Translated from ***Rev Prescr*** **June 2002; 22 (229): 464-466**

European pharmaceutical policy is turning its back on public health

It is on the basis of its practical impact at the Member-State and pan-European levels that current European pharmaceutical policy should be judged.

Is the policy transparent? Is it part of a coherent overall public health policy? Does it aim to strengthen the responsibilities and roles of the different players (patients, health professionals, regulators and manufacturers)?

Readers of la *revue Prescrire* find answers to these questions in each issue of the journal, and especially in our year-end reports. We have often criticised the French medicines authorities for their administrative secrecy, the secrecy of postmarketing studies, and the weaknesses of their drug pricing policy.

At the European level, our readers will have noted that:
– centralised marketing authorisation does not always mean therapeutic advance (1-3);
– the European Medicines Evaluation Agency (EMEA) is financially dependent on fees paid by pharmaceutical firms to balance its budget (**a**)(4);
– EMEA, as illustrated by its website, is lacking transparency towards citizens and health professionals alike (5);
– current European regulations hinder effective price controls on drugs at the member-state level (6,7).

We are not the only organisation to denounce the current inadequacies of national and European measures driving pharmaceutical policy away from its initial objectives. Here are three other examples.

ISDB: minimal agencies

At its creation, EMEA undertook to guarantee transparency, in the same way as all other European institutions, in line with the spirit of the Charter of Fundamental Rights of the European Union (**b**)(8). EMEA made systematic publication of public assessment reports (EPARs) on drugs authorised through the centralised procedure the cornerstone of its communication policy. These documents, which include about ten pages of useful scientific data, were supposed to be written by EMEA then released to the public and updated regularly.

Independent European drug bulletins belonging to ISDB (the International Society of Drug Bulletins) initially praised this initiative, and proposed ways of further improving to the EMEA (9).

Following the deteriorating quality of EPARs, the European ISDB group published a detailed study of nine consecutive EPARs (September 1996 to August 1997), which it then extended to cover all EPARs published in 1999 and 2000. These studies compared the information distributed by EMEA and that collated by ISDB members. The results were very negative: the EPARs were not harmonised, reliable or correctly updated (10,11).

The *Prescrire* staff that analyses the files of new drugs considers that things have now got even worse. EMEA has no documentary resources independent of drug companies (**c**). In many cases, analysis of EPARs suggests that these documents are totally or mainly written by the firms themselves, or edited by copying and pasting from the firm's application (**d**). Too many EPARs are vague or even inconsistent. In addition, irregular publication of their updates on the EMEA website means that their value is highly uneven (5).

EPAR are only released for drugs authorised through the centralised procedure, yet the bulk of products are approved through the totally secretive and increasingly popular mutual recognition procedure, which gives rise to no usable centralised information. Hardly any national agencies make public the results of their evaluation, even when they operate as rapporteur (the Netherlands recently introduced a few exceptions).

Worrisome results of an independent survey

The results of a 5-year follow up and analysis of the European regulatory system published by two British researchers provides food for thought during the run-up to the submission of the draft Directive and Regulation for approval by the European Parliament (**e**)(12).

John Abraham, a sociology professor and head of the Centre for Research in Health and Medicine at the University of Sussex, and Graham Lewis, a consultant in international drug regulations, examined, between 1994 and 1999, European bodies handling medicines-related matters, together with the role of individual member states.

Their work, funded principally by the British Council for Social and Economic Research, was based on interviews with staff in about fifty industrial organisations and administrative bodies in European Member States (especially Germany, the United Kingdom and Sweden – countries with strong pharmaceutical industries), and on the numerous published and unpublished documents they were able to gather.

The authors first recall the economic, sociological and political context in which the European pharmaceutical system was build up. They then describe its functioning, illustrated by a number of examples. They con- ►►

a- In 2002, the industrial contribution to the EMEA budget rose to 69.46% (ref 14) from 53% in 1998 (ref 4).

b- The transparency principle figures in the Citizenship Chapter of the Charter, in articles 41 (Right to a good administration) and 42 (Right of access to documents) (ref 8). A Regulation on access to documents, adopted in 2001, came into effect on 3 December 2001, and provides for application of the transparency principle (ref 15).

c- It must be stressed that EMEA is not the only medicines agency in this position. For example, the French agency for health product safety does not have solid industry-independent documentary resources that it can use systematically to analyse both the literature (including independent journals) and the conclusions of other drugs agencies worldwide.

d- According to EMEA internal procedures, EPARs are sent to the firms concerned, for their opinion, before publication. We recommend that EMEA states how and by whom EPARs are actually written, and who gives the pass for press.

e- A 243-page textbook with more than 400 references reports the results of this work, and represents a major source of information on European drugs policy (ref 12).

Quoted from: ***The Lancet* – Volume 358, Number 9275 – 07 July 2001**

CPMP members' standpoint

EMEA under DG health control. *"EMEA is located in an industrial institution of the European Commission (initially called Directorate General [DG] III, now called DG Enterprise) despite the fact that its mission is "to promote the protection of human health … and of consumers of medicinal products". Public health should be the fundamental concern of EMEA because it is the final outcome of improved availability of medicines (…). If public health issues were paramount, EMEA approval of new drugs would depend on their benefit to patients, and would be granted only for well defined indications after extensive research (…)".*

For a financially independent EMEA. *"Financial support for EMEA comes from two sources: a European Community grant, and the fees EMEA charges industry for the assessment of dossiers and other services. EMEA is forced to compete with national agencies for these fees, because – apart from biotechnology products – industry can apply to these agencies via the decentralised procedure, and hope to obtain approval with greater ease than through the EMEA. To eliminate this conflict, all applications for the European market should be made to one agency, the EMEA.*

EMEA should be allowed to do its own research (or to contract research out to third parties) to confirm or disprove data reported by industry. EMEA should also be equipped to deal with pharmacovigilance, to review drug use, and to make active investigations rather than relying on spontaneous reports and secondhand data.

Europe should acknowledge the need for the EMEA to take on these new roles, and supply the substantial investment that they would require. EMEA is still much smaller than the US Food and Drug Administration, although it covers almost double the population of its transatlantic cousin. If the European Community's grant were adequate, fees paid to EMEA by industry would be a small proportion of its income, and allow the agency to be free and independent".

Experts must be independent, not judge and jury. *"It is unusual for the same organisation and especially the same individuals--ie, CPMP members--to advise industry about the best way to develop a drug, to decide on approval of that drug, and, in appeal cases, to decide on approval for a second time. Scientific advice should not be a systematic activity, and should be given more on the CPMP's initiative than at the request of companies. If the CPMP were to give a negative opinion on a drug, it should not be able to change its opinion on the same dossier within a mere 120 days. Appeals should only be possible for serious reasons, such as deliberate misuse of information in the dossier. The appeal should be judged by an independent group of experts who come from outside the CPMP.*

Assessment of the dossiers could also be improved. One of the two CPMP rapporteurs is normally suggested by the company. This situation is difficult to condone. A company would be unlikely to select its rapporteur from CPMP members who are thought to be critical (…). In addition, a report by an independent expert is a required part of the dossier.3 In practice, these "neutral" experts tend to extol the virtues of the new drug rather than give a balanced view of its pros and cons. A summary of the dossier prepared by the company would be a less hypocritical document (…).

Industry can stop the procedure several times, for several months if required, but the CPMP must follow a rigid schedule. The CPMP should be allowed equal flexibility in the timing of the assessment process".

Comparative assessments are lacking. *"European Union legislation repeatedly states that drugs should be assessed for their quality, efficacy, and safety. However, this statement has been interpreted and acted on as if each drug were to be made available in a therapeutic vacuum. Industry has determined that once quality is acceptable, efficacy is suggested even if not shown, and safety raises no serious concerns – any drug should be allowed on the market. The apparent aim of industry is to produce a European catalogue from which physicians, or even in some cases patients, can select which medicine to use, and national health services can select drugs to be reimbursed. However, if there is no way of making valid comparisons between products, how can physicians or patients make informed choices?*

This point is made in several guidelines, including the E10 document of the International Conference for Harmonisation last year, that medicines should be tested against comparative drugs rather than placebos. These guidelines generated a strong reaction from the European Federation of Pharmaceutical Industries and Associations, which stated that for legal, scientific, and public-health reasons "quality, safety, and efficacy must remain the only criteria to assess the applications for marketing autorisation (…)".

Few therapeutic areas and indications exist, besides rare diseases, for which there is no treatment; in these cases only must placebo be used rather than an active comparative drug (…)".

Drug cost overlooked. *"Despite regular appeals to take economic aspects into consideration and contain healthcare costs, the CPMP works in an ideal world in which there are no financial limits on new drugs (…)".*

SPCs are not comparative. *"However, in these summaries, drugs are described as if they were the only ones on the market; comparisons should be made with other drugs with a similar mechanism of action that are available for the same indications (…). Distribution of the summary among physicians should be done by national authorities (…)".*

Lack of Transparency. *"Information on withdrawn applications is confidential, and no data are made public. Public health interests would be served by publication of such data. Therefore, either no withdrawal should be allowed after preliminary assessment, or the essential characteristics of any drug whose application has been withdrawn should be reported (…).*

If a drug is not approved or rejected unanimously, the minority view is lost along the route to making the committee's opinion on the drug public. Reports of all views in all documents, including the summary of product characteristics and the EPAR (European Public Assessment Report) would enable people to make up their own minds. Although votes are needed to reach a decision at the regulatory level, the majority decision does not necessarily represent the truth".

Mutual recognition too lax. *"The decentralised system seems to contribute more to the free movement of pharmaceutical products in the European Union than to patients' interests (…)".*

Re-assessment of authorisations is needed. *"Public health interests would be better served by an updated analysis of the drug's benefit-risk profile (…)".*

▶ *Following of page 8* cluded that the tendency to produce and to authorise ever more drugs, increasingly rapidly, was overshadowing public health considerations.

They also analysed how medicines agencies compete with one another in a context of still inadequate harmonisation, and noted that they are financed mainly by the pharmaceutical industry, with the sole exception of the German agency which, at the time of the survey, received "only" 40% of its funds from industry. Like EMEA, national agencies mainly live off the taxes and fees paid by companies seeking marketing authorisations.

The two researchers also recalled the dangers inherent in the lack of independence of many scientific experts involved in the drug evaluation process. Finally, and above all, they described a total lack of transparency in the drug regulation, and the authorities' failure to explain their decisions.

The impact of these trends on European countries with smaller pharmaceutical industries is only briefly mentioned. A continuation of this survey would be welcome during this period of European expansion.

Severe criticism by CPMP experts calling for regulations adapted to public health requirements

Silvio Garattini, a director of the Italian Mario Negri Institute, a clinical pharmacology research centre with universally recognised expertise, especially in the cardiovascular field, is a CPMP member. Together with Vittorio Bertele, another expert at the Mario Negri lnstitute who is also a CPMP expert, he published in the *Lancet*, in July 2001, a detailed analysis of the weaknesses of the European medicines system, and proposed a series of amendments (13). The inset on page 9 contains parts of their analysis.

The two experts concluded that *"centralisation of at least one part of the marketing authorisations at the EMEA is satisfactory, and should be gradually increased, with the aim of unifying the approval, monitoring, and policies on medicinal products, including pharmacovigilance and review of drug use. The institutional location of EMEA should be changed so it reports to the directorate of public health, not industry. Approval of new drugs must involve comparative assessments. More criticism is needed in the approval of new drugs. To defend patients' interests, companies cannot be allowed to release drugs with the sole aim of obtaining a slice of the market. The increasing power of the pharmaceutical industry requires an equally strong counterpart to ensure that drugs continue to be beneficial to patients, and are not just a profitable business."*

Conclusion: urgent reform is necessary

Seven years have passed since the creation of EMEA and effective implementation of European pharmaceutical policy. It is time to draw lessons from this experience.

EMEA, depending on DG Enterprise, cannot properly serve European public health interests. On the contrary, it behaves mainly as an administrative service for the pharmaceutical industry.

European institutions have started to revise the Directive and Regulation on medicines. The Council of Europe has repeatedly stated that pharmaceutical policy must be part of a welfare protection system at the service of patients; that rational drug use must be promoted; and that new therapies offering patients real advance must be developed.

The draft modifications proposed by DG Enterprise would only worsen the pro-industry bias of the current policy in the short term. They disagree with the Council of Europe's guidelines, and carry major risks, both for patients and, in the long run, for the European pharmaceutical industry itself, by facilitating the marketing of drugs that provide no tangible therapeutic advance.

1- Prescrire Rédaction "Nouveaux médicaments à AMM européenne: cotation Prescrire en 1999" *Rev Prescr* 2000; **20** (202): 60.
2- Prescrire Editorial Staff "EU centralised procedure does not mean a drug is innovative" *Prescr Int* 2001; **10 (**52): 53**.**
3- Prescrire Editorial Staff "Our judgements on products approved through the centralised procedure in 2001" *Prescr Int* 2002; **11**(58): 60.
4- Prescrire Editorial Staff "Funding of Medicines agencies" *Prescr Int* 2000; **9** (46): 34.
5- see pages 17-19 of this issue.
6- Prescrire Editorial Staff "The real beneficiaries of European drug policy" *Prescr Int* 2002; **11**(58): 34.
7- Prescrire Editorial Board "Prix des médicaments remboursables: quelle logique? Deuxième partie - Prix proportionnels à l'innovation: principe raisonnable, maigres résultats" *Rev Prescr* 2001; **21** (223): 859-863.
8- Charter of Fundamental Rights of the European Union (2000/C 364/01) 18 December 2000: 22 pages.
9- Bardelay D "ISDB Euro-group relations with EMEA" *ISDB Newsletter* 1999: **13** (1): 4-5.
10- International Society for Drug Bulletins "ISDB assessment of nine European Public Assessment Reports published by the European Medicines Evaluation Agency (EMEA)" 26 June 1988: 12 pages.
11- ISDB European Group "The failings of the European Medicines Evaluation Agency" *ISDB Newsletter* 2001: **15** (1): 11-13.
12- Abraham J and Lewis G "Regulating medicines in Europe - Competition, expertise and public health" *Routledge, London & New York* 2000: 243 pages.
13- Garattini S and Bertele V "Adjusting Europe's drug regulation to public health needs" *Lancet* 2001; **358**: 64-67.
14- EMEA "Work programme 2002 - Annex 2 - EMEA budget summaries 2000-2002" 18 December 2001: 44.
15- "Règlement (CE) n°1049/2001 du Parlement européen et du Conseil du 30 mai 2001 relatif à l'accès du public aux documents du Parlement européen, du Conseil et de la Commission" [Editor's note: also applies to all agencies created by these institutions] *Journal Officiel des Communautés européennes, 31 May* 2001: L145/43 - L145/48.

An industry-serving pharmaceutical policy

The framework texts of European drug policy have undergone multiple amendments over the last four decades. Directive 65/65/EEC (1965) laid the groundwork for the definition of medicinal products and for the principle of marketing authorisation, which is now obligatory for all pharmaceutical preparations (i.e. industrially prepared drugs). Similarly, Directives 75/318/EEC and 75/319/EEC defined the foundations for analytical assessment of the pharmacological, toxicological and clinical properties of new drugs prior to their market release.

The current versions of these texts are Directive 2001/83/EC (26 November 2001) and Regulation 2309/93 (22 July 1993).

The Council of Europe's desire to protect public health has not been respected

The creation of the European Medicines Evaluation Agency (EMEA) in 1995, and its early marketing authorisation and pharmacovigilance activities, were important steps in the implementation of European legislation on medicinal products. Seven years on, it is time for the European authorities to draw lessons from this experience and to adapt current regulations accordingly. The Council of Europe's position on this need for change was developed at the Lisbon Conference on medicines and public health in April 2000 (1).

Taking into account current trends in the pharmaceutical market, the Council underlined the need to identify drugs with real added therapeutic value, to scrutinise drug costs in order to ensure more rational use, and to develop drug information resources that are independent of the pharmaceutical industry.

The Council considered it vital to identify drugs bringing real therapeutic advance, not only to protect the consumer, but also to promote a healthy pharmaceutical industry (1).

These objectives were restated at the Ghent conference on health in Europe in December 2001, towards the end of the Belgian presidency of the European Union. It was also recommended that the public health dimension be taken into account more effectively by the relevant European institutions (2).

The European Commission empowers " Enterprise Directorate General " (DG Enterprise). The European Commission, via DG Enterprise – on which EMEA is dependent – has drawn up a draft reform of European drug regulations. [Note that the Commission is the only European body able to initiate such changes (see pages 6).] The two draft texts, on drugs for human use (one Directive and one Regulation), have been in the discussion stage since 2001, with a view to their adoption by the European Parliament and the Council of Europe in late 2002 (3,4).

These draft texts are accompanied by two particularly interesting documents – a Memorandum clarifying the rationale behind the texts (5), and a document on likely impact of the proposed modifications on the drugs industry (6).

DG Enterprise has chosen its camp. The impression given by the Memorandum is that DG Enterprise has simply ignored the numerous criticisms that have arisen from both within and without EC institutions. The same applies to key guidelines of the Council of Europe. This impression is confirmed when one reads the document on the industrial impact of the proposed changes, and also the draft Directive and Regulation (3-6).

For example, DG Enterprise seems to base its opinion of the EMEA's first five years of operation only on an audit done in 2000, at the Commission's request, by Cameron-Mc Kenna and Andersen Consulting. The Memorandum refers to comments made by the interested parties (Member States, drug companies, pharmaceutical industry organisations, physician and pharmacist organisations, and patient and consumer groups) (5), but it fails to mention the documents in which these parties' opinions are expressed. It also mentions none of the documents critical of EMEA that we examined on pages 8-10.

The Memorandum underlines DG Enterprise' wish to take into account ongoing changes in the industrial landscape, such as globalisation. DG Enterprise considers that current regulations are unsuitable, and that they risk isolating Europe and weakening its pharmaceutical industry (5).

Double language

Some of the main objectives stated in the Memorandum are mutually incompatible:

« – to provide a high level of health protection for the people of Europe and tighter surveillance of the market;

– to complete the internal market in pharmaceutical products taking account of the implications of globalisation and to establish a regulatory and legislative framework that favours the competitiveness of the European pharmaceuticals industry sector;

– to meet the challenges of the future enlargement of the European Union;

– to rationalise and simplify the system as far as possible, thus improving its overall consistency and visibility, and the transparency of procedures and decision making» (5).

The Memorandum then summarises each of the points on which DG Enterprise proposes modifications. It is highly instructive to compare what is said on each of these points in the Memorandum (5); in the document on the impact on the proposed modifications on the pharmaceutical industry (6); and in the proposed Directive and Regulation that is shortly to be submitted to the European Parliament and Council of Ministers for approval.

Easier marketing authorisation. The Memorandum states that the quality of the scientific debate (on marketing application files) must be maintained when Europe expands to 20, 25 or 28 Member States (5). It briefly mentions the importance given by the Council of Europe to the identification of drugs that have substantial added therapeutic value relative to existing options, but states that regulations are not the appropriate way of achieving this aim.

The document on the industrial impact of the proposed changes states that firms will be able to obtain marketing authorisation more ►►

Dangers of the mutual recognition procedure

Marketing authorisation by mutual recognition (also known as the decentralised procedure) is granted by national medicines agencies on the basis of initial approval by another Member State. This "Reference Member State", establishes an assessment report that is then submitted for "recognition" by the other EU countries. The European Medicines Evaluation Agency (EMEA) is kept informed by the firm, and the Commission for Proprietary Medicinal Products (CPMP) is only called on to arbitrate if one or more Member States refuse to recognise the initial marketing authorisation.

A "transient" procedure that persists. This procedure was initially understood to be transient, pending full operation of the centralised procedure (for a description of this procedure, see page 5). Yet the mutual recognition procedure has developed over the years, and, little by little, become institutionalised under the impetus of some national medicines agencies and drug companies. And the draft Directive of DG Enterprise proposes, at length, to maintain manufacturers' right to use this procedure, and even to facilitate it.

There follows a list of fundamental objections to the mutual recognition procedure, which carries inherent risks for public and individual health (1,2).

A particularly secretive system. As responsibility for marketing authorisation is diluted in the mutual recognition procedure, and as transparency is not obligatory, the data on which national agencies base their decision to grant marketing authorisation are not made public (with occasional exceptions (**a**)).

True, this secrecy is shared by almost all national marketing authorisations in Europe, but the mutual recognition procedure is its most blatant illustration.

A "marketplace" for marketing authorisation. Most national medicines agencies are funded, totally or mainly, by the fees paid by drug companies to have their marketing applications examined (**b**) (3). It is therefore crucial, for their financial existence, that these agencies are appreciated by their clients, i.e. firms, who might otherwise opt for the centralised procedure.

Needless to say, drug companies are only too pleased to see national agencies competing with one another for their custom.

Down-grading of requirements. Firms will naturally choose those agencies which have the least stringent requirements and/or which examine applications most rapidly (the two are not always but often linked).

National agencies compete on the basis of their "flexibility", as specialists say (in fact, their pliability) (4). And each national agency is linked to all the other national agencies within the framework of the mutual recognition procedure: if a given agency voices too many objections, other agencies may "seek revenge" when the country in question is rapporteur, making it less attractive to its potential "customers".

Lack of harmonisation in decisions and expertise. In the mutual recognition procedure, the criteria on which decisions are based are not standardised, and the level of scientific expertise varies from one national agency to another, as do the independence and critical capacities of national experts. Companies are naturally quick to exploit these differences in their own best interests.

When a drug is intended for sale in more than one Member State, European health would be best served by the removal of the mutual recognition procedure, after a short transition period, in favour of a reinforced, efficient and transparent centralised procedure.

a- For the moment, only the Netherlands have made tentative steps towards transparency in this area. Representatives of the Swedish agency have suggested publishing assessment reports, but nothing has yet come of this project. French law makes it obligatory to publish such reports (art. L.5311-1 of the Code of the public Health), but is not implemented.

b- In a 1999 survey, only the German agency received more than half its funds from the public budget; industry funding nevertheless amounted to 40% of its budget (ref 2).

1- Garattini S and Bertele V "Adjusting Europe's drug regulation to public health needs" *Lancet* 2001; **358**: 64-67.
2- Abraham J and Lewis G "Regulating Medicines in Europe – Competition, expertise and public health" Routledge London – New York, 2000: 243 pages.
3- Prescrire Editorial Staff "Funding of medicines agencies" *Prescr Int* 2000; **9** (46): 34.
4- Bouzy C and Abadie E "L'Europe du médicament" *Rev Prat* 2002; **52**: 510-514.

▶ rapidly; that suppression of five-yearly re-evaluations will save time and money; and that the mutual recognition procedure, whose flexibility is appreciated by drug companies, will be maintained (6).

The proposed Directive and Regulation recommend:
– that the risk-benefit ratios of new drugs should continue to be assessed without any need for a comparison with existing reference treatments (yet this makes it impossible to identify drugs with real therapeutic added value);
– that the period allowed to examine marketing applications (for both national and mutual recognition procedures) be cut from 210 to 150 days (this would be unlikely to improve the quality of the scientific debate (**a**));
– that a fast-track procedure be created for "innovative" drugs (the term "innovative" is not defined). In our view such a procedure should be reserved for exceptional situations, such as new drugs likely to bring major therapeutic advance in life-threatening diseases without adequate treatment;
– that the current five-yearly re-evaluation of marketing authorisations be suppressed, and that the principle of permanent, once-and-for-all approval be adopted, whatever the assessment procedure followed;
– that the mutual recognition procedure be facilitated: most disagreements would no longer be arbitrated by the CPMP, but by a small, autonomous "facilitating" group representing the Member States involved in the dispute (3,4).

Cheap, secretive pharmacovigilance. The Memorandum speaks of maintaining a high level of drug safety, and better management of pharmacovigilance crises (5). But the document on the likely industrial impact of the proposed changes states that the proposed reinforcement of pharmacovigilance will not cost firms money, as they already have the necessary system (6). It is hard to see exactly how pharmacovigilance would be reinforced.

The proposed Directive and Regu-

lation in fact call for minimal changes in this area, mainly requiring firms to prepare pharmacovigilance reports on their products every 3 years instead of 5 years at present (**b**)(3,4). Note that the creation of a European pharmacovigilance database presently touted as a major advance by DG Enterprise and by the pharmaceutical industry, has been one of EMEA's tasks since 1995: it is therefore nothing new. In addition, this database is not accessible yet to health professionals or patients.

Generic drug development hindered. The Memorandum claims it will be easier to market generics (5). But the document on the industrial impact of the proposed changes states that harmonisation of data protection periods will delay requests for "light" marketing authorisation procedures by generics manufacturers (6).

The proposed Directive and Regulation in fact recommend a lengthening of data protection periods, which is an obstacle to the marketing of generics (3).

Direct-to-consumer advertisement facilitated. The Memorandum is very clear on this point, recommending a pilot phase during which three drug classes will be able to be advertised directly to the public (5).

On this point, which has been hotly debated in recent months, the proposal in the Directive is less explicit than that in the Memorandum, using the word "information" instead of "advertising". But as the relevant proposals are found in the section of the Directive devoted to advertising, it is clear they are not referring to independent information (3).

Transparency of procedures and decisions: half-promises. Greater transparency of procedures and decisions is announced in the Memorandum (5) but is not even mentioned in the document on the industrial impact of the proposed changes (6).

In contrast, transparency is mentioned in the proposed Regulation, which state that expurgated assessment reports on drugs authorised via the centralised procedure should be published (but this is already the case with EPARs, of uneven quality: see page 8); and that an appropriate level of transparency should be guaranteed by the adoption of rules ensuring public access to non confidential information (4). Somewhat vague terms for a draft regulation.

Industry first

In short, although the Memorandum, which precedes the proposed Directive and Regulation, hints at public health (5), the proposals themselves are mainly designed to strengthen the short-term competitiveness of pharmaceutical companies (3,4). The annex on the likely industrial impact of the proposals confirms this impression, as it reassures firms that the proposed texts will have only a limited impact on their activity (6).

Similarly, the conclusions of the G10 – an informal group with strong industry representation, convened by the European Commission to examine the draft proposals – confirms that the pharmaceutical industry welcomes the proposed changes with open arms (**c**)(7).

It is hardly surprising that some organisations of health professionals, patients, consumers, together with organisations paying for medicines, are extremely worried about the impact of these proposed measures on European public health. They have drawn up in many European countries joint counter-proposals aimed at preserving the initial spirit of European regulations, namely strict assessment of new drugs, active pharmacovigilance, tight controls on drug promotion, and a transparent pharmaceutical policy dedicated to public health (see page 14).

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a- *210 days may seem long. But when one examines all the steps involved, the time actually left for thorough study of a marketing application is in no way excessive. For example, in the centralised procedure, rapporteurs have no more than 70 days to prepare their report.*

b- *Currently, PSURs (periodic safety update reports) must be submitted to the relevant authorities (national or European) by the marketing licence holder every six months during the first two years, then once a year for three years and every five years thereafter. These reports are supposed to comprise data on sales volume, the numbers of prescriptions and of patients exposed to the drug, and adverse events known to the firm. The reports must, in principle, be accompanied by the results of trials conducted to complete the safety assessment. In practice, it is impossible to know what PSURs actually contain because they are not publicly available, at either the national or the European level.*

c- *The G10 is composed of 13 members: two members of the European Commission (DG Enterprise and the DG Health and Consumer Protection), five ministers, three representatives of manufacturers' organisations, the president of GlaxoSmithKline Europe (the leading European pharmaceutical group), one representative of mutuality health insurers, and one patient representative (ref 7,8).*

1- 2281st Council meeting – Health "Follow up to the Lisbon-Conference on medicinal products and public health – Conclusions" Luxembourg 29 June 2000: 8-9.

2- Mossialos E et al "The influence of EU law on the social character of health care systems in the European Union – Report submitted to the Belgian Presidency of the European Union – Final version" Brussels 19 November 2001: 60-80.

3- "Proposal for a Directive of the European Parliament and of the Council amending Directive 2001/83/EC on the Community code relating to medicinal products for human use (Text with EEA relevance)" 2001/0253 (COD): 87-119.

4- "Proposal for a Regulation of the European Parliament and of the Council laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products (Text with EEA relevance)" 2001/0252 (COD): 14-57.

5- "Explanatory memorandum" preceding texts 2001/0253 (COD) and 2001/0252 (COD): 77-86.

6- "Impact assessment form. Impact of the proposal on businesses, particularly on small and medium-sized enterprises (SMEs)" 68-75 (Directive) and 126-133 (Regulation).

7- Albanese V "Compétitivité industrielle en Europe. Le G10 émet 14 recommandations" *Pharmaceutiques* 2002; 96: 36-39.

8- European Commission "High level group on innovation and provision of medicines. Recommendations for action" G10 Medicines -Report - 07 May 2002: 30 pages.

Towards a medicines policy that supports basic public health needs

After carefully scrutinising the DG Enterprise' complex draft modifications of the Directive and Regulation on medicinal products (see pages 11-13), various organisations and high-ranking persons throughout the European Union have launched a counter-lobbying operation. Here are some examples.

Independent journals

The International Society of Drug Bulletins (ISDB (**a**)), has intervened in many European institutions (**b**).

ISDB stressed the specific role of the different players of the health care system in the field of drug information. In particular ISDB:

1- calls for the development of independent information sources on therapeutics;

2- denounces repeated major abuses of drug advertising towards health professionals;

3- considers that these past abuses automatically disqualify drug manufacturers from providing information to the public;

4- recommends the continued ban of all direct-to-consumer advertising of prescription drugs throughout the European Union;

5- considers that drug manufacturers have already enough on their hands, with the need to improve their drug packaging and patient leaflets. (1).

ISDB also denounces the negative impact of accelerated marketing authorisation procedures (shorter assessment periods, or unjustified use of accelerated procedures), as well as the continuation (instead of the disappearance) of the complex and opaque mutual recognition procedure, and the intention to suppress the current 5-yearly re-examination of marketing applications, which is poorly enforced at present (2).

CPMP members

In an open letter dated 25 February 2002, nine expert members of the Committee for Proprietary Medicinal Products (CPMP) belonging to seven countries (Finland, Iceland, Italy, Norway, the Netherlands, Portugal and Spain), addressed members of the European Parliament who will vote, in late 2002, on the proposed changes to the European Directive on medicinal products (3).

The letter lists current problems and laments the fact that EMEA currently serves the interests of the pharmaceutical industry rather than European public health. They especially denounce:

– the fact that EMEA depends on of the Enterprise Directorate of the European Commission rather than the Health and Consumer Protection Directorate;

– EMEA funding by the pharmaceutical industry to the tune of 70%;

– EMEA secrecy regarding its goals, data, and some of its decisions, whereas the Charter of Fundamental Rights of the European Union and European Regulation n°1049/2001 (on access to documents) provide for greater transparency;

– the fact that marketing authorisation is granted for many drugs that are only equivalent, or simply "not inferior", to those already on the market, for reasons that are not made public;

– the short period that experts are given to prepare their opinion of applications, which are often difficult to assess rapidly because of the lack of comparative data, among other reasons.

Consumers organisations

The non governmental organisations Health Action International (HAI (**c**)) and the European Public Health Alliance, a group of European non governmental bodies (EPHA (**d**)), organised an international symposium on direct-to-consumer advertising of prescription drugs (Brussels, 10 January 2002) (4).

HAI and EPHA issued a joint statement. Here are a few extracts :

« This meeting clarified a number of points:

*• **People want objective information on prescription medicines.** Everyone emphatically agreed that the public needs access to balanced, comparative, relevant, up-to-date, accurate and unbiased information on pharmaceuticals and non-pharmaceutical treatments but only DG Enterprise defended their proposal (to advertise prescription medicines).*

*• **No one claims responsibility for the commission's proposal.** No one could say who exactly is driving this proposal. DG Enterprise said that this proposal was based on expectations expressed by patient groups but it could not name a single patient group supporting this proposal.*

The director of the European Federation of Pharmaceutical Industries and Associations (EFPIA) claimed that they have no position on DTCA and representatives from AstraZeneca, Novartis and Merck Sharp & Dohme, who attended, offered no comment.

It became clear that some national health policy makers (such as the Dutch Ministry of Health) reject DTCA but want to improve the quality and accessibility of information about medicines (which does not require any change in legislation).

*• **There is evidence that direct-to-consumer advertising of prescription medicines threatens public health.** (…)»*

HAI and EPHA demand that the EU:

« – Reject this proposal in its current form, as it does not uphold the Community's Treaty obligation to ensure a high level of public health in all of its activities as set out in article 152 of the EU Treaty. Neither does it conform to the WHO's Ethical Criteria for Medicinal Drug Promotion as agreed on by all WHO member states in 1988.

– Vigorously enforce the present legislation with review, sanctions, and thorough monitoring of promotion to health professionals and the general public.

– Develop a robust consumer information and education strategy to ensure that people receive and can use quality, objective information on medicines. Specifically,

– Improve the quality of patient information leaflets to make them more reader-friendly, comprehensive, and understandable.

– Encourage the provision of independent and comparative information about medicines for health professionals and the public. Furthermore, promote

regular independent testing of the effectiveness of medicine information in educating and informing professionals and the public.
(…) »

Medicines in Europe Forum

The aim of the Medicines in Europe Forum, created in March 2002 in Paris, is to provide information to all those concerned by European pharmaceutical policy, and to propose amendments to the draft Directive and Regulation of the European Commission (**e**).

Here are some of the reasons underlying its creation (5).

«• Medicines are not mere consumer goods.

Medicines are used by people who are either sick or have risk factors for a particular disease. All medicines, whether used therapeutically or preventively, have potential adverse events. In addition, the medicines market is captive: patients take drugs when required, not by choice; they are not mere consumers. For these reasons, approvals of new medicines must be thoroughly assessed; known and potential side effects must be actively monitored; and health professionals and citizens must have access to thorough and reliable information on the medicines they may be called on to prescribe, dispense or use. (…)

• Reducing the time for assessing a marketing application from 210 to 150 days (see article 17 of the proposed directive) means the quality of assessment cannot be guaranteed. *It takes time to evaluate pharmaceutical, toxicological and clinical data on new drugs, and the process cannot be accelerated without compromising on quality. The experience of experts working with national agencies or with the European Medicines Evaluation Agency shows that it is already difficult to comply with the current period of 210 days. (…)*

The accelerated procedure should be reserved for exceptional circumstances, such as medicines likely to offer a significant benefit for patients who have no alternative treatment. (…)

• Given the rate at which new scientific knowledge now accumulates, medicines must be re-assessed regularly (contrary to article 24 of the proposed directive).

Re-assessment of adverse drug reactions in the light of new pharmacovigilance data is essential to guarantee patient safety and rational use.

It's also important to re-assess the comparative benefits of different drugs in the light of new international data so that patients can always be prescribed the most effective treatment. (…)

• Drug safety cannot be ensured if pharmacovigilance is passive and secretive (see articles 101-107 of the proposed directive). *EMEA already collates spontaneous notifications of adverse drug reactions, but what purpose do the data serve if those most directly concerned – health professionals and patients – don't have access to them? The database of adverse drug reactions must be accessible on request, and so must pharmacovigilance reports. (…)*

Above all the European Medicines Evaluation Agency must create an independent and proactive pharmacovigilance system. It must be given the means to conduct prospective surveys, in collaboration with the agencies of EU member states and those of other countries. (…)

• Three principles must be reinforced. *(…) Three principles need to be reinforced in all sections of the proposed directive and regulation if European citizens are to be given every public health guarantee:*

– The principle of transparency. *(…) Secrecy now prevailing at the European Medicines Evaluation Agency and in most national agencies is an obstacle to rational drug use. Transparency must be improved if patients and health professionals are to regain confidence in this key organisation, and if these interested parties are to join force for improving rational drug use.*

Real patient representation in the EMEA (articles 58, 50.3 and 51.1 of the proposed regulation)

Representatives of patients must be allowed to participate actively in all EMEA consultative bodies.

Article 58 must provide for balanced representation of patients and drugs companies on the EMEA Management board, as well as transparent procedures for selecting these representatives.

– The principle of independence. (…) *The proposed directive and regulation must restore key guarantees of independence. Community funding of the EMEA must be increased substantially to reinforce its independence and to provide it with the means required for its role and responsibilities to be fulfilled.*

– The principle of harmonisation. *A considerable effort has already been made to harmonise the regulation of medicines in Europe. But much remains to be done in the field of pharmacovigilance at the European and international levels, and also to improve marketing authorisation procedures. While the centralised procedure has a good performance in terms of harmonisation, the mutual recognition procedure is still chaotic, and its quality is highly variable. In addition the mutual recognition procedure is not trustworthy because it is totally opaque. (…) ».*

a- Created in 1986, the International Society of Drug Bulletins (ISDB) is an international network of drug bulletins that are independent from the pharmaceutical industry. Its web address is www.isdbweb.org
b- Its representatives participated in the Conference on European Integration and Health Care Systems: a Challenge for Social Policy, organised by the Belgian presidency of the European Union (Ghent, 7-8 December 2001, (ref.1)), and also in the consultation by the European Economic and Social Committee on "What are the consequences of the EU commission's proposals on the health of EU citizens, and especially on drug safety?" (Brussels, 6 March 2002), (ref.2).
c- Health Action International (HAI) is a network of some 150 consumer groups and bodies focusing on health and development in over 70 countries. Its web address is www.haiweb.org
d- European Public Health Alliance (EPHA) represents more than 80 organisations and non governmental organisations involved in health matters. www.epha.org
e- The Medicines in Europe Forum, created in Paris in March 2002, groups together family organisations, consumer groups, patient groups, mutual insurance systems, and health professional organisations.
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1- Bardelay D - European Group of the International Society of Drug Bulletins "Information for consumers" European integration and health care systems: a challenge for social policy" Ghent 7-8 December 2001: 8 pages.
2- International Society of Drug Bulletins "About the proposals of the EU Commission (COM 2001-404 Final) regarding drug approvals and pharmacovigilance" European, Economic and Social Committee, Brussels 6 March 2002: 8 pages.
3- Group of 9 experts of the Committee of Proprietary Medicinal Products "Dear Members of the European Parlement – Proposed amendments to the EU pharmaceutical legislation" Milan 25 February 2002: 2 pages.
4- Health Action International – European Public Health Alliance "Joint Statement on the proposed relaxation of the EU Ban on direct to consumer advertising of prescription medicines" 28 January 2002: 3 pages.
5- Medicines in Europe Forum *"Platform"* March 2002.