

# European healthcare products regulation: the increasing role of legal considerations

**The regulation of healthcare products in the European Union has significantly expanded during the last decade. It has considerably broadened in scope and is much more sophisticated. Peter Bogaert looks back briefly at this historical development and offers a detailed indication of where we are today.**

Regulation has become more centralised and in many areas replaces pre-existing national decision-making processes, although national authorities maintain a pivotal role in the operation of the EU system. To a great extent, these developments reflect progress in science and technological innovation, policy developments and an internationalisation of business. These factors also strengthen the need for more EU-wide decisions, not only on the general rules but also on specific products or applications.

The EU regulatory system has sometimes been hailed as an example for other countries in the world and the Financial Times, for instance, reported that, according to the Commission, “increasingly the world is looking to Europe and adopts the standards that are set here”. There are, indeed, many countries, including China and Russia, and also states in the US that look at Community legislation when preparing new rules. This article highlights some of the general trends of the expanding EU regulatory regimes and also stresses the need for more legal certainty and better procedural guarantees.

## ... complexity

Undoubtedly, Community regulatory systems have become more complex. This is the result of a variety of factors. Science constantly progresses and paves the way for new products or identifies new issues that require more detailed regulatory activity. Companies also see a need for more “performing” products, such as functional foods or active cosmetics, and consumers are interested in novel products for health, personal care or enjoyment. In addition, regulatory experience in a specific field can also identify needs that result in new legislation. A few examples can illustrate this.

In the pharmaceutical sector, the rapid progress of biotechnology has resulted in new regulatory principles. An important step, also from an international perspective, is the framework for follow-on biological medicines – also known as biosimilar medicinal products – which the EU formally put in place in 2004. The rules provide a pathway for approving follow-on products without requiring full data packages but whilst also addressing the uncertainties that are inherent to biological products, such as recombinant growth hormones, erythropoietins, or interferons. A specific issue that comes up in this context is how to adequately distinguish the original and the follow-on products, for instance through the use of different international non-proprietary names (INNs) for the active ingredient. The European Parliament and Council also recently adopted a new Advanced Therapies Regulation, which for the first time provides an EU framework for approving tissue engineered products, such as curative new heart cells. This will open an entirely new area of regulatory activity with the EMEA.

Examples of legislation developed to meet specific needs that are identified through the application of the general regime are the Orphan Medicines Regulation of 1999 – stimulating the development of medicines for rare diseases – and the Paediatrics Regulation. The latter was adopted in 2006 and will in many

situations require pharmaceutical companies to develop data on the potential use of their products in children. In return, the new rules provide a reward in the form of six months patent extension if all relevant conditions are met. The Regulation makes the conditions for obtaining this intellectual property right dependent on an assessment by regulators, who in principle must be guided only by criteria related to public health. It puts in place a system where regulatory decisions and intellectual property are strongly interconnected. A similar situation will arise in the future under rules that were adopted in 2004 and that allow an additional year of regulatory data protection to be gained as a reward for developing an important new indication for a medicine. Here again, a decision that is primarily based on criteria of quality, safety and efficacy, will also decide whether or not this IP right – at least in the broader sense as used in the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) – is granted. Similar situations arise under the Orphan Medicines Regulation and it is expected that these issues will become much more important in the future.

In the food area, the new Nutrition and Health Claims Regulation entered into effect in July this year. It imposes stringent new rules that replace national principles, including several national systems that are based on guidance or self-regulation. The provisions of the new Regulation rely on difficult distinctions, such as the difference between disease risk reduction claims and general health claims, and in general only allow nutrition and health claims that are generically or individually approved.

## ... increasing integrated approach

As the EU regulatory regime becomes more comprehensive, there is also more and more interplay between the various systems and often regulators try to adopt a more integrated approach. Water protection rules can influence the assessment of medicines; functional ingredients in cosmetics will be impacted by an assessment under the biocides rules; substances classified under the chemicals rules as class 1 or 2 carcinogens, mutagens, or substances that are toxic to reproduction (CMRs) cannot be used in cosmetics, etc. The most far-reaching example of this is the recently adopted REACH Regulation, which regulates chemicals, including also, in many respects, their use in finished products. There are varying exemptions for specific types of products, such as foods and feeding stuffs, medicines, cosmetics, medical devices, food contact materials, pesticides and biocides, but each of these product categories is to some extent affected by the new rules.

The dividing line between regulatory regimes also results in legal discussions, when regulators seek to apply criteria under one regime when making an assessment under another. Several cases are currently pending before the European Court of First Instance addressing these issues.

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### ... increased discretion

The increasing complexity of the regulatory regime also results in an increased discretion at the disposal of the regulators. In the food sector, for instance, the new Fortification Regulation allows for bans or detailed restrictions on specific ingredients in foods, and also contains a definitive mechanism for placing substances under “Community scrutiny”. The Nutrition and Health Claims Regulation requires the Commission to set nutrition profiles, with which food products must comply in order to be allowed to carry nutrition or health claims. This can include setting specific conditions for the use of claims with respect to nutrient profiles.

The 2004 revision of the Community pharmaceutical legislation also increases the discretion of the medicines regulators. For instance, the legal criteria for refusing and withdrawing product approvals are much more subjective under the revised Human Use Directive. They now state that a marketing authorisation shall be refused “if ... it is clear that ... the risk-benefit balance is not considered to be favourable ...”. Similarly, they provide that the “competent authorities shall suspend, revoke, withdraw or vary a marketing authorisation if the view is taken that the product is harmful under normal conditions of use, or that it lacks therapeutic efficacy, or that the risk-benefit balance is not positive under the normal conditions of use, or that its qualitative and quantitative composition is not as declared” (while the text in force before the 2004 amendment read “where that product proves to be harmful ...”).

Also the above-mentioned Paediatrics Regulation attributes broad assessment powers to regulators to decide whether a paediatric investigation is justified and under what limitations or restrictions. This is important for regulatory compliance but also for the reward under the Regulation, because the agreement on an investigational plan is the first step towards gaining six months of patent extension.

The broad discretion of regulators is reinforced by the precautionary principle, which is now recognised as a general principle of Community law throughout all regulatory regimes. The Court of First Instance held in *Pfizer v Commission* that “under the precautionary principle the Community institutions are entitled, in the interests of human health, to adopt, on the basis of as yet incomplete scientific knowledge, protective measures, which may seriously harm legally-protected positions, and they enjoy a broad discretion in that regard” (*Case T-13/99*, Decision of 11 September 2002). The authorities then take, in essence, a political decision, based on the risk level that is acceptable to the society on which the risk is imposed.

The precautionary principle can, however, also restrict the regulator’s discretion when it is applied as an obligation. This can happen when the political decision concerning what level of risk is acceptable is made in the framework legislation, within which the Commission then has to review a specific substance or product. In that way, the precautionary principle raises the hurdles for granting or maintaining authorisations for substances or products. Very recently, the Court of First Instance of the EC annulled the decision of the Commission placing paraquat on the list of permitted active ingredients in plant protection products. The Court held that under the Directive on Plant Protection Products, the approval of an active ingredient requires that its safety be demonstrated beyond any reasonable doubt (*Case T-229/04 Sweden v Commission*, Decision of 11 July 2007).

### ... transparency

Both the legislative and the administrative decision making processes have also become much more transparent. This was to a

great extent made possible by the development of the internet, and the days that a written request to the EMEA was needed to obtain a copy of a European Public Assessment Report are since long over. More importantly, the political principle of transparency of official functions is now widely accepted.

This can, however, also create further complications for regulators. Transparency is intended to stimulate more discussion and input from the civil society. When it is applied to procedures governing individual substances or products, it will most likely also stimulate intervention of interested parties in the decision making processes on products of competitors.

### ... the role of legal considerations

It is obvious that the role of legal considerations increases in the context of the above-mentioned developments in the regulatory arena. Complex regimes require more detailed legal analysis, especially when several regulatory systems interact. More importantly, however, the need for full compliance with the relevant legal principles also increases with the broadening of the discretion of the regulators. This applies both to the substantive legal criteria and to procedural guarantees. As the Court held in *Pfizer v Commission*, when the precautionary principle is applied to impose restrictive measures, “according to the settled case-law of the Court of Justice and the Court of First Instance ... the guarantees conferred by the Community legal order in administrative proceedings are of even more fundamental importance”.

Frequently, however, the Community legislation lacks sufficient quality in this respect. Many key provisions of the legislation lack precision and, in general, procedural guarantees are not laid down in detail. There is also no general Community administrative procedure code, as is in place at national level in some Member States. This is also becoming more relevant as a result of the gradual replacement of Directives by Regulations, which cannot be fine tuned or adopted by each Member State to fit into the existing national rules.

The situation is challenging for the institutions, such as the Commission and the independent agencies, as well as for the companies and other persons who are directly affected by the regulatory decisions. To some extent, this can be addressed by guidelines and administrative practice, but there is also a need for strong overall legal rigour in the regulatory decision-making process. Agencies such as the EMEA regulate complex products that are often also of very high commercial value, and their decisions – or, where relevant, Commission decisions based on their advice – often have significant financial impacts. This is all the more so where regulatory decisions will also form the basis for granting intellectual property rights, such as the patent extension under the Paediatrics Regulation – in the form of a supplementary protection certificate (SPC) – or recognition of the importance of a new therapeutic indication. These dynamics may put a strain on the regulatory processes and may ultimately also result in legal challenges before the courts. Detailed attention to the legal aspects will be needed throughout the scientific and regulatory evaluation process, requiring strong legal expertise within each agency. \*

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