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The key action Cell Factory, an initiative of the European Union

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When Louis Pasteur concluded in a biblical tone his speech describing the results that demolished the theory of spontaneous generation by saying: *Messieurs, c'est les microbes qui auront le dernier mot*, a new era for humankind had began. He discovered the rational basis for microbial fermentations, for the development of vaccines, etc. He developed, without knowing it, the scientific basis of modern biotechnology. Now, more than a century later, at the end of the 20th century, there is a general agreement among scientists, politicians and sociologists: that the 21st century will be the century of Biotechnology and of Life Sciences [1].

Since the early 1980's, the European Union (EU) has developed several research and training programmes in Biotechnology, Biomedicine and Health as well as on Food and Agro-industrial research. These programmes have succeeded in mobilising, in an interdisciplinary and collaborative way, the most dynamic scientific and industrial groups in Europe, and they have provided an excellent record for research for the life sciences. The Life Sciences Community programmes have also generated an explosion in the knowledge of the structure and habits of all living beings, and in particular of living cells. This leads to promising developments in the corresponding sectors, e.g. health-care, pharmaceuticals, agriculture, food, etc. These developments, however, have been fulfilled only partially, as Europe has not been strong enough to exploit the advances steaming from this research.

The socio-economic objective of the Fifth Framework Programme

The Fifth Framework Programme for Research, Technological Development and Demonstration (1998–2002) [2] has taken into account the new socio-economic reality and has, therefore, adopted a new approach. Its novelty is the political willingness

to couple the dynamics of massive knowledge production with the few areas from which desirable spin-offs are expected to arise. Meanwhile, the Programme will pursue the renewal of knowledge to reinforce European strength in fields associated with further growth and higher standards of life. This is the purpose behind European research, as indicated by the Commission in the *Inventing Tomorrow's* document [3], which has served as the basis for the preparation of the Fifth Framework Programme.

There is no doubt that scientific, technological progress increasingly determines the way and the speed at which society evolves. This raises inevitably a certain number of questions, in particular with respect to the speed of the changes and the directions which they are taking in society. But one can also turn the approach around: if the role of research and technological development is to innovate, is this not in order to respond to a large extent to social and economic needs and expectations?

From the perspective of Community policy, research is not an end in itself, but rather an extremely important tool to achieve common objectives. The EU considers that now it is time to change direction slightly in order to put research activities in the current socio-economic context. Hitherto, Community research activities have been largely based on a technology-driven approach. The aim of the Fifth Framework Programme is to make research more efficient, in terms of exploitation of research results, directed towards meeting basic social and economic needs by bringing about the changes which each individual citizen desires.

To sum up, the Fifth Framework Programme consists of four thematic programmes and three horizontal programmes. The thematic programmes with the corresponding budgets expressed in million of euros (M€) are:

- Quality of life and management of living resources (2,413 M€);
- User-friendly information society (3,600 M€);
- Competitive and sustainable growth (2,705 M€);
- Energy, environment and sustainable development (2,125 M€).

The horizontal programmes address the following three themes, respectively:

- Confirming the international role of Community research (475 M€);
- Promotion of innovation and encouragement of participation of SMEs (363 M€);
- Improving human research potential and socio-economic knowledge base (1,280 M€).

The Quality of Life and Management of Living Resources Programme

This Programme has a budget of 2,413 M€ [4], which is a significant increase over the RTD activities in Life Sciences from the Fourth Framework Programme (1994–1998). The strategic objective is to link the ability to discover with the ability to produce in order to address the needs of society, and to meet the requirements of the consumer, leading to future wealth and job creation and improvements in the environment. The strategy of the socio-economic drive of this programme is to focus on specific areas where growing knowledge may provide scientific and technical answers to some of the pressing questions asked by the European citizen, which requires tackling on a European scale.

The Quality of Life Programme will concentrate on the acquisition and utilization of knowledge on fundamental mechanisms affecting human life, especially in the fields of health, food and environment. Particular emphasis will be placed on the development of knowledge aimed at the prevention of disease (research on the brain, on the mechanisms of food poisoning, on the newly emerging infectious diseases, etc.). The exploitation of living cells for health, environment and agro-industry and fine chemicals is also equally considered.

The programme has an overall concern to maximize the quality, the safety and renewable nature of bioproduction while respecting the fundamental ethical values. The six key actions with their financial breakdown (in M€) are the following: (i) Food, Nutrition and Health (290 M€), (ii) Control of infectious diseases (300 M€), (iii) The "Cell Factory" (400 M€), (iv) Environment and Health (160 M€), (v) Sustainable agriculture, fisheries and forestry, and integrated development of rural areas including mountain areas (520 M€), and (vi) The ageing population and disabilities (190 M€).

The key actions will concentrate on targeted, clearly delimited socio-economic needs and on the Community's policy objectives, where European research should make a decisive contribution with innovative products, processes or services. The key actions are supplemented in the programme with research and technological development of a generic nature as well as support to research infrastructures. The activities of generic nature have a long-term impact. Their aim is to help the Community not only to maintain but also to improve its

scientific and technological capability in those areas of research, and to enable technologies that should be widely used. The budget allocated by the Council to generic activities is of 483 M€. Support will be focused on:

- Chronic and degenerative diseases (in particular cancer and diabetes), cardiovascular diseases and rare diseases
- Research into genomes and diseases from genetic origin
- Neurosciences
- Public health and health services research
- Research related to the disabled
- Study of problems related to medical ethics and bioethics in the context of respect for fundamental human values
- Study of the socio-economic aspects of life sciences and technologies within the perspective of sustainable development (the impact on society, economy and employment)

The activities on research infrastructures in the programme should be able to provide added value, complementary to national or multinational initiatives. The following classes of infrastructures will be supported within a budget of 70 M€ and will focus on:

- Biological data and collections of biological material
- Clinical research facilities, including pre-clinical research
- Facilities for aquaculture and fisheries research

The first call for proposals for the Quality of Life Programme has been published recently [5]. The text of the Work programme, and general information is available from the Commission services at the following addresses:

E-mail: life@dg12.cec.be

Web: <http://www.cordis.lu/fp5/home.html>

Key action: the "Cell Factory"

Worldwide sales of about twenty cell-derived molecules produced on a large scale (insulin, interferon, erythropoietin, etc.) already amount to 9.35 billion euros. The recent strategic changes in the chemical industry are now concentrating on life sciences, as opposed to the traditional chemical sectors. Those changes reveal the issues involved in the extremely rapid growth of this scientific and technological domain. In less than five years, the world market for bio-products, especially in the health and environment fields, could amount to 100 billion euros with the added perspective of creating 200,000 new jobs.

Europe possesses first class scientific groups and an excellent know-how of this exploitation of living resources. All too often, however, the commercial exploitation takes place elsewhere, particularly in the USA. This key action on Cell

Factory should make it possible to strengthen the European capabilities in this domain by encouraging multidisciplinary approaches, which are indispensable to understand how cells work, and to develop viable applications in health, agriculture and industry. The industrial mastery of the cell as a factory opens up revolutionary perspectives. Development of new kinds of drugs, foodstuffs with specific nutritional properties, techniques for biodegradation of recalcitrant compounds, industrial enzymes replacing less environmentally friendly chemical processes, etc.

The overall objective of this key action is to integrate the innovations into living cells (microbial, plant and animal cells) and into their productions. Thus, they would provide an environment in which results could rapidly be exploited and transformed into products and processes of interest to the society. The spin-offs in society will be particularly visible in the health, environment, food, agriculture, agro-industries and high value-added products.

Contrary to previous framework programmes, which were mainly knowledge and technology-driven, the Fifth Framework Programme, and in particular this key action, has taken a different approach. It consists of putting forward the main socio-economic objectives addressed by the key action, together with the anticipated deliverables to society. In order to attain such objectives and deliverables, the key action will mobilise any kind of research or technological development, including demonstrations geared to the fulfillment of the overall objectives.

European challenges to be addressed by the Cell Factory key action

Promoting the development of innovative technologies and mobilising mission oriented research The new knowledge on advanced research that will be generated by the functioning of the cells as biological factories needs to be integrated into the overall problem solving approach of the key action.

Exploitation of results The creation of wealth and employment requires close links between research and socio-economic needs, efficient risk capital markets, creation and development of high-tech SMEs and a fruitful dialogue between knowledge and technology producers. The challenge Europe faces is to set up a nurturing environment for the development both of established bio-industries and of a new generation of European entrepreneurs to start up and flourish.

Linking the ability to discover to the ability to produce Scientific and technological excellence of the selected project is, indeed, necessary but not sufficient. It should be closely committed to knowledge transfer and convincing exploitation potential.

Table 1 Action lines under the key action the Cell Factory

New and innovation health-related processes and products

- Development of new diagnostics, therapeutic substances and strategies
 - Diagnostics
 - Therapeutic substances
 - Therapeutic strategies — Gene Therapy — Tissue and cell engineering
- New and improved technologies for biological productions
- Novel in vitro testing as alternatives to animal testing

Energy-efficient bioremediation and waste biotreatment processes

- New bioprocesses for preventing industrial pollution, treating, upgrading, and/or recycling bioaccumulable wastes and industrial by-products
- Bioassays and biosensors
- Biodegradation of recalcitrant chemicals
- Biodiversity and ecological dynamics of natural and introduced populations
 - Microorganisms
 - Plants and animals
- Development of methods and strategies to ensure the safety of new biomolecules or bioprocesses, and for the identification of recombinant organisms and their residues in the environment and their impact on human and animal health

New biological and biotechnological processes and products from cell factories

- Exploiting the cellular and molecular characteristics of organisms
 - High value-added products and processes involving/derived from microorganisms, plants and animals
 - Microorganisms
 - Animals
 - Plants
 - Functional biomolecules and biocatalysts
 - Identification and sustainable use of metabolic and genetic diversity as a source of new valuable products
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Anticipated deliverables

The key action will mobilize the efforts to seize opportunities in the following three areas of high socio-economic interest:

Improving the diagnostic and therapeutic arsenal for health care: development of new or improved health related processes and products from living cells and biomolecules, particularly towards improved therapeutics: new antibiotics, anticancer therapies, etc.; in vitro alternative tests, diagnostic tests, innovative technologies for biological production and novel targets for drug discovery.

Improving environmental sustainability: development of cleaner technologies and improvement of bioremediation and waste biotreatment processes. These efforts will be driven towards environmental friendly products and processes, recycling and/or biodegradation of wastes and industrial by-products; bioassays to monitor the effects of toxic chemicals in biological systems, and methods and strategies for safe introduction, use, monitoring and tracing of genetically modified organisms (GMOs).

Improving quality in food, agro-industry and fine chemicals: the key action aims at the development of bio-processes and bio-products combining ecological, consumer and industrial advantages, particularly towards high value-added products and processes for food, agro-industry and the (bio)chemical sectors including fine chemicals, and products derived from improved crops and farm animals.

Research and Technological Development (RTD) to be mobilised to attain the socio-economic objectives

The EU has departed in the current Fifth Framework Programme from the classical linear innovation chain: that is to say from basic and applied research through technological and industrial development to industrial production. In fast developing high-tech fields such as those involved in life sciences, the innovation chain does not always proceed following the classical mechanism. In certain cases, the fast dynamics of the innovation and the competitive forces of the market do not allow the time to follow the classical innovation chain. The product may be already obsolete before reaching the market. In other cases, because the science and technology push are not in phase with the needs expressed by society or the market pull. Finally, in countries where scientific and industrial tissues have not reached the dimension and the level of the more advanced ones, scientific and technological communities are relatively small. Scientific activities usually constitute an end in themselves without sufficient integration in the other social spheres. As a result, the impact of the research reaching society is unsatisfactory.

The approach of the EU has been pro-active. Rather than having a passive role waiting for an uncertain transfer of results to industry and society, the Commission has identified the potential necessities with the help of external advisory groups (EAG's), (one EAG focused on the Cell Factory key action) [6], scientific and industrial communities, socio-economic groups, etc.

The EAG on Cell Factory has delivered a number of key messages and most of them have been incorporated in the Workprogramme. The projects supported must combine innovative and multidisciplinary technology platforms with convincing dissemination and exploitation strategies, either by established industries, small biotech firms, entrepreneurial initiatives or by the public sector. The Commission was asked to apply a reasonable flexibility to the RTD fields to be mobilised. The projects could address a wide spectrum of RTD targets, provided they focused on the main socio-economic objective of the key action. In short, good, scientific excellence is necessary but not sufficient. Knowledge transfer and exploitation commitment are also essential. Another important message is that the Cell Factory key action does not exclude basic or fundamental research, nor does it focus on applied research. It should mobilise whatever scientific excellence, innovative technologies and convincing exploitation strategies are needed to reach the socio-economic objectives. It should also address the problem-solving approach of this key action, thereby leaving room for innovative ideas from the applicants.

Notes and references

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4. Council Decision of 25 January 1999 adopting a specific programme for research, technological development and demonstration on quality of life and management of living resources (1998–2002). Official Journal of the European Communities. L64, 12 March 1999
5. Call for proposals for RTD actions under the specific programme for research, technological development and demonstration on quality of life and management of living resources (1998–2002). Official Journal of the European Communities. C64, 6 March 1999
6. Opinion of the External Advisory Group for the Key Action "Cell Factory". <http://europa.eu.int/comm/dg12/fp5/eag-cell1.htm>