**Template for responses (DEADLINE 12 May 2006 responses should be e-mailed to peter.arlett@cec.eu.int)**

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

*Your response will be put on the Commission's website.*

**Name:** Medical Products Agency, Sweden

**Type of stakeholder (e.g. patient/ healthcare professional/ regulator/ industry): Organisation (e.g. European patient group or National industry association - if relevant):** Regulator

**Your comments:**
**General:** The Medical Products Agency (SE) endorses the general aim and ambition of the Assessment of the Community System of Human Pharmacovigilance. Signals indicating lack of pharmacovigilance staff resources and difficulties with collaboration with health care professionals should be considered seriously and the core recommendations are in principle supported. However, detailed interpretation or generalization of the results should be treated with caution given that there may be undefined elements influencing the validity and reproducibility of the responses both between different NCAs and within the same NCA. The great variability of the responses to some questions such as for example duration of PSUR assessment may indicate that consulted staff has interpreted the question differently. Nevertheless, the report is an important tool for future planning of the European risk management system and safety surveillance in order to achieve improvements within the whole community. Below are listed specific comments on the main headings of the recommendations of the assessment report.

**Comments on the specific areas highlighted in the Commission sponsored study which can be summarised as follows:**

**1. Data sources and safety issue detection**
The Report has identified communication problems and suggests well-tried multichannel technologies to be developed in all countries. The MPA support the idea of improving technical resources and the development of support by electronic patient records for spontaneous reporting of ADRs. However, there is a need to further elaborate how this should be done and how the Community could support and release resources for this development in all MS.
A general pro-active attitude towards signal detection should be stimulated with the development of mutual algorithms for prioritising and strengthening of signals. Methods for quantitative signal detection (10.4.1. Signal detection – Soundness; bullet point 5) that attempt to dampen the effect of small numbers in disproportionality measurements already exists: the BCPNN (Baysian Confidence Propagation Neural Network) as implemented by theWHO, and the MIGPS (Multi Item Gamma Poisson Shrinker) implemented by Lincoln/FDA are two methods that have been used for some time. To the method currently implemented in Eudravigilance, the PRR

(Proportional Reporting Ratio) should ideally be added a baysian method such as BCPNN or MIGPS.

The Report states that regional PhV centres are a promising approach, especially in larger MS. A decentralised system with reporting from regional PhV centres to NCAs and from all NCAs to the EMEA is supported by the MPA and believed to increase reporting. TheWHO-model for education on pharmacovigilance and spontaneous reporting could be considered and delegated to NCAs with more extensive resources/experience in Pharmacovigilance to be responsible for organising courses for newly developed agencies and regional PhV centres.
The recommendation that one senior pharmacovigilance staff member in each agency should be reachable 24h a day will be difficult to implement in smaller agencies and the cost-benefit of this model is questionable. It is unlikely that urgent matters will be solved at night with other parties not being available and the public unreachable for information. However, the 24h availability could be applicable for staff of the Inspection unit.

The work sharing model should be further developed in all areas in order to support smaller agencies. However, the work load related to assessment should be distributed more equally with respect to the resources of the agency and not to the size of the population.

An additional source of safety information that has not been discussed in the Report is to request the MAHs to present cumulative and updated meta-analyses within each PSUR of all their performed clinic trials in order to get more information on for example type-C ADRs (i e myocardial infarction and rofecoxibe).
The idea of Centres of excellence for specific tasks such as different databases and pharmaco-epidemiology is supported.

**2. The legal framework and new legal tools**
The implementation of existing legal framework could be facilitated by mutual seminars on harmonisation of for example PSUR assessments, renewal assessments etc. The implementation process would also be supported and facilitated by introducing further templates. A system to navigate through regulatory requirements (a “super-guidance”) seems helpful. This should preferably be in the format of a guiding flow-chart – and not yet another guideline.
Furthermore, to facilitate the national implementation of harmonised decisions at the EU-level, e.g. work-sharing projects such as PSUR work-sharing, the Commission should consider the need to harmonise the legislation.
Efforts should also be made to help not only HCPs to report ADRs but also other parties such as academic sponsors to comply with expedited reporting requirements of adverse events.

**3. Decision making in pharmacovigilance**
Some of the bullet points have already been addressed at the EMEA. Furthermore it could be discussed how *adequate* time for *decision-making* in safety issues should be defined and how this interacts with the quality of the decision. However, the recommendation to review the decision-making process is supported. In order to be able to communicate and implement at a national level the pharmacovigilance decisions taken by e.g. the Pharmacovigilance Working Party, it is necessary to rapidly increase the transparency of the EU assessment reports and other reports that needs to be referred to in the process.

**4. Impact of communications and actions**

Essential for the impact of regulators' communication to prescribers is knowledge of the needs of the prescribers and of available tools in the different Member States. Co-operation with health care providers/prescribers on a regular basis is important. A thorough mapping of available - and used - tools in the individual Member States should be performed. Methods for evaluation of impact should be developed and these methods should be used on a regular basis. Since updates of SPCs and PLs are common, the development and use of electronic prescriber support should be encouraged within the EU in order to enable important messages reaching the prescribers and patients urgently when deemed necessary.

Tools for evaluation of the outcome of regulatory actions will be increasingly important. An example of one newly developed tool is a national register on dispensed medicines established in Sweden in 2005. It contains patient identities for all dispensed prescribed drugs to the entire Swedish population (9 million inhabitants).The information includes age, sex and a unique identifier of the patient as well as the prescriber's profession and practice (primary healthcare centre/hospital clinic). The register can be linked to national registers of births, deaths, hospitalizations and cancer.

**5. Facilitation and monitoring of compliance with pharmacovigilance requirements**

The monitoring should partly be implemented in daily routine activities (such as evaluation of the quality of presented PSURs) and also be performed on demand.

**6. The need for quality management and continuous quality improvement.**

There appears to be a great variation in the level of quality management. This outcome of the Report should, as previously mentioned, of course be interpreted with caution. However, apparently there is a need for continuous quality improvement.

• **on suggestions to strengthen the Community Pharmacovigilance System.**

- More education of MS is needed for handling and understanding of data-mining techniques
- The method currently implemented in Eudravigilance for quantitative signal detection, the PRR (Proportional Reporting Ratio) should ideally be complemented with a baysian method such as BCPNN or MIGPS
- Increase the use of clinically implemented disease registries. An additional proposal would be to develop a mutual database (including contact persons) of available registries within the Community
- A decentralised system with reporting from regional PhV centres to NCAs should be implemented in more MS
- The WHO-model for education on pharmacovigilance and spontaneous reporting could be considered and delegated to NCA's with more extensive resources/experience in Pharmacovigilance to organise courses for newly developed agencies and regional PhV centres
- Electronic prescriber support should be encouraged within the whole EU
- A thorough mapping of available - and used - tools for evaluation of the impact of communication in the individual Member States should be performed

- Mutual seminars on harmonisation of for example PSUR assessments, renewal assessments etc
- Rapidly increase the transparency of the EU assessment reports and other reports that needs to be referred to in the process.

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On behalf of the Medical Products Agency

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