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EMEA/CHMP Working Group with Patients Organisations

Outcome of Discussions: Recommendations and Proposals for Action

Executive Summary

The EMEA/CHMP Working Group with Patients Organisations was created following the EMEA/CHMP Workshop for Patients Organisations held on 31 May 2002.

The Working Group held four meetings whereby it looked at further improvements to be achieved in the areas of:

(1) transparency and dissemination of information,

(2) product information,

(3) pharmacovigilance, and

(4) interaction between the EMEA/CHMP and Patients Organisations.

Patients Organisations were encouraged to steer as much as possible discussions in the different areas, e.g. through the leadership of subgroups addressing the different topics, in order to take as much as possible patients' expectations into account.

As a result of the discussions, recommendations have been established. Such recommendations fall into three categories:

(1) recommendations which can be implemented as such by the EMEA,

(2) recommendations which require a harmonised approach at European Union (EU) level before implementation, and

(3) recommendations which require amendments to the current legal framework.

The CHMP, in its March 2004 meeting, agreed on a 3-month consultation exercise with the EMEA's partners and stakeholders.

The recommendations and proposals for action stemming from the Working Group are the first element of the EMEA's reply to the G10 Recommendations from the High Level Group on Innovation and the Provision of Medicines, and the Resolution of the Council of Health Ministers of 1 and 2 December 2003. The final recommendations from the Working Group will be incorporated in an "EMEA Strategy on Interaction with Patients".

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Introduction

The EMEA/CHMP Working Group with Patients Organisations was created following the 1st EMEA/CHMP Workshop for Patients Organisations "Information and Participation," held on 31 May 2002[1]. Building on the conclusions of the Workshop, the EMEA /CHMP Working Group with Patients Organisations looked at further improvements to be achieved in the areas of transparency, dissemination of information, product information and pharmacovigilance, in order to:

(1) provide information adapted to patients' needs,

(2) develop appropriate communication tools, and

(3) increase the awareness of the public in relation to the use of medicinal products, in the context of the EMEA activities.

The EMEA/CHMP Working Group is co-chaired by F. Lekkerkerker (Dutch CHMP Member) and N. Wathion (EMEA Head of Unit for Post-Authorisation of Human Medicines), who was replaced by I. Moulon (EMEA Head of Sector for Medical Information) as co-chairperson in February 2005; the list of participants is attached as Annex 1. The EMEA/CHMP Working Group met for the first time on 8 May 2003[2].

Methodology

The EMEA/CHMP Working Group decided to create three subgroups, i.e. on transparency and dissemination of information, on product information and on pharmacovigilance. The proposals stemming from each subgroup were discussed at the level of the EMEA/CHMP Working Group. In addition, it was agreed to discuss the more general topic of interaction between the EMEA/CHMP and patients organisations in the Working Group. It should be emphasised that patients organisations were encouraged to steer as much as possible discussions on the different topics, e.g. through the leadership of the subgroups, in order to take as much as possible expectations of the patients into account. Where possible, representatives from patients organisations consulted their respective associations.

It should be stressed that the recommendations made by the EMEA/CHMP Working Group have taken into account recent initiatives, such as the outcome of the EU Review 2001 of pharmaceutical legislation and the recommendations stemming from the G10 High Level Group on Innovation and the Provision of Medicines[3].

Three types of recommendations have been made by the EMEA/CHMP Working Group:

(1) recommendations which can be implemented by the EMEA within the current legal framework,

(2) recommendations which can be implemented within the current legal framework, but need to be further discussed with the European Commission and National Competent Authorities in order to achieve a harmonised approach at EU level, and

(3) recommendations which need amendments to the current legal framework.

The recommendations finalised by the EMEA/CHMP Working Group were forwarded to the CHMP for consideration. The CHMP, during its plenary meeting on 23-25 March 2004, accepted such recommendations (see Annexes 2-5) and agreed on a 3-month consultation exercise with the Agency's partners and stakeholders (see Annex 6 for the list of consulted parties). The recommendations were published on the EMEA website on 23 April 2004.

1 http://www.emea.eu.int/pdfs/human/patientgroup/245702en.pdf
2 http://www.emea.eu.int/pdfs/human/patientgroup/261303en.pdf
3 http://pharmacos.eudra.org/F3/g10/g10home.htm

Next Steps

Comments made in the context of the consultation exercise were reviewed by the EMEA/CHMP Working Group during its meetings on 31 August 2004 and 29 October 2004. The recommendations were finalised at a 2nd Workshop held on 3 December 2004 during which all organisations which had commented were invited to participate.

From the final recommendations, the Working Group will identify priorities for action which will be incorporated into their work programme.
Long term activities of the Working Group will be addressed in the EMEA strategy on interactions with patients.
However, the group would like to remain closely linked to the CHMP in order to avoid the dilution of its activities. The other EMEA Scientific Committees have already regular interaction with Interested Parties and there is no current justification for an overarching group.
The new Regulation also foresees representatives of patients associations as members of the Management Board and in this respect, they will have an overview of the EMEA activities. The organisation of joint workshop with Industry and Health Care Professionals will be considered when necessary on specific topics but the group will remain restricted to Patients' Organisations.

General remarks

Before considering the proposals made in the different 4 areas (see Annexes), it is important to state that these recommendations address only one aspect of the information to patients. The purpose of this exercise is not to preclude physicians and pharmacists from their professional duties or to interfere in the patient-doctor or patient-pharmacist relationship.

However, patients are empowered to get information in order to make their own opinion. It is the role of the EMEA to provide additional information for patients on medicines. The objective is to encourage the dialogue between health care professionals and better informed patients. Moreover, the need to provide better information to health care professionals is addressed in the EMEA road map especially in the context of Pharmacovigilance and urgent safety restrictions. It will also be included in the communication strategy to be prepared by the EMEA.

Every patient has the right to access information and there should be no barriers of language. Further discussion with national competent authorities will take place in order to find the appropriate channels to relay the information. It was reiterated that the information should be conveyed with a language and a format understandable by all the patients.

Specific expertise in medical information should be developed in order to address the appropriate audience i.e. the public and the healthcare professionals. The EMEA together with Member States is putting in place measures in order to develop this area of expertise.

Increase of the transparency is one of the most important topics addressed in the EMEA road map and further discussion will take place prior to the implementation of additional measures. The boundaries between confidentiality and transparency will be further considered in the light of the new rules on access to documents as laid down in the new Community legislation.

The role and responsibilities of all the partners involved will have to be defined and adequate resources will have to be secured in order to implement the proposed measures

The EMEA road map has already included a proposal to build a networking model in the field of transparency and information to patients. Networks are already in place in Member States and further discussion will take place with the National Competent Authorities in order to share their experience to reinforce networks and processes and improve their adequacy

across the European Union. Priorities will derive from discussion with the National Competent Authorities and the Commission taking into account the proposals made by the Commission as a consequence of the G10. Moreover, the Pharmaceutical Industry will be involved in these discussions considering their role as initiator of the information on medicinal products. In addition, in 2005, the EMEA will the start to put in place the recommendations linked to the implementation of the new Community legislation.

Annexes

EMEA/CHMP Working Group with Patients Organisations

Outcome of Discussions:
Recommendations and Proposals for Action

Annex 1

Participants

Patients Organisations

Charlotte de Roo (Member)	BEUC, The European Consumer's Organisation
Jackie Glatter (Alternate)	BEUC, The European Consumer's Organisation
Wendy Garlic (Alternate)	BEUC, The European Consumer's Organisation
Mauro Guarinieri (Member)	EATG, European Aids Treatment Group
Polly Clayden (Alternate)	EATG, European Aids Treatment Group
Andrew Hayes (Member)	ECL, European Cancer Leagues
Arlene Spiers (Alternate)	ECL, European Cancer Leagues
Mary Baker (Member)	EFNA, European Federation of Neurological Associations
Jean Georges (Alternate)	EFNA, European Federation of Neurological Associations
Christophe Talheim (Member)	EPF, European Patients Forum
Colin Webb (Alternate)	EPF, European Patients Forum
Emmanuel Trenado (Member)	EPHA, European Public Health Alliance
Andreas Reimann (Member)	EURORDIS, European Organisation for Rare Diseases
Lesley Greene (Alternate)	EURORDIS, European Organisation for Rare Diseases
Francois Houyez (Alternate)	EURORDIS, European Organisation for Rare Diseases
Albert van der Zeijden (Member)	IAPO, International Alliance of Patients Organizations
Rod Mitchell (Alternate)	IAPO, International Alliance of Patients Organizations

CHMP Members and Experts

Frits Lekkerkerker – Co-Chairman	CHMP Member, The Netherlands
Daniel Brasseur	CHMP Chairman, Belgium
Fernando de Andrés-Trelles	CHMP Member, Spain
Tomas Salmonson	CHMP Member, Sweden
Anne Castot	Acting PhVWP Chairman, France
Beryl Keeley	Expert, United Kingdom

EMEA

Noël Wathion – Co-Chairman	Head of Unit Post-Authorisation Evaluation of Medicines for Human Use
Isabelle Moulon	Head of Sector Safety & Efficacy of Medicines
Martin Harvey-Allchurch	Head of Executive Support
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Hilde Boone	Scientific Administrator
Alexios Skarlatos	Administrator
Leng Heng	Scientific Administrator
Anabela de Lima Marcal	Scientific Administrator
Nathalie Seigneuret	Scientific Administrator
Victoria Palmi-Reig	Scientific Administrator

Annex 2

Final Recommendations in the Area of Transparency and Dissemination of Information

Topic leader: **Albert van der Zeijden (IAPO)**

The EMEA/CHMP Working Group agreed on the recommendations in the area of transparency and dissemination of information, as listed below. The following general comments were made:

The EMEA and patients organisations should work together on the provision of patient-friendly information on medicines. In this respect, the EMEA and its role/activities should be better known to the general public.

i. Patients need information on the availability of medicines in the EU.

ii. Patients need independent and validated information to help them to understand and participate in the treatment decisions. This should be a collaborative process with all parties involved in the provision of healthcare.

iii. The EMEA communication should include more patient-focused items and should take into account the needs of different user groups.

iv. Patients should be taken into account in the EMEA communication strategy.

v. Other tools to disseminate the information should be made available in addition to the EMEA website.

I Recommendations implementable within the current legal framework

I.1 Recommendations implementable as such by the EMEA

Synthesis/presentation of information on medicines

In consultation with patients organisations, the EMEA should ensure that the information concerning specific medicines is designed to meet the needs of different user groups, e.g. acute and chronic patients or the general public. Ideally this should:

i. Include availability of all information intended for patients in all official EU languages.

ii. Take account of different levels of education and ability. Follow established health literacy guidelines, i.e. namely clear and easy to understand messages, relevant and tailored content, culturally and linguistically appropriate format.

iii. Involve readers, including pilot testing on key audiences.

iv. Allow feedback from patients on the readability of patient information (e.g. package leaflet, public statements).

Transmission/dissemination of information on medicines

a) While the EMEA website is the Agency's primary tool for information dissemination, other tools should be used in particular to inform patients and the public who do not have access to the Internet.

   i. The EMEA needs to further develop its website and printed general information.

   ii. All printed information should include a reference to the web site.

   iii. The EMEA and patients/consumers organisations should encourage the inclusion of alternative sources of information voluntary and statutory.

   iv. The structure of the EMEA website should be reorganised to facilitate access of patients to information (e.g. possibility of searching drugs by disease name, medication class, therapeutic indication, active substance (International Non proprietary Name)).

   v. The EMEA should introduce multi-lingual navigation of the website.

   vi. The EMEA should create disease specific e-mail lists of patients' organisations in order to provide alerts on any new information posted on the website (e.g. safety updates, summaries of opinions, European Public Assessment Reports (EPARs), guidance documents).

b) The EPAR has shown to be of benefit mainly for healthcare professionals, although not necessarily understandable for most patients.

   i. The EMEA should develop a patient friendly version of the EPAR, including a section reflecting any comparisons with other therapeutic options considered during the evaluation process

   ii. The EMEA needs to ensure that a clear description/presentation of post authorisation specific obligations and commitments, their deadlines and their completion will be available for patients and the general public.

c) The EMEA should produce "Questions and Answers " documents on a case-by-case basis to address specific situations affecting the use of medicines, i.e. safety issues.

d) The EMEA should consider making product-by-product press releases with patient friendly information (at time of opinion, withdrawals and post-authorisation).

e) Patients' organisations should be included in the EMEA press release mailing.

f) Timing of information dissemination should be reconsidered by the EMEA, acknowledging the need for information to be provided before CHMP opinion (e.g. confirmation of submission of applications, procedural timetable for specific products). The provision of additional information prior to CHMP opinion will be decided between the EMEA and the industry.

g) Access to data on the actual availability on the market in each Member State of a given medicine should be possible.

h) Written information about medicines should also highlight the importance of the relationship between patients and pharmacists/doctors.

Transparency and awareness of the EMEA

a) Freedom of access to information answers the needs of patients and so will be the starting point for the EMEA. The necessity of limitations to this freedom has to be demonstrated on a case-by-case basis.

b) The EMEA, after discussion with industry, needs to clearly define the concept of "commercially confidential information" in order to allow for transparent communication.

c) The EMEA and its role/activities should be widely publicised and better known by the public.

   i. In general the EMEA should collect, communicate and provide information to patients and the European citizens in general. While doing this the transparency of the Agency and the European system as a whole will naturally increase.

   ii. The EMEA should undertake a public awareness strategy. This should include:

   - proactive press and media campaigns;
   - a user friendly web site;
   - publication of information brochures and printed materials;
   - use patient and healthcare professional groups as relay points.

I.2 Recommendations requiring a harmonised approach at EU level before implementation

Screening, identification and collection of information on medicines

a) The collection of comprehensive information on medicines should be based on a collaborative approach between regulatory bodies, healthcare professionals, patients groups, consumers organisations industry and other parties involved.

   The EMEA should take the initiative to bring together representatives of these groups to improve the level of collection of information on medicines with regard to the interests of patients.

b) Information on all medicines authorised in the EU should be made available.

c) Data sources include EudraVigilance (database on pharmacovigilance), EuroPharm (database on information on all authorised medicines) and databases of National Competent Authorities.

   Patients organisations should provide input on their expectations on what information should be publicly available from these databases.

Analysis and validation of information on medicines

a) Levels of validation of information should be reflected on the information provided, including reliability of data source.

b) Patients' organisations should develop a template guidance against which information provided by patient groups and other external sources could be validated. Patient organisations could consider signing-up to some self-regulation mechanism concerning the information to be presented.

Transmission/dissemination of information on medicines

a) There is a need to inform European patients about the availability of medicines across Member States.

   The EMEA should include a link to the future EuroPharm database on its website to allow access to accurate and up-to-date information about the availability of medicines across Member States.

b) Member States should make a listing of national patients associations publicly available (e.g. on their website) in line with the criteria defined in the Policy on Patients and Consumers organisations involved in EMEA activities.

II Recommendations requiring amendments to the current legal framework

Information on withdrawal or premature cessation of a product under development which is not validated by a scientific assessment highlights an area which requires review. It is suggested that this issue will be referred to be considered by the Commission in the context of the discussion on Eudract and Europharm.

Annex 3

Final Recommendations in the Area of Product Information

Topic leader: Mary Baker (EFNA)

The EMEA/CHMP Working Group agreed on the recommendations in the area of product information, as listed below. It should be noted that, in the context of the discussions, "product information" refers to "package leaflets".

These recommendations specifically address the Package Leaflet, which is included in the medicinal product package and reflects the agreed use of the product as reviewed by the competent authority which has licensed the product. Similar recommendations will be drafted for the outer and inner labelling of medicinal products.

This document does not address other reliable sources of information which are available to the patient and which are acknowledged by the Group, in particular the patient-specific advice and information given by physicians, pharmacists and other healthcare professionals.

I Recommendations implementable within the current legal framework

I.1 Recommendations implementable as such by the EMEA

a) Companies using the centralised licensing route should involve patients associations when preparing/drafting a Package Leaflet (PL) at an early stage. In addition, patients associations could be involved in Readability Testing and in the review by the Quality Review of Documents Group (QRD) of the English PL (e.g. join the Day-150 meeting).

   The EMEA should contact the relevant European patients association in the disease area and invite 1-2 representatives to attend the Day-150 meeting at the EMEA where the PL will be reviewed together with the company. If no EU association would exist in the disease area concerned, representatives from a national organisation or a general consumer representative with the appropriate expertise could be invited. A confidentiality agreement should be signed by the patients representatives.

   A voluntary trial period for this initiative could be set-up with interested companies.

   EMEA should publish a list of European patient associations on their website as well as providing a link to the national authorities' website where national patient associations would be listed.

b) The PL of a Centrally Authorised Product should include a reference to the EMEA website where patients can find the latest information available on the product (as part of the EPAR).

   A statement at the end of the PL such as "The latest approved information on this product is available on the website of the European Medicines Agency (EMEA): + *web address*" should be included.

   As the PL printed on the EMEA website may be different from the PL included in the medicinal product pack, due to the time it takes for an updated PL to reach the market (printing, manufacture of new product batches, distribution, pharmacy etc.…) the EMEA website (EPAR) should also contain an explanation on the general process of updating of labelling and the delays to reach the market in order to avoid confusion.

For Orphan Drugs only, where appropriate, a reference to the Eurordis website should be given in the PL in addition to the EMEA website: “General information on rare diseases is available on the Website of the European Organisation for Rare Diseases (Eurordis): http://www.eurordis.org/”.

c) Patients should be given the possibility to send comments to the EMEA on the readability/quality of PLs published on its website (in the EPAR). The EMEA would review and ‘filter’ the feedback received and liaise with the marketing authorisation holder (MAH) as well as with patients associations, as appropriate, regarding any relevant feedback received.

   A statement such as “to send your opinion on the readability/quality of the package leaflet text, please click here. Relevant feedback will be compiled and provided to the MAH” could be included on the EMEA website (e.g. EPAR).

   In addition, patient associations should encourage their members to provide feedback on printed PLs to the EMEA.

d) Changes made to the PL should be identified:

   i. Although not a priority, it could be considered to add a tabulated tracking sheet to the EPAR, giving a concise overview of the chronology of the PL and its changes.

   ii. At the end of the PL itself it should be indicated which sections were last revised.
   The reference to the revised PL section should be clear and simple (e.g. section 2 – pregnancy).

e) The listing of Local Representatives of the MAH at the end of the PL for all Member States is considered not useful and takes up too much space in the printed leaflet which could be better used. Only the Local Representative(s) relevant for the Member State(s) (MS(s)) concerned where the pack is marketed should be included in the printed PL.

   Similarly, where different manufacturers have been authorised, only the one responsible for the release of the actual batch should be included in the printed PL in order to avoid confusion and irrelevant information.

   In addition, a reference to the EMEA website should be printed above the company contact details (see also point b above).

f) Important new or updated draft guidelines published on the EMEA website which will impact on the PL (e.g. relevant CHMP guidelines, EU guidelines, QRD guidance, etc.) should be flagged to patients and healthcare professionals associations so that they can provide comments and provide input during the consultation period on the draft documents.

   An electronic mailing list should be set-up, as well as a system to identify which draft guidelines need to be sent.

I.2 Recommendations requiring a harmonised approach at EU level before implementation

a) The PL of a specific product should give the same information to all patients in the EU. There should be no differences between Member States (MSs) and between patients. Whereas this objective is already achieved in the Centralised Procedure, harmonisation of the PL text for products approved via the Mutual Recognition Procedure would be desirable.

Standardised requirements should apply across EU. This should ideally also apply to the content of PLs of products containing the same active substance(s).

The legislation and PL guidance provide for a standardisation of structure and format of a PL, but the available guidance could be further developed and optimised (e.g. QRD recommendations, review of Commission's guidelines – see also point I.2.c).

Even if a PL should give the same content in all language versions, strict literal translations may lead to unnatural, unreadable PLs which are difficult to understand. Therefore, different language versions of the same PL should allow for regional translation flexibility, whilst maintaining the same core meaning. In addition, companies and authorities should work together to ensure good-quality translations, possibly involving patients associations.

The readability of PLs should be increased as to improve the quality of the leaflets to a level which is understandable to most patients. Companies are strongly encouraged to perform readability testing and to increase the font size of printed package leaflets.

b) In order to provide a good balance between information on benefits versus risks, the benefits of taking/using the medicine should be made more prominent and better explained in the PL without promotional claims. The text should also distinguish more clearly between prevention and treatment.

In this respect, the potential consequences of stopping treatment and the need to discuss this with the treating physician or pharmacist prior to reaching a decision should be addressed in the PL as appropriate.

Similarly, a recommendation to consult the treating physician or pharmacist in the event that the expected benefit is not achieved could be included in the PL, where relevant.

Although the first section of a PL is "what the product is and what it is used for", the information provided in this section is usually very short. Especially for long term treatment and prevention products, further information on the demonstrated benefits for the patient should be included to give full information to patients and in order to improve compliance/concordance. However, it should not lead to the inclusion of any additional and promotional claims from the company outside the approved indications.

Guidance on the issues above should be developed when reviewing the Guideline on Readability (see point c below)

c) It is recommended to review the Commission's Guideline on Readability (1998), with active involvement of patients associations at an early stage. The EMEA should co-ordinate this task and should set-up a working group involving people with different expertise (Patients Associations, QRD experts, industry representatives, experts on readability and information design, etc…). Appropriate benchmarks and standards against which to judge the leaflets and tests performed should be established, based on adequate PL performance requirements.

As part of the general review of the Guideline, the following points should also be addressed:

i. In the Review of the pharmaceutical legislation (Directive 2001/83) it is specified that “Results of consultations with target patient groups should be reflected in the PL”. The Group welcomes this new provision. Further details however on what is required and when should be developed.

ii. The inclusion, in the PL, of clear and unambiguous signs/symbols/pictograms harmonised across the whole EU to aid visual navigation and highlight important sections or statements should be investigated.

iii. Where a product has been approved with conditions, or under exceptional circumstances, or is available under a pre-authorisation programme, a patient-friendly statement should be included in the PL to alert patients to this.

iv. The issue of good-quality translations should be addressed (see also I.2.a)

v. The presentation of side-effects should be looked at: quantification, usefulness, comprehension, understanding and patients should be encouraged to talk to their doctor or pharmacist for advice if they have any problem with side effects.

vi. The inclusion of information on interaction with ‘illicit/recreational drugs’ should be considered. Interaction with herbal or alternative therapies should be addressed in the PL where necessary.

More information on teratogenicity needs to be included in the PL, where available (e.g. from databases in MSs)

vii. The issue of finding the right balance between providing relevant information on benefit/risks but without overloading the PL will have to be considered.

II Recommendations requiring amendments to the current legal framework

a) Rather than using the term “Package Leaflet”, the term “Patient Information Leaflet” would be preferred as this reflects better the purpose of the leaflet. It is noted that “Package Leaflet” is however the term used in the European pharmaceutical legislation.

Even though flexibility of this term in translations exist, it would be better if the ‘official’ English term in the EU legislation would be Patient Information Leaflet, because ‘package’ refers to the product and not to the purpose of such leaflet.

b) It was noted that the current and revised legislation (Dir 2001/83) provides for a specific order for the PL particulars. As experience with this order is currently lacking, relevant feedback should be kept and analysed for future recommendations to amend the Directive accordingly.

c) Alternative tools to disseminate the PL should be put in place.

Annex 4

Final Recommendations in the Area of Pharmacovigilance

Topic leader: Emmanuel Trenado (EPHA)

The EMEA/CHMP Working Group agreed on the recommendations in the area of pharmacovigilance, as listed below under I and II**.** In addition, the following general comments were made:

a) Pharmacovigilance encompasses surveillance and investigation of adverse drug reactions (ADRs) after short-term and long-term use of medicines in order to promote the appropriate and safer use of available medicinal products including risk minimisation.

b) When medicinal products enter the market, clinical experience is limited[1]. After marketing authorisation, further knowledge on their characteristics and safety and risk profile is gained continuously and previously unknown ADRs and interactions may be identified at any time.

c) One major tool in pharmacovigilance today is spontaneous reporting by healthcare professionals, a method of passive surveillance[2]. Throughout Europe, the level of spontaneous reporting of ADRs is low (so-called underreporting).

d) Due to underreporting and missing data in case reports (incomplete or low-quality information) of ADRs, spontaneous reporting systems have their limitations but have nevertheless identified previously unknown ADRs in many cases. However, one cannot be sure to efficiently identify all ADRs by means of spontaneous reporting.

e) Spontaneous reporting by patients to healthcare professionals will be encouraged by competent authorities in accordance with revised EU legislation on medicinal products.

f) Given the limitations of spontaneous reporting, epidemiological studies and other methods of active surveillance may be used to investigate and quantify the risks of medicinal products.

g) There is lack of adequate awareness among the public about pharmacovigilance as an issue of public health.

h) To effectively distribute new information to prescribers and patients remains a major challenge. This is in particular true for delivering information that balances the benefits and risks for individual patients appropriately. Safety information should not jeopardise therapeutic adherence.

i) The success of any pharmacovigilance system depends on the capacity to communicate safety information effectively to the users of medicinal products.

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[1] The nature of clinical trials is as follows: Study size of usually several thousand patients sets a threshold for detection adverse reactions at a frequency lower than 1:1000; limited length of studies of usually several months rather than years does not permit detection of long-term adverse effects; patients with special conditions (e.g. rare diseases, children) may not be studied at all.

[2] Spontaneous reporting here describes the notification of a suspected adverse drug reaction by a healthcare professional following his/her own observation in a patient or brought to his/her attention by the patient him/herself.

With a view to the implementation of the recommendations listed below under I and II, the following topics have been identified for further elaboration through the Patient Working Group:

(1) Public communication of safety information

(2) Education on pharmacovigilance

(3) Direct patient reporting

(4) Protocol guidance for surveys on adverse drug reactions at the level of patient organisations.

I Recommendations implementable within the current legal framework

I.1 Recommendations implementable as such by the EMEA

a) Audit of pharmacovigilance

<u>System and process audit of pharmacovigilance systems</u>

The EU pharmacovigilance system at the level of regulatory authorities will be assessed by the European Commission (EC). Efforts to develop good pharmacovigilance practices for implementation by Member States with the goal to achieve best practice should be completed. It is recommended to also assess the pharmacovigilance systems of the Marketing Authorisation Holders (MAHs).

i. The EMEA/CHMP/Pharmacovigilance Working Party (PhVWP) should finish ongoing work on the guideline for Good Pharmacovigilance Practices intended for regulators to facilitate both system and process audit (internal or external).

ii. There is a plan at the level of the CHMP/PhVWP to develop a similar guideline for industry (in addition to existing regulatory guidance). This plan should be followed-up.

iii. The EMEA should follow-up the implementation of the CHMP Position Statement on compliance of MAHs with pharmacovigilance obligations, now enforced by revised EU legislation on medicinal products.

iv. The EMEA should implement a transparent tracking procedure on post-authorisation commitments and make it available to the public.

b) Transparency and communication

<u>Public information and education campaigns on better use of medicinal products</u>

i. The EMEA should provide general and product-specific material directed to patients (for Centrally Authorised Products (CAPs) and products subject to Referrals).

ii. Each time a Direct Healthcare Professional Communication is provided on a safety issue for a CAP, a patient-tailored communication should be published by the EMEA.

iii. The EMEA should support the concept of 'tear-off fact sheets' to support prescribers in informing patients on drug safety[1].

[1] For example, the UK's Medicines Healthcare Products Regulatory Agency (MHRA) issues fact sheets called "Key Information for patients receiving treatment with medicines known as x" (http://medicines.mhra.gov.uk/ourwork/monitorsafequalmed/currentproblems/currentproblems.htm).

Public access to information on pharmacovigilance

The EMEA should publish on an as-needed basis the conclusions of product-related discussions within the CHMP/PhVWP.

c) Improved reporting

Education campaigns on pharmacovigilance directed towards healthcare professionals

The EMEA should follow-up plans at the level of the CHMP/PhVWP to develop good pharmacovigilance practices for healthcare professionals.

d) Active pharmacovigilance methods and pharmacovigilance planning

i. Risk management programmes

Risk management programmes for the collection of pharmacovigilance data and risk minimisation should be defined at the time of granting a marketing authorisation.

The CHMP has released the ICH-E2E guideline for public consultation and the EMEA has circulated such guideline to the EMEA/CHMP Working Group with Patients Organisations for comments. The EMEA will forward such comments to the CHMP/PhVWP and the ICH Expert Working Group.

ii. Collaborative post-authorisation safety studies

If appropriate, the EMEA should approach patients organisations to support appropriate studies for CAPs, which are often undertaken by the MAHs (e.g. as successfully done for the Oversight Committee on metabolic disorders for anti-HIV medication).

iii. Surveys on adverse drug reactions by patients organisations

Results from the French joint (TRT-5/AFSSAPS) pilot study on anti-HIV medication should be communicated by the EMEA to the EMEA/CHMP Working Group with Patients Organisations for consideration of further recommendations with regard to surveys.

The EMEA/PhVWP should support the development of a guidance for protocols for such surveys.

I.2 Recommendations requiring a harmonised approach at EU level before implementation

a) Audit of pharmacovigilance

Outcome audit of pharmacovigilance

i. The impact of regulatory decisions and public communications concerning appropriate and safer use of medicinal products should be assessed. Procedures for evaluating public health impact of the regulatory action and of public communication on drug safety should be set up.

ii. Patients organisations should set up procedures for evaluating public communication on drug safety within their membership, possibly in co-operation with the National Competent Authorities (NCAs)/EMEA and MAHs.

b) Transparency and public communication

Public information and education campaigns on better use of medicinal products (not related to one single product)

i. The EMEA and NCAs should provide support for patient education on better use of medicines. Funding of such campaigns should be addressed.

ii. The recommendations listed under section I.1.b (I,ii,iii) should preferably be taken up in a EU wide context, hence requiring Member States' involvement, in order to achieve a harmonised approach.

iii. Patients' organisations should prepare patient education programmes jointly with healthcare professionals on appropriate use of medicinal products.

Education on safe use of individual medicinal products

i. Patients organisations should be involved in preparing patient education programmes jointly with healthcare professionals on appropriate and safe use of individual medicinal products where such education programmes are proposed by or requested from marketing authorisation holders.

ii. Public access to information on pharmacovigilance safety and risks of medicinal products

iii. Public access to information on product-related pharmacovigilance safety and risks should be further improved.

c) Improved reporting

Education campaigns on pharmacovigilance directed towards healthcare professionals

i. Curricula for studies and continuous training for healthcare professionals should be reviewed in order to raise pharmacovigilance awareness.

ii. Learned societies should be approached to provide educational programmes on the benefit of pharmacovigilance and the application of proper diagnostic criteria for ADRs.

Reporting incentives for healthcare professionals

i. Feedback mechanisms to healthcare professionals should be established in order to stimulate reporting.

iii. Publication of safety-related information in scientific journals and in bulletins of healthcare professional associations, including observations on adverse drug reactions submitted by healthcare professionals to such journals/bulletins should be encouraged (after reporting to the NCAs and marketing authorisation holders).

Improvement of reporting forms

Feedback from healthcare professionals on available reporting forms and reporting via Internet should be obtained in order to further improve reporting by healthcare professionals.

Patient reporting

i. Patients are advised, through the package leaflets, to report adverse drug reactions to their healthcare professionals and patient organisations should encourage patients in this respect. Healthcare professionals report adverse reactions, in accordance with their national code of conduct, to competent authorities and marketing authorisation holders. In addition, patients may report to a patient organisation, or patient organisations may suspect a possible adverse reaction in a patient via their patient support work. Based on such patient reporting, patients organisations should be allowed to send in summarised reports to the NCAs. These reports should be based on direct patient reporting on ADRs to the patient organisations. In order to produce meaningful reports, the Patients organisations should have in place a standardised mechanism appropriate structure for producing meaningful reports. to validate reports. In addition, patient organisations should be encouraged to send such reports in parallel to the relevant marketing authorisation holders.

ii. First experience from patient reporting currently obtained in some Member States (e.g. in Denmark on direct-to-authority reporting, in the Netherlands on reporting through the national pharmacovigilance system LAREB, in the United Kingdom through a national healthcare-supported telephone helpline) should be communicated to the EMEA/CHMP Working Group with Patients Organisations for consideration of further recommendations on patient reporting.

d) Active pharmacovigilance methods and pharmacovigilance planning

Collaborative post-authorisation safety studies

When feasible, working groups between patients organisations and NCAs should be established at national level for general collaboration and more specifically, for setting up, together with MAHs as appropriate, collaborative studies.

Registries

i. Patients' organisations should promote the creation of patients registries to collect data on ADRs, tolerability and impact on quality of life, in particular for orphan drugs for rare diseases.

ii. Patients' organisations should share experience from already existing registries.

Surveys on ADRs organised by patients organisations

Patients' organisations should exchange best practice in undertaking this kind of surveys.

I.3 Recommendations requiring amendments to the current legal framework

a) Audit of pharmacovigilance

Outcome audit of pharmacovigilance

i. The impact of regulatory decisions and public communications concerning appropriate and safer use of medicinal products should be assessed.

ii. Competent authorities jointly with learned societies, and health insurance schemes and healthcare professionals should implement a policy to collect prescription and drug utilisation data. In some Member States this requires amendment to legislation.

Annex 5

Final Recommendations in the Area of Interaction between the EMEA/CHMP and Patients Organisations

The EMEA/CHMP Working Group agreed on the recommendations in the area of interaction between the EMEA/CHMP and Patients Associations, as listed below.

I Recommendations implementable within the current legal framework

I.1 Recommendations implementable as such by the EMEA

a) In collaboration with patients organisations, the EMEA/CHMP should produce a policy, clearly identifying the type of organisations it will interact with, based on criteria to be defined by the working group (e.g. representation at EU level, funding, how to address areas where no European patients organisations exist, etc).

b) The EMEA should subsequently publish the above policy and the list of patients organisations with whom it is interacting. The EMEA will invite other organisations fulfilling the defined criteria to express their interest to participate to the EMEA activities, as necessary.

c) The EMEA should identify one Staff Member as a contact point for interaction with patients organisations.

d) For each topic discussed by the Working Group, it is proposed to have one contact point from the EMEA and one from the patients organisations who could be contacted by patients for further information.

e) Different frameworks for interaction with patients should be defined, in particular with the view to better understand the impact of a disease and its management from a patient's perspective:

- interaction with patients as representatives of their association
- interaction with patients as experts

Clear rules will be established by the EMEA, especially to address the balance between confidentiality and need to share information with the patients' groups concerned. A patient invited as an expert will have to adhere to the same rules as all other experts participating in EMEA activities, especially with regard to confidentiality undertaking.

In all cases, patients either invited as representatives of their association or as experts will have to adhere to the provision defined in the EMEA policy on the handling of Conflict of Interests.

<u>Interaction with patients as representatives of their association</u>

i. The EMEA/CHMP Working Group with patients organisations should become an established working party. New terms of reference (e.g. mandate, scope, frequency of meetings) should be agreed upon to work in particular on the implementation of all recommendations stemming from the current exercise, as well as all the provisions foreseen in revised European pharmaceutical legislation relevant to interaction with patients.

ii. The EMEA should pro-actively consult appropriate disease specific patients' organisations when developing guidance documents, intended to give guidance on the development of new medicinal products. It is therefore proposed that the EMEA will send Concept papers to the relevant patients

associations asking for input which will be taken into consideration during the development phase. A Concept paper is a document which is primarily intended to state clearly the need for discussing specific issues, innovations or controversial key-points in any stage of the development of medicinal products with a view to laying down the foundation for a future guideline. It should point out what should be discussed in the guideline, but should not elaborate already on solutions.

iii. The same process would apply once the guidance document is released for public consultation before finalisation. Exceptionally, specific meetings could be organised to discuss with the relevant Working Parties some of the issues or comments, if needed.

iv. The possibility for having Ad-hoc on-call informal meetings between the CHMP and patients organisations to discuss disease-specific topics, as foreseen in revised Community legislation, should be further defined (e.g. assessment of quality of life, new emerging therapies, evaluation of individual risks associated with these emerging therapies).

v. Patients' organisations should be able to participate on specific topics to Working Groups of the CHMP (for example paediatric Working Party, Scientific Advisory Group) to present patients views.

vi. The EMEA should provide feedback from these meetings in a transparent manner. Reference is made to the availability of the minutes of the meetings of the EMEA/CHMP Working Group with Patients Organisations on the website, as an example of adequate transparency.

vii. The patients' organisations' representatives will be responsible for disseminating all information within their organisations and to consult with them as appropriate. Patients organisations should publicise their involvement in the EMEA/CHMP Working Group with Patients Organisations.

Interaction with patients as experts

The participation in the CHMP or its Working Groups/Scientific Advisory Groups on appropriate occasions should be envisaged. Reference is made to the positive experience with the Ad-Hoc Working Group on Anti-Retroviral Medicinal Products. For instance, the participant could use his expertise as a patient to provide input for instance into the design of pivotal trials, the data required for licensing a new medicinal product and the elaboration of a risk management programme.

f) The EMEA should develop training to make sure that all patient representatives that are involved in EMEA/CHMP activities understand the regulatory background of these activities.

I.2 Recommendations requiring a harmonised approach at EU level before implementation

The EMEA should promote its model of involvement of patients to the Heads of Agencies in order for National Competent Authorities to consider any appropriate action at national level.

II Recommendations requiring amendments to the current legal framework

In order to further increase the transparency of EMEA/CHMP activities it is proposed to have public hearings in the context of the scientific evaluation process, in line with the FDA. It needs to be emphasised that this is not foreseen in current or future Community legislation. There will be further debate on this issue in the light of the divergent views expressed on this topic.

Annex 6

List of Consulted Parties

European Institutions

European Commission – Enterprise Directorate-General

European Commission – Health and Consumer Protection Directorate-General

European Commission – Information Society Directorate General

European Parliament – Committee on the Environment, Public Health and Consumer Policy

National Competent Authorities in the EU Member States (including Accession Countries) and EEA/EFTA Countries

Ministries, responsible for human medicines

Heads of Agencies, responsible for human medicines

European Industry Associations

AESGP –Association of the European Self-Medication Industry

EFPIA – European Federation of Pharmaceutical Industries and Associations

EFPIA/EBE – European Federation of Pharmaceutical Industries and Associations / Emerging Biopharmaceutical Enterprises

EGA – European Generic medicines Association

EPFA – European Plasma Fractionation Association

EuropaBio – European Association for Bioindustries

Europharm SMC – European Pharmaceutical SMEs Association

Eye-Care Industries EEIG

European Healthcare Professionals Associations

CPME – Standing Committee of European Doctors

ICN – International Council of Nurses

PGEU – Pharmaceutical Group of the European Union

UEMO – European Union of General Practitioners

European Patients Associations

BEUC – European Consumers' Organisation

EATG – European AIDS Treatment Group

ECL – European Cancer Leagues

EFNA – European Federation of Neurological Associations

EPF – European Patients' Forum

EPHA – European Public Health Alliance

EURORDIS – European Organisation for Rare Disorders

IAPO – International Alliance of Patients' Organisations

Other Organisations

British Medical Journal Publishing Group Ltd

CCNet – Cochrane Consumer Network

European Academy of Sciences and Arts

GIRP – European Association of Pharmaceutical Full-line Wholesalers

Annex 7

List of Abbreviations

ADR: Adverse Drug Reaction

AFSSAPS: Agence française de sécurité sanitaire des produits de santé

CAP: Centrally Authorised Product

CHMP: Committee for Human Medicinal Products

EC: European Commission

EMEA: European Medicines Agency

EPAR: European Public Assessment Report

EU: European Union

FDA: Food and Drug Administration

ICH: International Conference on Harmonisation

MAH: Marketing Authorisation Holder

MS: Member State

NCA: National Competent Authority

PL: Package Leaflet

PhVWP: Pharmacovigilance Working Party

QRD: Quality Review of Documents Group