Dr Peter Arlett
European Commission
B-1049
Brussels
Belgium

1st February 2008

Dear Dr Arlett

STRATEGY TO BETTER PROTECT PUBLIC HEALTH BY STRENGTHENING AND RATIONALISING EU PHARMACOVIGILANCE

Thank you for the opportunity to comment on the Commission's proposals to strengthen and rationalise the EU pharmacovigilance system. The UK believes that this exercise provides a unique opportunity to transform the way in which pharmacovigilance is undertaken across the EU and to introduce provisions that ensure that we have a modern, efficient and effective regime within which to operate, with responsibilities and obligations clearly set out and effective sanctions for failure to comply. This will enhance public confidence in the safety of medicines available across the EU.

The UK very much welcomes the Commission's proposals, which, in summary, clarify legal obligations on companies, provide for a single, binding EU decision making regime for safety issues, introduce proportionate safety monitoring for products and reduce certain administrative procedures. We believe that the Commission's proposals will ensure that we strengthen our ability to provide a high level of public health protection whilst meeting the objectives of Better Regulation.

However, we would also like to draw your attention to a number of areas where we believe the proposals could be further enhanced. In particular, and in acknowledgement of the unique opportunity that the Commission's proposals represent, we consider that the following five key issues should be given greater consideration before the legislative texts are finalised for negotiation:

- We believe that throughout the provisions and in particular in the rules governing communications, there should be a better balance of the benefits associated with a product as well as the risks. At present the focus is almost exclusively on risk;
- We also believe that the concept of, and procedures for, signal management should be explicitly drawn out to ensure a transparent and flexible system where roles and responsibilities are clearly defined. The Pharmacovigilance Committee should be given responsibility for monitoring and management of all safety issues and for appropriate allocation of work arising from them;
- Given the unique opportunity that the review of the legislation governing pharmacovigilance presents, we would like to see the Commission taking a more

fundamental approach to the rules governing the way statutory information is provided to healthcare professionals and patients. We think this would best be achieved by the Commission establishing a working group to explore this issue in detail, and to offer proposals to the Commission before the formal legislative proposals are finalised later this year. The implications of the work on patient information already underway in the Pharmaceutical Forum, and of the Commission's commitment to make legislative proposals on patient information under Article 88a of Directive 2001/83EC will of course need to be taken into account;

- In line with Better Regulation principles, we believe that the new pharmacovigilance legislation should support worksharing arrangements for a range of functions, not only PSURs;
- We need greater clarity on funding arrangements for pharmacovigilance activity, including how to provide funding for safety studies on medicines no longer protected by patent.

The UK's detailed comments on the Commission's proposals follow, presented in the order in which they appear in the consultation document:

Decision-making and roles and responsibilities

We welcome the proposals to establish a formal committee to replace the Pharmacovigilance Working Party which will coordinate pharmacovigilance and make recommendations on safety issues to the Committee on Human Medicinal Products (CHMP). We welcome the principles of the new referral procedures proposed but there will need to be absolute clarity on their scope to ensure that only substantive issues with serious public health implications follow this route. Absolute clarity over respective roles and responsibilities of the Pharmacovigilance Committee and CHMP – especially in situations in which certain hearings are to be held in public – will also be crucial to operating a successful regime in which the Community and its citizens can have absolute confidence. The consequence of formal decision making on a safety related matter should not necessarily be to bring nationally authorised products into future MRP/DCP processes.

We expect that safety signals for nationally authorised products with less significant public health impact will be dealt with by the Pharmacovigilance Committee alone, with input from CMD(h) on implementation aspects as necessary. For these cases, agreement at the Pharmacovigilance Committee should enable them to issue a binding decision with regard to any MR or DC authorised products and to issue a "persuasive opinion" with regard to any purely national MAs. A divergence of opinion at the Pharmacovigilance Committee could allow for a referral to CHMP and Commission Decision for those MAs approved in MR or DC procedures only. Knowledge from practical experience of updating safety information for large numbers of products can be used to inform practice.

We would welcome greater clarity about how the work associated with the new Committee is to be financed.

Good Vigilance Practice

We strongly welcome the proposal to establish the concept of Good Vigilance Practice (GVP) in the legislation, to be followed by the adoption of a regulation on GVP. The UK is already developing a Good Pharmacovigilance Practice (GPP) Guide, which is due to be published towards around mid 2008. This guide is aimed at MA holders in the UK and will complement the EU legislation, making it clear that the document is practical guidance to complement any EU GVP regulation.

We would also like to see inclusion of a provision that will allow inspections to be undertaken to confirm adequacy of, for example, pharmacovigilance systems, before a medicinal product is placed on the market. At present if a company does not already have a product on the market there is no provision that allows for such an inspection to take place. We note that the proposals envisage that in the future the Commission will collate inspection reports. We would prefer to retain current arrangements under which inspection reports can be made available on request. However, we would welcome a minimum EU standard set for inspections to ensure consistency of approach across Member States.

Risk Management Planning and post-authorisation studies

We are pleased to see inclusion of proposals that will enable regulators to ask for risk management plans for authorised products where necessary. However, we also believe that there should be scope within the legislation to ensure that risk management plans can cover a number of products – “common, or core risk management plans” – for example all pandemic flu vaccines, or all products containing the same substance (including generics).

The plan to annex the risk management plan to the summary of product characteristics is also strongly welcomed as this will improve the legal standing and transparency/availability of these documents. However, we are concerned that the current text makes no reference to the safety specification section of the risk management plan. This section is essential for understanding the rest of the plan and it is important that it should be included. We also welcome the introduction of clear rules governing the requirement to undertake post-authorisation studies, including sanctions to ensure studies are completed.

We are concerned that the amended text suggests that the provision for authorisation under “exceptional circumstances” is to be removed, and replaced by a provision that specifies the post-authorisation requirements that, in granting an MA, may be placed on the MAH. The existing provision refers to situations described in Annex 1 to Directive 2001/83EC in which an MA may be granted on the basis of a limited data package (such as the rareness of a condition that the product is intended to treat, where it would be unethical to conduct a full programme of clinical trials or where the current state of science precludes a full dossier of data being developed). We do not believe that the proposed replacing text provides a proper alternative to the current provision, which is most often used for products to treat Orphan diseases.

Simplification of Adverse Reaction Reporting (ADRs), intensive monitoring, patient reporting, Eudravigilance

We welcome the proposals for reporting of single ADRs from industry and the new requirement for reporting expected serious reports from outside the EU and non-serious reports from within the EU. However, we would support further simplification and believe that all ADR reports (serious and non-serious) should be reported, regardless of whether the ADR occurred, within or outside the EU. This would remove the burden of making the relevant judgements and modern electronic data management systems are capable of handling the volume of data. We support the proposal that the public may have access to the data and that such requests must be provided within 90 days. However, it is vital for public confidence that a transparent access policy is agreed by all Member States.

We also welcome the provision of a legal basis for patient reporting which experience in the UK has shown to be a valuable additional source of information for pharmacovigilance.

We strongly support greater proportionality in ADR reporting, depending on the level of knowledge about the safety of a drug. In line with this approach, we welcome the proposals to establish an intensive monitoring regime for new drugs, and scope to restrict use of a drug under safety review, although it needs supporting with a system that would clearly identify intensively monitored drugs to reporters, such as the Black Triangle system in the UK.

We do not support the proposal that patient reports for intensively monitored drugs should go directly to industry, rather than competent authorities. Whilst we acknowledge that industry needs urgent access to these reports, it is essential that the regulator receives these reports at the same time. We also believe that although electronic reporting should become the norm, there must remain the option for submission of reports on paper for the foreseeable future so that those without access to, or confidence in, electronic systems are still able to report.

We also have concerns about the proposal that healthcare professionals and patients will, within 5 years, report direct to Eudravigilance. Encouraging healthcare professionals – and more recently patients – to report adverse reactions to medicines has for 40 years been the responsibility of national regulators, and although Member State approaches to this task differ, essentially their success in gaining compliance is determined by their understanding of the culture within which they operate. The fact that citizens are encouraged to report to a national body which they understand to have responsibility for safeguarding public health in that Member State significantly increases their engagement – at least in the UK. We have serious concerns that a fundamental change to this system would lose the engagement of those whom pharmacovigilance systems are intended to serve, and have a significant negative impact on reporting rates in the UK and in other Member States. This is wholly incompatible with the fundamental objective of pharmacovigilance which is to safeguard public health.

We also consider that the proposal that all industry reports should go direct to Eudravigilance will place an unreasonable burden on the EMEA because the whole Community will be dependent on them to download and route all reports to the correct competent authority in a timely manner so that Member States can undertake signal detection. There is also no mention of foreign reports being provided to Member States although we presume this would be done passively through Eudravigilance.

We support the proposal for the EMEA to carry out all literature monitoring, since this would provide a significant reduction in duplication of work. However, we believe that the residual responsibility must rest with the MAH to ensure that important cases are not missed.

Periodic Safety Update Reports (PSURs) and worksharing

We strongly support these proposals. The reduction in frequency or removal of the requirement to submit PSURs for older and well established products will be helpful in achieving a proportionate approach to the regulation of lower risk products, including certain herbal medicines. We support the introduction of a legal basis for worksharing on PSURs and, as stated above, we believe that there are other areas in which worksharing arrangements can be developed.

Communication, Transparency

We welcome these proposals, but believe that in implementing them it will be important to take account of the fact that Member State communications take place in different cultural contexts and under different time pressures. We would not want the EU requirements to prevent Member States from operating in an appropriate way in the best interests of public health in their own country.

Product information

In supporting the current proposals to enhance communication with healthcare professionals and patients via product information, we strongly suggest that this opportunity is taken to make both PILs and SPCs more useful, user friendly and coherent. The proposals at present represent only a small part of what should be a much broader effort to improve the accessibility and relevance of patient leaflets. We propose that the Commission sets up a working group to explore what healthcare professionals and patients need – to be working on proposals during 2008, whilst the Commission is finalising the legal texts.

Finally, we congratulate the Commission on developing a coherent package of proposals to improve the current pharmacovigilance regime, but we believe that in undertaking this exercise, the Commission has created a unique opportunity for an even more radical approach to revising this fundamental aspect of medicines regulation. We hope that there remains the opportunity for these ideas to be included in the Commission's formal legislative texts, and we would also welcome the opportunity to discuss further our views on the additional issues we have identified above.

Yours sincerely

Kent Woods
Chief Executive