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Response to the consultation on the review of pharmacovigilance regulation in the EU

It is widely accepted that pharmacovigilance (PV) includes not ony the identification of adverse drug reactions(ADR) but the promotion of the safe use of drugs and the creation of appropriate structures and means of communication needed to perform its tasks.

At present PV in Europe is an activity performed almost exclusively by drug authorities and the pharmaceutical industry, focussed mainly on the identification of ADR. Very little is done to achieve progress in the other two important fields of PV. Thus the needs of physicians and patients are neglected to a large degree. ADR are common and contribute considerably to the economic burden of health care.

Thus I would like to draw the attention to the following issues:

Preventability of ADR

There are ADR which are absolutely inherent to a drug and there are ADR which can be avoided by high quality prescribing (e.g. by taking into account patient characteristics like impaired renal function, low body weight or comorbidity). Meta-analyses have shown that about a third of all serious ADR are preventable, but the current PV regulations neglect this chance. The avoidance of serious ADR would save considerable amounts of money and improve at the same time the quality of care.

In this context it is important to emphasize that we know a lot about ADR but alarmingly little about how to successfully modify physicians prescribing habits. The Dear Doctor letter, and changes in the summary of product characteristics and /or the patient information leaflet have repeatedly shown to have very little impact if at all on the use of a particular drug.

Therefore PV has to broaden its scope, doctors working in patient care have to be involved, and research has to be funded with the aim to promote the safer use of drugs. Not only the ADR itself has to be investigated but the context in which the ADR occurred too.

Cooperation with the Patient Safety alliances has to be established.

Rational risk/benefit decision-making

Even officials of drug authorities admit in private conversation that decision making of drug authorities re drug safety issues can be quite arbitrarily. Rational decision-making requires reliable quantitative data about the benefits and harms of the treatment under investigation and of its therapeutic alternatives, and of the harms of the natural history of the disease that is treated. These data are usually not available when decisions have to be taken. Data about the natural history of disease, drug utilization data and data about the ADR profile of drugs are needed. The EMEA should start to establish such data bases.

The EU member states show a considerable variability with regard to the incidence and prevalence of diseases, the drugs used, the comedications, the medical cultures and traditions. Thus one may expect a considerably variation of type, frequency and severity of ADR across the EU member states. (Cars, for example kill highly different numbers of people in the different EU member states). Very little attention has been paid to this issue, although there are a number of hints that drugs may be harmful in one member state but without any excess risk in an other state. Thus all EU member states should have a standard PV system which allows for a cross state comparison of incidence, type and severity of ADR. As most drugs which achieve approval within the EU have been shown to be effective, it has to be taken great care that the use of these drugs is restricted only in those regions where the drug has shown to be more harmful than acceptable or is likely to do so.

Improvement of current ADR monitoring systems

Although the spontaneous reporting system is an essential approach in this field the administrative collection of incomplete and unvalidated reports (as it is the case in many countries) is no longer acceptable. Quality control procedures as known from clinical trials like source data verification etc. are needed (e.g.in the sense of Good Pharmacovigilance Practice) as are more attempts to estimate the incidence by the use of regionalized drug consumption date. More use of pharmacoepidemiological data banks, the development of new approaches to monitor long term effects and ADR in inhospital patients are urgently needed. Data mining approaches to screen the data which are available in the various drug authorities have to be regulariloy used and refined.

As drug authorities usually do not provide the working conditions scientists like and need, a much closer collaboration between drug authorities and academia is needed. One should definitely discuss to establish a long term collaboration between drug authorities and certain qualified research groups/departments including even the exchange of staff for a certain time etc. and respective outsourcing of tasks, which require academic expertise.

In general, transparency and access to all data needed for an efficient PV should be free for all those who are active in PV.

Final comments

The EU has to take greater responsibility re that all states have at least one ADR monitoring system in common so that comparability is granted. PV has to provide the data physicians seeing patients and patients need. Avoidable bureaucracy should be reduced. Evaluation of current methods, e.g. PSURs, extensive exchange of data e.g with

ethics committees etc in necessary. There is definitely more money needed for PV research. The responsibility for PV should be in the Health Directorate of the European Commission.