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# A free hand

In this supplement we review the performance of the European Medicines Evaluation Agency (EMEA), and the European drugs policy.

Time is pressing, as draft Directive and Regulation will be submitted for adoption by the European Parliament and the Council. These drafts are prepared and sponsored by Enterprise Directorate of the European Commission, on which EMEA has so far depended.

We believe, like many other independent observers, that EMEA's performance is not that good. And things may get even worse over the next seven years if the current drafts, which are supported by a powerful industrial lobby, are adopted.

Some hold that the European community is a technocratic juggernaut that disregards its own citizens' interests and stifles national vitality.

We believe this is far from the truth. On the contrary, harmonisation is an effective way of optimising scientific and human resources, and European institutions are not ill-designed and sclerotic, but open to public influence.

The real problem is one of public apathy: who, apart from drug companies, is monitoring, and trying to influence, European pharmaceutical policy?

So it is hardly surprising that this policy is increasingly industry-oriented, or that EMEA has been linked to Enterprise Directorate General (and not Health and Consumer Protection Directorate General), and receives most of its funds from industry (like most national medicines agencies). Medicines are now seen as simple goods serving the European economy, rather than as a cornerstone of citizens' health. A "free market" policy that disregards public health regulations will be detrimental to European citizens.

This trend is not inevitable. It is not too late to act. We can, and must, demand that change serves the public interest first and foremost. The pharmaceutical industry must not be given a free hand to ride roughshod over the rest of society.

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# REORIENTING EUROPEAN MEDICINES POLICY


## Pharmaceutical policy is now decided at the European level

For about a decade now, pharmaceutical policy has been decided and organised mainly at the European level, within a context of international harmonisation. Some national responsibilities persist, but they are almost all governed by rules that apply throughout the European Union.

A firm grasp of the functioning of European institutions is therefore required to understand the new legal framework of the countries in which we live and work.

First, a short glossary.

• **Marketing authorisation.** Marketing authorisation allows a drug company to sell a proprietary (industrially manufactured) drug. Europe currently has three types of marketing authorisation:

*National marketing authorisation* is granted by a national medicines agency, on the basis of an application file, after approval by the national licensing authorities. This form of authorisation is only valid in the country in which it is granted;

*European centralised marketing authorisation* is granted by the European Commission, after examination of the file by the European Medicines Evaluation Agency (EMEA) and taking into account the opinion of the European Commission for Proprietary Medicinal Products (CPMP). This marketing authorisation is valid in all EC Member States;

*Marketing authorisation by mutual recognition* (also known as the decentralised procedure) is granted by national medicines agencies through recognition of marketing authorisation initially granted by another Member State. This latter Member State is known as the Reference Member State (**a**), because it builds up the assessment report that is submitted for recognition by other Member States. EMEA is kept informed of the procedure by the company, but the CPMP is only consulted when arbitration is required between Member States.

• **EMEA (European Medicines Evaluation Agency).** Created by a European Regulation in 1993, and in operation since 1995, EMEA is based in London. It co-ordinates the scientific resources provided by the different Member States for assessing and monitoring human and veterinary drugs.

EMEA has no deciding power, but offers an "opinion" to other ►►

*a- "Rapporteur country", now called "Reference Member State", i.e. the country which initially granted marketing authorisation within the mutual recognition procedure should not be confused with "rapporteurs" and "co-rapporteurs", who are CPMP members working within the framework of the centralised procedure. The latter are responsible for analysing drug assessment files on behalf of their CPMP colleagues. They act as members of a European expert Committee, not on behalf of their countries of origin.*

## Distribution of roles within the European Union

• **European Council: impetus and direction of general policies.** Each Member State is represented by the head of government (or head of state) and minister for foreign affairs.

• **European Parliament: shared legislative power and budgetary power.** The European Parliament has legislative power (in conjunction with the European Council), budgetary power and control power. It is composed of members of the European Parliament, who are elected by European citizens for 5-year terms of office. This is the only EC institution that meets and debates in public.

• **European Council: shared legislative power.** The Council (of ministers) of the European Union is also a legislative body (in conjunction with the European Parliament). It includes one ministerial representative from each Member State, and its composition can vary according to the issue in hand. Drug related matters can be discussed by ministers of health or industry according to the decisions taken.

• **European Commission: sole legislative initiative.** The European Commission is the only EC institution with the right to propose new legislation. It prepares legislation, in principle in keeping with the large directions laid down by the Council of the European Union. The draft Directive and Regulation now being discussed were prepared by the Enterprise Directorate General of the European Commission. The European Commission is also the European Community's executive body, responsible for ensuring that community treaties and decisions are enacted. It employs about 20 000 staff.

• **Advisory committees.** The Economic and Social Committee, which comprises three groups (employers, workers and miscellaneous activities), has a consultative role. For example, it organised a consultation on the drug regulation now undergoing discussion. The Committee of the Regions, created with the aim of bringing European institutions closer to the citizen and comprising local and regional representatives, also has a consultative role.

• **Directives and Regulations.** The scope of Directives and Regulations is defined by article 249 of the European Treaty:

*« In order to carry out their task and in accordance with the provisions of this Treaty, the European Parliament acting jointly with the Council, the Council and the Commission shall make regulations and issue directives, take decisions, make recommendations or deliver opinions.*

*A regulation shall have general application. It shall be binding in its entirety and directly applicable in all Member States.*

*A directive shall be binding, as to the result to be achieved, upon each Member State to which it is addressed, but shall leave to the national authorities the choice of form and methods.*

*A decision shall be binding in its entirety upon those to whom it is addressed.*

*Recommendations and opinions shall have no binding force. »*



### Further information

European Communities. "Annuaire interinstitutionnel – Qui fait quoi dans l'Union Européenne?" Office des publications officielles des Communautés européennes, Luxembourg 2002. Besides general information on EU institutions, this directory contains lists of all Members of Parliament and of the different institutions. All this information can also be accessed via the Europa server of the European Parliament (see below).

• Sauron JL "L'application du droit de l'Union européenne en France" La Documentation Française Collection Réflexe Europe, Paris 2000: 135 pages.

• The ABC of Community Law "Borchardt KD"– Fifth edition. European Communities 2000; European Commission, Directorate - General for Education and Culture - Publications Unit, rue de la Loi - Wetstraat 200, B-1049 Brussels (available in all EC languages).

Website:
-European Parliament
http://www.europarl.eu.int (mostly in all EC languages).
-European Union online
http://www.europa.eu.int/inst-fr.htm (mostly in all EC languages).

► European institutions (mainly the European Commission, which grants or refuses marketing authorisation, and Member States for pharmacovigilance matters).

EMEA has a number of consultative committees (mainly the CPMP) and expert groups composed of members seconded by the different Member States.

In 2001, EMEA employed 208 salaried staff (2002 estimate: 251), and its budget was 65 866 000 euros (2002 estimate: 70 547 000 euros), 69% of which came from taxes and fees paid by companies to have their marketing application files examined (1).

• **CPMP (Committee for Proprietary Medicinal Products).** The CPMP is one of EMEA's consultative committees. The CPMP currently comprises two experts from each Member State, chosen for their experience in drug assessment and appointed for a renewable period of three years. These experts are scientific experts, not political representatives of their countries of origin.

The role of the CPMP is to offer an opinion on drugs intended for human use, through the centralised procedure. It also arbitrates in disputes over mutual recognition.

The CPMP is assisted by working groups on efficacy, safety, pharmacovigilance, biotechnics, blood-derived medicinal products, and phytotherapy, among others. In addition to EMEA, another committee is now responsible for giving opinions on orphan drugs (Committee for Orphan Medicinal Products).

• **EPAR (European Public Assessment Report).** EPARs are EMEA publications on drugs that have been authorised through the centralised procedure. They are supposed to reflect the assessment file submitted by the manufacturer, its analysis by

the CPMP, and the reasons underlying the CPMP's opinion. In fact, these brief documents have been expurgated of all data considered confidential from a commercial or industrial point of view, and are approved by the manufacturers concerned before being released to the public.

EPARS relate only to marketing authorisations granted through the centralised procedure. No assessment report is available on products that are refused marketing authorisation. Similarly, none of the numerous decisions taken through the mutual recognition procedure give rise to EPARs.

• **SPC (Summary of Product Characteristics).** Attached to the marketing authorisation, these "identity cards" recap the state of knowledge on a drug when marketing authorisation is granted, and are revised after each five-yearly reappraisal of the assessment file.

Drafted by the manufacturers, SPCs are submitted along with the marketing application. They are finalised when marketing authorisation is granted, and are translated (European marketing authorisation only) into the different languages of the European Union.

The SPC is written according to a standard layout. Further information can be added throughout the lifetime of a drug, such as warnings on side effects that were not identified during the initial assessment phase.

The SPC contains the information that companies must mention on all advertising aimed at health professionals (such as brochures, adverts, and monographs in a datasheet compendium).

Another annex to the marketing authorisation (now called Annex III) sums up the information contained in the SPC in plain language. This annex forms the basis for compulsory information in the patient leaflet.

• **Blue box.** This is the information box, surrounded by a blue line that figures on the packaging of preparations approved through the centralised procedure. It carries information specific to Member States where the product is marketed. This includes the drug's legal status (e.g. classificaton of controlled substance) and any restrictions on its prescription (these elements are not yet fully harmonised within the EU).

• **European marketing authorisation number.** When a product is granted European marketing authorisation through the centralised procedure, the marketing authorisation number (which can be found, for example, on the packaging or in the SPC) is composed of the following elements:
-the letters "EU", for European Union;
-the number "1" or "2", according to whether the drug is designed for human use ("1") or veterinary use ("2");
-two figures corresponding to the year of initial authorisation (95 for 1995, etc.);
-three figures corresponding to an identification number given to each drug;
-three figures for each product in the range, corresponding to to its formulation, dose strength and package contents.

For example, EU/1/97/031/044 corresponds to the human drug NeoRecormon°, in injectable form, 6 000 IU per syringe, sold in boxes of 6 syringes, and authorised in 1997 through the European centralised procedure.

• **ICH (International Conference on Harmonisation for technical requirements of registration of pharmaceuticals for human use).** The ICH process was launched in 1990, driven by the regulatory authorities and pharmaceutical industries of the United States, Europe and Japan.

The aim is to harmonise marketing authorisation procedures by adopting common recommendations for drug evaluation and similar administrative procedures.

Through international conferences held every two years, and especially the work of a 14-member committee supported by industrial and administrative experts, ICH has seen more than a hundred common recommendations adopted by pharmaceutical firms and medicines agencies

This rapid harmonisation is welcome because it saves time and money (for example, fewer redundant clinical trials and animal studies). However, there is also a risk that international requirements for drug evaluation will be reduced to the lowest common denominator.

Health professionals and patient organisations have made virtually no contribution to this process, which should be monitored closely (by consulting the website of a major medicines agency such as EMEA) and opposed when necessary.



**1-** The European Agency for the Evaluation of Medicinal Products "Work Programme 2002" 18 December 2001: 62 pages ("Annex 1 – EMEA establishment plan 2000-2002" pages 42-43; "Annex 2 – EMEA budget summaries 2000-2002" page 44).

## Further information

Key information on European pharmaceutical regulation can be obtained from the following sources:

• History of the construction of European drug legislation: Campion G "Clefs pour l'Europe du médicament" Éditions de Santé, Paris 1996: 251 pages.

• Current EC drug regulations; definitions, concepts, and list of current texts: Brunet P "Dictionnary of the main reference terms – Pharmaceutical law in the European Union" Éditions de Santé, Paris 1999: 236 pages.

• Marketing authorisation procedures in theory and practice: "La réglementation des médicaments dans l'Union Européenne – Volume 2A. Avis aux demandeurs – Médicaments à usage humain" Office des publications officielles des Communautés européennes 1998: 175 pages.

• Current European texts (Directives and Regulations) and proposed amendments to these texts: European Union website http://europa.eu.int/eur-lex