medicine made available by competent authorities. However, the principles identified in [XV.B.3](#), would also apply to these type of safety information.~~

~~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 the information which is made available through different means. Transparency provisions applicable to each pharmacovigilance process are provided in each relevant GVP Module.~~

Experience so far has demonstrated the need ~~for and the benefits of streamlining and to~~ coordinating safety communication ~~processes effectively~~ within the EU regulatory network. ~~This is of particular relevance to safety communication. In these cases, Higher~~ levels of public interest from the public are anticipated ~~when new safety concerns arise on issues requiring safety communication,~~ and it is ~~most~~ important that clear and consistent messages are provided across the EU ~~in a timely manner~~. The new legislation on pharmacovigilance therefore includes a number of provisions to strengthen safety communication and its coordination¹.

~~Safety c~~ommunication of important new [safety](#) information on medicinal products should ~~be involve~~ a two-way process ~~interaction~~, taking into account the views and expectations of [concerned parties](#), including patients and healthcare professionals, ~~with due consideration of the current legal.~~

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).

~~framework given to relevant legislation. This Module addresses some aspects of this two-way interaction process and with concerned parties 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.~~

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

~~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 Section XV.B. of: 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) because of their central importance in targeting healthcare professionals and the level of coordination required between. The reason for focusing specifically on DHPC is that it is a specific tool which involves both marketing authorisation holders and competent authorities. Section 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 coordination and dissemination of DHPCs safety communications within operation of the EU network in relation to safety communication and its coordination. Both sections give particular consideration to direct healthcare professional communications (DHPCs), and provide specific guidance for preparing them. This is because of the central importance of DHPCs in targeting healthcare professionals and because of the level of coordination required between marketing authorisation holders and competent authorities in their preparation.~~

~~In Throughout this Module, all applicable legal requirements obligations are referenced to as stated in the way explained in the GVP Introductory Cover Note and are usually identifiable by the modal verb "shall". (e.g. 'the marketing authorisation holder shall...'). When guidance for the implementation of legal requirements is provided on how to implement legal provisions, using the modal verb "should" is used (e.g. 'the marketing authorisation holder should...').~~

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.~~

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XV.B.12. 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~~In addition to the above ~~effective, high quality-~~ safety communication should ~~support help~~ ~~bolster can support~~ public confidence in the regulatory system.

XV.B.23. Principles of safety communication

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

- The need for ~~communication communicating safety information~~ should be considered throughout the pharmacovigilance and risk management process, and ~~the planning of safety communication~~ should be part of risk assessment (see **Module XIJ**).
- ~~There should be For the communication to be effective, a~~ Adequate coordination and cooperation ~~should be initiated~~ between the different parties involved ~~in issuing safety communication~~ (e.g. competent authorities, ~~other~~ 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 ~~for them to take appropriate action~~.
- Safety communication should be tailored to the appropriate audiences (e.g. patients and healthcare professionals) by using appropriate ~~terminology language~~ and taking account of the different levels of knowledge and ~~information~~ needs. ~~The whilst maintaining the Safety~~ ~~Communication may include specific recommendations for the different audiences, however the accuracy and consistency of the communication to the different target audiences should always be maintained~~ ~~information conveyed~~.
- Information on risks should be presented in the context of the benefits of the medicine and ~~should~~ include ~~available and relevant appropriate~~ information on the seriousness, severity, ~~frequency~~, risk factors, time to onset, ~~and~~ reversibility of ~~potential~~ adverse reactions ~~and, if available,~~ ~~expected time to recovery~~.
- ~~Safety communication should address the uncertainties related to a safety concern and should be updated as further evidence becomes available available.~~ This is of particular relevance for ~~emerging information which is often communicated earlier while the information is being assessed by a competent authorities are conducting their evaluations;~~ the usefulness of ~~its~~ communication at this stage needs to be balanced against the potential for confusion if uncertainties are not properly ~~addressed~~ ~~represented~~.
- ~~Emerging safety communication needs to be complemented with safety communication on the resolution of the safety concern.~~
- Information on competing risks, such as the risk of non-treatment, should be included where appropriate and possible.

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- ~~The most~~ Appropriate quantitative measures should be used when describing and comparing risks, ~~i.e.g.~~ 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 ~~the risk~~ and/or the ~~risk-benefit-risk~~ balance ~~should may~~ also be ~~considered used~~.
- Patients and healthcare professionals should, where possible, be consulted and, ~~if possible, asked to be used to pre-test~~ provide feedback on the intended messages pre-tested 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 the need to repeat communication, strengthening messages by repetition, especially particularly whenever a change in behaviour is sought over time.~~
- Where relevant ~~S~~safety communication should be complemented at a later stage with relevant follow-up communication e.g. on the resolution of a safety concern or updated recommendations.
- The effectiveness of safety communication should be evaluated where appropriate and possible (see **XV.B.7.**).
- Safety communications should take account of comply with relevant requirements relating to individual data protection and confidentiality.

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XV.B.34. Target audiences

The primary target audiences ~~of for~~ safety communication issued by regulatory authorities and marketing authorisation holders should be patients and healthcare professionals who use (i.e. prescribe, handle, dispense, administer or take) medicinal products.

~~As primary target audiences, 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 play an essential role.~~ Effective safety communication ~~on medicines, including medicines being investigated in clinical trials,~~ enables ~~healthcare professionals them~~ to give clear and useful information to their patients, thereby promoting patient safety and confidence in the regulatory system. Both healthcare professionals in clinical practice and those involved in clinical trial should be provided with appropriate information on any safety concern at the same time.

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~~This applies also to communication on medicines undergoing clinical trials, where healthcare professionals involved in the trials should be fully informed of emerging safety issues relating to the medicine being studied. It is important that information reaches all different relevant audiences at the same time in a coordinated manner as to avoid confusion. Safety information related to a medicine which is also under development in clinical trials should be for example provided to prescribers as well as to clinical trials investigators at the same time.~~

Patient, consumer and healthcare professional organisations can play a role as multipliers ~~in as they can~~ disseminating important safety information to target audiences.

The media ~~should is~~ also ~~be considered as~~ a target audience ~~of for~~ 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 safety information is communicated through the media will influence the public perception ~~and confidence in the regulatory system i.~~ It is therefore important that the media, ~~which may obtain safety information from~~

~~other sources, also receives also safety information directly from the competent authorities in addition to the information they receive from other sources, such as from the marketing authorisation holders.~~

XV.B.45. Content of safety communication

Taking into account the principles in ~~XV.B.23~~, safety communication **should contain:**

- ~~any should describe in a clear and concise way any new important emerging information on an authorised medicinal product which has an impact on the medicine's risk-benefit-risk balance of under any conditions of use:-~~
- ~~t~~The reason for initiating safety communication ~~should be~~ clearly explained ~~to the target audience:-~~
- ~~a~~Any ~~related~~ recommendations to healthcare professionals and patients on how to deal with ~~any a~~ 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)]. Safety 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.~~
- ~~w~~When applicable, a statement on the agreement between the marketing authorisation holder and the competent authority on the safety information provided ~~should be included:-~~
- ~~information on any proposed change to the product information (e.g. the summary of product characteristics (SmPC) or package leaflet (PL)):-~~
- ~~—~~
- ~~a~~A list of literature references ~~should be annexed~~, when relevant ~~or a reference to where more detailed information can be found:-~~
- ~~w~~Where relevant, ~~the information should include~~ a reminder of the need to report suspected adverse reactions in accordance with national spontaneous reporting systems.
- ~~The information in the safety communication should shall not be misleading and should shall be presented objectively [DIR Art 106a(1)]. Safety 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. The Agency or national competent authorities shall delete any information of a personal or commercially confidential nature unless its public disclosure is necessary for the protection of public health [DIR Art 106a(4)].~~

XV.B.45. Means of communication

Communication tools and channels² have become more numerous and varied over time, offering the public more information than was previously possible. ~~Safety communication should make~~The use of ~~an~~ ~~thise~~ increasing variety of means **should be considered when issuing safety communication** 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 different communication tools and channels are listed discussed below in sections XV.B.5.1.-XV.B.5.9. -~~

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.

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XV.B.56.1. Direct healthcare professional communication (DHPC)

A direct healthcare professional communication (DHPC) is defined [in this document](#) 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 enquiries~~ from ~~individual~~ healthcare professionals, ~~nor are they meant as educational material for routine risk minimisation activities.~~

~~A The preparation of DHPCs is a specific tool which should involve cooperation between 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 before a DHPC is issued by the marketing authorisation holder, and also, whenever possible, when issued by a competent authority. The agreement~~ This will cover both the content of the information (see [XV.B.54.](#)) and the communication plan, including the intended recipients and the timetable for disseminating the DHPC (see [Module XI](#)).

~~Where there are several marketing authorisation holders of the same active substance for which a DHPC is to be issued, a single consistent message should normally be delivered.~~

~~Whenever possible, it is advised that healthcare professionals' organisations or learned societies are involved as appropriate during the preparation of DHPCs to ensure that the information they deliver is useful and adapted to the target audience.~~

A DHPC may be complemented by other communication tools and channels and the principle of consistent information should apply ([XV.B.24.](#)).

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

A DHPC should be disseminated in the following situations [when there is a need to take immediate action or change current practice in relation to a medicinal product](#):

- ~~the 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 use of a medicine due to the restriction of an indication, a new contraindication, or a change in the recommended dose due to safety reasons;](#)
- ~~an important change to the product information, in particular, the restriction of an indication, the introduction of new contraindication, and a change in the recommended dose, major warnings or precautions for use;~~
- [a restriction in availability or discontinuation of a medicine with potential detrimental effects on patient care.](#)

~~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:

[new major warnings or precautions for use in the product information](#):

- ~~_____~~

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- ~~• 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 of a known risk;~~
- ~~•~~
- substantiated knowledge that the medicinal product is not as effective as previously considered;
- new recommendations for preventing or treating ~~or preventing~~ adverse reactions or to avoid misuse or 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).

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A competent authority ~~should may disseminate or~~ request the marketing authorisation holder to disseminate a DHCP in any situation where the competent authority considers it necessary for the continued relevant to the safe and effective use of ~~the a~~ medicinal product.

XV.B.56.2. 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 concern~~. Lay language documents should contain the competent authority's recommendations and advice for risk minimisation ~~to for~~ 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.

Competent authorities publish lay language documents on their website- national medicines web- portals and may additionally disseminate them to relevant parties such as patients and healthcare professionals' organisations. For lay language information to be effective, it should be made available in an the official languages- or official languages of the Member States(s), as specified by the Member States(s) 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.56.3. 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, in addition to who may also obtaining information from other sources, receive information that is consistent with the authority's scientific assessment. By targeting Interaction with the media, it is expected that the message will is an important way to reach out to a wider audience. ~~Adequate use of press communication is also an important factor which contributes to as weill as to building~~ trust in the regulatory system.

Press releases may also be prepared and published 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~~ make reference to any and regulatory action taken by the competent authority. ~~It is also recommended encouraged that R~~relevant ongoing reviews should 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. In cases where a DHPC is also prepared, healthcare professionals should ideally receive it prior to or around the same time of the publication or distribution of a press release so that they are better prepared to respond to patients.

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.56.4. 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 published on websites under their control is easily accessible and understandable by the public. Information on websites should be kept up-to-date, with any information that is out-of-date marked as such or removed.

The new legislation on pharmacovigilance foresees the creation of an EU medicines web portal which will contain information on all medicines authorised in the EU [Article 26 of Regulation (EU) No 1235/2010]. This web portal will become a key tool for communicating up-to-date safety information to EU citizens and will contain information in all EU official languages. Documents on websites should be found easily via search engines as well as by navigating from the home page. Each Member State shall set up and maintain a national medicines web-portal which shall be linked to the EU medicines web-portal. [DIR Art 106a]. Until the web portal is fully established and into operation, the Agency's website will be acting as an interim platform to convey this important up-to-date safety information.

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XV.B.56.5. 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, special attention should be paid to ensure that the accuracy of the information ~~released is not compromised. should be ensured as for all communication.~~ Communication practices should ~~be reviewed regularly and kept up to date with~~ take into account emerging communication tools used by the various target audiences.

XV.B.56.6. Bulletins and newsletters

Bulletins and newsletters provide at regular intervals 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.56.7. Inter-authority communication

When one competent authority takes regulatory action on a particular safety concern, other competent 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~~ Lines-to-take are documents specifically prepared by a competent authority to assist its own staff and those of co-operating authorities in answering-responding to external enquires or communicating on a specific safety issue ~~of concern~~.

XV.B.56.8. Responding to enquiries from the public

Competent authorities and marketing authorisation holders should have systems in place for responding to enquiries 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 relevant 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) and Article 98(1) of Directive 2001/83/EC applies to marketing authorisation holders.

XV.B.56.9. Other means of communication

In addition to those discussed above, there are o~~ther~~ tools and channels ~~exist~~, such as publications in scientific journals and ~~;~~ journals of professional bodies ~~and their websites~~.

Some 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 outside the scope of this module and are described in more detail in Module XVI. 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.~~

Comment [MN1]: Text removed as it is outside the current scope

XV.B.67. Effectiveness of safety communication

Safety communication is considered effective when the message 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~~ introduced 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 when possible~~ will normally be appropriate in order to establish that safety communications have met the standard of XV.B.32. 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 the case of DHPCs, the marketing authorisation holder should ~~at least~~ be responsible for evaluating the ~~effectiveness of its~~ the dissemination of the DHPCs they prepare and should inform the competent authorities of the outcome and of any difficulties identified (e.g. problems related to the list of

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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.78. 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.23, as appropriate ~~for each intervention.~~

In particular, the communications should be subject to ~~quality controls to procedures ensuring~~ their accuracy and clarity. For this purpose review ~~processes-procedures~~ 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 ~~within the EU regulatory network³. between the different parties involved.~~

A good level of coordination of safety communication ~~within the EU regulatory network⁴~~ 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.56~~. 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, considering the potential for overlap between transparency measures and active communications 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 substances contained in medicinal products authorised in more than one Member State ~~should be exchanged and require~~ coordinated within the EU regulatory network:

- ~~the~~ suspension, withdrawal or revocation of a marketing authorisation due to changes to its ~~risk-benefit-risk~~ balance;
- ~~the~~ start or finalisation of an EU referral procedure- for safety reasons;
- ~~restrictions of indications or treatment population or the addition of a new contraindication (i.e. changes to summary of product characteristics section 4.1);~~
- dissemination of a DHPC agreed by ~~relevant the Pharmacovigilance Risk Assessment Committee (PRAC) / Committee for Medicinal Products for Human Use (CHMP) or the Coordination Group for~~

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

⁴ i.e. the competent authorities in the Member States, the Agency and the European Commission.

~~Mutual Recognition and Decentralised Procedures – Human (CMDh) competent authorities of a Member State or the Agency~~ (see XV.C.2.1.);

- other emerging safety concerns ~~judged by a national competent authority or the Agency to be likely to that may~~ give rise to public or media interest ~~in more than one Member State~~ (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 ~~the safety announcement shall be sent to the network under embargo no less than 24 hours in advance of publication a publication embargo of 24 hours shall be provided~~ [DIR Art 106a (2)], in order to allow ~~Member States the members of the EU regulatory network to prepare or plan their own communication if necessary 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 ~~further~~ action in addition to the dissemination of the safety announcement is needed, ~~to ensure an adequate level of coordination. This action may such as be:~~

- ~~the~~ preparation of lines-to-take (see ~~XV.B.56.7.~~) 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 ~~request for demand of~~ information which may follow the publication of the safety announcement;
- ~~the~~ 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. ~~Any information of a personal or commercially confidential nature shall be deleted unless its public disclosure is necessary for the protection of public health [DIR Art 106a (4)].~~

The exchange and coordination of safety announcements within the EU regulatory network should make use of the ~~EU Early n~~Notification ~~s~~System (ENS). The ~~early notification system-ENS~~ 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~~ing and coordinat~~ing~~ of safety announcements.

The ~~early notification system~~ ENS includes the Heads of Medicines Agencies (HMA), the members of the PRAC, CHMP, CMDh, ~~the~~ 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 any~~ specific confidentiality arrangements in place.

As ~~a compliment to part of the~~ the coordination of safety announcements within the EU regulatory network, competent authorities in Member States and the Agency should interact with concerned stakeholders in the EU (mainly patients', ~~consumer~~ and healthcare professionals' organisations), ~~acknowledging who can play a key their~~ role in reviewing and disseminating ~~key~~ information ~~on the safe and rationale use of medicines to~~ the end users (patients and healthcare professionals). ~~It is recommended that national competent authorities and the Agency keep up-to-date contact details of relevant patients, and healthcare professionals' organisations.~~

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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 (e.g. scientific journals, learned societies). 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~~ evaluation of the information, the Agency should prepare and disseminate a lines-to-take document or an Agency's safety announcement to address the ~~information issues raised from by~~ information from the third parties (see XV.C.1.1.).

In the context of collaboration with authorities outside the EU, the Agency or a competent authority of a Member State 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 any~~ relevant confidentiality agreements with non-EU regulatory authorities 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, the marketing authorisation holder shall be required to inform the competent authorities in Member States, the Agency and the European Commission [DIR Art 106a]. This should ~~relate~~ apply to announcements intended for the EU as well as outside the EU (when they concern products authorised in the EU or those for which an opinion under Article 58 of Regulation (EC) 726/2004 has been given). Informing the authorities at the same time as the public (i.e. without advance notice to the authorities) ~~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 (see XV.C.1.2.) intends to issue a communication that could potentially impact the 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 in Member States and the Agency and make every effort to share so that the content of the communications information with the relevant authorities is shared.

XV.C.1.4. Consideration for other third parties

~~Any other~~ third parties (e.g. scientific journals, learned societies, patients' organisations) ~~is~~ are 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 and, if publication is planned, to share the information under embargo ahead of its publication if publication is planned.

XV.C.1.5. Languages and translations

Consistent messages should reach the public across the EU in a timely manner and in ~~an~~ the official languages ~~or official languages~~ of the Member States as specified by the Member States 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~~ should be provided.

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

In the EU, a direct healthcare professional communication (DHPC) (see XV.B.65.1.) is usually disseminated by ~~one or a group of~~ the marketing authorisation holders for the respective medicinal product(s) or active substance(s), either at the request of a national competent authority in a Member State or the Agency, or ~~at~~ on the marketing authorisation holder's own initiative. ~~The marketing authorisation holder should seek the agreement of the relevant national competent authorities or the Agency regarding the content of a DHPC (and communication plan) prior to dissemination.~~ 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.65.1. When drafting a DHPC, the template (see ANNEX ~~TEMPLATE~~) and the guidance provided in the annotations in the template should be followed as appropriate.

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~~A draft DHPC and communication plan relating to medicinal products authorised in more than one Member State in relation to a safety concern being discussed by the PRAC should be referred to the PRAC for its recommendation to CHMP and CMDh. part of the PRAC assessment of the draft DHPC safety concern 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 concerned:

~~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 centrally authorised products and for products subject to an EU referral procedure for safety reasons, the relevant marketing authorisation holder should submit the draft DHPC and communication plan (including the intended recipients and the timetable for disseminating the DHPC) to the Agency, which should coordinate the review process by its scientific committees (i.e. PRAC and CHMP) and CMDh.~~

- ~~_____~~

- 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, not authorised through the mutual recognition or decentralised procedure, the marketing authorisation holder should submit the draft DHPC and any communication plan to the competent authorities of the Member States where the products is-are 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.

~~The Agency will coordinate the review of DHPCs within its scientific committees/groups as appropriate (i.e. involvement of PRAC, and finalisation by CHMP or CMDh). The competent authorities or the Agency may consult the PRAC on any DHPC. The PRAC should always be consulted involved in the review of draft DHPCs related to a safety concern being discussed at the PRAC and the DHPC should form part of the PRAC assessment (see Module XII). The Agency may also request advice from consult the PRAC on issues related to other safety communications.~~

Once the content of a DHPC and communication plan from the MAH are agreed by national competent authorities or the Agency, -

~~the national c~~ompetent authorities in a Member State and/or the Agency should exchange the 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. The early notification system is only used if the DHPC concerns an active substance authorised in more than one Member State.

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-risk balance of a medicinal product [REG Art 16(2) and DIR 23(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.

A flow chart describing the processing of DHPCs is provided in ANNEX II.

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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 the~~ official ~~language of official~~ languages of the Member States 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 relevant marketing authorisation holder should provide the Agency with a complete set of all final EU official language versions as well as ~~and~~ any additional 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.~~

1 | **ANNEX ~~Template L~~ for Direct Healthcare Professional Communications**

2 <Date>

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

5 Dear Healthcare provider,

6 <Name of company> ~~Company X~~ would like to inform you of the following:

7 **Summary**

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

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

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

15 **Further information on the safety concern and the recommendations**

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

20 <A statement on any previous DHPCs related to the current safety concern that have recently been
21 distributed.>

22 <If ~~needed~~applicable, details on the recommendations for risk minimisation.>

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

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

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

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

29 **Further information**

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

32 <Therapeutic indication of the medicinal product if not mentioned above.>

See websites for contact details

European Medicines Agency www.ema.europa.eu
Heads of Medicines Agencies www.hma.eu

The European Medicines Agency is
an agency of the European Union



33 **Call for reporting**

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

36 <Mention if product is subject to additional monitoring and the reason why.>

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

39 **Company contact point**

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

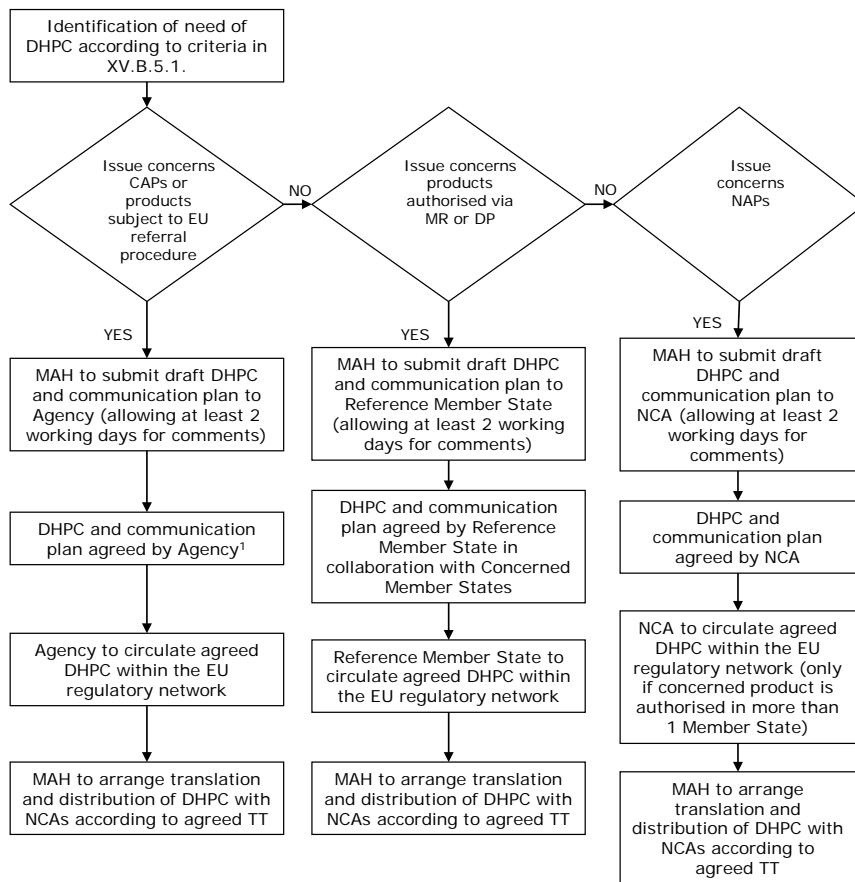
42 **Annexes:**

43 < Relevant sections of the ~~Text of the revised~~ Product Information that have been revised (with
44 changes made visible), ~~if applicable~~>

45 <Detailed scientific information, if necessary>

46 <List of literature references, if applicable>

47 | **ANNEX II Flow chart for the processing of DHCs**



¹ Agency to consult scientific committee evaluating the issue.