COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, 10.12.2008
SEC(2008) 2671

COMMISSION STAFF WORKING DOCUMENT

Accompanying document to the

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

and the

Proposal for a

DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use

SUMMARY OF THE IMPACT ASSESSMENT

{COM(2008) 664 final}
{COM(2008) 665 final}
{SEC(2008) 2670}

1. INTRODUCTION

Medicines contribute considerably to the health of EU citizens. The discovery, development and effective use of drugs have improved many people's quality of life, reduced the length of time spent in hospital and saved many lives. Consumption of drugs is increasing, with pharmaceutical market value reaching €141 billion in 2006.

Medicines can, however, also have adverse (negative) effects. Adverse drug reactions (ADRs – a response to a medicine which is noxious and unintended) present a major public health burden in the EU. It is estimated that 5% of all hospital admissions are due to an ADR, 5% of all hospital patients suffer an ADR and ADRs are the 5th most common cause of hospital death. It is estimated that 197,000 deaths per year in the EU are caused by ADRs and that the total societal cost of ADRs in the EU is €79 billion.

Medicines regulation and particularly the system of authorising medicines are critical for ensuring that only high quality, efficacious medicines of acceptable safety are allowed on the EU market. However, the established limitations of drug development, particularly the limitations of clinical trials in terms of their size, duration and controlled conditions means that some side effects will only be detected after a medicine has been authorised and entered the market.

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects of drugs and comprises: collecting and managing data on the safety of medicines, scrutinising at the data to detect 'signals' (any new or changing safety issues), evaluating the data and making decisions with regard to safety issues, acting to protect public health (including regulatory action), and, communicating with stakeholders about the safety of medicines.

Key stakeholders involved in pharmacovigilance are:

- patients as the users of medicines and families and carers as advisers and carers of patients,
- all healthcare professionals but particularly:
  - doctors (to advise patients, prescribe medicines and report ADRs)
  - pharmacists (to advise patients, dispense medicines and report ADRs)
  - nurses (to advise patients, administer medicines and report ADRs)
  - academia (to conduct studies into the safety of medicines)
- medicines regulators including Member States National Competent Authorities (including regional centres), the European Medicines Agency (EMEA) and the European Commission,
- Healthcare service providers and governments and social insurance schemes,

- Pharmaceutical industry, including Marketing Authorisation Holders (innovative, generic and over-the-counter medicines sectors), manufacturers and distributers of medicines (comprising a wide range of company sizes including a high proportion of small and medium-sized enterprises -SMEs).

Of these stakeholders the current EU regulatory framework, made up principally of provisions in Regulation (EC) No 726/2004 and Directive 2001/83/EC (supported by implementing guidelines), place direct obligations on medicines regulators and the industry only. However, the impact of these provisions can affect indirectly all those listed above, particularly in terms of the public health burden of ADRs.

2. PROBLEM DEFINITION

Significant weaknesses of the current EU system of pharmacovigilance have been identified through an independent Commission sponsored study, extensive public consultation (in 2006 and again in 2007) and through detailed analysis by the Commission services. These weaknesses include:

- A lack of clear roles and responsibilities for the key responsible parties and a lack of clear obligations against which they perform their roles (resulting in poor compliance);

- Slow EU decision-making on drug safety issues particularly for nationally authorised products and frequent disharmony in action taken by the Member States;

- Low levels of transparency relating to pharmacovigilance and relatively limited EU coordination of communication about the safety of medicines, plus complex product information with poor penetration of key warnings;

- Cumbersome oversight of companies' pharmacovigilance systems by the authorities;

- A lack of proactive and proportionate monitoring including a lack of risk management and structured data collection in the form of post authorisation safety studies and duplicative reporting rules for the industry and authorities relating to both 15-day, literature and periodic (PSUR) reporting of ADRs;

- Lack of inclusiveness of stakeholders including a lack of direct patient reporting of ADRs and their virtual absence from decision-making.

Overall these weaknesses mean that limited resources are diverted to meet complex and duplicative administrative requirements, there is an over-reliance on poor quality reactive data, decision-making is slow and measures to reduce risk to patients are not only sometimes late but frequently of limited effectiveness. Taken together these problems mean that the safety of EU citizens is not optimally protected so that there is an opportunity to reduce the public health burden ADRs by improving EU pharmacovigilance. In addition, the diversity of Member State pharmacovigilance requirements and the disparate Member State action on safety issues for nationally authorised products means that the single market in pharmaceuticals is not fully achieved.

3. OBJECTIVES

The specific objective of the proposals is to improve the health of EU citizens by strengthening and rationalising pharmacovigilance.

The operational objectives of the proposals can be summarised as:

(1) Providing for clear roles and responsibilities for the key responsible parties and clear obligations against which they perform their roles;

(2) Rationalising EU decision-making on drug safety issues in order to deliver measures that are equally and fully implemented for all relevant products and across the community with a view of preventing unnecessary patient exposure to risks;

(3) Strengthening medicines safety transparency and communication to increase the understanding and trust of patients and health professionals in the safety of medicines and improve the penetration of key warnings;

(4) Strengthen companies' pharmacovigilance systems, allowing companies to improve their systems constantly while reducing administrative burden;

(5) Ensure the proactive and proportionate collection of high quality data relevant to the safety of medicines through risk management and structured data collection in the form of post authorisation safety studies, together with rationalised single case and periodic reporting of suspected adverse reactions;

(6) Involve stakeholders in pharmacovigilance including through direct patient reporting of suspected adverse reactions and inclusion of patients and heath-care professionals in decision-making.

4. POLICY OPTIONS

Four basic policy-options were developed for the impact assessment:

(1) No policy-change;

(2) Deregulation;

(3) Self-regulation, and;

(4) Amendment to the existing European Community legislation.

Enhanced implementation and enforcement work within the current legal framework (i.e. option 1) will improve pharmacovigilance and EU public health protection and it is for this reason that work to improve implementation of the current EU pharmacovigilance system is an integral part of the Commission "Strategy to Better Protect Public Health by Strengthening and Rationalising EU Pharmacovigilance" announced in February 2007. However, the impact overall of improvements of the current EU system will be limited and the step change improvement in public health protection can only be realised with a

change to EU legislation. On this basis only option 4 proved a realistic way of meeting the objectives proposed.

A large number of potential policy options were highlighted by the independent study and by stakeholders during the first public consultation. The specific policy options were selected and modified based on an iterative process of problem investigation, process understanding, expert dialogue and stakeholder consultation with options being fine-tuned while others were excluded during the process. Fifteen specific policy options were selected on the basis that they provided the best sum of the impacts and an overall coherence of the EU regulatory system. These fifteen were included in the legal proposal.

These are:

- Clarification and codification of the tasks and responsibilities of involved parties and establish standards;

- Establishment of a clear EMEA committee structure for pharmacovigilance scientific assessment and decision making coordinating activities and making recommendations on the safety of medicines at the EU level;

- Rationalising the EU pharmacovigilance referral procedures;

- Increasing drug safety transparency;

- Improved EU coordination of communication about major new or changing safety issues and establishment of an EU portal on the safety of medicines;

- Introduction of a new section in the Summary of Product Characteristics and Patient Information Leaflet on ‘key information' with a transitional implementation period;

- Introduction of a "Pharmacovigilance System Master File" to ensure robust but un-bureaucratic oversight of companies pharmacovigilance systems;

- Provision of a clearer legal basis for risk management plans for new and authorised products with safety concerns, including post-authorisation safety studies;

- Codification of guiding principles and oversight for the conduct of non-interventional post-authorisation safety studies;

- Simplification of ADR reporting using the EU Eudravigilance database as a central tool;

- Scanning of the scientific literature by the EMEA with a clearly defined in scope;

- Exchange of data on medication errors that result in an adverse reaction including between the competent authorities for medicines and those for patient safety;

- Removal of the current routine requirement for industry periodic reports (PSURs) for low risk, old and established products;

- Provision of the legal basis for the new EMEA pharmacovigilance committee structure to require submission and coordinate assessment of PSURs and make consequent recommendations for product labelling;

- Provision of the legal basis for patients to report suspected adverse drug reactions.

5. ANALYSIS OF IMPACTS

The chosen policy options were found to be coherent with existing international harmonisation in pharmacovigilance and will lead to further convergence with the systems in place or being introduced in the United States, Canada and Japan.

The chosen policy options were not found to have a significant environmental impact. However, the increased use of information technology will reduce the need for duplicate paper reporting and the increase in transparency will allow pharmacovigilance assessments to be widely available though the internet.

With regard to impact on public health (the key social impact) none of the chosen policy options have a negative impact and those with the greatest positive impact were found to be: codified roles, responsibilities and standards; fast robust EU decision-making; transparency and EU coordination of drug safety communications; improved product information; improved risk management including high quality post-authorisation safety studies, data sharing on medication errors and work-sharing on the assessment of periodic reports (PSURs).

Overall the most conservative estimate of the saving to society of the proposals is €237 Million per year across the EU with a maximum estimate of €2.4 Billion per year. The most conservative estimate of the public health impact of the proposals suggested 591 lives saved across the EU per year with a maximum estimate of 5910 lives saved per year.

Currently the EU pharmaceutical industry sector spends an estimated €833 Million annually on meeting the EU regulatory requirements for pharmacovigilance and the policy options proposed would redirect the industry spend from duplicative ADR, periodic, literature and system reporting to proactive monitoring, with higher quality data collection through risk management planning and post-authorisation studies. Overall, and including this redirection of spending, the package of proposals will save the EU industry sector an estimated €145 Million per year representing 17.4% of their current EU spending on pharmacovigilance.

In 2004 the EU medicines regulators employed 317 staff in pharmacovigilance activities and staff numbers have increased slightly over time. The proposals will lead to costs incurred by the regulators with estimated one-off implementation costs of €3,9 Million for the EMEA and €3.0 Million across the EEA National Competent Authorities and ongoing annual running costs of €10.1 Million for the EMEA and €4.6 Million across the EEA National Competent Authorities. The proposals explicitly foresee industry fees to cover these pharmacovigilance costs and these fees are included in the calculations of industry costs which revealed 17.4% overall industry savings. It should be noted that these figures will not necessarily result in direct fee increases as, at least for the EMEA, fee income is currently in surplus.

6. CONCLUSION

This impact assessment has shown that increasing the clarity, efficiency and quality of the EU system of pharmacovigilance, through amendments to the existing EU legal framework, presents a win win situation with major public health improvements of at least 591 lives and €237 Million of public health burden saved per year across the EU and overall cost savings of €145 Million per year to the EU industry sector.