Prescrire

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Paris, 2 March 2009

Excessive secrecy beyond the law!

Prescrire answer to Draft of "EMEA policy on the practical operation of access to EMEA documents" (deadline 2 March 2009) (1)

Dear Sir, Dear Madam,

We've read with great attention the Agency draft on policy of access to EMEA documents (1).

In agreement with article 255 of the Treaty establishing the European Community, citizens have a right of access to European Institution documents in application of transparency principles.

However, since decades, the international scientific community and the public are aware of the different strategies used by the regulatory agencies to practice excessive secrecy in drug regulation (read "Development of excessive secrecy" section of the Uppsala Declaration in annex).

The draft "EMEA policy on the practical operation of access to EMEA documents" released for consultation unfortunately uses many of these strategies to justify its secrecy ("Specific principles" section on page 3) (1).

Progress needs to be made in stamping out the hypocrisy of "commercial confidentiality". Clinical data concerning patients, exposed to a medicine, as well as the incidence and prevalence of diseases, and the frequency of adverse effects, are scientific data. Also, there is no reason to consider consumption data as "commercially sensitive": this information is sold to the firms by companies specialising in the sale of economic data. Consumption data are of major public health interest: being aware of the size of the population likely to be exposed to an adverse effect is a necessary factor for establishing the risk-benefit balance.

EMEA should remember that transparency at European level is key to encourage transparency at National level in EU Member States.

For EMEA to substantially improve its transparency policy, we request EMEA to apply the general principles available in the international Uppsala Declaration, namely make transparency the norm and secrecy the exception.

Commercial confidentiality must not supersede general interests, especially when European citizens' safety is at stake.

Sincerely,

Olivier HUYGHE
For Prescrire editorial team

1- http://www.emea.europa.eu/pdfs/general/direct/11019606en.pdf

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Annexe

Statement of the international working group on transparency and accountability in drug regulation *"Uppsala Declaration"*

1. Introduction

Health Action International (HAI)-Europe and the Dag Hammarskjoeld Foundation jointly convened an International Working Group to seek ways of promoting openness and accountability in drug regulation, both in industrialised and developing countries. The Working Group met in Uppsala, Sweden from 11-14 September 1996.

In recent decades, most countries of the world have established agencies to ensure the efficacy, safety and quality of pharmaceuticals, the validity of information relating to them, and to monitor patterns of utilisation and matters relating to rational use. These agencies must be regarded as servants of the public, acting to protect and advance health where drugs are concerned.
The regulatory agencies have assumed major responsibilities and large amounts of drug information are entrusted to them; the agencies themselves also generate policies, procedures and decisions. The scientific community and the public need this material but much of it is not available to them. It is needed both to ensure the effective and safe use of drugs, and to guarantee accountability, i.e. to provide a sound basis for scrutinising the activities of these agencies so as to ensure that they are acting efficiently and honestly in the public interest.
In recent years, freedom of information has become an increasingly accepted principle in democratic societies; many national governments subscribe to it, as do the European Commission and the World Health Organization. The principle of openness applies to pharmaceuticals as it does in other matters - often even more so because of the direct importance of drugs to people's health.
For these reasons, the Working Group set out to consider how essential information could be mobilised from drug regulatory agencies and their associated bodies without injuring any valid interest.

2. The origins of confidentiality in drug regulation

Most regulatory agencies and similar bodies have been established by law, and specific clauses in these laws usually require that they handle certain data confidentially. In addition, the employees of agencies are commonly bound by oaths binding upon civil servants requiring them to maintain secrecy on matters entrusted to them.
Two main arguments originally underlay the principle of regulatory secrecy in the drug field:
- First, it was considered that a commercial company which had used creativity and funding to devise and develop a drug could only reap a proper reward and fund future research by protecting it from immediate imitation by others. While patent law would protect certain matters, others could be protected only by maintaining secrecy.
- Second, it was realized that information relating to individual persons (for example those participating in a drug research project or those in whom adverse reactions had been reported by physicians) would have to be dealt with having full regard for personal integrity. These principles need not be questioned but they need to be more fully defined. On which matters does the need for secrecy really outweigh the general need for openness? Where is the dividing line between legitimate trade secrets and "commercially sensitive" data? How do secrecy clauses in the law need to be changed?

3. Development of excessive secrecy

Drug agencies and inspectorates often maintain secrecy to a much greater extent than law or logic actually demand. Some laws, for example, only strictly require secrecy as regards personal data and the method of preparation of a drug, yet one often sees that no part of a regulatory file is accessible, and that reports about adverse reactions or poor manufacturing standards are sealed. Various reasons underlie excessive secrecy:
- **lack of legal obligation**: in some countries, the law establishing regulatory bodies does not impose on them any duty of providing information.
- **lack of clarity in the law**: agencies or their staff may consider it safer to apply confidential clauses broadly

rather than narrowly.
- **lack of tradition**: many countries have no tradition of transparency in government.
- **lack of consistent policy**: particularly in some developing countries there are (very) frequent changes in regulatory staff and general policy matters such as the provision of information receive little attention.
- **absence of explicit routines**: within the agency, who is competent to release a particular type of information, to whom, and in what circumstances?
- **lack of capacity and resources**: particularly in under resourced regulatory agencies, the time required to process requests for information may in itself be a barrier.
- **paternalism**: the frequent belief that those outside of the agency do not need, could not cope with or would misinterpret the information.
- **embarrassment**: an agency may hesitate to make fully public those decisions which are poorly documented or internally contested, papers which reflect poorly upon the agency's performance, or matters on which it might be criticised for not yet having taken a decision.
- **industrial influence**: many companies clearly prefer that entire regulatory files be regarded as secret.
- **over-caution**: there may be an exaggerated fear of upsetting commercial susceptibilities.
- **bureaucratic habit and inertia**: in agencies which are not subject to critical and transparent review, habits can form which discourage exchange of information.

4. The benefits of openness of drug information

Full availability of information is essential if all parties involved in health care are to participate effectively. Openness facilitates adequate feedback, proper setting of priorities and development of trust. A culture of openness protects conscientious individuals working in organisations of all kinds. Knowledge relating to all drugs evolves constantly, as do standards and expectations relating to them, their producers and health care providers. However thorough the investigations made before a drug is licensed and marketed, much more will be learned about its efficacy, proper use and risks once it is marketed and used on a much larger scale. Almost no new element of knowledge emerges suddenly; as a rule it begins with impressions, suspicions and hypotheses. Where these arise - for example in reports of possible serious side effects in the journals - all existing relevant information will need to be mobilised to verify or discount this evidence so that the truth can be established as quickly as possible. Much of the information needed for that purpose, including data on both animal and human experience, is unpublished and lies only within the files of agencies. By using it, the truth can be established much more quickly than if one is reliant purely on published evidence.

5. Consequences of excessive secrecy in drug regulation

Where secrecy is excessive the benefits set out in Section 4 will be lost. The risks that arise include the following: if a substantial part of the information existing on drugs remains hidden within regulatory agencies, and sometimes fragmented between them, the development of knowledge will be impeded. This is particularly dangerous where suspicion arises of a hitherto unknown risk. Malpractice can be hidden from view; legal discovery in the course of litigation has for example revealed cases of falsification or suppression of unfavourable data by certain companies, or submission of inconsistent files on the same drug to different agencies. Secrecy facilitates the circulation and use of sub-standard drugs. Where a drug is subject to negative findings, the failure of a drug agency to explain its conclusions or provide background data can leave the way clear for the sometimes very different and emphatic account given from the manufacturer.
In a climate of secrecy and mistrust, the public is unlikely to believe even accurate and meticulously prepared official statements--assuming that they cannot be taken at face value and that some relevant information has probably been withheld. The incomplete availability and irregular release of information promotes a climate in which suspicion is generated and in which sensational and poorly founded stories on drugs break in the popular press; their reliability cannot be checked and unnecessary panic can be caused.
Secrecy has consequences which can be wasteful and even inhumane; scientific work, e.g. in humans or animals, which has already been performed by one company but hidden within regulatory files, may be repeated unnecessarily. If drug utilisation data are not available irrational drug use may continue unrecognised and unchecked.
If research is sponsored by companies, unfavourable or unclear results may be withheld or the research it self may be stopped.

6. Current trends

The Working Group noted several current trends which can affect the free availability of drug information, favourably or otherwise.
First, the move towards adoption of Freedom of Information legislation continues, though only a few countries have as yet taken this step and existing laws contain important exceptions. The current trend towards semi-privatised, industry-financed rather than tax-financed drug regulation can increase the degree of industrial influence on the regulatory process. The industrial preference for a high degree of confidentiality is likely to be pressed strongly. Consolidation of drug regulatory activities into regional and multinational agencies is increasing, and collaboration between certain agencies is growing. This does not in principle lessen the challenge of ensuring sufficient openness; large regional groupings can practice excessive secrecy as much as national bodies.

7. General principle: Freedom of Drug Information

In principle information available within regulatory agencies should be freely available to any party requesting it.
This basic principle applies at least as strongly here as in other fields of governmental activity, and exceptions to it must be defined restrictively. There must also be a right of appeal to an independent higher authority if the regulatory authorities initially refuse to disclose. The Working Group further noted that:
- Availability of information must extend not only to data reaching the agency from the outside, but also to its own deliberations, conclusions and actions.
- Data should where possible be released with some indications as to what is fact and what is hypothesis, but the release of the basic facts must not be restricted or delayed in order to add such commentary.
- The provision of information should not only be passive; agencies should actively provide and publish information in the public interest wherever possible.

8. Valid exceptions to the principle of free drug information

The two most important exceptions that can reasonably be made to the principle that drug information must be freely accessible are as follows:

a. Protection of legitimate business interests

The protection of innovative products and processes is primarily the concern of patent law and not of drug law. However on certain issues patent protection cannot be obtained yet there may still be a valid interest in maintaining secrecy to protect an innovation (e.g. relating to a manufacturing or finishing process) from competition. A feasible approach would be for a manufacturer, when submitting a file to an agency, to state, with reasons, which specific parts of the file are considered confidential and for what period. This specification would be made on a standard form allowing the authority to confer in confidence about the types of matters accepted as justified under this exception.

b. Protection of confidential personal information

Personal data which enter the files of regulatory agencies or adverse drug reaction agencies can include the identity of the individual patient or health professional (or sufficient information to enable him or her to be identified indirectly) as well as information on the illness from which the patient is suffering and the drug treatment received. Information which might lead to the identification of individual patients should not be released by an agency to any party. A feasible approach would be to ensure that all personal data entering an agency is coded in advance in such a way that the individual cannot be individually identified, even by the agency itself. Other limited exceptions to the principle of openness can arise.

9. The need for transparency at the international level

There is an increasing trend to exchange data and views between national regulatory and adverse reaction monitoring agencies. One example is the International Conference on Harmonisation (ICH) which aims to harmonise regulatory requirements between the United States, Japan and the European Union. In time, this will also have a major impact on data handling by agencies in other regions. To date, ICH has concentrated primarily on accelerating the process of new drug approvals; it has scarcely considered the problems of the developing world, monitoring of existing drugs, and the broader aspects of drug safety. Information on ICH activities has been presented in such a way that their full repercussions have not been widely recognised. There is little possibility for developing countries with their special needs to influence the ICH process, and a broader process of consultation and full accountability is lacking. Mechanisms to ensure transparency and access to information

should be integrated into harmonised procedures.
The Working Group noted that, although the WHO International Centre for Adverse Reaction Monitoring has been able to provide an increasing degree of public access to the data which it holds, some of the countries contributing data object to the release of their own information through the Centre, even when aggregated with data received from other centres. It was considered that these countries should be urged to allow the public use of their data through the Centre so as to enhance the usefulness of this international database in generating and examining early signals of possible side effects. Conversely, agencies should be encouraged to make fuller use at the national level of the signals now provided by the Centre on matters of potential concern.
An important form of international exchange is that of certificates of good manufacturing practice issued by drug exporting countries under the WHO Certification Scheme by federal, national or provincial authorities. Unfortunately, the reliability of these certificates varied very greatly. The Scheme will not be of optimal value to importing countries until there is some means of checking that a certificate has indeed been issued on the basis of competent and independent inspection.

10. Continuing Commitment

Secrecy in medicine is a serious obstacle to the attainment of health, in the drug field as in others. The participants in this Working Group made a continuing commitment to promote the further development of openness in drug regulation. They will do this by continuing to publicise the issue, stimulating discussions on the problems surrounding secrecy in drug regulation, surveying current disclosure policies of regulatory agencies and promoting the development and implementation of freedom of information laws applicable to drug regulation. The International Working Group invites other committed groups and individuals working towards greater access to drug information such as drug regulators, consumer organisations, interested NGOs, the World Health Organization, health professionals and public health associations to join its effort and work together in an expanding network.

Uppsala, Sweden, 11-14 September 1996

Statement (with the list of the working group participants) freely available online at:
www.isdbweb.org/pag/uppsala.php

APPENDIX to Uppsala Declaration

Some examples of the types of information to which access is needed

As noted in Section 7, availability of information must extend not only to data reaching the agency from the outside, but also to its own deliberations, conclusions and actions. Some examples of the type of documents and data which can be of particular value and can be made available without undue effort are given below. The list is not exhaustive and the general principle of full availability of all data continues to apply.
- Public assessment reports providing the essential reasons underlying the licensing of a drug and any conditions attached to the licence, or relating to the modification of an existing licence. Where an agency has not compiled reports for these specific purposes, its own internal assessment reports must be made available.
- Copies of the pharmacological, toxicological and clinical reports submitted to obtain the initial or modified registration of a drug and those added to the file subsequently.
- Items (a) and (b) above should be accessible from the date of marketing anywhere in the world, onwards, (as should the texts of the approved data sheet and package insert).
- Inspection reports of pharmaceutical plants, subject only to the deletion of personal details and material details relating to industrial secrets and individual privacy (as defined earlier).
- Adverse drug reaction reports received from health workers, manufacturers or other agencies, subject only to the deletion of personal data.
- Collected pharmacoepidemiology data including data on drug sales and drug consumption.
- The internal evaluation of the relevant regulatory authority regarding current adverse reaction reports.
- Where essential drug lists exist: publication of motivated decisions to include particular drugs on the list or to amend the list.
- Reports relevant to the suspension, restriction or withdrawal of drug product licences or of manufacturing licences.
- Reports on agency meetings, including meetings of scientific committees, and hearings subject to the deletion of personal data.