

New Safe Medicines Faster

A Proposal for a Key Action within the EU's 6th Research Framework Programme (without Appendix)

Executive summary

The global competitiveness of the European pharmaceutical industry is under threat. Technology currently available for the development of new medicines is unable to match the pace of drug discovery and design; and the ever-growing demand for safety, efficacy and quality documentation has increased the cost and time involved in getting new medicines on the market.

Although the pharmaceutical industry is one of the strongest in Europe in terms of research, innovation, exports and employment, there are severe restrictions on its ability to create wealth and launch safe, drugs for the treatment of common and rare afflictions.

The present situation must not be allowed to continue. For this reason, the European Federation for Pharmaceutical Sciences (EUFEPS) proposes a key action under the title *New Safe Medicines Faster* for the forthcoming 6th Reserach Framework Programme.

The key action has three main objectives: to seek new technologies capable of more effective selection of potential drug candidates for innovative medicines while accommodating safety demands; to use such technologies to speed up the pharmaceutical development process and eliminate bottlenecks created by initial exploratory drug research; and to cultivate a pan-European interdisciplinary network that bridges the gap between industry and academia.

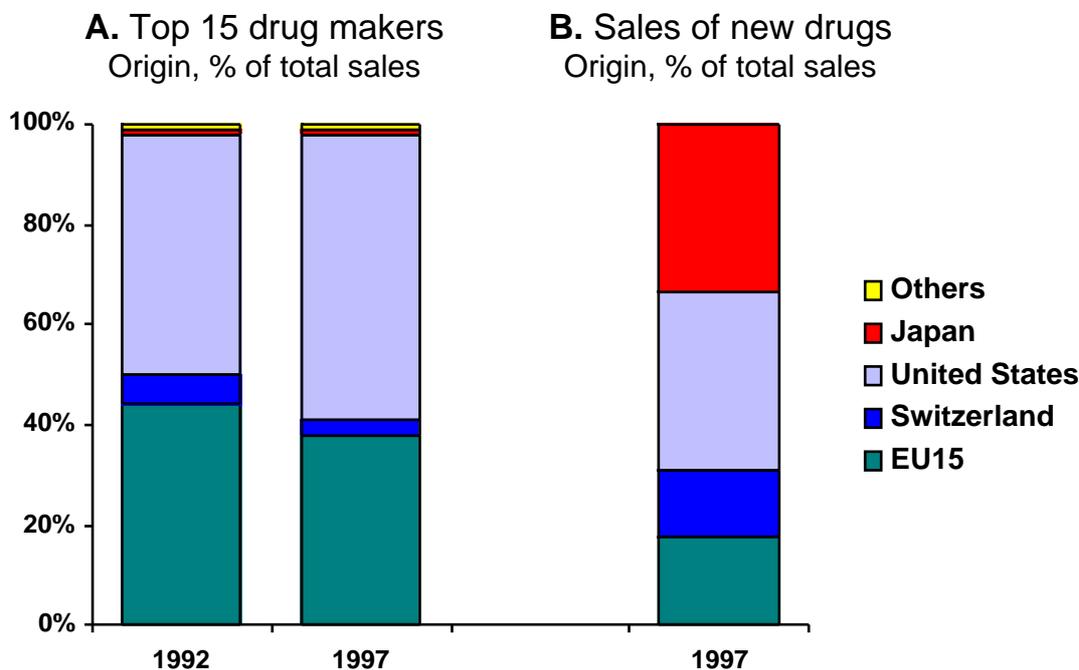
By breaking down the barriers put up by the legislation of individual nations and initiating a new set of recognised European standards, new medicines can be brought onto the market faster and cheaper — with the ultimate aim of making Europe's pharmaceutical industry the best and most competitive in the world.

The situation today

Europe's pharmaceutical industry is a major employer, with 397,000 employees working within the European Union in 1995^{1,2} — the equivalent of one in every 300 workers and just less than half that of the motor vehicle industry. Ranked the fifth largest industrial sector in the EU, the pharmaceutical industry makes an increasing contribution to the EU balance of trade, in 1995 accounting for 3.5% of total manufactured goods^{1,2}.

The fact that no less than 16 of the top pharmaceutical companies resided in the EU in 1997 — while Switzerland boasts three, the USA 13 and Japan eight — underlines the strength of the European industry. However, in 1996, the world-leading position held by the European pharmaceutical industry in sales terms was taken over by the USA, representing 33% of the world market compared to Europe's 29%^{1,3}.

That the European strength is gradually being undermined is clear from the breakdown of pharmaceutical sales given in figure 1⁴. This shows the US industry's superior ability to translate new technology into marketable medicines, as their recently introduced products account for a larger share of total sales than in the EU, where companies depend considerably more on older products. A report published by Europe Economics in December, 1998 confirms this trend, warning that the EU pharmaceutical industry may be falling behind the US in terms of innovative efforts¹. Opportunities to improve the competitive situation were the subject of an EU round table discussion held in Frankfurt in December, 1997.



Source: IMS Health, *The Economist*, December 1998

Figure 1. Development in market shares for the top 15 drug manufacturers (A) according to origin from 1992 to 1997 and (B) the corresponding distribution of sales of new drugs released since 1988⁴.

Consolidation and co-operation

The global pharmaceutical industry comprises several tiers. At the top lie a number of large multinational corporations conducting broad research and worldwide marketing. The second tier consists of hundreds of medium-sized companies that often rely on niche products or their national market. Then, there are numerous minor and start-up companies and specialist ventures, the latter becoming increasingly important as a source of new technology, targets and drug candidates and for contract research.

Like other manufacturing sectors, Europe's pharmaceutical industry has undergone dramatic consolidation, with a 10 to 15% reduction in employees over the past decade. This is primarily due to market pressures and the call for increased shareholder value. Whether consolidation has affected the industry's capacity to innovate remains to be seen. The high cost of developing drug candidates and marketing the end product, however, does require financially strong corporations. With only around one in ten drug candidates making it onto the market and less than a third of those launched recouping the cost of their development, the pharmaceutical industry is up against difficult odds.

Many European pharmaceutical companies choose to co-operate with specialist companies or buy in specialist knowledge from contract research organisations rather than merge with others, spending up to 40% of their research expenditure outside the company. This way, the risk of jobs being transferred abroad is avoided, allowing the EU to retain and enhance important skills. Although more financial research support given to biotechnology by some member states — the UK, France and Germany — has aided the drive to remain competitive, this has only been at a modest level. There is, though, no doubt the application of emerging drug discovery technology and new science would have a major impact on the future of the EU industry^{1, 5, 6}.

The key action

The EU lost important ground in the first phase of the biotechnological revolution in drug discovery. Using this focused key action, the second phase concerning the implementation of the most efficient, swift and safe drug development processes can be led by the European pharmaceutical industry. A key action, as defined in the EU's 5th Research Framework Programme (see box), is an excellent way to create consortia of research groups representing all the specialist areas involved in drug development — pharmacology, toxicology, pharmaceuticals, scale-up processing, analytical chemistry and clinical trials. A new and highly important discipline, pharmacogenomics, will also play a major role in the future when determining the effect of specific drugs on individual patients. In addition, the key action should comprise clusters, centres of excellence, a strategy for specialist training and dedicated support for small and medium-sized enterprises.

Thus on this background anticipating the timing is right we have taken the opportunity to suggest a new key action *New Safe Medicines Faster* to the forthcoming 6th Research Framework Programme.

Definition of a key action:

- Research action addressing major socio-economic challenges facing European society
- Mission-oriented problem-solving approach
 - integrating all necessary disciplines and sectors
 - from basic research to development and demonstration
- Strong networking component
 - between the projects financed
 - and with related national/international activities
- Designed and implemented in consultation with all stakeholders
 - including the ultimate beneficiaries

from the EU's 5th Research Framework Programme

Objectives of the key action**Promoting new technology**

Innovative new technology is vital in order to improve the process of converting a drug candidate into an approved medicine. In a world characterised by the increasingly rapid development of new generic techniques in the fields of biochemistry, genetic engineering, bioinformatics and so on, it is imperative that EU-funded research projects define ways of applying such techniques to create new, highly efficient pharmaceutical technologies. Work on these new disciplines should include as many of the pharmaceutical sectors and EU member states as possible. As a result, the new pharmaceutical methods, techniques, tools and procedures that emerge will more easily obtain regulatory approval and, at the same time, represent the most competitive solutions for increasing the speed, cutting the cost and improving the quality of drug development.

Efficiency cuts costs

A drug candidate's chances of success as a marketable product are to a large extent determined during the phase of exploratory development, when efficacy, safety and technical studies are carried out (see figure 2). At the same time the costs are lower than the later clinical phase. For this reason, it is clear that any shortening of this phase, due to an improved ability to predict the successful outcome of the development process, contributes most to reducing the cost of producing a new drug.

High throughput screening methods and the use of combinatorial libraries have already paced previously time-consuming processes in the drug discovery phase. For example, the task of finding a drug target and identifying a new drug candidate is considerably cheaper and faster than in the past. To avoid bottlenecks, then, it is imperative that the capacity and speed of drug development and assessment are increased to match the growing number of new drug candidates. Efficient methods for selecting the right drug for a given purpose are a sure means of reducing time to market, enabling the EU pharmaceutical industry to launch major new products early in the life of the protecting drug patents.

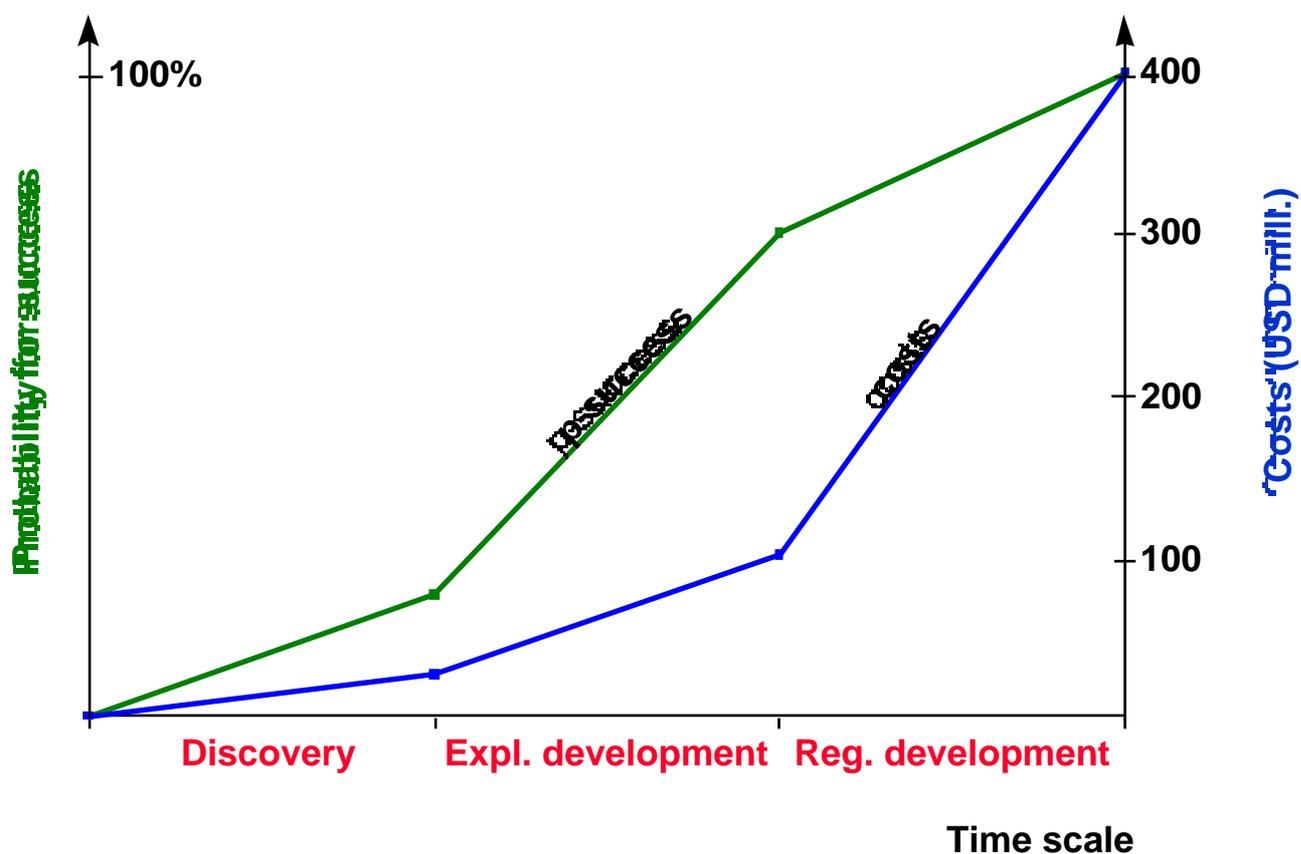


Figure 2. Relative risk and cost of carrying a drug through discovery to registration. Expl. = exploratory, Reg. = regulatory

The interdisciplinary network

The research, technology and development involved in creating new medicines rely on input from so many scientific areas that interdisciplinary European co-operation is the only way to ensure success.

The proposed key action *New Safe Medicines Faster* invites cross-sectional collaboration between all scientific research areas, expanding and consolidating the networks already in existence among Europe's pharmaceutical scientists. By bridging the gap particularly between academia and industry, the transfer of new knowledge and technology from one to the other will become considerably easier, to the benefit of all.

At present financial support for academic pharmaceutical research in general is noticeably lacking in the EU research framework programmes. The pharmaceutical sciences are distributed among many European schools and universities, making it difficult to create enough critical mass to be at the forefront with regard to new science and technology. Often pharmaceutical studies are considered too applied to gain support from basic research funds or too biological to qualify for technological funding. By combining these diverse groups within the various member states into effective consortia and networks, enough synergy can be obtained to promote innovation and scientific excellence.

Large international research projects made possible by co-ordination and combination of the diverse techniques employed by Europe's pharmaceutical companies and research institutions are thus important to speed up the production of innovative medicines.

Benefits of the key action *New Safe Medicines Faster*

Streamlined drug development

The co-ordination, concertation, and concentration of all the disciplines involved in research, technology and development, from early target identification and validation through safety and efficacy tests to market launch, will result in a whole new streamlined approach to the production of new medicines — a fast track in which drug development is viewed as one continuous transformation process. Central players within research, industry, the finance sector and patient associations will, thus, be mobilised to address the objectives of the key action.

The benefits of streamlined drug development are:

- faster transition from drug candidate to new medicine
- improved speed and efficacy of the research, technology and development process
- less risk of missing a potential drug candidate
- improved quality, efficacy and safety assessments
- reduced need for animal experimentation
- optimised scale-up, production and quality control
- more widespread use of environmentally sound production methods
- reduced observation time and number of patients required for clinical testing
- improved validity of clinical trials and prediction of large-scale use in man
- eased drug approval process

New front-line technologies have already been supported by former EU research framework programmes. This includes technological tools obtained from basic sciences, such as molecular genetics, biomedicine, bio-engineering and information technology, which can be implemented in traditional pharmaceutical disciplines. Robotics and miniaturisation in pharmacology and pharmaceuticals and structure activity relations in absorption, distribution, metabolism and excretion studies and toxicology will also contribute to faster, more efficient drug development, as will further progress in the auxiliary disciplines of analytical and processing chemistry. In an attempt to give an impression of the many research subjects and technologies, linked to this proposed key action, some of the current research issues for each discipline along with important interfaces and proposed deliverables were specified in an appendix to this position paper.

Stimulated industry

The energising of pharmaceutical research and development will stimulate the growth of both established pharmaceutical companies and smaller start-up companies. In a climate of increasingly tough competition, even the largest companies lack the resources to sustain specialist in-house laboratories with front-line expertise. This is resulting in a growing number of start-up and spin-off enterprises which carve themselves a niche in the market by supplying advanced know-how and services and by developing pioneering technology in their particular field. Such small, highly specialised companies are essential to the future growth of larger pharmaceutical concerns.

By encouraging interdisciplinary co-operation between companies, the issue of intellectual property rights is expected to become a less sensitive one as opportunities arise to share rights to methodology. Pharmaceutical companies are highly protective of their rights with regard to new drug candidates — the essence of their future survival. This may also be a major reason why many companies have not participated in earlier EU research framework programmes on a larger scale⁷.

The prospect of shared rights and technologies, though, may diminish such reservations, aided by positive past experiences of EU-supported initiatives.

A highly qualified work force

PhD and post-graduate students trained in the most up-to-date technology and research areas will help to close the current gap between academia and the needs of industry. As an EUFEPS survey from 1997 confirms, the present level of European research training in pharmaceutical disciplines is either limited or non-existent, resulting in a chronic shortage of suitably qualified scientists⁸. The key action is intended to remedy this situation.

The EUFEPS survey lists the main training deficiencies in the following order of importance: combinatorial chemistry, bio-engineering, drug delivery, pharmaceutical technology, biopharmaceutics, pharmacokinetics and high throughput screening. In the years ahead, a lack of trained scientists is also expected in the fields of gene therapy, diagnostics, classical pharmacology, bioinformatics, statistics, synthetic chemistry, computational chemistry and molecular pharmacology. Clinical development and clinical pharmacology are additional problem areas.

These deficiencies are largely thought to be due to small individual faculties, a lack of academic and industrial integration and inadequate post-doctoral programmes. But, by combining training and mobility, the key action provides a basis for solving these problems, resulting in:

- A strong educational framework that combines top level university research with front-line technology in areas where there is little or no training in Europe today.
- A pool of experienced researchers born of the advanced level of collaboration between academia and industry and trained in integrated applied science and technology, making them suitable for jobs in the regulatory environment, large pharmaceutical concerns and, new specialist companies.
- An enhanced capacity for innovative development within further education to meet the needs of industry.

In conjunction with the key action, it is proposed that a European school of pharmaceutical excellence is established to address many of the pharmaceutical industry's current shortcomings. The school could comprise five to 10 academic centres with minimal administration attached to one of the major academic partners. Affiliated to a university department, each centre would provide theoretical and experimental training courses of three to 12 months' duration complemented by the expertise and technological know-how of other academic departments, pharmaceutical companies, instrument manufacturers, contract research organisations and research institutes.

The concerted effort put forward by the key action *New Safe Medicines Faster* has clear benefits that speak loudly in favour of its inclusion in the EU's 6th Research Framework Programme. By crossing the divide currently between individual fields of research and development, industry and academia and transforming drug development into an integrated process, the European pharmaceutical industry is better armed to tackle the health and employment challenges of the future.

References

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Postscript

European Federation for Pharmaceutical Sciences - EUFEPS

Founded in 1991, the European Federation for Pharmaceutical Sciences is a federation of 25 societies representing pharmaceutical sciences in 23 European countries — a total of around 18,000 individuals.

EUFEPS is governed by a ten-member executive committee, comprising outstanding pharmaceutical scientists who report to a council. One of the advisory committees of EUFEPS is the Committee on Industrial Relations (CIR), consisting of 15 senior industrial research scientists and directors from 8 countries and 3 members from educational institutions. CIR is particularly concerned with advanced education, drug discovery and early research and development in the pharmaceutical industry.

The mission of EUFEPS is to promote excellence in the pharmaceutical sciences and innovative drug research in Europe and to represent the interests of scientists engaged in drug research and development, drug regulation and drug policy-making. New processes and technologies which may lead to faster development of new safe medicines form part of EUFEPS' work in promoting the European pharmaceutical industry in the global arena. Pharmaceutical education and training is also seen by EUFEPS as an important factor in achieving its mission.

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