European Medicines Agency

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OVERVIEW OF COMMENTS RECEIVED ON THE GUIDELINE

EMEA/CHMP WORKING GROUP WITH HEALTHCARE PROFESSIONALS' ORGANISATIONS (HCP WG)

FINAL RECOMMENDATIONS AND PROPOSALS FOR ACTION

Table 1: Organisations that commented on the draft Guideline as released for consultation

1	*The Association of the European Self-Medication Industry (AESGP)*	Belgium
2	*Portuguese National Association of Pharmacies (AFN)*	Portugal
3	*European Federation of Nurses Associations (EFN)*	Belgium
4	*European Federation of Pharmaceutical Industries and Associations (EFPIA)*	Belgium
5	*The European Society of Clinical Pharmacy (ESCP)*	Norway
6	*European Union Geriatric Medicine Society (EUGMS)*	U.K.
7	*International Federation of Associations of Pharmaceutical Physicians (IFAPP)*	Austria
8	*International Plasma Fractionation Association (IPFA)*	The Netherlands
9	*International Federation of Anthroposophic Medical Associations (IVAA)*	Belgium
10	*H Lundbeck A/S*	Denmark
11	*NOVARTIS Pharma AG*	Switzerland
12	*Pharmadanmark*	Denmark
13	*Plasma Protein Therapeutics Association (PPTA)*	France
14	Task-force in Europe for Drug Development for the Young (TEDDY)	Italy

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Table 2: Discussion of comments

GENERAL COMMENTS - OVERVIEW
The Association of the European Self-Medication Industry (AESGP) AESGP presumes that the recommendations were primarily written with prescription medicines in mind. Although some recommendations and proposals for action may also apply to non-prescription medicines, AESGP believes that a sentence should be incorporated in the introduction stating that the applicability of the recommendations and proposals for action to non-prescription medicines should be further considered. *A sentence clarifying this fact has been added*
Portuguese National Association of Pharmacies (AFN) • The creation of the HCP WG was an important step in the field of issues related to medicines and so a positive contribution for a better Public Health in Europe. • This WG is a very useful tool to EMEA as a source of information, obtained near those who interact everyday with patients. • Healthcare professionals exchanging information, meeting periodically, creating formal or informal networks and carrying knowledge to other competent levels of EMEA will certainly contribute to the consolidation of a strong basis/platform to improve the safety of medicines. • The chosen priority areas are those that in the short/medium term need to be improved and actively implemented. In fact, they also match some of the European Commission initiatives. The recommendations made within the competence of the WG will certainly contribute for the objectives to be reached by those initiatives. • The recommendations that HCP WG developed for those priority areas – information of medicines, pharmacovigilance and the involvement of healthcare professionals' organisations in the work of the EMEA's scientific committees - focus the most relevant aspects in each one, having in mind the state of the art, and in full respect with the independence and professional duties of healthcare professionals.

European Federation of Pharmaceutical Industries and Associations (EFPIA)

- The recommendations to enhance involvement of HCPs in the identified priority areas are generally supported. For example harmonisation of medicines information and the attempts to improve the HCPs reporting practises on adverse drug reactions can be endorsed.
  However, it should be assured that the processes do not become even more complex or longer, or actions do not unnecessarily increase the workload of EMEA and other stakeholders.
  In addition, it should be guaranteed that there is a well-balanced representation of different HCP organisations in the activities such as in consultations.
- The will to promote EMEA as a source of validated and official information on medicines, which can be easily located by users among other sources of information is welcome.The project of increasing collaboration between EMEA and health care professionals' organisations, through the countries, will be useful, generating connections

The European Society of Clinical Pharmacy (ESCP)

In general, the draft covers most relevant aspects and issues regarding the three areas of consultation.
However, many Healthcare professionals throughout Europe do not have enough understanding of the quite formal English that EMEA is using; if EMEA wants to disseminate information about medicines, something should be done about that.

European Union Geriatric Medicine Society (EUGMS)

- The EUGMS welcomes the establishment of a Working Group with Healthcare Professionals within the EMEA, with the aims to improve the safe and effective use of medicines. Problems with medicines are responsible of a great share of suffering by older subjects, including a significant proportion of hospital admissions. Older people use more drugs than their younger counterparts. Any action to improve safety and effectiveness is expected to have a major impact on health and wellbeing of older European citizens.
- The creation of a Geriatric Medicine Committee, that parallels the Paediatric Committee, is strongly recommended to improve safety, effectiveness and appropriateness of research and use of drugs in older people. This recommendation is supported by the European Union Geriatric Medicine Society & the European Region of the International Association of Geriatrics and Gerontology, and has also been included as a strong recommendation in the European Silver Paper on the future of health promotion and preventive actions, basic research, and clinical aspects of age-related disease that has been produced at the recent Summit on Age-Related Disease sponsored by the French Presidency of the EU (Wroclaw, September 2008).

International Federation of Associations of Pharmaceutical Physicians (IFAPP)

- IFAPP is a global federation representing 30 National Associations of Pharmaceutical Medicine, with some 7000 members all over the world. The European part of the Federation is by far the largest one: in fact in 19 European countries is established a National Association of Pharmaceutical Medicine: the European network is estimated in approximately 4500 professionals, all involved in the different areas of drug research and development activities. In fact Pharmaceutical Medicine is defined as "the medical scientific discipline concerned with the discovery, development, evaluation, registration, monitoring and medical aspects of the marketing of medicines for the benefit of patients and the health of the community".
- IFAPP is therefore a healthcare professionals' organization with a large European coverage of the countries and also with a significant competence in all areas of pharmaceutical medicine.

International Federation of Anthroposophic Medical Associations (IVAA)

- The International Federation of Anthroposophic Medical Assosciations (IVAA) welcomes the in-depth work of the EMEA/CHMP Working Group with Health Professionals' Organizations on information on medicines, on pharmacovigilance and on the further involvement of healthcare professionals' organizations in the activities of EMEA.
- IVAA takes the assessment of these three topics, the development of recommendations and proposals for actions as well as the decision, to ask for a public consultation of the recommendations, as proof that the Working Group with Healthcare Professionals' Organizations has not only worked successfully in the framework of EMEA/CHMP but contributes substantially to overall objectives and activities of EMEA.
- In view of the convincing work of the Group between 2006 and 2008, IVAA recommends to continue with a Working Group with Healthcare Professionals' Organizations in EMEA/CHMP. The practical experience of these organizations as well as their direct link to healthcare professionals and to patients offers indispensable added value to EMEA's tasks. IVAA underlines that the involvement of these organizations enables EMEA to generate a multi-level support of the public administrations of health in Europe and opens its considerations to advice of professionals which otherwise might be lost. By involving these professional organizations EMEA adds as well a certain democratic aspect to its work, which is, in general, more concentrated on the administrative strata of our societies.
- In this context and as the representative of an integrated medicine, IVAA asked for a balanced representation of healthcare professionals' organizations in the EMEA (CHMP) Working Group with Healthcare Professionals' Organizations. IVAA points to the fact that the use of CAM medicines and therapies by patients and citizens in Europe is increasing. IVAA would therefore appreciate if EMEA would invite healthcare professionals' organizations from the strand of CAM medicines and therapies to take part in the Working Group of Healthcare Professionals.
- The development of a set of criteria about how to contact and to engage these organizations and their experts in EMEAs activities will certainly be a first and necessary step. IVAA underlines that these criteria should enable healthcare professionals' organizations from all stands of medical treatment to participate in these activities, including organizations from the CAM sector. Specific criteria of the involvement of healthcare organizations and of healthcare professionals as experts might be helpful.

The CHMP Working Group with Healthcare Professionals' Organizations is a group of the CHMP and therefore, its extent of activities do not currently go beyond the scope of activities of the CHMP.

H. Lundbeck A/S

Lundbeck welcome the opportunity to provide comments on this document. Below please find some general comments:

- There is not information on defined criteria that EMEA will use to determine eligibility of Health Care Professionals
- In the proposed list of representative from HCP, 3 representatives from the neurological societies are listed, whereas there is not representative for Psychiatry. Representatives from HCP in this field with important unmet medical need should also be included.
- HCP will be involved in revision of EPAR. Will the sponsor be involved in the discussion?
- It is clearly stated (annex 4) that HCP will be involved in the evaluation of medicine as individual experts in the European regulatory network, more information on the role of HCP in advising the EMEA/CHMP is requested on the following points:
    - clinical development of innovative medicine to treat unmet medical needs
    - identification of specific target groups for innovative medicine
    - availability of specific scales and validation tools to allow conduct of clinical trials

NOVARTIS Pharma AG

Overall, the work of the EMEA/CHMP Working Group with Healthcare Professionals' Organisation to improve the current Pharmacovigilance system is to be congratulated and welcomed. However, a number of clarifications and improvements to the draft Recommendations and Proposals are needed.
First of all, QRD template needs to be updated, if some of these proposals described at the document will be implemented.
As regard on the role of health care professional organisations: Although it may not be their intent, the draft recommendations are worded in such a way as to imply that health care professional organisations may in fact take on a legal role in the EU regulatory process. (We acknowledge that the recommendations mention that EMEA/161660/2005 is under consideration for use in "establishing clear boundaries" for health care professionals in addition to patients, the target group for the current version). The document should clarify the legal status and role of health professionals in the regulatory process.

Plasma Protein Therapeutics Association (PPTA)

The information on the nature and use of medicinal products to health care professionals and patients is an important tool to ensure efficacy of the treatment and transparency about the effects and possible side effects. Public assessment reports, SPCs and PILs contribute to the safe, efficacious and transparent use of medicinal products. However, PPTA strongly believes that in the recommendations and proposals for action the specific nature of needed information to both groups is not appropriately reflected and might cause more confusion than clarification. The European SPC is intended, as stated in its name, to summarize the characteristics of the product in compliance with the respective licensing dossier and providing regulatory statutory information. The SPC is not intended to provide detailed guidance to the treating physician on the specific therapy for the individual patient. Manufacturers of medicinal products provide information separately in specified brochures with the aim to provide specific information relevant to specific groups of healthcare professionals and patients. In all cases the product specific SPC forms the basis and is part of such information material. In addition the PIL gives information on the use and dosage as well as other information important to the physician and the patient. PPTA believes that there is no added value in trying to cover regulatory statutory information plus therapy-specific detailed information in the current EPARs, SPCs and PILs. In view of their different purposes these two types of document classes should be kept separately. PPTA is concerned that the involvement and consultation of multiple healthcare professionals and patient organisations for the generation and review of SPCs and PILs will cause procedural delay and add unnecessary costs. PPTA member companies, due to the nature of their products, work very closely with healthcare professionals and patient organisations during product development. The PPTA welcomes the idea on the future EU database on medicines (EudraPharm) being a single, controlled reference source of information. In addition, Annex 3 needs clarification on how HCP organizations perceive their interaction with the industry (Applicants/MAHs) especially regarding consultation for preparation and use of risk minimizations measures set out in product specific RMPs. In general it appears to be of benefit if the industry could consult – depending on the product, indication, patient population etc - with a selected 'expert' HCP organization for preparation of efficient risk minimization measures.

In order to avoid unnecessary delays due to a lengthy consultation process with multiple healthcare professionals and patient organisations in the early phase of the development of SPCs and PILs PPTA would respectfully like to propose to introduce a formal consultation process after 5 years when the first renewal of the product license is due. At that point of time all involved parties have gathered sufficient experience with the cSPCs and PILs to enter into a constructive and focussed review process.

Information on medicines:

The recommendations were largely supported. In particular, all stakeholders welcome that EMEA becomes a source of information on medicines to health-care professionals, which can be easily located by users.
Pharmaceutical Industry considers that there is no added value to make cross- reference between product information and public assessment report. Pharmaceutical Industry expressed some concerns on the recommendations to consider the possibility to add a summary to the SmPC and to add new information in the package leaflet, and, on the recommendation to voluntary test readability of labelling. On the other hand, Industry would welcome clearer guidelines on labelling and package leaflet. Attention should be given to their concern when further considering those initiatives. Pilot analysis could be helpful to gain experience on the added value of these proposals and to balance it with the possibility to improve guidelines (e.g. on package leaflet and labelling). Finally, an impact assessment was also requested prior to engage in further activities toward harmonisation of information on medicines in EU.
The Plasma Protein Therapeutics Association (PPTA) challenged the objectives of regulatory information on medicines, considering that the European SPC is not intended to provide detailed guidance to the treating physician on the specific therapy for the individual patient and that the PIL gives information on the use and dosage as well as other information important to the physician and the patient.
Overall, only minor changes were necessary to the recommendations on information on medicines including a clarification on their application to non-prescription medicines, some special considerations for older people, restriction of the proposed voluntary testing of labelling to emergency medicines was requested.
Some comments were related to the implementation of the recommendations and could therefore be considered at a later stage.

ANNEX 2 – DRAFT RECOMMENDATIONS: INFORMATION OF MEDICINES		
Line no. + paragraph no.	**Comment and Rationale**	**Outcome**
Product information	IFAPP network may be a key success factor in the harmonization of product information. In addition we would propose a more "patients friendly" information, with more emphasis on safety aspects and less room for technical information as animal data and PK results.	Comment acknowledged. Comments to be taken into account when considering the recommendation
	QRD template needs to be updated, if some of these proposals described at the document will be implemented.	QRD templates will be updated as appropriate following the outcome of the implementation of the recommendation.
Recommendations that can be implemented within the current legal framework		
Page 9 Para (a)	We agree that HCP organisations should be consulted on the revision of the SmPC guideline. It may be beneficial if, as part of that consultation, HCP organisations were asked to review a representative sample of authorised SmPCs, and to provide feedback on the	Suggestion consistent with the present recommendations.

	usefulness of the information provided. This feedback could then be used by the EMEA to improve the quality of the SmPC guideline.	
Page 9, paragraph a)	The SPC is the most important point: a special design focused on paediatric medicines and ADR for young infants Carefully structured and designed and easily available. The paediatric web page should include information tailored for children	See SmPC guideline.
Page 10, first paragraph	The UN proposed in 1995 to adapt our vocabulary, not using the words "elderly", "old", "aged", and using instead the term "older persons", a more respectful approach. This should also hold for translations of the final document to other languages. (United Nations Committee on Economic, Social and Cultural Rights. The economic, social and cultural rights of older persons. Geneva: UN High Commissioner for Human Rights, 1995) Line 7: Change the term "elderly" to "older persons"	Wording revised accordingly.
Page 10, first paragraph	One of the main problems of older patients is the need to use multiple drugs (Polypharmacy), with a risk of interactions that increases exponentially with the number of drugs. Information on interactions is especially relevant for this population. Add, from line 8: "Adverse reactions should be described in terms of frequency and seriousness. Drug interactions should also be described in clear and precise terms. The information provided…"	Agreed.
Page 10 Para (b)	The stated objective of reducing "over-information resulting in an overall loss of awareness" is welcome. However, there is concern that the current draft revised version of the SmPC guideline is unlikely to meet this objective. For example duplication of information within the SmPC will not help the prescribers to have clear and comprehensive information. The scope of the statement '*the information provided should always be based on validated, robust and clinical relevant data'* is somewhat too broad. For example it is expected that for products which have been marketed for a number of years the safety profile should be established based on accumulated post-market surveillance experience (notably in the PSURs) rather than on the basis of clinical trial data.	Both these recommendations and the SmPC guideline ask for clear and concise information. For clarity, the statement has been replaced with a reference to core quality principles on information as agreed by the Pharmaceutical Forum

Page 10 Para (b)	Similarly the statement making reference to the CHMP assessment report needs to be carefully considered. It is important that the SmPC provide the necessary information for safe and effective use of a drug product and it is not necessary to have to cross refer to another document such as the CHMP assessment report for the purposes described in the recommendation.	The statement has been clarified has follows: "To avoid excess of information in the SmPC and to provide healthcare professionals with access to the data justifying its recommendations, the SmPC should systematically cross-refer to the public assessment report."
P 10, top, section b, line 8	*"The information provided should always be based on validated, robust and clinically relevant data. Those data may be better described in the public version of the CHMP assessment report to which a cross-reference should be systematically included in the SPC."* Novartis position has been to avoid the reference to the EMEA website in the EU SmPC. Feasibility of adding a weblink should be evaluated, with particular focus about updates of information (consistency between EMEA website and available SmPC to HCP) and access directly to the relevant product.	Referring to EMEA website in the SmPC and in the PL is already offered in QRD templates. This possibility is much more used in the PL. EMEA website publishes the latest approved product information. See above
Page 10, paragraph b), line 7	Besides frequency and seriousness of ADR, an extensive description of the type of event, the age of patients and the dose per body surface should be given.	See SmPC guideline
Page 10 Para (c)	Reporting should focus on serious or unlisted reactions. c) "To help improve pharmacovigilance reporting, the SmPC could include a statement reminding healthcare professionals to report **serious or unlisted** adverse drug reactions".	Proposal for encouraging reporting is welcomed; however, it is proposed to delete this recommendation and to consider it as part of the pharmacovigilance recommendations and the ongoing review of the pharmacovigilance system. See also comment below.
Page 10, section c	*"To help improve pharmacovigilance reporting, the SPC could include a statement reminding healthcare professionals to report adverse drug reactions"* Proposal to delete this point, as in section 10 b just above, it is indicated that the SmPC shall be "comprehensive, clear and correspond to healthcare professionals expectations". This is in contradiction to adding a further sentence reminding HCP on their duties. In case this proposal will be kept the QRD template would need to be updated.	Comments acknowledged. See above.

	A different media should be used to remind healthcare professionals on their duties than the SPC.	
Page 10 c)	Encouraging health care professionals to report adverse drug reactions (ADR) is only of value, when the health care professionals are sufficiently trained to judge the relevance and severity of the observed ADR. Above comment should consider that most of the spontaneously reported ADRs received by the industry come from health care professionals (HCPs). Encouraging reporting would therefore increase the safety database for the products, i.e. would be of benefit. However it should be emphasized that HCPs should always report suspected ADRs to the concerned MAH/manufacturer, i.e. in such cases in which local (MS) legislation requires (primary) reporting to a national PV centre. " …. reminding health care professionals to report suspected adverse reactions to the concerned marketing authorization holder / manufacturer, its distributor(s) respectively regardless of whether local (Member State) legislation requires primary reporting to a national Pharmacovigilance Centre."	See above.
Page 10, paragraph c) line 1	It seems to be necessary to unify the same report for all EU Countries. To include some legal obligation for professionals, Hospitals or Associations, to be obliged to inform on any ADRs reported in children.	See above.
P 10, middle, section d	*"Other regulatory guidelines related to product information should be flagged to health care professionals organisations providing them with a possibility to submit comments and input during the preparatory phase"*. Proposal to delete this point, as the preparatory phase of the SmPC and the PL is always a very active phase due to inclusion of new safety data. Any input at this stage would require a good knowledge of the product from the healthcare professionals organisations to be valuable. More clarity on the guidelines especially for the PL would be more	The recommendation does not consider product-specific input but proposes to involve HCPs in the preparation of guidelines which would give specific recommendations for the preparation of product information (e.g. in a specific therapeutic area).

	welcomed by the industry.	
Page 10 Para (e)	The possibility for HCP organisations to provide input on product information may be helpful in ensuring that the information is useful to HCPs in "real world" clinical practice. If HCP input is sought, it should be focussed on the SmPC, as HCPs are the main audience for this document. Any such product-specific HCP review of product information is likely to be of most benefit if it is conducted once HCPs have gained experience with the product in clinical practice. Product information is already subject to a number of separate reviews by different groups (e.g. PIQ, QRD, Member States), and MAHs often receive conflicting feedback from these groups. If an additional review is to be conducted by another group (i.e. HCP organisations), the EMEA should establish a "hierarchy" of reviewers, so that clinically meaningful comments are appropriately prioritised over less important comments. EMEA should also try to improve their processes to ensure that MAHs do not receive multiple sets of inconsistent comments on their product information.	Comment consistent with the proposal. Practical considerations to take into account when further investigating this proposal.
P 10, middle, section e	"*The possibility for healthcare professionals' organisations to provide input on product information should be investigated. For example, healthcare professionals' organisations could be consulted prior to the 5-year renewal of a marketing authorisation to provide feedback and summarise the practical experience gained in relation to the quality of the product information"* With the NML, there is only the need to renew the MA once. If the HCP would like to have a possibility to comment on the product information on a regular cycle, the renewal which happens only more once is maybe not the best choice. More information is needed on the involvement of Healthcare Professionals in reviewing PI at the time of the renewal. Please provide more information on this involvement about the process and the timelines. (How would this be organized? Who would drive this process?)	Comment to take into account when further investigating this proposal. Renewal is given as example. Safety related procedure is proposed as another example.
Page 10 d) and e)	When health care professionals are consulted in the development or revision of an SPC it should be kept in mind that detailed information on the medicinal product and therapy options are provided in separate	The SmPC is part of the marketing authorisation and sets out the agreed position of the medicinal product as distilled during the course of the

	product specific information. Pertaining to e). it is difficult to understand how from a procedural perspective practical experience and other feedback from health care professionals might be integrated into an SPC (or core-SPC) and at the same time obtaining some standard labelling across classes of medicines.	assessment process. Recommendations will have to be considered within the appropriate procedural framework. In this respect, it should be noted that product-specific procedure and non-product procedures are separate.
Page 10 Para (f)	We question the value of user testing readability of labelling, and in particular the practicality of doing so under "stressful conditions". The invented names of medicinal products are already subject to close scrutiny by the EMEA and Member States with respect to the potential for confusion with other medicinal products. It might be more helpful if clear guidance could be provided to help MAH ensure that product labelling is distinctive in order to minimise the potential for confusion with other products. This test for 'look alike" would be useful only for injectable drugs/hospital /emergency drugs. Feasibility and reliability of the test remains to be explored. Delete paragraph (f).	Comment acknowledged; recommendation revised as follows: "The presentation of the labelling (i.e. how it looks like) can be a safety issue when using a medicine in particular medicines for emergency or parenteral use. It is therefore suggested to invite applicants to perform a user test on readability by healthcare professionals in working conditions of dispensation or administration of those medicines (as a way of tackling the 'look alike' and 'sound alike' issues) "
P 10, middle, section f	*"The presentation of the labelling (i.e. how it looks like) can be a safety issue when using a medicine. It is therefore suggested to invite applicants to perform a user test on readability by healthcare professionals in stressful conditions of dispensation or administration (as a way of tackling the 'look alike' and 'sound alike' issues)"* Proposal to delete this point, as by labelling, we understand the secondary packaging (folding boxes) and labels on the primary packaging materials. As Novartis fully supports the principle that a user test can be beneficial to improve the readability of the package leaflet, it is very doubtful that a user test on the labelling (very reduced amount of information) would improve the quality of the labelling. Instead of conducting a user testing of the labelling which would be very difficult to conduct due to the huge variety a medicines on the market (the "look alike" test would therefore be rather irrealistic), it is expected that more guidance should be given on quality standards	Guideline on the readability of the labelling is already available. This labelling user test is proposed to be performed on a voluntary basis. Depending on the situation, different part (e.g. the outer packaginging or the immediate packaging) may be interesting to study. See also above.

	regarding labelling (e.g. company logos, size of letters, colours, etc) to limit dispensation mistakes. In case this point will be kept, results of such a test should be provided at D120 (not at the time of the submission as the testing should be done with a labelling available at a later stage of the application process).	
Page 10 f)	To our knowledge there is no standardised model for health care professionals in stressful conditions and therefore, we do not believe that such a situation could be scientifically designed and evaluated. The current practice of PIL user testing includes representation by healthcare professionals and patients. *..on readability by health care professionals ~~in stressful conditions~~ of ….*	See above
Page 10, paragraph g)	Patients are the final users of medicines. Some patients (in many cases older ones) may have problems reading the package or the insert or manipulating the content. Mentioning patients with problems in this paragraph may be important. Add, from line 3: "…organisations should provide further recommendations on the content of labelling and package leaflet, <u>with special consideration for disabled patients, who may be more exposed to risk</u>. For example, guidance is necessary…"	Agreed.
Page 10 Para (g), last sentence	It is not clear what is meant by the statement about maintaining strong links between the SmPC, labelling and package leaflet. The legislation already clearly states that the package leaflet must be drawn up in accordance with the SmPC, and it is obvious that the labelling must also be consistent with the SmPC. As noted in other comments, the SmPC and the package leaflet are targeted at different audiences, so their respective content and the presentation of that content should not be confused. Delete the last sentence ("It is also of utmost…healthcare professionals.")	Not agreed; the HCP WG stressed the relevance of this recommendation since HCPs are the Patients' main source of information on medicines. Consistency between SmPC and PL is therefore necessary to avoid confusion. The statement has been clarified as follows: "It is also of utmost importance to maintain a strong consistency between the SmPC, the labelling and the package leaflet to facilitate communication between patient and healthcare professional."
Page 10 g)	Many if not all hospitals have standard operating procedures and instructions regarding the handling of medicines. By adding specific instructions as per request by certain healthcare professionals might be	The recommendation should be considered in view of existing hospitals standard operating procedures and instructions regarding handling of medicines.

	confusing.	
Page 10, paragraph g)	Very important to avoid unnecessary medicines preparation which could lead to a wrong dosage, especially in very young children SPC should be consciously designed with selected information: exactly how to administer the medicine specially in infants. Dilution must be eliminated, trying only to give the exact amount for the body surface.	Comments acknowledged. See SmPC guideline
Page 10 Para (h)	The role that both patients' and HCP's organisations will have in "considerations on the package leaflet" should be clarified. Applicants are already required to ensure that the package leaflet reflects the results of user testing with target patient groups. Additional reviews conducted on behalf of competent authorities by patients' or HCP's organisations would, therefore, appear duplicative and unnecessary. The role that both patients' and HCP's organisations will have in "considerations on the package leaflet" should be clarified, ensuring applicant user testing is not duplicated or undermined.	HCPs often use the package leaflet and should therefore have the possibility to contribute. Acknowledging that the package leaflet is first addressed to patients who already participate to their preparation, the recommendation plans that HCPs' consideration is addressed jointly with patients' representative to avoid duplicative or contradictory outcome.
Page 10 i)	By suggesting considering all health care professionals as opposed to only medical, this will increase the volume of information and might make it even more difficult to reach one acceptable labelling text.	The use of term "healthcare professionals" - as in the legislation – should be promoted to avoid confusion induced by the use of too many different terms with no specific definitions.
European Public Assessment Report – "EPAR" p.11/20	Establishing a benefit-risk assessment must be done on a comparative base: i.e. by considering benefits and risks of other therapeutic agents. Grosso modo 4 categories of medicines can be considered: 1. The medicine is appropriate and the risks are minimal. 2. The medicine is appropriate but there are considerable risks. 3. The medicine is not appropriate, but there are no considerable risks 4. The medicine is not appropriate and there are considerable risks. ***Proposed change:*** EPARs should provide a clear description of the benefit-risk of the product as well as an increased level of detail of the rationale for the outcome of the discussions and the recommendations	Comments to be taken into account when considering the recommendation.

	given by the CXMP . This would include information coming from the comparison with other medicines with the same therapeutic indication during the evaluation of its benefit-risk. There is a need for a system of assessment questions when evaluating benefits and risks of therapeutic agents on transparent way.	
	HCP will be involved in revision of EPAR. Will the sponsor be involved in the discussion?	Yes, Pharmaceutical Industry could be involved in the revision of the EPAR structure.
Page 11, paragraph k)	Older subjects may be interested in outcomes not usually included in the list of benefits of drugs: i.e. they may be more interested in functional benefits and quality of life than in mortality. To tailor drug treatments to older people, this information is important. Whenever it is available for a given drug, it should be clearly included in the EPAR. Add at the end of the paragraph: "…of its benefit-risk. Information on all outcomes (not only mortality or the specific effect of the drug on an organ, but also quality of life and disability) should be also made available for a context appreciation of its benefit-risk ratio".	Agreed as follows: "Information on all relevant outcomes, especially those demonstrating an effect on the quality of life or a reduction in disability should be also made available for a context appreciation of its benefit-risk balance."
Page 11 k)	It is unclear on what regulatory basis, a comparison with other medicines can be made during the evaluation of a products benefit-risk, other than on the basis of the clinical data supplied with a formal application.	As stated in Part I of Annex of Directive 2001/83/EC, "In general, clinical trials shall be done as 'controlled clinical trials' if possible, randomised and as appropriate versus placebo and versus an established medicinal product of proven therapeutic value; any other design shall be justified."
Page 11, paragraph Product information a)	Promptly spread information of an important ADR mainly in young patients with automatic warnings previously structured. The system has to be designed with the capacity to generate an automatic warning.	Support acknowledged.
Page 12, paragraph Product information b)	Try to make the same paediatric formulation available in all EU Countries.	Issue outside of the scope of these recommendations.
Page 12, paragraph Product	Note that medicines used on daily practice have a diverse way of prescription, that increases the bureaucratic workload and worsens the children treatment, by delaying the administration of the medicine or	Issue outside of the scope of these recommendations.

information c)	even not achieving it. To unify the medicines´ availability for each Country in order to avoid examples like the following: prescription as compassionate use in one Country, and as off label use in others, or need to ask for them as foreign medicines in others. This incoherence should be reduced also by applying a 'unique' definition of 'off-label' and 'unlicensed' use of medicines. (as resulting from the TEDDY survey results).	
Pages 12/20 Dissemination of information	Need to ensure that appropriate quality systems are established, implemented and maintained in relation to this activity.	Comment acknowledged.
Dissemination of information p.11/20	A clearly defined network is necessary as well as a well described process when promoting EPARs and other EMEA documents. The statement under 'o' has to suggest a commitment. ***Proposed change:*** Knowledge of product information, EPARs and other EMEA documents should be promoted by the allies of EMEA in mutual agreement. Accessibility to product information on the EMEA website should be improved, in particular for safety announcements.	Comments to be taken into account when considering the recommendation.
Page 11 Para (p) and (q)	EFPIA welcomes the suggestions made in para (p) and (q).	Comment acknowledged.
Recommendations requiring amendments to the current legal framework		
Page 12 Product Information Para (a)	Various measures are already in place that are aimed ay achieving harmonisation of safety information in particular - the safety information will be harmonised within 3 years through EU PSUR harmonisation. - many art 31 referrals are also carried out. This requires a major commitment and huges resources from industry and regulatory bodies. The impact of these activities will need to be assessed before	Comments to be taken into account when considering the recommendation.

	additional activities are considered.	
Page 12 Para (b)	For ease of use there should be one SmPC for all formulations: • This proposal is usually supported. However there should be some flexibility e.g. in relation to cases where the indications differ (in that case it may be appropriate to have different SmPCs).	Comment acknowledged; wording revised to refer to different formulations of a product in the same indication(s). In addition, this recommendation has been moved under "Recommendations requiring a harmonised approach at EU level before implementation".
P 12, section b	*"To facilitate the daily use by healthcare professionals, information related to the different strengths or pharmaceutical forms of a product should be presented in a single combined SPC to avoid multiplicity of documents and dispersion of the information"* This proposal on different strengths or pharmaceutical forms presented in a single combined SmPC is welcomed whenever possible. It is already the case in the Novartis Core Data Sheet.	Comment acknowledged. See also above.
Page 12 Para (c), sentences 1-3	The paper proposes that the SmPC could be complemented by a summary of key prescribing information. On a similar note, the Commission has separately proposed to amend Article 11 of Directive 2001/83/EC to include "Key Safety Information" in the SmPC (included in the Commission's December 2007 public consultation on legislative proposals under their "Strategy to Better Protect Public Health by Strengthening and Rationalising EU Pharmacovigilance"). The proposed revisions in this paper need to be considered in concert with these legislative proposals, as well as revisions to the Guideline on the SmPC, in order to ensure the best possible presentation of important information, and to avoid unnecessary multiple revisions to existing SmPCs.	Comments to be taken into account when considering the recommendation. See below
P 12, section c	*"The current SPC could be complemented with a summary providing key prescribing information for daily practice. The summary should include appropriate references to the complete SPC for detailed information. The summary could also include a section highlighting key information that the healthcare professional should convey to the patient when prescribing, dispensing or administrating a medicine. This key information could also appear in the package leaflet."* It is the same trend than in the US.	Comments to be taken into account when considering the recommendation. See below

	More information about the selection of keys messages should be provided. Consistency with US highlights would allow worldwide consistency in labelling e.g. for CDS.	
Page 12 Para (c), sentences 4-7	The package leaflet is primarily addressed to patients, so the addition of sections addressed to HCPs could be confusing to the leaflet's main users. If key-prescribing information is to be provided in a summary, complementary to the SmPC, the inclusion of the same information in the package leaflet is completely unnecessary. Delete the 4th to 7th sentences ("This key information could also appear…from patients' organisations.")	The relevance of this proposal was confirmed by the HCP WG who confirmed that it could improve communication of information to HCPs and Patients. It has been made clear that it should be investigated when, how, and which of these proposals will be beneficial.
P 12, section c	*"This key information could also appear in the package leaflet. For this purpose, new sections addressed to healthcare professionals could be added in the package leaflet (e.g. "When prescribing, please note…", "When dispensing, please note…" and "When administrating, please note…")"* Package leaflet to be complemented by sections as "When prescribing, please note/ when dispensing pls note/ when administrating, pls note...:" should not create confusion for the patient. Therefore a careful assessment of the need of these additional sections in the current format of the EU PL should be done. Especially as we already receive the feed-back from the users in the current tests that the PLs are quite long. Are consequences on PL readability due to lack of place taken into account? More guidance should be provided on the contents to evaluate the feasibility.	See above
Page 12 c)	It is suggested to have a summary in the SPC providing key prescribing information for daily practice. Given the culturally differences across Europe across the health care professions, it should be assessed whether it is at all possible to find and agree on one set of meaningful, harmonised, valuable information. The SPC/PIL is licensing documents reflecting the content of the licensing dossier and with a structure and content clearly defined by EU regulations (SPC guideline, EU core-SPCs, QRD Templates;	See above

	Readability Guideline etc). By this it is guaranteed to have legible and understandable documents for healthcare professionals and patients. The documents already focus to key messages and a further summarizing/highlighting is not deemed to be necessary.	
Page 12 Para (c)	Furthermore it should be noted that increasing the size of the leaflets may become technically not feasible, in particular in the case of multilingual leaflets. When leaflets are too large they cannot be managed by the currently available machines. The size of the leaflets has some limits that cannot be exceeded. At present for the biggest leaflets, the only solution is to use triple sheet leaflets for which only one vendor exists (patented process) with all the consequences that such lack of choice of vendors may cause. Additional difficulties include: difficulties to introduce these leaflets in the boxes, too hard folded leaflet causing damage to blisters => decrease of the rate of production => lower stocks => risk of out of stock situations => risk for the patients at the end of the chain and no back-up solution in case of delays in delivery. Major issues may result from this recommendation if it is not carefully considered.	Comments to be taken into account when considering the recommendation. See above
Page 12 Para (d)	The paper proposes that the content and structure of the SmPC be updated to address compatibility with future information systems. This should be used as an opportunity to also explore how to increase the availability of additional clinically relevant data to HCPs. Currently, the information allowed in the SmPC (in section 5.1) is very limited, but there may be additional data that would be useful to HCP's and to the benefit of patients. HCPs could help identify the additional information that would be useful for inclusion in the SmPC.	The possibility for HCPs to made suggestion regarding the content of the SmPC is already foresee in the first recommendation.
P 12, section e	"*Based on the experience gained through voluntary user test of the labeling for dispension and administration, it could be proposed to make this test a mandatory requirement for new labelling*". Please refer to comment from page 10, section f.	See outcome of comments on recommendation presented in page 10 section f.
p. 13 Para (f)	The proposal to change the terminology used in the EU regulatory framework for over 40 years would have to be carefully considered as it could create confusion. Furthermore 'medicinal product' is the	Comments to be taken into account when considering the recommendation.

	English term corresponding to e.g. the word 'médicament' in French, 'Artzneimittel' in German, 'medicinale' in Italian etc.	
Page 13 Para (b)	The information to be made public from the EudraCT database is already subject to separate consultation from the Commission, and we expect a similar consultation on EudraVigilance to be conducted. HCPs and patients' organisations have an opportunity to provide input through that consultation. The Commission's proposals suggest that a significant amount of information from EudraCT will already be made public. The value or appropriateness of public availability of some of this information is questionable, so any proposals for an "increase in transparency" must be carefully scrutinised.	This recommendation could be revised according to the outcome of ongoing activities in this field.

ANNEX 3 – PHARMACOVIGILANCE

Line no. + para no.	Comment and Rationale	Outcome
Page 14 Spontaneous reporting Para (a)	We agree that adverse drug reactions affecting quality of life are very important. We support the proposal to look at the existing data from a new 'platform. However it is not clear how expediting all suspected cases will serve this purpose. All non-serious ADRs are being submitted with PSUR reports and signal detection being performed by companies on all cases. Periodic submission of non-serious cases will be much less resource demanding and fully supports the need for regulators to perform signal detection by e.g. generic name - not limited to one manufacture. According to our experience such events may have less attention from HCPs and as a result may be underreported. In addition, transient but important adverse drug reactions may be forgotten by the patient and therefore never reported. Perhaps, HCPs could be encouraged to focus more on the use of patient diaries for collection of ADR's, in this way non-serious and transient, but important reactions could be remembered and reported e.g. vaginal bleeding or breast tenderness and nausea in connection with early hormone treatment.	This comment rather relates to the new legislative proposals in the area of Pharmacovigilance developed by the European Commission. As not relevant to this public consultation, the comment was not reflected.

	(EFPIA)	
P. 14, section (a) Adverse Drug Reactions	Re the Working Group's support for spontaneous reporting provisions in the proposed EU legislation, we iterate the following points made by Novartis during the consultation period for that document. Eliminating the distinction between serious and non-serious events for the purpose of reporting to health authorities is a burdensome task with no added value. "MAH's shall submit electronically to Eudravigilance no later than *15 days* following the receipt of the report, **all** ADRs that occur in the community…." One can understand why these should be populated in Eudravigilance for signal detection purposes but not clear why rapid reporting has been extended to non serious reports that occur in the Community. This represents a major process change for MAHs that negates the purpose of conducting case triage to process and transmit the most important cases first. It greatly restricts the ability of MAHs to managed fluctuations in workload, as there will no longer be any flexibility to postpone non-serious processing for short periods of time when workload is high. More costs will arise for more resources to cope with the increased expedited data entry. *In our comments on the proposed EU legislation, we recommended dropping the requirement for expedited sponsor reporting of non-serious cases We support maintaining adherence to requirements for ADR submission set forth in Vol 9A.* This significant impact is further compounded by the proposal's absence of language specifically excluding non-serious reports from observational studies. Such data is inherently low in quality, has usually not been vetted by the treating physician, and is not stored in the safety database by MAHs. To do so is an inefficient use of resources that could better be deployed on activities with higher value. *At a minimum, any expanded expediting requirement for spontaneous reports should specifically exclude none-serious reports that arise from observational studies.*	See above.

	Moreover, The definition of Adverse Reaction in the proposed EU legislation is too broad and does not distinguish between the concepts of 'reaction' and 'event'. If this is applied to observational studies, where it is often rare to receive a causality assessment from the treating physician, this could lead to a significant over-expediting of relatively low-value cases, particularly if the MAH is not given the legal means to use medical judgment in assessing possible causality in the absence of a treating physician's attribution statement. *The current ICH definition of adverse reactions should be retained. If this standard is no longer appropriate, a revised definition should be developed through ICH consensus.* (Novartis)	
Page 14, Spontaneous reporting Para (a)	The importance of non-expedited reports of minor ADRs is huge, since it is essential for populating safety databases and for performing comprehensive signal detection and drug safety profile evaluation. The proposed guideline asks to drop the threshold for spontaneous reporting, so that all suspected reactions are made 'expeditedly' reportable. Expedited reporting is time consuming and resource draining. Making all ICSRs expedited, or even lowering the threshold for expedited reporting by itself, does not add any scientific knowledge to the drug safety profile. Individual cases are almost always confounded: it is not the individual case, but the overall assessment of a case series, also taking into account epidemiological and pharmacological data, that permits to identify new signals. Lowering the threshold for expedited reporting drains resources from intelligent signal detection and evaluation, the activity at the basis of patients' protection. Proposal: *"The HCP WG recognizes that to better understand the impact of minor adverse reactions affecting quality of life, these need to be thoroughly assessed in documents evaluating the overall product safety profile, such as comprehensive documents issued by regulators and safety documents specifically issued by the MAHs (e.g the PSUR and the RMP). Whenever minor ADRs lead to many patients discontinuing*	The issue of thresholds for expedited reporting is related to the Community legislation, and not releveant for this public consultation. The proposal of the new text does not bring any new information, it just describes the current situation in communication between MAHs and regulators. It is unclear how such a text would fit in the recommendation made by Health Care Professional organisations. Therefore, the proposed text was not accepted.

	the drug and may therefore jeopardize therapy success, they should also be evaluated in the drug's benefit-risk assessment and risk-management plan (when applicable). " (EFPIA)	
p. 14, section (b) Patient reporting	<u>Re the Working Group's support for increased consumer reporting, we iterate the following points made during the consultation period for the proposed EU legislation:</u> Patient adverse reaction reporting forms are to be part of the patient information leaflet for intensively monitored drugs, with reports going to the Marketing Authorisation holder. Is there any evidence that such a system will 1- increase reporting from patients or indeed? 2- provide better quality data? Two elements of the proposed EU legislation are problematic and confusing; • The first requires the submission of adverse reactions for reports where the *patient* or the health care professional has made a statement of possible attribution for spontaneous reports (currently, the health professional attribution is used). This will create a new EU requirement for MAHs to submit non-HCP cases as individual reports. Is the intent to rely on consumer causality as part of the ADR reporting paradigm? This has significant implications for the number and quality of reports in Eudravigilance. • The second requires the submission of all reports where no causality statement is made or the causality is unknown. This has negative connotations, particularly if it is intended to include observational studies, for which it is often rate to receive a causality statement from the treating physician. MAHs are often	This comment rather relates to the new legislative proposals in the area of Pharmacovigilance developed by the European Commission. As not relevant to this public consultation, the comment was not reflected.

	required to conduct epidemiology studies, product usage surveys, and other observational activities for which extensive medical data and reporter causality are lacking and follow-up is not possible. This requirement could lead to a significant over-expediting of relatively low-value cases, particularly if the MAH is not given the legal means to use medical judgment in assessing the possible causality in the absence of a treating physician's attribution statement. In addition, encouraging patient reports may reduce the incentive for health providers to submit ADRs. It can also lead to situations where patient and provider submit two dissimilar and conflicting versions of the same report. *Urgent clarification is required concerning the purpose, mechanisms and scope of patient ADR reporting, which appears to be new and is currently not an EU requirement.* *We strongly recommend that spontaneous report and observational study assessments as part of the reporting paradigm are limited to health professionals, as patients are not qualified to make such evaluations.* *In general, companies should apply a conservative approach in the assessment of causality for cases with missing reporter causality. However, their decisions should be based on medical and scientific assessment, (e.g. events or outcomes which are expected in high morbidity or mortality populations could be assessed as non-suspected in the absence of a reporter causality). To consider all cases with missing reporter causality as 'suspected' is very problematic, as reflected in the comments and rationale.* *In order to achieve optimal transparency and communication on safety information, we suggest coordinated and transparent interactions between the EMEA Committees (CHMP, COMP, PDCO, PhVig Com etc.) and interlinkage between the various EU databases, such as Eudravigilance, Eudrapharm etc.). Safety information should be publicly presented in a balanced way considering risks* ***and*** *benefits of the product. Therefore, the PhVig Com should coordinate any publication of its safety opinion with the overall scientific assessment*	

	and opinion of the CHMP.	
Page 14 Para (c)	Underreporting should be systematically addressed, but also the quality of the received reports should be addressed. Receiving bigger amounts of non-serious listed/labelled reports is of little value, whereas receiving better-documented unlisted reports addressing all confounding factors would be of big help. Training of HCPs should be encouraged. Proposal: *"d) The quality and completeness of the submitted reports should be systematically addressed. HCPs should be trained on the principles of drug-event causal relationship (including confounding factors). "* (EFPIA)	The notion of the low quality of reports was added. The issue of training was already reflected in the respective area.
P. 14, section (c) Under - reporting	Under-reporting should indeed be systematically addressed, but in an manner that encourages submission of high-quality reports for adverse events that can further defines the drug's safety profile. A massive proliferation of non-serious, listed events serves only to divert valuable sponsor and agency resources that could be put to more effective use. *Education efforts for health professionals should focus on increasing reports for significant adverse events, not for growing overall volume.* (Novartis)	We agree with the comment, the issue of education is already included in the respective area.
Page 14 Spontaneous reporting c)	ADR reporting by all health care professionals directly into the Eudra pharmacovigilance data base would lead to a flood of unprocessed information, particularly when health care professionals have not received appropriate training in recognising ADRs and judging their severity. Therefore, obligatory training and education is a prerequisite for a meaningful communication of ADRs. Proposal: *"Each medical institution should have an internal review system for reported ADRs."* (PPTA)	The notion of the low quality of reports was added. The issue of training was already reflected in the respective area.
Spontaneous	Our network is strongly involved in a project of observational studies	Thank you. Your proposal might be further discussed in the context of

reporting	and spontaneous reporting: IFAPP believes that these activities can be easily disseminated over EUROPE with the help of our council of education, an IFAPP working group	other EMEA activities. Please, submit you detailed offer.
Spontaneous reporting p.14/20	One reason for not reporting is that health professionals find it too time consuming. This is due to the fact that the reporting forms are perceicved as complicated and that the amount of information to be submitted is found to be too massive. Hence, the reporting form should be made as simple as possible viewed from the perspective of the health professionals. The information required should ideally be submitted in a way as schematic as possible, e.g. by ticking boxes. *Partner organisations can play an important role by promoting reporting as one of the items in their mission statement and/or objectives.* (ESCP)	Thank you.
Page 14, paragraph Spontaneous reporting c)	Adverse drug reactions resulting from the off-label use of medicines (e.g. paediatric use) are particularly affected by lack of reporting, presumably due to liability issues. Current guidelines include the minimum criteria for reporting the identification of the reporter. *These criteria should be revised and/or the current legislation amended in order to allow the anonymous reporting of adverse reactions to be considered as a consequence of medication errors and off-label use.* (TEDDY)	Recommendation for anonymous reporting as an acceptable form of spontanoues reporting was not accepted by the HCP WG. Nevertheless, there is always a possibility for separate, anonymous reporting to regulators, which does not enter the database of spontannous reports, but may trigger an interest in further study of the issue raised by an anonymous reporter.
Page 14, Spontaneous reporting section	In many cases, ADR, including many minor or non-specific reactions, are due to interactions or associations of different medicines. The current reporting system is not very good to identify this group of problems. This may be improved by using a reporting system that is especially careful in the inclusion of any medicine used at that time, and a systematic analysis of ADR looking for interactions. Add a paragraph d) Spontaneous reporting and analysis of ADR should be adapted to be more sensitive to detect interactions between drugs, not only reactions	Comment accepted, a new paragraph was added.

	to individual drugs. (EUGMS)	
Signal detection and evaluation p.15/20	Regarding signal evaluation: Measures should be in place to avoid the kind of uncertainty that has lately arisen with regard to the safety of ezetimib, i.e whether or not its use leads to an increased risk of cancer. Evaluation should possibly be performed by well trained epidemiologists, who have also a practicing role in healthcare.	Thank you. This is already the case in many authorities and companies.
Page 15 Signal detection & evaluation Education and training	See above. At least one person within a given organisation who is familiar with the principles of ADR reporting should review the potential cases before submission into the Eudra system Considering that **ANNEX 3** refers to **co-operation between the EMEA and HCP's organization,** at least sub-paras a) and c) need clarification that involvement (consultation) of HCP's organizations in preparation & use of risk minimization measures set out in Risk Management Plans is something which – if deemed appropriate /of benefit - has to take place between a concerned / qualified HCP organization **and the concerned Applicant / MAH** which is the one being in charge of preparation and follow-up with product specific RMPs (not the EMEA). (PPTA)	This communication is already happening. Nothing prevents Applicant of MAH to consult relevant HCP organisation. Nevertheless, it is irrelevant to the document under public consultation, as that is expected to address issues between EMEA and HCP organisations. Risk Management Plan is an agreement between the regulator and MAH. Regulator is normally shaping the RU RMP proposal from MAH quite significantly already. Involvement of HCP organisations in this process would be beneficial to the whole outcome.
P. 15 Signal detection and evaluation	The contribution of health professional organisations to signal detection and compliance with related regulatory action can in theory be an asset. *The document should clarify the legal status and role of health professionals in the regulatory process. It should also address how these activities will be handled across the 27 Member States.* (Novartis)	This document relates to co-operation at European level only, therefore between EMEA and the Working Group. Detailed legal aspects are not discussed, as this is just a set of recommendation.
Spontaneous reporting	Spontaneous reporting: Direct patient reporting seems to be an effective and valuable source of information about adverse drug reactions. Denmark has very good experiences with direct patient reporting – the share of direct patient reports is constantly increasing, in 2007 direct reports constituted	Thank you for the comment. We believe the text of recommendations is in line with it.

	19,5% of all ADR reports. With reference to the concern raised in section a) (page 14) that adverse drug reactions affecting the quality of life are not adequately detected in the current system, it seems worth noticing that Danish patients have reported minor and sometimes diffuse ADRs such as: loss of appetite, nausea and pain. These patient ADRs may be crucial in understanding the background and mechanisms for discontinuation of treatment and non-adherence. In order to strengthen direct patient reporting it could be relevant to consider how e.g. community pharmacy could help facilitate such reports. Pharmacists working at community pharmacies are in contact with many patients. As a part of the individual patient counselling pharmacists could – on a systematic basis encourage patients to report experienced adverse drup reactions. In case of chronic use of medicine the pharmacist could actively ask for any indications of adverse drug reactions when the patient comes to collect his or her medicine – especially, if there has been a change in medicine. However, Pharmadanmark finds, that if the threshold for expedited reporting is lowered, so *all* suspected adverse drug reactions are reportable this may lead to an unproductive and major increase in the administrative burden on both industry and national authorities. The current procedure for handling incoming non-serious ADRs works to secure an acceptable balance in regard to the benefits of patients, authorities and industry as non-serious ADRs are registered and evaluated in the product PSUR. Making it possible for patients to report non-serious ADRs directly to national authorities should not be mixed with industry requirements to handle serious ADRs. (Pharmadanmark)	
P. 15 Risk Communication (a) Education and training	We agree that there is a need for better basic education for health professionals about the safety of medicines. Historically, adverse event information has sometimes been released with little or no frame of context for practitioners. To best serve the health community and patients, it is important to do more than issue communications on adverse events. Such information must be placed into the proper	This comment relates to the best practice of risk communication, and therefore it is outside the scope of this public consultation.

(b)	context. In addition, both sections recommend involvement of health professional organisations in drafting risk communication and preparing sponsor risk management plans. This again raises issues about the legal role of such groups in the regulatory process. *In addition to adverse event information, safety communications should address:* • *The risk in the context of the drug's benefits* • *The risk in the context of risks with other treatments for the disease* • *The risk of stopping treatment* • *What is known and what is not known about the adverse event* • *What actions, if any, health professionals should consider taking* • *How to discuss the event with patients* *The document should clarify the legal status and role of health professionals in the regulatory process. It should also address how these activities will be handled across the 27 Member States.* *(Novartis)*	
Signal detection and evaluation	Signal detection and evaluation Pharmadenmark fins that the development of tools for better signal detection and evalutation is primarily the responsibility of authorities and industry. New and better tools are currently in the process of being developed – and in this process Pharmadenmark supports all kinds of collaboration between authorities and industry but also academia and healthcare professionals' organisations (especially scientific societies). Individual healthcare professionals report cannot be used as basis for signal detection and evaluation. (Pharmadanmark)	Thank you. Spontanneous reports serve as a basis for signal detection and evaluation for decades, and the methodology today is using epidemiological approaches to their evaluation. This is reflected in the document already.
Page 16 Areas of research	Pharmacovigilance is a part of the mandatory requirements for manufacturers of medicinal products. Any research and new developments in this area should therefore be jointly discussed with industry associations. Health care professionals can only have a limited	Pharmacovigilance is both science and activities, and it involves many stakeholders. Discussion between regulators and health care professionals is needed to the same extend as discussion with patients, industry associations, politicians, academia and others. No change to the document

	perspective on the complex pharmacovigilance system in place. (PPTA)	needed.
Risk communication	Risk communication Pharmadanmark welcomes that focus is set on ways to improve risk communication and that this includes stronger involvement of healthcare professionals' organisations. Healthcare professionals' organisations can play an important role in linking regulators with individual healthcare practitioners – communicating experiences, mindsets and goals. With the objective of developing new and effective risk communication methodologies Pharmadenmark finds that university researchers should have access to ADR databases. (Pharmadanmark)	The need for access to ADR databases was added to the document.
Education and training p.15/20	When addressing pharmacovigilance in curricula etc. it is equally important to address the context in which it operates. This will contribute to a balanced approach where the risk of overemphasis is minimised. Otherwise there may develop a culture of fear where health professionals will get too anxious to prescribe or recommend use of certain medicines. (ESCP)	Thank you, yes, indeed, that will be needed. Nevertheless, as the current curriculum is almost exclusively focused on benefits, there is no risk of inbalance when there will a bit more about safety and pharmacovigilance.
Education and training	Education and training Pharmadanmark sees education and training of healthcare professionals as a key element in improving the pharmacovigilance system. Drug safety and pharmacovigilance should be included in the core curriculum at universitites for graduate as well as post-graduate education. Pharmadanmark finds that healthcare professionals' organisations should work closely together with regulators and universities (and other relevant providers of post-graduate education) in the specification of educational/training requirements. Requirements should reflect that healthcare practitioner's need a basic understanding of drug safety and that healthcare practitioners hold a key position in the pharmacovigilance system securing that high quality ADR reports are	Thank you.

	produced. (Pharmadanmark)	
Education and training p.15/20	When addressing pharmacovigilance in curricula etc. much attention should be given to the interpretation of results from safety studies with regard to the terms "association" and "causality". Currently, causality is often inferred while the results from most studies merely show an association (at best).	Yes, that will be a matter of development of the curricula, which is out of scope of this document.
Page 16, area of research, paragraph a)	Appropriateness of drug treatments should be included in the list of research areas, including both under and overuse of drugs. Proposal: *"Research in the area of pharmacovigilance includes drug utilisation studies, studies on the appropriateness of drug treatments, pharmacoepidemiological studies and clinical safety trials."* (EUGMS)	Comment accepted and new text implemented.
Page 16, paragraph b)	As older people are the group disproportionately involved in ADRs, it is important that the research is also directed to ageing as well. Proposal: *Research in elucidation of biological causes and possible prevention of ADRs, e.g. pharmacogenomics, should be promoted by regulators, with a particular emphasis on the groups most at risk, particularly older people.* (EUGMS)	The comment was partly accepted, and the emphasis on populations most at risk was added.
Area of research	Area of research Pharmadanmark strongly supports a substantial increase of research activity in the area of pharmacovigilance. One area missing in the draft recommendations is pharmacokinetics. The relationship between knowledge/use of pharmacokinetic information and drug safety is an area with great potential for improving drug treatment, as many adverse drug reactions can be traced back to little control of actual blood level of active medicinal substance. In order to strengthen and facilitate such research contacts should be made ot experts within pharmacokinetics	Thank you. The notion of pharmacokinetic studies and Therapeutic Drug Monitoring was not reflected as this is an ongoing activity already.

	and Therapeutic Drug Monitoring. (Pharmadanmark)	
New approaches in pharmacovigilance	Observational studies on new medicines will generate very important data to complete the safety profile of the drug and to better assess the benefit/risk ratio. (IPFA)	Thank you.
Page 17, new approaches, paragraph a)	This paragraph is worded for complex strategies for individual diseases. However, in most cases, complex strategies are used for complex patients with multiple comorbid diseases and multiple treatments for each of them. Surveillance methods in this group may be different that those used for single diseases, as in oncology. Complex patients, not only complex diseases, have to be mentioned. Proposal: "In a majority of cases, medicines are used in combination, as a part of a complex therapeutic strategy of a single disease, or in the treatment of complex patients with multiple comorbid diseases . Methods of surveillance of such complex therapeutic strategies and patients should be developed and implemented as part of the pharmacovigilance system. Relevant examples include different standards of diabetic care, combination therapy of HIV, protocols used in oncology, or polypharmacy in complex, frail, older individuals." (EUGMS)	Comment partly accepted, with less emphasis on any specific population of patients.
New approaches in pharmacovigilance	New approaches in pharmacovigilance The proposal to develop methods of surveillance of complex therapeutic strategies seems very relevant, but a more complex approach should wait until basic procedures are optimal – and that is not the case yet. The proposal to develop new IT methodologies that can share information from different databases (e.g. ADR data and data on genetic variability) would constitute a great break through. Pharmadanmark strongly support such initiatives. Pharmadanmark agrees to the need for further strengthening of co-	Thank you.

	operation between food safety surveillance and drug safety surveillance. (Pharmadanmark)	
Page 16, paragraph New approaches in pharmacovigilance	The setting up of new data sources for pharmacovigilance, such as automated healthcare databases, must be encouraged, in particular in areas such as paediatrics where the spontaneous reporting is less efficient (TEDDY)	Thank you.

ANNEX 4 – DRAFT RECOMMENDATIONS: INVOLVEMENT OF HEALTHCARE PROFESSIONALS' ORGANISATIONS IN ACTIVITIES OF THE EMEA'S SCIENTIFIC COMMITTEES		
Line no. + paragraph no.	**Comment and Rationale**	**Proposed change (if applicable)**
European Federation of Pharmaceutical Industries and Associations (EFPIA)		
Page 17 Para (a)	Other stakeholders, including the pharmaceutical industry, should be consulted on the criteria for Agency contacts with HCP organisations, as the definition of these selection criteria will be important.	
Page 17 Paras (b) and (c)	The criteria should also stipulate a need to evaluate that representatives of HCP organizations are truly representing the positions and views of their organization, and not simply expressing personal views. There should be regular evaluation of the organizations and their representatives.	The criteria will ensure that HCP organisations selected truly represents the positions and views of their members. Specific rules for involvement will be drafted, which will define the differences in the involvement of members of HCPs' organisations as experts or as representatives of their organisation.
Page 18 Para (ii)	It is not fully clear from the document why the EMEA should always consult HCPs in a more pro-active way when developing guidelines, in comparison to other stakeholders.	The text has been amended to reflect that the procedure to consult healthcare professionals in early stages of guideline preparation will reach other satkeholders
Page 18 Paras (ii) and (iii)	The paper includes proposals for increased involvement of HCP organisations during development of EMEA guidelines. As these guidelines primarily concern the development and authorisation of medicinal products, the same possibilities for involvement must be available to the pharmaceutical industry, as a stakeholder with greater	The "Procedure for European Union guidelines and related documents within the pharmaceutical legislative framework (EMEA/P/24143/2004)" already foresee involvement with relevant interested parties. The recommendations refer in particular to HCPs in particular without

	interest and experience in these topics.	excluding other relevant stakeholders/interested parties.
Page 18 Para (vi)	The EMEA plan to create a database of organisations and groups with potential interest in EMEA guidelines to guarantee adequate dissemination of guidelines early in development to when they are implemented. Pharmaceutical companies or at least trade associations such as EFPIA should be included in this database, as they would also benefit from prompt notification of new guidelines to ensure they are efficiently implemented when they come into force.	Pharmaceutical companies and trade associations as EFPIA are to be entered in the database.
Page 18 Paras (vii) and (viii) and Page 19 Paras (i) and (ii)	We support greater interactions and sharing of opinions between Healthcare Professionals' Organisations and EMEA Scientific Committees. This should result in greater consistency between the information given in the SmPC and medical practice.	Agreed.
European Society of Clinical Pharmacy (ESCP)		
Regarding point a) p.17/20	It should be stated which groups of healthcare professionals (preferably represented by their respective Societies etc.) EMEA will collaborate with in defining the mentioned set of criteria. In collaboration with the pertinent Societies and Organisatons of healthcare profesionals (see attachment...)....See also earlier in these comments. To what extent would a kind of charter be possible?	The criteria will be developed by the EMEA in collaboration with the EMEA/CHMP Working Group with Healthcare Professionals. The text has been rephrased to be more specific.
International Federation of Associations of Pharmaceutical Physicians (IFAPP)		
Interaction with HP as representatives of their organization	IFAPP and its European network can be of great help to EMEA in collecting, analyzing and disseminating information to HP, and also to receive immediate feedback on EMEA proposals and guidelines. IFAPP members are used to interact with regulators, and are very familiar with EU regulations related to drugs	IFAPP's proposal is noted
Interaction	Among IFAPP membership we have hundreds of very experienced	

with HP as experts	pharmaceutical physician professionals who are involved in educational programs: they may represent a significant pool of experts willing to help EMEA in its activities.	IFAPP's proposal is noted