Open letter
To interested parties:
- EU Commissionner Verheugen (Enterprise Directorate-General)
- EU Commissionner Kyprianou (Health Directorate-General)
- Members of European Parliament
- Medias

José Manuel BARROSO
President of the European Commission
European Commission
200, Rue de la Loi
B-1049 Brussels
Belgium

October 2007, 10

Dear President Barroso,

On 31 July 2007, the European Commission launched a consultation on the future of pharmaceutical products for human use in Europe (1).

The Medicines in Europe Forum (MiEF), Health Action International Europe (HAI), and the International Society of Drug Bulletins (ISDB) are wondering about the real reasons for this "consultation". Indeed, it seems to ignore the fact that fundamental regulations and directives on human medicinal products have just been adopted by the European Community. Moreover, the allotted time is very short and spans the summer holiday months.

The MiEF, HAI Europe and ISDB disagree with the diagnosis made by the instigators of this "consultation". The Forum considers that the solutions proposed for the issues raised fail to take patients' interests into account. Instead they pander to the pharmaceutical industry's wish list of legislative changes. Patients and healthcare professionals, and European citizens in general, cannot fail to see that this "consultation" ignores their uppermost concerns.

Protecting the competitiveness of European industry must not be allowed to turn healthcare in general and medicines in particular into simple consumer products. Public health must be the overriding concern of EU legislators.

The signatories of this contribution remind the Commission that it is responsible for protecting the health of European citizens (article 152 of the EU Treaty). They therefore call on the Commission to review its priorities, first among which should be patients' interests, not short-term interests of the private sector.

While underlining the biased nature of the so-called consultation, the MiEF, HAI Europe and the ISDB nonetheless wish to respond with a summary of proposals for a more ambitious strategy based on a long-term outlook. You will find their joint contribution annexed to this letter.

We sincerely hope that the Commission will come to see the importance of reorienting European policy towards the preservation and improvement of public health.

Sincerely,

The Medicines in Europe Forum **HAI Europe** **The ISDB**

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The Medicines in Europe Forum was launched in March 2002 and it covers 12 European Member States. It includes more than 70 member organizations representing the four key players on the health field, i.e. patients groups, family and consumer bodies, social security systems, and health professionals. Such a grouping is unique in the history of the EU, and it certainly reflects the important stakes and expectations regarding European medicines policy. Admittedly, medicines are no simple consumer goods, and the Union represents an opportunity for European citizens when it comes to guarantees of efficacy, safety and pricing.

Health Action International (HAI) is an independent global network of health, consumer and development organisations working to increase access to essential medicines and improve rational use. More info: www.haiweb.org

The International Society of Drug Bulletins (ISDB), founded in 1986, is a world wide Network of bulletins and journals on drugs and therapeutics that are financially and intellectually independent of pharmaceutical industry. Currently, their members include 60 members in 35 countries around the world. More info: www.isdbweb.org

Answer to the consultation
Deadline for answer: October 2007, 12
(Open letter and answer sent to nicolas.rossignol@ec.europa.eu: 5 pages)

The future of the European pharmaceutical industry depends on companies' capacity to meet patients' real needs

The Medicines in Europe Forum, HAI Europe and ISDB are circumspect with regard to the real motivations of this "consultation", which is presented as a "democratic debate" but which focuses almost exclusively on issues of concern to the pharmaceutical industry (**a**) (1). Our response to the questions posed is followed by a list of concrete proposals for a more ambitious strategy based on a long-term perspective.

1. Do you agree with the analysis of the main challenges outlined above?

The Medicines in Europe Forum, HAI Europe and ISDB do not approve the analysis of the "main challenges". These "challenges" mainly concern parts of the current European legislative framework that the pharmaceutical industry would dearly like to modify. Worse, there "challenges" are abusively presented as being in patients' best interests. The list includes a "softening" of pharmacovigilance, variations of marketing authorisation and clinical trials with the pretext of "facilitating patients' access to treatment"; direct-to-consumer "communication" on all drugs, under a smokescreen of "patients' right to information", in order to introduce DTCA (Direct-To-Consumer Advertising); restriction of parallel imports, under the pretext of the "fight against counterfeiting"; dropping standards to the lowest common denominator, and accelerating reimbursement procedures, price setting, and the assessment of "added therapeutic value", under the pretext of "accelerating access to new drugs".

Another example of bias is that the consultation paper highlights the harmonisation and construction of the internal market with respect to issues like pricing and reimbursement, but not for marketing authorisation itself. Yet, during the debate on the new EU legislative framework for human medicines adopted in 2004, the Medicines in Europe Forum defended the concept of centralised authorisation for all new drugs (for reasons of public health), while the Commission and industry representatives took a contrary stance (**b**).

Do you see other challenges?

The most urgent challenge is to end the confusion between the role of drug companies and that of other stakeholders in the healthcare arena (2).

The Vioxx° scandal is not so much "an important problem for the EU domestic market" as a human tragedy, with thousands of deaths. It further undermines the credibility and legitimacy of drug companies and medicines agencies alike. Affairs of this type help to reveal that the healthcare authorities are currently incapable of correctly evaluating drugs before approving them for general use, incapable of ensuring effective pharmacovigilance, and incapable of taking timely decisions to protect European citizens.

The Vioxx° affair once again underlines the dangers of granting marketing authorisation for potential "blockbuster" drugs solely on the basis of clinical trials designed, funded, conducted and published by the manufacturer. The notorious "data massaging" with respect to the adverse effects and efficacy of cox-2 inhibitors shows just how unreliable the information provided by drug companies to the public, healthcare professionals and even the healthcare authorities can be.

It should be mentioned in passing that the reference to a Wikipedia article on Vioxx° suggests those responsible for the consultation have a somewhat curious concept of what is reliable medical information (**c**).

Another challenge is to encourage the generics market which, through the cost savings it engenders, can help to finance the use of recent and often extremely costly drugs, if they provide therapeutic advances. In this respect, more transparency is needed on the real costs of drug research and development as unrealistic cost estimate are often used by companies to justify very high prices for their products.

2. Do you see other areas than those already targeted by the Commission where regulatory action should be taken?

The Medicines in Europe Forum, HAI Europe and the ISDB are astonished by the way the Commission ignores the fact that the legislative framework was recently modified in depth, through the Regulation on orphan drugs in 2000, the Directive on clinical trials in 2001 (only recently transposed in many member states), annex I of the Medicines Directive adapted to new therapies in 2003, the complete revision of Directive 2004/27/EC and of Regulation (EC) 726/2004 in 2004, the Regulation on pediatric drugs in 2006, the Regulation on "advanced therapies" in 2007, etc.

Most issues raised in this consultation were dealt with during the review that gave rise to Directive 2004/27/EC and Regulation (EC) 726/2004. Even the European Pharmaceutical Forum, which has already been asked to examine several of these questions, did not conclude that the current legislation needed to be modified.

3. What would you suggest as concrete measures to ensure the safety of medicines supplied in the EU, addressing in particular counterfeit medicines, and provision of high quality and affordable medicines also to third countries?

Here again the question is partial and biased. Yes, counterfeiting is a public health issue, especially outside Europe, and it must be dealt with notably by re-organizing the healthcare system so that pharmacists can play their role to the full (**d**). But this issue is also exploited by some drug companies so as to discredit generic drugs, and especially legal parallel imports. There are other, far more important priorities when it comes to drug safety.

As regards re-importation of drugs exported outside Europe at differentiated prices, the main problem is that it deprives needy patients in the poorest countries. There is already an ad hoc system for some drugs (Regulation (EC) 953/2003, 26 May 2003), and it could easily be extended if re-importation becomes a major problem.

Currently the main issue in drug safety is the inadequate evaluation of new products before, but also after, marketing authorisation is granted. Studies of the risk-benefit balance prior to marketing authorisation must be reinforced. Post-market studies should be developed, and companies that fail to conduct these studies should be penalised financially. Such studies are still too infrequent in Europe, yet they can help guarantee the efficacy, safety and correct use of drugs in normal conditions of use. Company run risk-management programmes must not be used as an excuse for undermining public pharmacovigilance systems.

A variety of accelerated drug approvals facilitating early marketing now complicate the general framework; these include the accelerated procedure, the exceptional, simplified, or conditional marketing authorisations, etc. Marketing authorisation through these facilitated procedures can only be justified when there is a real need in terms of public health. And they must be accompanied by strict post-market pharmacovigilance, the results of which must be made public.

Furthermore, direct reporting of adverse effect by patients, and public access to data on adverse drug reactions (measures that are regularly rejected by the Commission), are simple solutions that would offer substantial progress.

4. What can be done to improve Europe's international competitiveness?

This is not something of general concern to patients and healthcare professionals. What matters is access to safe and effective drugs that correspond to real healthcare needs.

If the aim of the consultation is to improve access to drugs that represent a real therapeutic advance, and that benefit patients, then the Commission is on the wrong track: European medicines policy must be refocused on risk-benefit balance and real therapeutic advance (added therapeutic value).

5. What can be done to foster convergence and transparency as regards pricing and reimbursement in the EU?

Here again, the question is biased away from patients' interests, and particularly the interests of patients in the poorer member states. Unlike many other products, the prices of drugs have fundamental implications for society and public health, because it conditions access to potentially vital treatments. The intention to set the same price for each drug throughout the EU is to ignore the real situations of European patients.

Decisions on pricing and reimbursement lie with individual member state. And transparent pricing decisions are essential for a harmonious relationship between the supplier, the payer, and the user.

Increasingly high and sometimes excessive prices can create problems of access and availability. A fair and equitable price should strike a balance between investment (yielding reasonable or "ethical" profits), therapeutic benefits for patients, and cost for the payer.

6. Do you think the current EU regulatory framework can accommodate emerging technologies like regenerative and personalised medicine, as well as nanobiotechnology?

The very recent Regulation on advanced therapies should be sufficient to deal with this issue. One of its principles states that, when there is a doubt as to whether a medicine is a "medical device" or a "drug", the latter status should be adopted, because it offers the best safety guarantees for the patient. It would be dangerous to ignore this public health rule under the pretext of not hindering "the creation of highly innovative small and medium-sized enterprises".

The general framework governing advanced therapies will require supplementary protective measures for nanobiotechnology for example, given the total lack of experience in this field.

Concrete, ambitious, long-term proposals

The market for healthcare products is not like any other market, and patients cannot and must not be considered as mere consumers.

The long-term health of the European pharmaceuticals industry depends above all on the development of drugs with added therapeutic value. The idea of therapeutic advance is clear and best defined in terms of tangible clinical benefits for patients (**e**) (3). And it is the documented therapeutic advantages offered by a new drug that should form the basis not only for marketing authorisation but also for pricing and reimbursement.

The current dearth of pharmaceutical innovation must not be allowed to serve as a pretext for deregulating the European medicines market.

The following concrete proposals would markedly improve the system:

- **confusion between the roles of drug companies and those of other stakeholders in the healthcare arena must be brought rapidly and permanently to an end**, notably by refusing to allow companies to "accompany" (actually influence) caregivers, patients and their relatives. Companies cannot be both judge and jury. This will mean maintaining the ban on direct-to-consumer communication on prescription drugs by industry (article 88 of Directive 2001/83/CE), even if it is dressed up as "compliance programmes" and "disease information", which boils down to promotional campaigns (4,5);
- **existing legislation must be vigorously applied** so that marketing authorisation guarantees patient safety and does not become a simple administrative formality; pharmacovigilance must receive effective public funding, as stipulated by Directive 2004/24/EC, in order to guarantee its independence; institutional review boards and ethics committees must be strengthened in order to put an end to unethical trials; and nanomedicines must be covered by the Regulation on advanced therapies;
- **the therapeutic advance offered by a new drug must be systematically determined**, and the precise costs of research and development must be available in order to establish fairer prices;
- **the transparency of medicines agencies must be guaranteed** so that the public can access data on drugs' efficacy and dangers, before and after they are marketed, so that adverse effects can be effectively prevented;
- **patients must be allowed to participate directly in the reporting of adverse drug reactions**, thereby contributing to better use and earlier detection (6).

The medical and legal issues raised by the proposed deregulation inherent in the consultation paper cannot be ignored. Furthermore, the Commission cannot continue to ignore the economic consequences of market deregulation on healthcare expenditure by EU member states: direct expenses linked to increased sales and earlier marketing of poorly assessed drugs; adverse effect management; with drug prices bearing no relation whatsoever to added to therapeutic value. In the long run, the consequences of such deregulation would be detrimental to all healthcare stakeholders, and that includes the pharmaceutical industry.

In short. The Medicines in Europe Forum, HAI Europe and the ISDB disapprove of the method used for this consultation and are sceptical about the Commission's real aims: the consultation period is very short and includes the summer holiday period; the literature references are unprofessional; and the regulations and directives on medicinal products that have just been adopted are just ignored.

The Medicines in Europe Forum, HAI Europe and ISDB disagree with the analysis presented in the "consultation" and consider that the proposed solutions are biased in favour of drug companies, largely ignoring patients' interests and public health in general. More than ever before do we see how placing medicines within the Enterprise Directorate's sphere of activity has led to a fundamental imbalance in the Commission's proposals. Patients and healthcare professionals, and European citizens in general, cannot possibly identify with the tone of this "consultation".

The competitiveness of Europe's pharmaceutical industry should not lead to healthcare being treated as a commodity and patients' interest loosing priority status.

The Medicines in Europe Forum **HAI Europe*** **The ISDB**

* HAI Europe is also submitting a response to the report.

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Notes:

a- Interestingly, the "preoccupations" presented in this "consultation" document precisely match the EFPIA agenda, as described in a speech by its President (ref 7).

b- During the recent consultation on variations of national marketing authorisation, the Medicines in Europe Forum and ISDB underlined that the decentralised and mutual recognition procedures (sources of heterogeneity and competition between national agencies) were detrimental to the global efficiency of the healthcare system and to the health of European citizens. A more transparent process is needed, which would be fairer for companies and would also be in patients' best interests (ref 8).

c- Wikipedia, the online encyclopedia, is not a reliable source of information: drug companies themselves have been known to modify key information on their own products (ref 9).

d- Industry pressure to promote self-medication, direct-to-patient communication on prescription drugs, and the development of internet sales are bypassing pharmacists and depriving patients of their advisory and controlling roles.

e- Application of the Regulation on drugs for pediatric use provided an opportunity for the European Commission to specify what was meant by an "important therapeutic benefit" (ref 10).

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References:

1- European Commission – Enterprise and industry Directorate-General "The future of pharmaceuticals for human use in Europe – Making Europe a Hub for Safe and Innovative Medicines – Have your say" Public consultation 19 July 2007. Http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/new.htm#j07: 4 pages.

2- Joint position statement by MiEF, International Society of Drug Bulletins, and Health Action International Europe "Health information: Everyone has their part to play and should keep to it" March 2007: 4 pages.

3- ISDB "Paris Declaration on therapeutic advance in the use of medicines" Paris 15-16 November 2001. www.isdbweb.org: 12 pages.

4- Joint Declaration by HAI Europe, ISDB, BEUC, AIM and MiEF "Relevant health information for empowered citizens" 3 October 2006. Websites www.prescrire.org: 9 pages, and www.isdbweb.org.

5- "Patient "information" in Europe: many concerns" press review and extracts from contributions to the consultation organised by the "patient information" group (May 2007). www.prescrire.org (full dossier).

6- ISDB "Berlin Declaration on Pharmacovigilance" Berlin 31 October-1 November 2003. www.isdbweb.org: 28 pages.

7- "Higgins set out aims for EFPIA as its new president" Scrip June 8th 2007 N°3266: 3 pages.

8- Medicines in Europe Forum and International Society of Drug Bulletins "Pour des AMM centralisées et de qualité et une meilleure transparence du processus" Contribution à la consultation publique sur les variations d'AMM nationales ; September 2007: 2 pages.

9- Rhys Blakely "Exposed: guess who has been polishing their Wikipedia entries? No hiding place after a new website shows that a rash of companies are editing entries on the world's most popular online reference work" Times Online 2007 (August 15). Http://business.timesonline.co.uk: 2 pages.

10- "Commission guideline on the format and content of applications for agreement or modification of a paediatric investigation plan and requests for waivers or deferrals and concerning the operation of the compliance check and on criteria for assessing significant studies" European Commission January 2007: 19 pages.