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Response to the European Commission public consultation on legislative proposals as part of a "Strategy to better protect public health by strengthening and rationalising EU pharmacovigilance"

Joint Position Paper

of

the Medicine Evaluation Committee (MEDEV)

of the European Social Health Insurance Forum

Submitted 1 February 2008

About the *Medicine Evaluation Committee* (MEDEV)

The *Medicine Evaluation Committee* (MEDEV) was established in 1998 as a standing working group of the European Social Health Insurance Forum, which comprises 16 national liaison agencies, associations and institutions for social health insurance in the EU Member States and Switzerland. Today, MEDEV represents the drug experts and pharmacologists of the national social health insurance organisations and other competent bodies in 14 EU Member States. The principal purpose of MEDEV is to provide the national health insurance organisations and other competent bodies with timely analyses about drug related trends and innovations at both national and European level. Further, with the overall objective of providing a necessary counterweight to the pharmaceutical industry, especially at EU level, MEDEV aims to support the EU's activities in formulating drug policies by giving input from the point of view of the statutory health insurers' and other competent authorities. MEDEV can offer expert advice to all EU bodies from the earliest stage of the pharmaceutical decision-making process and help them analyse the possible impact of drug-related policies on national health schemes.

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MEDEV welcomes the opportunity to comment on the Commission's strategy to better protect public health by **strengthening and rationalizing** EU pharmaco-vigilance. The strategy announced in February 2007 by Vice President Verheugen has two parts:

1. better implementation of current framework
2. proposals for change to legal framework

As a first comment we remark that the current framework for EU pharmacovigilance as laid down in Regulation (EC) 726/2004 and Directive 2001/83/EC (as amended in 2004) was the result of a major review of pharmaceutical legislation in 2001 and has only been in effect since 2004. As such MEDEV strongly believes that it would be premature to consider changing the legal framework until full efforts have been made for the better implementation of the existing legislation (1).

Having said that, our further comments will be addressed to the subject of the current public consultation: proposals for change to the legal framework (2).

Forward

Experience with thalidomide in the1960s, diethylstilbestrol in the 1970s, triazolam in the 1980s and more recently, cerivastatine, rofecoxib (Vioxx), olanzapine and rosiglitazone has demonstrated the need for:

1. Strict legislation to secure as far as possible the **placing on the market** of safe and effective medicines and

2. Strong **pharmacovigilance procedures** to monitor the safety of those medicines in general public use over the medium to long-term, to identify and rapidly warn of any adverse effects that pose a risk to patients and to take effective actions to prevent these effects from being replicated.

Rationalisation should not *weaken* current requirements for marketing authorization at the expense of patient safety

Since the introduction of the Medicines Directive in 1965, Community legislation has required demonstration of quality, ***efficacy*** **and** ***safety*** of a new medicine as prerequisites for obtaining marketing authorization (MA). In recent years a number of derogations have been introduced to the legislation to facilitate the process and allow quicker passage to market of some medicines under specific conditions – conditional MA, exceptional circumstances. The proposals described in the consultation document go further in this sense such that conditional MA becomes the norm rather than the exception (Article 22).

- With the proposed change to **Article 22** of Directive 2001/83/EC it seems that an **exceptional or conditional marketing authorization** is possible for *all* new medicinal products. In this way the exceptional procedure is no longer restricted to cases in which the applicant can show that he is unable to provide comprehensive data on the efficacy and safety under normal conditions of use. Even an optimal pharmacovigilance system can never be a substitute for comprehensive data on safety at the moment of marketing authorization and before use in an uncontrolled setting of daily practice. Doing so will put patients unnecessarily at risk. An alleviation of the obligation to provide comprehensive safety data **should remain reserved for exceptional cases** as outlined in Annex 1 of the Directive.
- More detailed safety studies will only be implemented post-MA and only "if there are *serious concerns* about the risks affecting the risk – benefit balance" (Art 101g(1)). MEDEV believes that **post-marketing safety studies** should be compulsory.
- Art 8 states that the required **risk management system** should be proportionate to the level of the foreseen risk. What about unforeseen risks? The proposed changes to Art 1 (13) and (16) of the Directive remove the specific references to "**unexpected adverse reaction**" and harmful effects due to "abuse of medicinal products". MEDEV strongly opposes the deletion of these articles.
- In Art 26, the requirement to demonstrate *therapeutic efficacy* as a prerequisite for obtaining MA is simply deleted. This is unacceptable and far beyond the scope of a revision of the legislative framework on pharmaco-vigilance. It is indeed the opinion of MEDEV that marketing authorization requirements should be strengthened further, preferably by including the demonstration of "***added*** **therapeutic benefit**". Demonstration of therapeutic efficacy should remain a *minimum* requirement.
- It is equally unacceptable to delete the provisions under Art 116 and 117 for withdrawal of marketing authorization and withdrawal of product on the grounds of lack of therapeutic efficacy.

MEDEV believes that the above mentioned Commission proposals, contrary to the aims of the strategy to better protect public health by strengthening pharmacovigilance, seriously **weaken the current legislative framework** regarding the placing on the market of safe and effective medicines. This would greatly increase the risks to patients and the public.

Centralisation and clear definition of responsibility

MEDEV congratulates the Commission on its efforts to establish clear roles and responsibilities for the different players and to centralise activities related to the coordination, communication and monitoring of pharmacovigilance data. In particular we welcome:

- the establishment of a **Pharmacovigilance Committee** within EMEA with responsibility for coordinating pharmacovigilance in the EU

- the establishment of an **EU portal on the safety of medicines**, with links to competent authority websites in the Member States (MSs), for better transparency and communication of drug safety information, including the publication of an intensive monitoring list (Art 101j)

- better use of **Eudravigilance database** with electronic reporting and responsibility by EMEA for scanning the literature and updating the database, as well as for monitoring of the database for signals of new or changing risks and for informing the market authorization holder (MAH), MSs and Commission (Art 101d).

Further to the above, MEDEV recommends **strengthening the mandate of the proposed Pharmacovigilance Committee by giving it the right of decision** on pharmacovigilance issues within the EMEA rather than being limited to an advisory role as proposed by the Commission. In particular, we believe it would be more appropriate to assign the prerogative to ask for post-authorisation safety studies and risk management plans to the pharmacovigilance committees whether at national or European level. This would avoid the conflict of interest that arises if this prerogative is assigned to the authorities granting marketing authorisation (e.g. the CHMP) as the Commission proposes.

Patient reporting should be to the competent authorities not to the MAH

Art 59 referring to the package leaflet states that for medicinal products included on the EU list of intensely monitored products, "All suspected adverse reactions should be reported to …the *MAH* in the MS where the MAH will receive suspected adverse reaction reports." Further the MAH is only required to register notifications where it considers "that a causal relationship is at least a reasonable possibility" (Art 101e). This gives the opportunity to the MAH to filter and even bury adverse reaction reports it considers harmful to its product.

MEDEV recommends that patients are encouraged to **report adverse effects directly to their national competent authority**, preferably with the support and advice of a health professional. Direct reporting by patients could be facilitated by including a pre-printed form in the product package.

Guaranteed independence of pharmacovigilance activites through public funding

Public financing of activities vis à vis pharmacovigilance to guarantee their independence is conferred in REG (EC) 726/2004 (Art 67.4). The new proposals expressly nullify this guarantee by listing the financial means available to authorities to carry out their pharmacovigilance duties as not excluding "fees charged to MA applicants or MAH for these activities" (Art 101c).

A clear distinction of the role and financing of bodies responsible for pharmacovigilance (including decision-making) from those responsible for marketing

authorization should avoid conflict of interest and guarantee the independence of pharmacovigilance activities.

Complete transparency and access to information on pharmacovigilance

MEDEV calls for complete transparency regarding pharmacovigilance activities to include not only the publication of the *agreed* risk management plans and the post authorization safety study protocols on the EU medicines safety web-portal as proposed but also details of the decision-making process (demands, responses, reasons), the periodic safety update reports (PSURs), inspection reports and sanctions taken in case of non respect of obligations, as well as full details of meetings, decisions, votes, and minority opinions (as laid down in Dir 2004/27/CE (Art 126)) also in cases of suspension, revocation or non-renewal of MA on the basis of safety issues.

Appropriate measures to enable easy **access to safety information on medicines for all stakeholders** (health professionals, patients, consumers, carers) should be put in place.

This position paper has the support of the following MEDEV member organisations:

AUSTRIA	HVSVT	Hauptverband der österreichischen Sozialversicherungsträger, Vienna
BELGIUM	INAMI/RIZIV	Institut National d'Assurance Maladie Invalidité - INAMI / Rijksinstitut voorziekte- en Invaliditeitsverzekering - RIZIV, Brussels
FINLAND	PPB	Pharmaceuticals Pricing Board, Helsinki
FRANCE	HAS	Haute Autorité de santé, Paris
	CNAM	Caisse Nationale d'Assurance Maladie, Paris
GERMANY	AOK-BV	AOK-Bundesverband, Bonn
	BKK-BV	Bundesverband der Betriebskrankenkassen, Essen
	IKK-BV	Bundesverband der Innungskrankenkassen, Bergisch Gladbach
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LUXEMBOURG	UCM	Union des Caisses de Maladie, Luxembourg
THE NETHERLANDS	CVZ	College voor Zorgverzekeringen, Amstelveen
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