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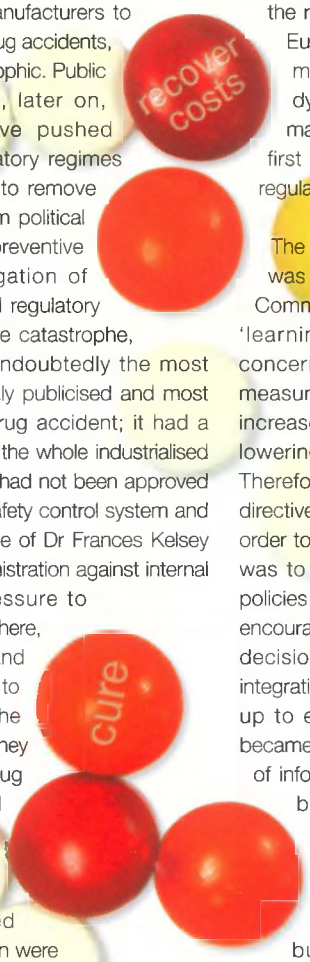
Catastrophes, regulation and interest accommodation

Jürgen Feick examines market entry regulation for pharmaceuticals within the EU and concludes that it still fails to satisfy the Single Market goal.

From industrial self-regulation to accident-induced governmental regulation

The pharmaceutical industry was first subjected to more or less stringent pre-marketing controls in the 20th century. Around the turn of the century industrial mass production of pharmaceutical specialties had largely overtaken the tradition of individual preparations by local pharmacists. This development, along with the growth of international trade, dramatically increased and spread the risks associated with the consumption of pharmaceutical products. Governments, however, were reluctant to intervene, despite the early warnings from physicians, and the demands of health insurers and public health care providers, who disliked spending their members' money or public budgets for possibly ineffective or even outright dangerous drugs. But, except for a few countries like the USA, Sweden, or Norway, national discussions before World War II were regularly stalled by the argument that strict pre-marketing controls would burden companies with additional costs and endanger the growth and international competitiveness of an innovative industry. There were strong lobbies against effective governmental intervention in the pharmaceutical industry in all industrialised countries. And in these early decades it was not too difficult to convince politicians that industrial self-regulation would assure product quality most adequately, most efficiently, and with the least disruption to the industry. This position made sense insofar as it was the pharmaceutical industry itself which possessed the scientific and technological means to test and control the assurance of product standards. This informational asymmetry between governmental regulators and pharmaceutical industry is still effective today, although to a much lesser degree.

Motives such as consumer protection against fraud, cost control in health care or rationalisation measures in war-time economies may be cited for compelling governments to introduce systematic pre-marketing controls. But the single most important factor for governmental intervention obliging pharmaceutical manufacturers to obtain approval has been drug accidents, some verging on the catastrophic. Public outcries in national and, later on, international arenas have pushed politicians to set up regulatory regimes whose political function is to remove the possibility of blame from political decision-makers through preventive measures and the delegation of control tasks to specialised regulatory authorities. The Thalidomide catastrophe, surfacing in 1961, was undoubtedly the most dramatic, most internationally publicised and most politically consequential drug accident; it had a strong impact on practically the whole industrialised world. In the USA, the drug had not been approved due to an already existing safety control system and to the courageous resistance of Dr Frances Kelsey of the Food and Drug Administration against internal and outside political pressure to licence the drug. Yet even there, foetuses were damaged and crippled children were born to mothers who had taken the sedative during pregnancy; they had either acquired the drug outside the USA or received the medicine from their family doctors as part of a testing/pre-marketing campaign. An estimated 10,000 handicapped children were born worldwide, mainly in Europe, except for France which had not yet approved the drug due to bureaucratic delays. This major catastrophe was publicly understood as proof that industrial self-regulation had failed; a situation that could not be handled by merely symbolic policies.



National responses and the European Community

In the US the Thalidomide catastrophe saved a pharmaceutical regulation bill that was close to failure in the US Congress. The bill ultimately introduced the strictest market entry regulation so far, based on proofs of pharmaceutical quality, toxicological safety and therapeutical efficacy (the Kefauver-Harris Amendments of 1962). It became the regulatory model for policy formation in the European countries. While American policy-making and implementation profited from the dynamics of the 'new social regulation', in many European countries industry lobbying first tried to preserve as much industry self-regulation as possible.

The upcoming wave of new national regulation was a challenge for the still young European Community. Despite lively communication and 'learning' between national governments concerning this new regulatory task, differing measures in the member states threatened to increase non-tariff barriers to trade, instead of lowering them as stipulated in the EEC treaty. Therefore, the EC-Commission prepared policy directives, the first coming into effect in 1965, in order to harmonise national legislation. Its intention was to arrive at functionally equivalent national policies and implementation practices that would encourage mutual recognition of national regulatory decisions. But this mode of European market integration by and large either failed or did not live up to expectations. European harmonisation became increasingly dense and detailed, measures of information, communication, and cooperation between national authorities were introduced, and semi-formalised procedures supported by a European evaluation committee (CPMP) were supposed to foster regulatory consensus-building between national agencies. Nonetheless, national regulatory decision-making did not converge sufficiently to create a single market for pharmaceuticals.

Table 1: No single market for medicines
Mutual availability of active ingredients (Country 1 > Country 2 in %)

COUNTRY 1	COUNTRY 2 AUT	B	DK	F *	GER	NL	S	UK
AUT	–	59	49	43	81	57	48	54
B	72	–	55	52	79	66	52	60
DK	81	73	–	60	84	76	73	71
F *	74	69	58	–	75	68	58	63
GER	68	54	43	42	–	50	42	49
NL	80	76	65	56	84	–	61	69
S	79	71	74	59	83	72	–	70
UK	68	62	55	60	73	62	53	–

Selected countries; active ingredients categorized according to ATC-Code.
Source: EURO-Medicines Database; Folino-Gallo, P. et al., 2001, Availability of medicines in the European Union, in: European Journal of Pharmacology, 57: 443
Source: EURO-Medicines Database, www.euromedicines.org (date: 23.11.2001)

Incrementalism and a module of structural change

Until the early 1990s, the development of pharmaceutical regulation within the EC had been one of incremental institutional evolution. The single incremental steps may be regarded as attempts to correct failures on the road to mutual recognition. They were largely without success, since final regulatory decisions remained national and the European implementation input was non-binding. A fundamental structural change was introduced in 1995 with the regulatory module of the Centralised Procedure establishing an original European regulatory infrastructure, with the European Agency for the Evaluation of Medicinal Products as its focal institution, and a decision-making process within which marketing authorisations are issued by the EC-Commission and are valid in all member states. Furthermore, a semi-Europeanised approval procedure came into force in 1998, the Decentralised or Mutual Recognition Procedure, containing the very rarely utilised provision for a binding European arbitration stage should mutual recognition fail.

A 'policy-patchwork' accommodating a variety of interests

This leaves us with a 'policy-patchwork' (Héritier) of three different marketing authorisation procedures in the European Community, all for the same regulatory task, and all based on a maximally harmonised legal framework. These three procedures discriminate between types of medicine, distinguished essentially by their degree of innovativeness and the number of markets targeted by the pharmaceutical entrepreneur. In order of degree of Europeanisation the three procedures are:

1. the Centralised Procedure, obligatory for all bio-hightech medicines, optional for all otherwise innovative medicines, leading to a single EC-wide valid marketing authorisation;

2. the Decentralised or Mutual Recognition Procedure, based on coordinated national decisions and applicable whenever a medicinal product shall be marketed in more than one member state and if (1) is not applied;

3. purely *national procedures* for marketing applications, targeted at only one member state's market, provided (1) does not apply.

This complex procedural configuration reflects a large variety of economic, political, administrative and therapeutic interests. In fact, their accommodation within a differentiated regulatory landscape has been a precondition for the acceptability of the most Europeanising implementation framework, the Centralised Procedure. The latter satisfies the interests of the innovative, internationally oriented pharmaceutical industry by opening up a large market with one, even more efficiently organised, procedure. This part of the industry, as well as national governments and the Commission, views it as a measure to reestablish and enhance the innovativeness and competitiveness of the European pharmaceutical industry and Europe as an industrial site. The Commission gains implementation competences at the expense of national authorities, but these authorities may content themselves with extensive participation rights in the procedure. The two other procedures are in the interest of pharmaceutical companies whose product range, regulatory capabilities, or territorial marketing approach are tuned to national or regional markets and to traditional regulatory liaisons. National governments appreciate the contribution of these firms to GDP and high-qualification jobs, and national authorities' regulatory capacity and autonomy is guaranteed by the continuation of these nationally based procedures. The diversity of procedures leading to the output of a variety of medicines, some with a rather national focus, also serves the heterogeneous therapeutical interests of doctors and patients. One is tempted to speak of an 'institutional isomorphy' (DiMaggio/Powell) between interest and regulatory structure. But the original European goal, that of creating a single market for pharmaceuticals, is only achieved for the most innovative medicines. As long as the mutual recognition of national regulatory decisions is not automatic, and as long as the Centralised Procedure is not obligatory for all applications, there will be no EC-wide access to all medicines available within the EC (see table 1).

The limits of 'private interest government' and the quest for transparency

This overall analysis does not mean that all interests are served equally well. Since the strengthening of market entry control for pharmaceuticals in the second half of the twentieth century, an unresolved dispute has been underway between those who claim that tight regulation might impede medical innovation and economic growth and those who make the criticism that patients might be less well protected than commercial interests. Critics would also argue that even though these new regulations have not been established on behalf of large parts of industry, and even against their resistance, their further development and, especially, their implementation have become increasingly biased towards industrial interests; this is mainly due to changes in administrative orientation and behaviour. Nevertheless, there are clear limits to what has been called 'private interest government' (Bernstein). After the catastrophe of the 1960s, public awareness is too great to allow major regulatory problems to pass unnoticed. Politicians fear that they might lose support and votes, and companies that their commercial image could be damaged and that they might face liability claims. For this mechanism of public control to function properly, transparency is a necessity. Given the complexity of this highly technical product, full transparency of application data and procedures is demanded by external expert 'watchdogs' and 'whistle blowers'. There are objections in the name of commercial secrets and, furthermore, warnings that this would strengthen an innovation-averse, precautionary attitude, because of a potentially over-anxious public. If so, all parties would have to prove their case in public; the argument is that an open society can not tolerate secrecy simply because matters become complicated. Otherwise, the establishment of technocratic power structures and the misuse of appeals to complexity for the protection of partial interests seem inevitable.

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