



Comments of the International Primary Care Respiratory Group (IPCRG) and European Federation of Allergy and Airway Diseases Patients' Associations (EFA) on the Commission Public Consultation: An Assessment of the Community System of Pharmacovigilance

12th May 2006

For the attention of Dr. Peter Arlett, European Commission

We are writing on behalf of the International Primary Care Respiratory Group (IPCRG)ⁱ and European Federation of Allergy and Airway Diseases Patients' Associations (EFA)ⁱⁱ in response to the European Commission's consultation on the community system of pharmacovigilance. The IPCRG is a charitable organisation committed to improving respiratory care in primary care on a European and worldwide scale. EFA is a non-profit network of allergy, asthma and chronic obstructive pulmonary disease (COPD) patient organisations committed to improving the health and quality of care of patients with these diseases in Europe. We would like to firstly fully support the thrust and importance of these proposals. We have a number of specific comments we would like to make about particular sections:

1. Data sources and safety issue detection

As stated in the consultation many different data sources provide pharmacovigilance data and welcome moves towards a common pharmacovigilance database. The challenge with many of these is that such recording is often haphazard and dependent on a prescribing physician recognising a temporal link between a prescription and an adverse event. Such event monitoring would not have picked up less clearly linked events such as cardiac events linked to prolonged prescribing of COX-2 inhibitors or to an increased risk of asthma deaths in association with prescribing of long-acting beta agonists in the absence of inhaled steroids. It is also likely to under-report problems associated with use of medicines either that are unlicensed, as is often seen in paediatric practice, or used beyond their licensed dosages e.g. problems seen again in children with use of high and unlicensed dosages of inhaled steroids as well as nasal steroids for infants. This also applies to new 'so-called' immunomodulating agents such as tacrolimus and pimecrolimus. We would therefore welcome proactive methods to evaluate the safety of all newly licensed medications and also those with any existing concerns – such methods might include:

Role of patients and patient organisations

Patients are an underutilised source of adverse event reporting and methods should be developed for them or their representatives to submit adverse event data.

Targeted Active Data Collection

We believe this could be an important method for future reporting. We believe it is essential that primary care networks in addition to specialist networks should be utilised here, since even if a drug is prescribed predominantly in specialist practices, adverse events may only be noted in primary care settings. In such instances combined data recording with primary and secondary care data linkage may be extremely important.

Issues about consent and confidentiality merit consideration. Limiting data to consenting patients or parents may limit representativeness and should be unusual. Confidentiality should be explicit in methods used to monitor drug safety.

It is also important that datasets used should provide sufficient quality and validation for safety purposes. An important issue here is the accuracy of diagnosis; e.g. many patients are often misdiagnosed as suffering from asthma, but in fact have COPD (Chronic Obstructive Pulmonary Disease) and vice versa.ⁱⁱⁱ It is important to ensure that adequate support is provided to practitioners supplying data for this purpose, as their primary use of such systems is rarely for registering drug safety.

Post authorisation safety studies

We believe these are extremely important but think a number of key issues need to be considered in relation to current designs used.

- a. There should be a normal procedure for all newly licensed drugs for children and adults.
- b. It is essential that the design of such studies should be scrutinised by regulatory authorities in conjunction with independent data monitoring committees which include patient representatives as well as physicians. This should be a required element of any studies set-up. It is imperative that endpoints are relevant, duration adequate, recording methods adequate and that the studies are adequately powered with appropriate numbers of controls.
- c. It is imperative that representative patients are included in such safety studies. Current pharmaceutical company approaches based on Good Clinical Practice (GCP) and licensing requirements tend to make this impossible. In this context designs should be considered that allow anonymised data to be used so avoiding necessity for consent. Such designs should in our view be actively encouraged. To this end wherever possible the methodology of data collection should as closely as possible fit in with best normal clinical practice.

2. The legal framework and new legal tools

We support the use of new legislation to tackle safety issues more proactively.

3. Decision making in pharmacovigilance

We believe that the decision making process is complex with the current divisions between European Medicines Agency (EMA) / Committee for Medicinal Products

for Human Use (CHMP) functions and those of regulatory bodies in Member States. This may lead to real confusion with doctors in certain member countries receiving very differing or no advice. The recent example of salmeterol where the UK Medicines and Healthcare products Regulatory Agency (MHRA) provided advice, but many other Member States did not, has created confusion with many doctors in Europe turning to the IPCRG for advice or the US Food and Drug Administration (FDA) website.

Furthermore, it is important that the EMEA becomes more consistent in its actions, i.e. that the work of the Pharmacovigilance Working Party is adequately reflected by other CHMP Working Parties to ensure a coherent approach to monitoring the safety of medicines and reviewing marketing authorisations. For this reason, we fully endorse the initiative to optimise “the interaction between the CHMP and the PhVWP”, and to establish “the interaction between the newly created CMD(h), building on the work already undertaken through the best Practice Guide on the cooperation between the MRFG and the PhVWP”, as expressed in the EMEA “Implementation of the Action Plan to Further Progress the European Risk Management Strategy: Rolling Two-Year Work Programme (Mid 2005 – Mid 2007)”

4. Impact of communications and actions

Whilst we recognise that communication and responsibilities are extremely complex within pharmacovigilance, it is important that all stakeholders are included both in terms of reporting issues of concern and in terms of disseminating and receiving information on drug safety. Communication which may be factually accurate may have adverse effects. For example, in the past communication regarding safety issues with inhaled steroids in children resulted in a significant minority of patients stopping regular asthma therapy without consulting their physicians.

5. Facilitation and monitoring of compliance with pharmacovigilance requirements

Whilst the marketing authorisation holders are primarily responsible for the safety of their products we fully support the need for adequate monitoring of their obligations to monitor drug safety. We also endorse the view that this should be a helpful and supportive role as well as a policing role. We are particularly keen on prospective evaluation of drug safety and believe this should be normal for all newly authorised medications and should be undertaken specifically in both adult and paediatric populations. To ensure the design of such studies is appropriate it should be scrutinised by regulatory authorities in conjunction with independent data monitoring committees which include patient representatives as well as physicians.

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

We fully support the proposals put forward for this in the consultation.



Additional comments

• comment on how you could better contribute to the Community pharmacovigilance system

We believe we can assist in contributing in a number of specific ways:

- a. We are delighted as both IPCRG and EFA to participate in providing input into the ongoing review process for pharmacovigilance.
- b. We are eager to provide potential members for any advice required in developing pharmacovigilance strategies for newly licensed drugs in allergic and respiratory disease or formulations for paediatric asthma.
- c. We are happy to review advice that may be provided on issues of drug safety either by Member States or the EMEA.

• Make suggestions on how to strengthen the Community pharmacovigilance system.

We have put forward an extensive array of comments above about strengthening this but would like to add the importance of thinking specifically about paediatric pharmacovigilance as undertaken in the recent EMEA consultation on a draft guideline on pharmacovigilance for medicines used in children.

We would also like to recommend the monitoring of “off-label” use of licensed medicines in the context of a European Risk Management Strategy and that usage should not just be monitored but also reported – the method of doing so should be agreed prospectively with regulatory bodies. It is striking in our area of expertise that there is limited awareness of prescribing of unlicensed and high doses of inhaled and nasal steroids in children. In fact recent evidence presented at the British Thoracic Society in December 2005 showed that almost one in ten children prescribed inhaled steroids are prescribed both high and unlicensed doses.^{iv} Such mechanisms should ensure this does not happen in the future. This may also be the case with new treatments, for example new immunomodulating agents for the treatment of atopic dermatitis in very young infants.



ⁱ **About the IPCRG**

The IPCRG is a charitable organisation that acts as an international umbrella organisation for national primary care respiratory interest groups. Our aim is to use our international network to undertake research in community settings; to lead the production of evidence-based guidelines appropriate for primary care professionals; and to disseminate these findings.

The IPCRG website is available at: www.theipcr.org

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ⁱⁱ **About EFA**

The EFA is a non-profit network of allergy, asthma and chronic obstructive pulmonary disease (COPD) patient organisations who represents its 33 members on European level and provides a platform for members to exchange experiences and for capacity building. Our aim is to reduce the frequency and severity of allergies, asthma and COPD, minimise their societal implications, improve the health-related quality of life and ensure full citizenship of people with these conditions, as well as pursuing equal health opportunities in the field of allergy and airways in Europe.

The EFA website is available at: www.efanet.org

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ⁱⁱⁱ Tinkelman D, Price D, Nordyke R, Halbert RJ. Misdiagnosis of COPD and Asthma in Primary Care Patients 40 Years of Age and Over. *Journal of Asthma* 2006;43:1–6

^{iv} Thomas M, Turner S, von Ziegenweidt J, Price D. Prescribing of high-dose inhaled corticosteroids and add-on therapy in children from 1999-2004: an observational study. Presented at British Thoracic Society December 2005.