14 May 2006

Peter Arlett
European Commission
DG Enterprise & Industry
Unit F2 'Pharmaceuticals'
EUROPEAN COMMISSION
B - 1049 Bruxelles
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By e-mail: Peter.arlett@cec.eu.int

Subject: Public Consultation on the Community System of Pharmacovigilance

Dear Mr. Arlett,

We are pleased to provide you with our comments on the Community System of Pharmacovigilance following the European Commission workshop with industry groups held on 21 April 2006.

We encourage the efforts made up to this point and acknowledge the significant measures implemented, which potentially allow efficient exchanges of Pharmacovigilance data within the European Economic Area. Our main comment concerns the system's complexity, which represents a substantial impediment to the development of small and medium companies (SMEs), as they struggle to allocate sufficient resources to respond to increasing regulatory and administrative requirements. Through our activities and collaboration with SMEs we have gained experience in the field, and considered it useful to provide you with some comments on difficulties encountered by such SMEs, in addition to recommendations on how the system could be improved from a small structure point of view.

Please find attached Voisin Consulting's comments on the Community System of Pharmacovigilance.

Sincerely,

Voisin Consulting

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SIGNATURES

1. Introduction

This document summarizes Voisin Consulting's comments on the Community System of Pharmacovigilance from a small company's point of view. Our comments have been organized in compliance with the template provided for responses to the "Commission Public Consultation: Assessment of the Community System of Pharmacovigilance".

RESPONSE TO: Commission Public Consultation: As Assessment Community System of Pharmacovigilance

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COMMENTS

1. Data sources and safety issue detection

Firstly, as the pharmacovigilance system, and particularly the Eudravigilance electronic database, has become very demanding in terms of resources for the industry, we believe that there is a need for transparency on how the industry could benefit from such database. Through a guideline these benefits could be emphasized by indicating the:

- Database objectives (briefly listed from a patient, industry and agency point of view),
- Added value for the pharmaceutical and biotechnology industry,
- Detailed instructions for the use of pharmacovigilance data in support of new marketing authorization application, with brief case studies,
- List of advantages for innovative companies (such as conditional marketing approval procedure).

Secondly, below are further comments based on our experience.

Slow responsiveness

Our experience with safety issue detection and follow-up actions has highlighted the difficulty several member states are experiencing to provide fast and efficient safety issue detection and guidance for action.

As an example; in the past, we have assisted a SME developing a medicinal product already commercialized in a different indication. Genotoxicity studies showed positive. As required, expedited reporting was observed on the basis of available results. Given the absence of response from the concerned member state, assistance from external experts was sought to determine appropriate action and communication with the company commercializing the active substance. Similar non- or slow responsiveness is observed following PSUR and renewal submissions.

This phenomenon is clearly due to pharmacovigilance clearly lacking resources within member states.

It is easily understandable that small member states cannot allocate sufficient resources for pharmacovigilance. To circumvent lacks of resources, we believe that experience on organizational good practices and working tools should be extensively shared between agencies. To respond to lack of personnel, an up-to-date official list of experts at the European level could be provided. As a result, member states could seek assistance and relevant guidance from such experts and communicate their conclusions to the industry within an acceptable timeframe. These member states would still be responsible for safety issue detection, but not –partially or fully- for the analysis and subsequent action guidance for serious adverse events.

The availability of an official list of experts could be further extended to the industry so that pharmaceutical companies would approach agencies with well-informed, more appropriate propositions for concise and efficient actions.

Loss of control on the safety of medicinal products

We know from experience that many SMEs, as well as foreign companies, do not have a sufficiently broad picture of pharmacovigilance requirements in the EEA to establish an efficient safety information communication path. The situation is in fact becoming more complex with the need to appoint pharmacovigilance representatives and local representatives in certain member states. From that perspective, we welcome the obligation for pharmaceutical companies to provide a description of their pharmacovigilance system and, where appropriate, their risk management system as part of the application for a marketing authorisation. Nevertheless, the complexity of the system obliges these companies to subcontract their pharmacovigilance activities.

From our experience, we notice the following difficulties resulting from subcontracting:

- Loss of vision on the safety of the medicinal product
- Lack of responsiveness (this is also applicable for member states fully outsourcing pharmacovigilance)

The difficulties are further emphasised by somewhat unclear guidance associated with the outsourcing of the Eudravigilance database registration and use, for example due to:

- Lack of clarification of who can replace a registered person when absent (signature).
- Start-ups cannot afford Eudravigilance courses for several members of the company and to train newpeople as staff leaves the company
- Need to clarify the status of consultants/CRO who will fill in the Eudravigilance database on behalf of MAH/sponsors. Such situations will be more and more common and should be clarified
- Need to be more transparent between the requirements for post-marketing reporting and SUSAR reporting.

2. The legal framework and new legal tools

The increase of pharmacovilance regulatory texts has been important through various directives and regulations over the past years. Generally, SMEs cannot cope with the integration and implementation of such texts. They lack distance for a global view of the system.

Although complex, we believe the legal framework is quite appropriate. We would rather improve the means of communication rather than try to rearrange it at this stage.

We encourage any action that draws the system towards harmonization. Member States should bear in mind that national requirements impede the efficiency of SAE reporting and follow-up action as pharmaceutical companies must double their efforts and staff to remain compliant on a national level. Such efforts could be more effective if allocated to signal detection and decision making.

We believe that there is a clear need for enhanced implementation and simplification of the pharmacovigilance system by Member States with all efforts made towards harmonization. We understand that measures in that direction are already in place and we welcome them. We believe that there is no need for further regulations/guidelines/directives as the system is already sufficiently complex. On the contrary, if possible, grouping of all pharmacovigilance regulatory texts should be achieved on one single source/website (e.g. the Eudravigilance website), including the national implementation texts as soon as possible following the day of their national publications. Additionally, one could consider a correlation table of specific requirements from each Member State. This could be made available and updated by Member States, in collaboration with the Community within a specific timeframe.

Regarding the Pharmacovigilance database, we believe that one could turn around national electronic reporting requirements by installing a single interface for electronic reporting both to the EMEA and national agencies. As a result, national databases could therefore still exist, while avoiding double reporting.

3. Decision making in pharmacovigilance
As described above.

4. Impact of communications and actions

Communication
As mentioned earlier, communication is more an issue than the pharmacovigilance system itself. We believe that the communication paths from the agency towards industry should be further investigated. For instance. some member states communicate directly with MAHs to inform them about new national requirements (e.g. MHRA for new fees). This is also the case in Switzerland. Guidance on pharmacovigilance could be provided to clinical trial sponsors and MAH though the issuance of a short user guides referring to the applicable regulations in the EU, including national regulations. Such user guide would have to be regularly updated.

Language

If a fully centralized pharmacovigilance system with centralized contact points is not feasible in practice, Member States should be encouraged to appoint English-speaking contact points. These English-speaking contact points would act on pharmacovigilance issues within their agency instead having all pharmaceuticals companies to appoint local pharmacovigilance representatives.

5. Facilitation and monitoring of compliance with pharmacovigilance requirements
No specific comment.

6. The need for quality management and continuous quality improvement.
No specific comment

CONCLUSION

To summarise, we believe that the current pharmacovigilance system could be improved by responding to the following needs:

- Need for a better implementation of the pharmacovigilance system by Member States with all efforts made towards harmonization.
    1. No need for further guidelines/directives as system already very complex, only amendments inserted into current documents.
    2. Differences between European directives and national implementation texts should be published in English. A centralised correlation table of specific requirements from each Member State should be made available and updated by Member States, in collaboration with the Community within a specific timeframe
- Language: if a fully centralized pharmacovigilance system with centralized contact points is not possible in practice, Member States should be required to appoint an English-speaking contact point for Pharmacovigilance issues within their agency instead of requiring all pharmaceuticals companies to appoint local representatives
- Pharmacovigilance database:
    1. Need of explanatory guidance (for transparency) on
        1. Database objectives (further information)
        2. Added value for the pharmaceutical industry
        3. Detailed instructions for possible use of data by the industry (present and future)
- Need for a single interface for electronic reporting both to the EMEA and national agencies (national databases could therefore still exist, while avoiding double reporting)
- Need for sufficient allocation of resources in each Member State by:
    1. Additional hired resources
    2. Sharing member states' working tools / experience at a centralized level would improve overall efficiency, and draw member states toward harmonisation, while avoiding unnecessary efforts
    3. An official list of pharmacovigilance experts available at community level that would help smaller Member States complete their lacking national resources
- Eudravigilance, codes of access:
    1. Need to clarify the situation as to who can replace a registered person when absent (signature). Start-ups cannot afford Eudravigilance courses for several members of the company
    2. Need to clarify the status of consultants/CRO that will fill in the Eudravigilance database on behalf of MAH/sponsors. Such situations will be more and more common and should be clarified