Document	**Comments on European Commission Consultation on Draft legislative proposals regarding Pharmacovigilance 5.12.2007**
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Status / Date	Final version / January 31, 2008

Our comments are structured as follows:

1. General comments
2. Comments regarding Section 3 Legislative strategy and the key proposals for legislative change
3. Comments regarding Annex I: Detailed proposals for legislative changes

1. General comments

ECHAMP welcomes this series of consultations of the European Commission to strengthen and rationalise EU pharmacovigilance.

It is the aim and the obligation of industry to watch over the quality and the safety of the medicinal products we produce. Pharmacovigilance is an indispensable tool related to public health and patient safety and has to be a main priority in an unchallenged way.

At the beginning we would like to introduce the particularities of homeopathic approval procedures in the EU and their relationship to pharmacovigilance: The products can be authorised according to article 16 of Directive 2001/83/EC. For this type of products chapter IX of the Directive fully applies as regulated in article 16.3. Or they may be registered according to articles 13-15 of the Directive. Here chapter IX does not apply as a matter of principle; however, some Member States (MS) have individual rules putting these products also under pharmacovigilance provisions. On a long-term perspective we support a common and adequate application of chapter IX also to these products in the whole EU as necessary according to the status as medicinal product.

Homeopathic medicinal products are widely distributed in a lot of EU MS while the process of finalisation of the re-authorisation has different status from MS to MS.

There are further special characteristics of homeopathy and anthroposophy which should be considered when discussing efficient pharmacovigilance measures in the EU:

- The range of essential medicinal products is considerably larger compared to other fields of the pharmaceutical industry. Due to the strongly individualised character of the therapeutic approaches homeopathy and anthroposophic medicine need a large range of starting materials (in the range of thousands) and of specific medicinal products. A large number of them have a low to very low turnover.
- They are old established products well known in the EU for decades.
- As a matter of principle, they have a comparatively low risk profile.
- In the MS familiar with homeopathic medicinal products these products are available without prescription and they are not re-imbursed by health assurances. This means that consumers frequently use the products without advice of a healthcare professional. This has strong impact on the dealing with possible ADRs reported by patients.
- Our present experience with the literature cases of ADRs relevant to our medicinal products shows that the quality of the case reports is predominantly poor and often contains mistakes due to lacking knowledge.

Therefore, it is of extreme economic importance for homeopathic and anthroposophic industry, which consists mainly of SME’s, that the regulatory and administrative burden linked to Pharmacovigilance should be rationale, efficient and restricted to a minimum while of course guaranteeing the quality and the safety of the products. It goes without saying that the relevant fees should be fair as well.

So, a strong but efficient system of pharmacovigilance which is not overloaded by purely administrative measures without added value to patient safety is needed for homeopathic and anthroposophic industry in Europe. In this perspective we are very satisfied with the intention to create a ‘Strategy to better protect public health by strengthening a rationalising

EU pharmacovigilance' which can surely improve regulation in the field of homeopathic and anthroposophic medicinal products.

Basically, we appreciate the idea of this Commission initiative to reduce the formalistic burden which will be an alleviation for small and medium sized companies regarding measures which are purely administrative and do not contribute to patient safety. In order to achieve this basic idea, it has to be realised that there are branches with highly different product ranges regarding the potential safety risk. The necessary measures have to be adequate.

We realise some proposals which we really appreciate as a good step into the right direction. These proposals are most welcome.

In contrast to this, we perceive other proposals which will create a new and cost-intensive administrative burden where we see a big distance to the conditions of practical regulatory experience and no real added value to safety issues. Considering homeopathic medicinal products these proposals will be contra-productive to the original intention of the present consultation.

Among others, we welcome the proposal to establish a Pharmacovigilance Committee at the EMEA as adequate measure regarding the importance of the topic. However, up to now there is no expertise about our products at the EMEA. Therefore we recommend the involvement of experts on homeopathic and anthroposophic medicinal products.

In our comments on the present consultation we intend to direct your attention to different aspects of the proposals which are particularly relevant from the perspective of European homeopathic and anthroposophic industry:

2. Comments regarding Section 3 Legislative Strategy and the Key Proposals for Legislative Change

3.1. Legislative strategy

In view of the fact, that up to date the implementation of the pharmacovigilance articles of the Directive is widely disharmonised among the MS we strongly recommend to lay all rules down in a Commission Regulation. Otherwise the door is open for further divergent procedures which will not reduce the burden for the companies. The positive effect of this initiative will fail, if national Member States keep the possibility to maintain on a national level, what will be cancelled by Europe.

Proposal: Transfer the complete chapter IX to a new Commission Regulation on Pharmacovigilance.

3.2. Key proposals for legislative change

3.2.1. Fast robust EU decision-making on safety issues by rationalising the existing EU referral procedure and reinforcing the committee structure

We welcome the proposal to establish a Pharmacovigilance committee at the EMEA as adequate measure regarding the importance of the topic. However, up to now there is no expertise about our products at the EMEA. We strongly demand the involvement of experts on homeopathic and anthroposophic medicinal products.

3.2.2. Clarify /codify roles and responsibilities and codify standards for industry and regulators

We welcome the principle of the proposal to establish a common Pharmacovigilance standard. This is especially necessary for homeopathic and anthroposophic medicinal products due to the current situation where divergent national regulations dominate.

3.2.3. Simplify informing the authorities about the company pharmacovigilance system

We highly appreciate the proposal as essential measure decreasing the administrative burden. This is extremely relevant to homeopathic and anthroposophic industry, where the companies are characterised by a broad range of products and respective numbers of marketing authorisation dossiers.

3.2.6. Simplify and make proportional reporting of single serious adverse drug reaction (ADR) case reports

We highly appreciate the proposal as essential measure decreasing the administrative burden concerning reporting of serious cases of ADR.

Anyhow, regarding some planned concomitant measures we have severe concerns.

1. Expedited single case reporting of *all non serious* ADRs will create an additional workload for pharmaceutical companies offering old established products.

More personnel will be necessary in order to keep the narrow time lines for reporting but no increase of knowledge of the safety of the products can be expected.
This will have particular impact on SMEs. For detailed explanation refer to our statement given under Annex I, Directive 2001/83/EC, article 101e (2).

2. Additionally patients are proposed to report ADRs directly to the authority. We understand the interest of consumer/patient associations to be free to report ADRs directly to agencies. However, from our practical experience it is extremely difficult to evaluate patient reports without medical knowledge in the field of homeopathy and anthroposphic medicine. Usually the patient reports are of poor quality and therefore merely assessable. They do not add useful information to the evaluation of the risk profile of the products.

   In addition, missing harmonised nomenclature regarding active substances hinders a general evaluation of these cases without product knowledge.

   Before introducing the new element of direct patient reporting without oversight on practical consequences we urgently recommend to ask the MHRA, who introduced this instrument recently, for a summary of their experience.

3. Regarding the transfer of the evaluation of literature to the EMEA in the field of homeopathic medicinal products we would like to make clear, that there are more than 2000 substances used in homeopathy and anthroposophy in Europe.

   The evaluation of literature cases is extremely hindered e.g. by the fact, that there is no unique drug terminology for herbal and homeopathic substances. A unique scientific plant classification is not available. In addition it remains a challenge to guarantee that all substances listed in the future database will be so unambiguously defined, that an attribution to homeopathic and anthroposophic substances will be possible.

In addition, for the evaluation of ADRs (from direct reports or from literature cases) in context with homeopathic medicinal products the degree of dilution of the substance in the finished product has to be considered.

3.2.7. Simplify and make proportional to risk periodic safety update report submission by industry (PSUR)

As a matter of principle, we appreciate the consideration to cancel the PSUR for old established products.

However, as mentioned above, we have serious concerns about the expedited reporting of all ADRs from inside the Community. If the ECHAMP member companies could chose between the two measures of widening the definition of ADRs to be reported within 15 days on the one hand or of writing PSURs in regular periods of time on the other hand, we clearly indicate that we see more benefit and sense regarding the safety of old established products in limiting the 15 day reporting to serious ADRs according to the old definition and to keep the PSUR.

3. Comments Regarding Annex I: Detailed Proposals for Legislative Changes

Article	Comment on Commission Proposal	Reason
Directive 2001/83/EC		
1(11)	Keep old text	Not acceptable. The evaluation of a medicinal product must be seen in context with the prescribed dose, because everything (including food) will be potentially harmful if taken in too high doses.
(13)	Keep the old term and definition	The term unexpected adverse reaction is a useful tool for the evaluation of safety of a product. Inconsistent with article 101a new.
1 (16)	Keep old text	Abuse and adverse reaction have to be differentiated. These are essential terms for an adequate safety evaluation.
8 (3) (ia)	A summary of the pharmacovigilance system which shall include: …, contact details for the qualified person, a statement signed by the qualified person …	Also this reduced content is vulnerable to changes, because it contains personal data, which will change with respective staff change. In this case also variations have to be made for each marketing authorisation. This can only be circumvented by submission of an independent Pharmacovigilance dossier and a cross reference in the marketing application dossier. It is of great importance, that the contact data for the qualified person is not available for the entire public. It should be stored in closed sections of the authority internet pages.
21 (1) sentence 2:	Add: The risk management system shall be annexed to the marketing authorisation, <u>where appropriate.</u>	For clarity reasons.

Title IX		
101e (1)	1. MAH shall record… (a) Reports where the ~~Patient or the~~ Healthcare Professional… (b) Reports where the ~~Patient or the~~ Healthcare Professional… (c) <u>Patient reports have to be recorded and reported when the QPPV considers at least a reasonable causal relationship between the the ADR and the medicinal product</u>	The given definition of reports to be included actually means that nearly any case has to be reported irrespective of any reasonable relation. This is contra-productive with respect of the goal of the Commission initiative, to simplify and to make pharmocovigilance more efficient. It would mean that a lot of adverse events will be reported.
101e (1)	"The marketing authorisation holder shall accept reports of adverse reactions electronically". Please clarify: Does it mean that acceptance of xml-files or E2B conform reports directly in the company has to be possible?	In view of the deadlines to be kept, such a requirement would be unrealistic and extremely difficult to SMEs, which because of low frequency of reports mainly work in co-operation with contract companies.
101e (2)	"The MAHs shall submit electronically to Eudravigilance, no later then 15-days following the receipt of the report, all adverse reactions that occur in the Community…" We have serious concerns with this requirement. Only serious adverse drug reactions (occurring within and outside the Community) should be submitted electronically within 15-days to Eudravigilance.as it is currently valid If electronically single case reporting for non-serious cases is deemed as necessary we suggest extending the reporting period, for example up to 90 days.	The planned extension for electronically reporting of all adverse drug reactions in the Community as single cases (ISCR) means an additional workload and financial burden for pharmaceutical companies without additional benefit for the safety evaluation of old established products. This will have particular impact on SMEs offering well known products, where the staff capacity in the pharmacovogilance departments is not adapted to frequent expedited reporting in the same way as in big exploring company with mostly new drug substances. This is because each ISCR takes additional time for preparation and documentation of the whole procedure. This is especially true, if all cases have to be reported in a 15-day period, because this short period is mostly not sufficient to gain all necessary information. Therefore one has to make at least one follow up report, per case, which means another additional time.

		For homeopathic and anthroposophic companies with a big product spectrum of comparatively low safety risk and predominantly non-serious adverse drug reaction this will bring much more workload than reporting the cases in a line-listing enclosed in a PSUR. For demonstration of the importance: As an average in our member companies, there is a 100fold amount of non-serious ADRs compared to serious ADRs. For this a longer reporting period for non-serious reports will save time and capacity for MAH and authorities because - the number of follow-up reports can be reduced, - and they can be processed more organised and therefore time-saving.
101k (7)	Reference should be made to paragraph 6.	The referral to paragraph 5 seems to be an error.
101l (4) f	Do not include reports of audits into files which are open to external authorities.	This is against all common practice in pharmaceutical industry (GMP). We strictly refuse this as it would be contra-productive with respect to the original intention of audits.