

## **HEADS OF AGENCIES WORKING GROUP**

### **ESTABLISHING A EUROPEAN RISK MANAGEMENT STRATEGY**

#### **OVERVIEW OF PHARMACOVIGILANCE RESOURCES IN EUROPE – SURVEY OF NATIONAL COMPETENT AUTHORITIES**

##### **Introduction**

Pharmacovigilance is a vital preventive public health function which is dependent on effective systems for monitoring safety of medicines in clinical use. Such systems need to be capable of detecting and analysing reports of drug toxicity, and assessing changing risk:benefit so that appropriate, prompt regulatory action can be taken to minimise risk and communicate effectively to health professionals and patients.

This overview summarises the findings of questionnaire surveys of the pharmacovigilance resources of national competent authorities, carried out between 2003-4 by an Ad Hoc Working Group of the Heads of Medicines Agencies. The surveys covered staff, data, tools (IT systems, signal detection procedures), expert advisors and communications support.

The immediate conclusions of the Working Group on the results have led to an initiative in collaborative work-sharing between Member States and a move towards use of a wider range of more robust sources of evidence than individual case reports. The results of the surveys have also been fed into the European Commission assessment of the community system for Pharmacovigilance which is currently underway and will define priorities for the future operation of pharmacovigilance in Europe.

##### **Background**

The report of the High Level Group on Innovation and Provision of Medicines in the European Union (G10 Medicines Report) published in May 2002, recommended that systems for post marketing surveillance should be optimised to ensure that co-ordinated processes are in place to gather data on adverse events and patient safety (<http://pharmacos.eudra.org>).

In Autumn 2002 Heads of Medicines Agencies agreed on a mandate for an ad hoc Working Group on establishing a European risk management strategy. The Working Group, comprising participants from Denmark, France, Germany, Spain, UK and EMEA and later joined by Netherlands and Sweden, identified as a key priority the conduct of a high level survey of EU pharmacovigilance resources (<http://heads.medagencies.org/heads/docs/summary.pdf>). It was envisaged that such a survey would enable future planning to optimise utilisation of resource and expertise, and encourage collaborative working.

##### **Methodology of survey**

The responsibilities of the National Competent Authorities are outlined in detail in Volume 9A of the Rules Governing Medicinal Products in the European Union: Guidelines on Pharmacovigilance for Medicinal Products for Human Use (<http://dg3.eudra.org/f2/pharmacos/new.htm>). Questions which reflect these responsibilities were formulated in order to build a picture of the distribution of resources and the local evolution of systems and approaches to the conduct of pharmacovigilance.

## **Findings**

As expected there was considerable variation between NCAs in the majority of parameters included in the survey.

### **Human resources for pharmacovigilance**

The total human resource is limited to around 400 staff in all NCAs with 70% of Agencies contracting out some assessment work. The deployment of the pharmacovigilance staff was almost equivalent in data management and risk assessment, with less than 10% monitoring industry compliance and very few engaged in audit of pharmacovigilance action. The skill mix includes a high proportion of staff with health professional training, with only a small number of Agencies utilising scientific resources and few employing in-house epidemiologists. The majority had access to expert advice from a pharmacovigilance committee.

### **Data resources – spontaneous ADR reports**

The annual number of spontaneous ADR reports received by NCAs was over 100,000, with reporting rates varying widely. In terms of reporting mechanisms, the majority of suspected ADR reports were received on paper, which reflects the fact that healthcare professionals remain the major source of reports. While the access to electronic reporting is largely limited to industry, the burden of resource – intensive manual data entry will remain. In relation to industry, readiness for implementation of electronic standards was a key concern.

Most NCAs devoted resource to initiatives to strengthen reporting, ranging from feedback to reports, to education and training. In over half the member states ADR reporting is mandatory for some or all health care professionals. A growing number have introduced patient/consumer ADR reporting or are planning to do so. A number of NCAs utilise regional monitoring centres to strengthen their pharmacovigilance capability.

### **Detecting signals of new safety issues**

Spontaneous ADR data remain an important resource for the detection of potential drug safety hazards. The more extensive the data, the more appropriate it is to use automated signal detection methodologies. Effective signal detection programmes require large volumes of reports but only a small number of key data fields. Only a minority NCAs operated an automated signal detection process (two had one under development). Others relied on regular case by case review of ADR reports.

### **Access to other data sources**

Access to and utilisation of other data sources over and above spontaneous reports is variable across the EU, reflecting the continued reliance on spontaneous ADR data. Robust decision making relies on the best evidence available and spontaneous data is considered to be at the lowest level of the “evidence hierarchy”.

Periodic safety update reports (PSURs) constitute a major workload for all NCAs, and this work is mostly duplicated across the EU. Evidence that PSURs have contributed to ongoing evaluation of risk:benefit in clinical use is not readily available. Since PSURs represent a major use of both industry and Agency resource, it will be important to assess their value in terms of signals detected and marketing authorisation changes made to enhance risk:benefit.

All NCAs have access to data on consumption of medicines. The majority have access to sales data and prescription data (non-hospital) split by age, sex and geographic

region. Most NCAs have the capability to perform reporting rate calculation if necessary. Computerised prescription registration is operated in the majority of NCAs, but the data may not be readily available to some, or comprehensive.

### **Pharmacoepidemiological tools**

Over half NCAs had utilised pharmacoepidemiological studies to confirm and or quantify a signal, most commonly requesting the marketing authorisation holder or collaborating with academia. Slightly more had considered using pharmacoepidemiological studies for early post marketing surveillance of new products. All NCAs have access to some of the main types of disease registries in the member state – inpatient/outpatient medical care, cancer registries, cause of death, intrauterine drug exposure or congenital abnormalities. Individual NCAs have access to a wide range of specialist registries for disease groupings.

### **Communications**

As would be expected, all NCAs have access to support in the dissemination of drug safety information to healthcare professionals and the public. There is considerable variability between NCAs in the number of enquiries from healthcare professionals and the public. For some this is a considerable burden whilst others utilise their regional centres.

### **Interpretation of key findings**

The purpose of the survey was to identify key findings to inform future strategies to strengthen pharmacovigilance in the EU. The main findings from the survey are first the variability between NCAs in how pharmacovigilance is resourced, and secondly the limited nature of those resources. This underlined the need to optimise the use of resources within the European network. The collaborative work-sharing pilot for PSURs is an important step forward which could be extended to other areas of pharmacovigilance and provision of information.

The move from reactive to proactive pharmacovigilance via Risk Management plans will require coordinated use of more robust forms of evidence than spontaneous reports. This in turn requires appropriate expertise, access to sources of evidence and adequate sources of funding, perhaps via a central European source. A collaborative initiative by the network of Agencies could be a major step forward in making best use of collective scientific knowledge in this evolving area.

### **Next steps**

The action Plan published in May 2005 by Heads of Agencies and EMEA has brought together an agreed strategy for strengthening pharmacovigilance in the EU. The adoption of the revised remit of the European Risk Management Strategy Facilitation Group will provide a mechanism for monitoring progress in the delivery of the action plan, ensuring the optimal use of resources and available methodologies, together with maximising the opportunity of the new legislation.