

Mr Nicolas Rossignol
European Commission
Enterprise and Industry Directorate-General
The Future of Pharmaceuticals for Human
Use in Europe
B232 8/102
B-1049 Brussels, Belgium

12 October 2007

Re: Consultation on the Future of Pharmaceuticals for Human Use in Europe

Dear Mr Rossignol

Thank you very much for the opportunity to input into the above Discussion Document.

EuropaBio is the European Association for Bioindustries, solely and uniquely bringing together bioscience companies from all fields of research and development, testing, manufacturing and distribution of biotechnology products. It has 84 corporate members operating worldwide, 12 associate members and 5 BioRegions, as well as 25 national biotechnology associations representing some 1800 small and medium sized enterprises involved in research.

Healthcare biotechnology has already had a tremendous impact on meeting the needs of patients and their families, and will continue to represent the state-of-the-art evolution of science as applied to human medicine. These therapies present novel approaches to patient disease management, and the technology itself is providing us with a better understanding of the course and mechanisms of disease. They are:

- personalized and targeted;
- patient-focussed;
- often aimed at treating rare diseases, therefore coming on to the market with limited sets of evidences;
- based on strong SME commitment and involvement in research; and
- complex in their development and modes of action - meaning that the highest level of knowledge sits within biotech companies, with little share heritage within the scientific community.

This is why EuropaBio welcomes this current Commission initiative. Innovative biotechnology companies are soon set to introduce further breakthrough therapies based on a cascade of new discoveries in European labs, and this move to improve the regulatory, non-regulatory and RTD framework related to bio-pharmaceuticals and advanced bio-therapies ó in addition to the Advanced Therapies Regulation ó therefore comes at an opportune time.

As a general comment, the distinctive features of the biotechnology industry (the strong relationship between innovation and competitiveness, the collaborative basis of research in this field, and the importance of small firms) have made pricing and reimbursement the main, if not unique, tools with which to reward its innovation. Improvements in ensuring certainty and in defining value in this area will ensure sustainability and growth to this fragile, but extremely high-added value sector.

Question 1. Do you agree with the analysis of the main challenges outlined in the Consultation Paper. Do you see other challenges?

We agree with other stakeholder submissions stating that, in addition to the challenges outlined in the Consultation paper, the protection - globally - of intellectual property rights is a big challenge facing the European pharmaceutical industry. While countries have a right to use the flexibilities introduced into international legislation, better results will be achieved through collaboration with the innovator to ensure that health needs are met and that IPRs are protected. Europe should be pioneering this approach at an international level and ensuring application of this approach by Member States.

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

We are supportive of other submissions requesting the Commission to avoid subjecting products not reimbursed by Member States to price controls. The development of an EU integrated strategy for biomedical research, supported through increased R&D spending under the Commission's 7th Research Framework Program, should also be undertaken.

Question 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?

We see a number of concrete measures that could be taken to ensure the safety of medicines in Europe, and are supportive of overall comments made in this regard by organizations such as EFPIA and PhRMA. Specifically from a biotech perspective, however, we believe that the following concrete acts could be undertaken for these complex and advanced therapies:

- implementation of a system that allows industry to be a source of information, so as to ensure the empowerment of European patients to seek information;
- introduction of regulation to ensure clear labelling to distinguish different biosimilars;
- the establishment of bio- networks to share and disseminate information;
- simplification of Package Information Leaflets; and
- strengthening of penalties for counterfeiting.

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

EuropaBio strongly believes that agreement on, and implementation of, a streamlined, affordable European patenting system would go a long way towards improving Europe's international competitiveness. Agreement also on a workable definition of the scope of patenting possible for human gene sequences and pluri-potent stem cells will also assist (provided, of course, any broader interpretation is then enacted and implemented in national law).

The existing clinical trials Directive should be amended to recognise the importance of genetics and pharmaco-genetics in order to facilitate the development of the next generation of treatments. In addition, a minimum of administrative burdens should be introduced. Allowing the sharing and acceptance of data, and increasing clarity in the Directive, will also facilitate harmonisation across all Member States, and reduce delays in the start of trials due to varying systems. In this regard, we welcome the current initiative by the Commission and hope that such changes can be achieved.

More consistency is also needed in the approach to orphan drugs and biosimilars across all Member States. This could be assisted by agreeing on common, Europe-wide practices for rewarding innovation (see our answer to Question 5 for details), and by starting a Europe-wide educational campaign to explain the real benefits of biotechnology in thereby encouraging a more positive research and evaluation environment.

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

Pricing and reimbursement procedures set by Member States in the European Union continue to show structural difficulties in encompassing and capturing the value, and subsequent rewarding, of the use of biotechnology in bringing and delivering innovative treatment to patients - due to their innovative character and, hence, lack of adequate comparator products.

The healthcare biotechnology industry is characterized by the way it is structured: the underlying multiplicity of small and medium-sized purely biotech companies, the use of highly innovative technological platforms, as well as by its sophisticated network of collaborations - both biotech-to-biotech and biotech-to-big pharma - all of which form the core of this specific healthcare sector. In addition, the innovation component of healthcare biotechnology results in extremely high costs, (especially as far as both R&D and manufacturing is concerned), as well as in a very long-winded path to ROI (return on investment) estimated at about 12-15 years.

For the Bio-Healthcare Industry, rewarding innovation by appropriate levels of pricing and reimbursement in a timely fashion therefore often means the survival and growth of these intensive knowledge-based biotech SMEs, and is the way to ensure a substantial reinvestment in R&D by more mature biotech companies. Considering that many of these products aim to respond to previously unmet medical needs - often of a severe nature - timely patient access to these products is also crucial.

EuropaBio believes that the reimbursement of biotech medicines should not only take into consideration the benefits of biotech products, but should also differentiate rewards according to the disease areas that the products cover (ie: a relatively higher reward not only for innovative medicines, but also medicines that treat serious and chronically debilitating diseases and for those medicines which address unmet medical needs). We would suggest agreeing on common, Europe-wide practices for rewarding innovation through harmonized application of the following common principles:

- a. *Separating pricing from reimbursement.* Pricing, as a definition of the ex factory price, should fall under the responsibility of the manufacturers or sponsors. While reimbursement, as a definition of the level of funding made available by governments, payers or reimbursers, should fall under the responsibility of Member States. The Commission, through the Transparency Committee, should monitor and ensure that biotechnology-derived centralized approved medicines are made available to patients and consequently reimbursed in a timely manner.
- b. *Rewarding value.* Medicines should be rewarded for the added-value that they bring to the treatment of patients. There should be clarity and consistency on the criteria on which added value is identified and assessed - indicator measures of value can take various forms, such as mortality and morbidity data, side-effects, tolerability, medical need etc. Evaluation mechanisms should look at the impact of healthcare interventions, including medicines, on the total healthcare system (including the value to society of having patients contributing to the workforce - particularly in the case of the 30 million Europeans suffering from rare diseases). The benefits of so-called incremental innovation should also be acknowledged.
- c. *Predictability, transparency and flexibility.* Pricing and reimbursement systems should support business planning for long-term supply of medicines and encourage R&D investment in medicines of value. The fact that data may be incomplete at the time of launch creates a temporary uncertainty as to the full therapeutic value of a new product in use. New policies should be implemented that give payers and industry a flexible partnership approach to handling this uncertainty. We would support products enjoying early, reimbursed launch, on the understanding that the provision of further clinical outcomes data may lead to changes in reimbursement (which could benefit either the payer or supplier).

- d. *Faster and timely patient access.* The length, complexity and diversity of current pricing and reimbursement procedures in general, conducted prior to the effective launch of a product, can significantly delay the marketing and, thus, the availability of medicines for patients. The European Commission and member states should continue efforts to reduce market access delays in Europe. Pricing and reimbursement processes in all Member States need to continue comply with the timelines set by the Transparency Directive. In addition, GIO Recommendation 3, which addresses market access, should be implemented. A pan-European system of Compassionate Use for Orphan Drugs, as well as for innovative therapies for life-threatening diseases, should be equally implemented across the Member States.
- e. *Respect for intellectual property.* Reimbursement systems can ensure a proper balance between recognition of therapeutic added value on the one hand and drawing the full benefits from generics on the other without undermining patent protection or making assumptions over the therapeutic interchangeability of medicines.
- f. *Adequate Data and Marketing Protection for New Indications.* Bioindustries are often small and medium size undertakings and it is vitally important for them that the Community regulatory framework grants adequate data and marketing protection in the event of the development of new therapeutic indications or other innovations on molecules that have already been placed on the Community market.

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

The introduction of the Advanced Therapies Regulation goes a long way towards enabling the EU regulatory framework to accommodate emerging technologies, and EuropaBio has been at the forefront of this debate. The new regulation creates for the first time a single, harmonized European market for these products, which could offer revolutionary treatments for a number of diseases or injuries, such as cancer or skin burns. Appropriate implementing rules that are science-based, along with adequate funding for the EMA's new Committee for Advanced Therapies, are now needed.

However, this will mean nothing if there continues to be no commonly shared European 'consensus' on how to reward such healthcare innovation. The variety of national requirements causes difficulties for the increasingly global biotech-based industry. In addition, the perception that health technology assessment (HTA) of new technologies on a product-by-product basis is a higher priority than the search for inefficiencies of the healthcare systems as a whole, or for outdated products and procedures, has to be counterbalanced. In this context, EuropaBio proposes the **development of the following series of shared European standards for HTA** to ensure the highest level of transparency, dialogue and trust amongst stakeholders and public authorities - including social values, which are part of our solidarity-based healthcare systems and are the foundation of our European society:

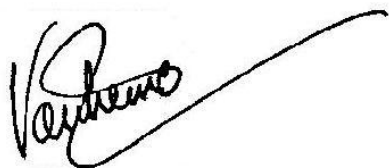
1. *A broader perspective.* HTA should seek to determine the value of a technology, whilst considering a wide range of perspectives that include economic, medical, technological, social, ethical, psychological and anthropological aspects. This evaluation should include all relevant stakeholders and take place in the context of the whole budget for healthcare, and be equally made for processes, procedures, service costs and products.
2. *Improved early-stage dialogue.* HTA should be based on an in-depth interaction to discuss specific data required in order to decide on the reimbursement of a product, and looking at its specific field and patient need. This would create predictability by clarifying payer expectations and the ability of industry to meet these expectations. At present, dialogue generally starts when a medicine has been approved.

3. *Flexibility.* HTA is a flexible process that should be used collaboratively. The use of HTA to make reimbursement decisions should have as its key objective to improve health outcomes for patients through the rapid uptake of beneficial health innovations and technologies, without losing sight of social values. A proper use of clinical and/or cost-effectiveness assessment of medicines should be aimed at increasing the understanding of its different benefits, value to patients and of public health and healthcare system impact.
4. *The right timing.* A one size fits all approach to the timing and methodology of appraisals will fail to take account of the complexity of conducting assessments and would ignore differences in diseases, treatments, and patient populations. Often the sort of data needed to confirm cost- and clinical effectiveness, and efficiency, is data on real-life clinical use of an intervention. These data can only be collected once the intervention is on the market for some time, and will depend on prevalence. Manufacturers should therefore be able to submit health outcomes information to the relevant government bodies throughout a product's lifecycle. This evidence should receive appropriate attention and reward from payers.
5. *Managing uncertainty.* Uncertainty in economic evaluation of innovative therapies is often managed by a call for more evidence. However, the willingness to invest in research to obtain additional evidence may be limited by the number of patients, the heterogeneity and natural history of the disease, the mechanism of action of the therapy, and the ethical issues surrounding a specific patient population. If the region of uncertainty is wide, but the treatment has significant potential benefits, conditional funding should be considered in the interim - provided that data are collected during further use of the therapy in order to improve an informed decision.
6. *Patient and public involvement.* Both patients and the public have to be regularly informed about what the use and procedures of HTA are and how it fits in making the healthcare system more efficient for them. They should have the same right as other stakeholders and actors of the process in the evaluation of new therapies, which should not just be based on economics but also on other factors, including social values. Patient and public involvement needs to be clear, transparent and become a key structural element of any evaluation of innovative therapies.

In relation to nanobiotechnology, EuropaBio believes that biological entities in the cell, while small enough to be labelled as "nano" are biological in the first instance, and therefore not the kind of nanostructure that would warrant new supervision. Where biological effects are the main target of the efforts of this research, the area of biotechnology is already well regulated. Nano structures that are not biological entities per se, but that can be used in the body, cell, or in the human animal or plant environment, would then fall under current product approval procedures for that sector. As such, the current EU regulatory framework is well placed to accommodate this emerging field

Thank you very much again for the opportunity to comment, and we look forward to being involved in the next stages of this process.

Yours sincerely



Johan Vanhemelrijck
Secretary General