CONFLICT OF INTERST OF EXPERTS IN EUROPE IMPACT ON PUBLIC HEALTH

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Author: Christophe Kopp, editor with *la revue Prescrire*, a French continuing education journal for healthcare professionals (www.prescrire.org), published by *Association Mieux Prescrire* (AMP). All *Prescrire* editors and AMP members have to sign a No Thanks Charter each year, where they declare to have no conflict of interest with the pharmaceutical and device industry. The speech will focus on experts involved in regulatory work

1- Management of conflicts of interest by European health authorities

Freedom of information in Europe is guaranteed by a regulation providing for access to public documents of all EU institutions, including the European Medicines Agency. Regarding conflicts of interest, we can rely on the EU Regulation 726/2004 on medicines. When the authorities refuse to give access to key information we can appeal to the EU Ombudsman and finally to the European Court of Justice.

Conflicts of interest start when pharmaceuticals laws are drafted by EU Commission

It has been shown that a group of experts, the Competitiveness in Biotechnology Advisory Group with Industry and Academia (CBAG), dominates EU drafting in its field. This expert group includes 20 industry representatives and 6 academics, but no representative from public health advocates independent of the pharmaceutical companies.

Another example is the way the EU Commission has built partnerships with patient groups so that it can claim to work for patients' wellbeing. Indeed, the EU Commission's Directorate Enterprise has co-opted the European Patients' Forum (EPF) as the main representative of patients. Yet this Forum is heavily sponsored by big pharma.

European Medicines Agency's fails to manage conflicts of interest

Failure to manage conflicts of interest transparently and efficiently begins with the management board of the European Medicines Agency. This management board includes 2 representatives of patients belonging to industry-sponsored groups.

When it comes to marketing approval and pharmacovigilance we are unable to check whether the binding rules on conflict of interest are properly applied. We can't check how conflicts of interest are managed for a given meeting. We can't see if "conflicted" experts are excluded from entering the rooms when issues in which they have conflicts of interest are addressed.

When *Prescrire* editors suspect a distorted drug evaluation they request information on conflicts of interest of experts. Erlotinib was a case in point. Erlotinib is a gefitinib me-too

with severe adverse effects such as skin rash, cardiovascular reactions or interstitial pneumonia. In July 2006 the European Medicines Agency rejected an application for use of erlotinib in metastatic prostate cancer. The licensing committee considered that the adverse effects of erlotinib in this setting outweighed its limited efficacy. The company, Roche, was not happy and appealed the decision.

Then the European Medicines Agency convened a special meeting with other experts. The new panel of experts issued a positive opinion and the drug was finally approved for this clinical use. The same clinical data had actually been submitted, apart from a retrospective subgroup analysis with a low level of evidence that favored the product.

Prescrire requested the declarations of conflicts of interest of experts and we found that 3 out 4 experts had significant links with the company Roche. This is evidence that disclosing conflict of interest is not enough to prevent distorted drug evaluation.

EU member states' health agencies are no better than EMEA at managing conflicts of interest: the French case

At the French drug regulatory agency (Afssaps), conflicts of interest of experts are disclosed annually, but with much delay: 2007 declarations were not available as of 9 April 2008. The French regulatory agency uses 2 categories of conflicts of interest: minor and major. A minor interest includes having 5000 euros stakes or less in a drug company that markets the product being evaluated, or strong links with the same company dating between 3 and 5 years. Yet there is no evidence that these minor conflicts of interest protect experts from being willy-nilly influenced.

Reports on pharmacovigilance and market approval meetings do not allow health professionals and the public to check how conflicts of interest are managed before the meetings start. Declarations of conflict of interest are made by word of honor. There is no independent body for auditing these declarations; no penalty for dishonest experts.

In France experts are paid around 330 euros for participating in a half-day meeting. Badly-paid expertise and lack of academic recognition means experts are vulnerable to conflicts of interest.

In France there is a new law that makes an obligation for academics and physicians who are involved in health matters to disclose their conflicts of interest when they communicate with the public or the media. Unfortunately this law is not properly applied and much campaigning is still needed.

We understand that in other European countries the situation is no better. In short, transparency and management of conflicts of interest in regulatory and health agencies of EU member states are apparently not in line with EU law.

2- ICH: a clear case of institutional abuse of power

The ICH was created in 1990 for harmonizing drug regulation in the 3 biggest pharmaceutical markets: the United States, the EU and Japan. The key members of the ICH,

the only one with votes, include regulators from the FDA, the European Medicines Agency (EMEA) and the Japanese Ministry of Health, Labour and Welfare (MHLW).

ICH also includes representatives of brand-name pharmaceutical companies: the Japan Pharmaceutical Manufacturers Association (JPMA), the European Federation of Pharmaceutical Industries and Associations (EFPIA), the Pharmaceutical Research and Manufacturers of America (PhRMA). The International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) has been, in its own words, "*closely associated from the start by providing the ICH Secretariat*".

There is no voting representative from companies or drugs agencies from developing countries, or the generics industry, no representative from public health advocacy groups, the medical profession or consumers.The ICH has produced numerous guidelines related to efficacy, clinical safety and quality of medicines that have direct influence on day-to-day functioning of drug regulation worldwide, and especially on pharmacovigilance.

ICH regulatory guidelines have huge influence on drug registration and pharmacovigilance worldwide. Actually the ICH is behind the trend towards faster approval of medicines since 1990.

3- Proposals: Disclosure of conflicts of interest is not enough, elimination is best

Regulatory agencies should disclose and manage conflict of interest of experts and staff for each regulatory meeting in a transparent manner so the public can check rapidly whether "conflicted" experts are excluded, including experts with so called minor conflicts of interest. And expertise contributing to regulatory decisions should be reasonably paid (no voluntary work), and recognized by academia as Publications and Research.

Two publicly accessible databases are needed: one registering conflicts of interest declarations from experts, regulators, and academics so the public and healthcare professionals can easily monitor regulatory work; the other one registering drug companies' monies given to health professionals, experts, key opinion leaders, with payment description.

Governments should reconsider the funding of regulatory agencies that should be totally funded by public money. That is one key condition for restoring integrity and credibility of regulatory decisions; governments should increase public funding of clinical trials based on true research needs.

There is a need for education about conflicts of interest and their serious consequences on public health during training of healthcare professionals.

Last but not least we should blow the whistle on the ICH, which should be controlled by the WHO with equal votes by representatives of patients, health professionals, UN member states and all pharmaceutical and device industries.

Joint campaigning is needed to achieve these goals

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