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[1]: Professor Saad Shakir

Type of stakeholder (e.g. patient/ healthcare professional/ regulator/ industry): Academic/Pharmacoepidemiologist/Drug Safety Research Physician/Practicing Clinician

Organisation (e.g. European patient group or National industry association - if relevant): Director of a Charitable Research Unit which studies the safety of medicines Director of a Charitable Academic Research Unit which studies the safety of medicines

Your comments:

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

  1. Data sources and safety issue detection
  2. The legal framework and new legal tools
  3. Decision making in pharmacovigilance
  4. Impact of communications and actions
  5.Facilitation and monitoring of compliance with pharmacovigilance requirements
  6. The need for quality management and continuous quality improvement.

- **on your experiences of the Community system overall**

- **on any part of the Community system (section 1 of this consultation paper describes the system and those involved directly)**

- **on how you could better contribute to the Community pharmacovigilance system**

- **on suggestions to strengthen the Community pharmacovigilance system.**

- **any other comments**

Below is my response to the Consultation by the European Commission on the review of pharmacovigilance regulations in Europe. I understand the task of Commission is complex. The aim of my suggestions is to drive regulations towards a better scientific base, less bureaucratic hindrance, more openness and efficiency.

[1] requests for attendance at the workshops should be sent separately to peter.arlett@cec.eu.int and should include the organisation you represent and your contact details. The deadline for these requests is 31 March 2006.

Risk management for newly introduced products is perhaps one of the most important recent developments in pharmacovigilance. Its precise impact can only be known in the next few years. However, this development perhaps provides only the foundation to build on to expand and enhance pharmacovigilance. More is needed. The revision of the regulations is an excellent opportunity to introduce improvements. With all the effort that will be put in such an exercise the improvements need to be bold, yet scientifically well founded. Points which I hope the Commission will consider include:

1. Spontaneous Reporting

Spontaneous reporting is very important for signal generation for rare adverse drug reactions (ADRs). However, it utilises enormous resources as it is managed now. Complex regulations have bureaucratised the system to a degree that drains its scientific spirit. There is a need to harmonise case reporting to a single point in the EU which disseminates the reports electronically to Member States and the EMEA. This is technically feasible and must be implemented as a unified procedure to all licences (centralised, mutual recognition and national). Evaluation can be shared by Member States to spread the workload. Simplification of the processes will save enormous resources both within pharmaceutical companies and regulatory authorities. If the new regulations succeed to streamline spontaneous reporting, they should ensure that any freed resources are kept within the system to develop and support other methods of pharmacovigilance.

2. Periodic Safety Update Reports

Similarly, the revision of the regulations provides an opportunity to review the effectiveness and scientific contribution to pharmacovigilance of Periodic Safety Update Reports (PSURs). The benefits of PSURs have not been evaluated (nothing in the public domain to my knowledge). Their evaluation is long overdue. For example, are PSURs necessary for established products which have been on the market for many years? Updating an internet document for each product may be all that is needed for this group. Scaling down the PSURs only to those that are useful will save enormous resources. Again all freed resources from reduced requirements for PSURs (which will be enormous) must be channelled to support other methods of pharmacovigilance.

3. Other pharmacovigilance and pharmacoepidemiology methods

Many regulatory decisions, including important public health decisions, such as product withdrawals, have been based on limited data, e.g. spontaneous reports with or without data from another study.[(1)] There is general agreement that the evidence-base for pharmacovigilance decisions must be enhanced. Risk management planning attempts to address this imbalance, but more is needed. The revision of the pharmacovigilance regulations is an opportunity to:

3.1 Address the methodological imbalance which currently is in favour of spontaneous reporting with the aim to place more emphasis on other methods such as intensive monitoring schemes, observational studies and using automated databases and simple randomised clinical trials.

3.2 Intensive monitoring schemes must become obligatory for new products in situations and in EU countries where such schemes are feasible.

4. Expanding the scope and stakeholder-base of risk management

4.1 At present pharmacovigilance and risk management plans are driven by the pharmaceutical companies (with or without external advice) and subsequent regulatory approval. This small and closed circuit must be opened and expanded. Contributions to risk management planning must be extended to other stake holders such as interested healthcare professionals, researchers and patients' representatives. This reflects policies across the EU for open governments, freedom of information and patients' participation.

4.2 The main public health burden of medicines is not from rare events with new products, but from common ADRs for established and frequently widely used drugs. Risk management must extend to all areas where it is needed, not only to new products where pharmaceutical companies are prepared to spend money to facilitate their introduction to the market. In many cases risk management needs to be disease-based and not drug-based, certainly not exclusively drug-based for profitable new products.

5. Methodology research

Pharmacovigilance and pharmacoepidemiology are very young sciences. The methods are evolving. Observational studies have their strengths and weaknesses. Advances can only be achieved by methodological research. Funds for such research are limited from grant offering bodies and the pharmaceutical industry usually (with a few exceptions) only funds research that is of immediate or medium term direct benefit to them. Since regulatory authorities are one of the principal users of pharmacovigilance and pharmacoepidemiological research, the Commission needs to ensure that methodological research is adequately funded.

6. Research networks and collaborations

There is ample scope for establishing pharmacovigilance and pharmacoepidemiology research networks between research groups in the EU. Scientific convergence and telecommunications render such collaborations feasible. The review of the regulations is an opportunity to facilitate the establishment and funding of research networks and collaborations in pharmacovigilance and pharmacoepidemiology within the EU.

7. Training

The numbers of competent researchers in pharmacovigilance and pharmacoepidemiology researches in the EU is limited. This hinders existing research activities in these fields and blocks expansion. The Commission ought to take the opportunity of the regulations review to put in place measures to ensure high quality training of researchers in these fields.

I wish you the best. Please do not hesitate to contact me if you wish any advice, input or any other contribution for this important project.

Best wishes.

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References

1. Clarke A, Deeks J and Shakir S. A Review of the Publicly Disseminated Evidence of Safety Used in Decisions to Withdraw Medicinal Products from the UK and US Markets. Drug Safety. 2006;**29(2)**:175-181.