COUNCIL DECISION

of 15 December 1994

adopting a specific programme of research and technological development, including demonstration, in the field of biomedicine and health (1994 to 1998)

(94/913/EC)

THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 130i (4) thereof,

Having regard to the proposal from the Commission (1),

Having regard to the opinion of the European Parliament (2),

Having regard to the opinion of the Economic and Social Committee (3),

Whereas by its Decision No 1110/94/EC (4), the European Parliament and the Council adopted a fourth framework programme for Community activities in the field of research, technological development and demonstration (RTD) for the period 1994 to 1998 specifying inter alia the activities to be carried out in the field of biomedicine and health; whereas this Decision takes account of the grounds set out in the preamble to that Decision;

Whereas Article 103i (3) of the Treaty stipulates that the framework programme shall be implemented through specific programmes developed within each activity under the framework programme and that each specific programme shall define the detailed rules for its implementation, fix its duration and provide for the means deemed necessary;

Whereas the amount deemed necessary for carrying out this programme is ECU 336 million; whereas the appropriations for each financial year shall be laid down by the budgetary authority, subject to the availability of resources within the financial perspectives and the conditions set out in Article 1 (3) of Decision No 1110/94/EC;

Whereas RTD activities in biomedicine and health should be encouraged in order to improve public health within the Community;

Whereas this programme may make a significant contribution to the stimulation of growth, to the strengthening of competitiveness and to the development of employment in the Community, as indicated in the White Paper on 'Growth, competitiveness and employment';

Whereas the content of the fourth framework programme for Community RTD activities was established in accordance with the subsidiarity principle; whereas this specific programme specifies the content of the activities to be carried out in accordance with this principle in the field of biomedical and health reserach;

Whereas Decision No 1110/94/EC lays down that a Community action is justified if, *inter alia*, research contributes to the strengthening of the economic and social cohesion of the Community and the promotion of its overall harmonious development, while being consistent with the pursuit of scientific and technical quality; whereas this programme is intended to help meet these objectives;

Whereas the Community should only support RTD activities of high quality;

Whereas basic research in biomedicine must be encouraged to reinforce the scientific and technological bases of European health undertakings and to promote medical advances with the aim of improving the health of the European citizen;

Whereas the rules for the participation of undertakings, research centres (including the Joint Research Centre (JRC)) and universities and the rules governing the dissemination of research results specified in the measures provided for in Article 130j of the Treaty apply to this specific programme;

Whereas provision should be made for measures to encourage the involvement of small and medium-sized enterprises (SMEs) in this programme, in particular through technology stimulation measures;

Whereas the Commission's efforts to simplify and accelerate the application and selection procedures and make them more transparent must be continued in order to promote the implementation of the programme and to

(1) OJ No C 228, 17. 8. 1994, p. 119.
(2) OJ No C 341, 5. 12. 1994.
(3) Opinion delivered on 14 September 1994 (not yet published in the Official Journal).
(4) OJ No L 126, 18. 5. 1994, p. 1.

facilitate the action which undertakings, and particularly SMEs, research centres and universities have to undertake in order to participate in a Comunity RTD activity;

Whereas this programme will help to strengthen synergy between the RTD activities carried out in the field of biomedicine and health by research centres, universities and undertakings, in particular SMEs, in the Member States and between these and the corresponding Community RTD activities;

Whereas it may be appropriate to engage in international cooperation activities with international organizations and third countries for the purpose of implementing this programme;

Whereas this programme should also comprise support activities and activities for the dissemination and exploitation of RTD results, in particular towards SMEs, notably those in the Member States or regions which participate least in the programme, and activities to stimulate the mobility and training of researchers within this programme to the extent necessary for proper implementation of the programme;

Whereas an analysis should be made of possible socio-economic consequences and technological risks associated with the programme;

Whereas progress with this programme should be continuously and systematically monitored with a view to adapting it, where appropriate, to scientific and technological developments in this area; whereas in due course there should be an independent evaluation of progress with the programme so as to provide all the background information needed in order to determine the objectives of the fifth RTD framework programme; whereas at the end of this programme there should be a final evaluation of the results obtained compared with the objectives set out in this Decision;

Whereas the JRC may participate in indirect actions covered by this programme;

Whereas the Scientific and Technical Research Committe (Crest) has been consulted,

HAS ADOPTED THIS DECISION:

Article 1

A specific programme of research and technological development, including demonstration, in the field of biomedicine and health as set out in Annex I, is hereby adopted for the period from the date of adoption of this Decision to 31 December 1998.

Article 2

1. The amount deemed necessary for carrying out the programme is ECU 336 million, including a maximum of 8,5 % for staff and administrative expenditure.

2. An indicative breakdown of this amount is given in Annex II.

3. The budgetary authority shall lay down the appropriations for each financial year, subject to the availability of resources within the financial perspectives and in accordance with the conditions set out in Article 1 (3) of Decision No 1110/94/EC, taking into account the principles of sound management referred to in Article 2 of the Financial Regulation applicable to the general budget of the European Communities.

Article 3

1. The general rules for the Community's financial contribution are laid down in Annex IV to Decision No 1110/94/EC.

2. The rules for the participation of undertakings, research centres and universities and for the dissemination of results are specified in the measures envisaged in Article 130j of the Treaty.

3. Annex III sets out the specific rules for implementing this programme, supplementary to those referred to in paragraphs 1 and. 2.

Article 4

1. In order to help ensure, *inter alia*, the cost-effective implementation of this programme, the Commission shall continually and systematically monitor, with appropriate assistance from independent, external experts, progress within the programme in relation to the objectives set out in Annex I, as amplified in the work programme. It shall in particular examine whether the objectives, priorities and financial resources are still appropriate to the changing situation. It shall, if necessary, in the light of the results of this monitoring process, submit proposals to adapt or supplement this programme.

2. In order to contribute towards the evaluation of Community activities, as required by Article 4 (2) of Decision No 1110/94/EC and in compliance with the timetable laid down in that paragraph, the Commission shall have an external assessment conducted by independent qualified experts of the activities carried out within the areas covered by this programme and their management during the five years preceding this assessment.

3. At the end of this programme, the Commission shall have an independent final evaluation carried out of the results achieved compared with the objectives set out in Annex III to Decision No 1110/94/EC and Annex I to this Decision. The final evaluation report shall be forwarded to the European Parliament, the Council and the Economic and Social Committee.

Article 5

1. A work programme shall be drawn up by the Commission in accordance with the objectives set out in Annex I and the indicative financial breakdown set out in Annex II, and shall be updated where appropriate. It shall set out in detail:

— the scientific and technological objectives and research tasks,

— the implementation schedule, including dates for calls for proposals,

— the proposed financial and managerial arrangements, including specific modalities for implementing technology stimulation measures for SMEs and other measures, including preparatory, accompanying and support measures,

— arrangements for coordination with other RTD activities carried out in this area, in particular under other specific programmes, and for ensuring appropriate interactions with other Community activities, such as in the field of public health and with the European Medicines Evaluation Agency (EMEA), as well as with activities carried out in other frameworks, such as Eureka and COST,

— arrangements for the dissemination, protection and exploitation of the results of RTD activities carried out under the programme.

2. The Commission shall issue calls for proposals for projects on the basis of the work programme.

Article 6

1. The Commission shall be responsible for the implementation of the programme.

2. In the cases provided for in Article 7 (1), the Commission shall be assisted by a committe composed of representatives of the Member States and chaired by the representative of the Commission.

3. The representative of the Commission shall submit to the committee a draft of the measures to be taken. The committee shall deliver its opinion on the draft within a time limit which the chairman may lay down according to the urgency of the matter. The opinion shall be delivered by the majoritiy laid down in Article 148 (2) of the Treaty in the case of decisions which the Council is required to adopt on a proposal from the Commission. The votes of the representatives of the Member States within the committee shall be weighted in the manner set out in that Article. The chairman shall not vote.

4. The Commission shall adopt the measures envisaged when they are in accordance with the opinion of the committee.

5. If the measures envisaged are not in accordance with the opinion of the committee, or if no opinion is delivered, the Commission shall, without delay, submit to the Council a proposal relating to the measures to be taken. The Council shall act by a qualified majority.

6. If, on the expiry of a period of three months from referral of the matter to the Council, the Council has not acted, the proposed measures shall be adopted by the Commission.

Article 7

1. The procedure laid down in Article 6 (2) to 6 (6) shall apply to:

— the preparation and updating of the work programme referred to in Article 5 (1),

— the content of the calls for proposals and establishment of criteria and mechanisms for project approval and selection,

— the assesment of the RTD activities proposed for Community funding and the estimated amount of the Community contribution for each activity where this is equal to or more than ECU 0,2 million,

— any adjustment to the indicative breakdown of the amount as set out in Annex II,

— specific modalities for the financial participation of the Community in the different activities envisaged,

— the measures and terms of reference for programme evaluation,

— any departure from the rules set out in Annex III,

— participation in any project by legal entities from third countries and international organizations.

2. Where, pursuant to the third indent of paragraph 1, the amount of the Community contribution is less than ECU 0,2 million, the Commission shall inform the committee of the activities and of the outcome of their assessment.

3. The Commission shall regularly inform the committee of progress with the implementation of the programme as a whole.

Article 8

Participation in the following programme areas: brain research; research on diseases with major socio-economic impact; human genome research; public health research, including health services research; and research on biomedical ethics may be open on a project-by-project basis, without financial support from the Community, to legal entities established in third countries, where such participation contributes effectively to the implementation of the programme taking into account the principle of mutual benefit.

Article 9

This Decision is addressed to the Member States.

Done at Brussels, 15 December 1994.

For the Council

The President

A. MERKEL

ANNEX I

SCIENTIFIC AND TECHNOLOGICAL OBJECTIVES AND CONTENT

This specific programme fully reflects the orientations of the fourth framework programme, in applying the selection criteria and in specifying its scientific and technological objectives.

Paragraph 4.B of Annex III, first activity of the above-mentioned framework programme, is an integral part of this programme.

This programme will be implemented in synergy with other specific programmes in the field of life sciences and technologies, as well as in such fields as telematics, measurement and testing, and targeted socio-economic research.

Background

Health is of the highest value for every European citizen and the competence of the Community has been extended recently by Articles 129 and 130f of the Treaty so as to include public health research. Health care is a first economic sector absorbing 7,25 % of the GDP and creating work for more than six million people or 7 % of the active population. There are more than one million qualified nurses, 850 000 medical doctors, 250 000 pharmacists, three million hospital beds and 0,8 % of the population per day is in a hospital bed.

Research is essential to any strategy to protect the health of the citizens, to fight diseases and to support health industries. It is important to target the research towards projects of interest to the Community and consumers, and promote the transfer of research to clinical practice.

The challenge for health research is to combat the great scourges such as cancer, AIDS, cardio-vascular diseases, allergic disorders, neuro-mental diseases and problems linked with age and handicaps. Rising health care costs have become a concern for all EC countries, while the European citizen is demanding more and more high-quality health care. New health technologies and health care systems are expected to face these common problems. The development of new medicines has become more and more expensive in both time and money, mainly due to the need to satisfy increasingly complex regulatory requirements which need to be streamlined within an international context.

Certain fundamental health problems are in the domain of the health industry the competitivity of which must be safeguarded and improved. Rather than adding a supplement to substantial investments already made by the Member States and European industry, the Community research will bring added value by an integration action, by synergy of national efforts and by interaction of all disciplines from basic to clinical research towards problem-solving activities.

Measures intended to encourage participation of SMEs will be implemented, in particular technology stimulation measures and interaction between science parks and biomedical and health SMEs, taking account of the needs of those from less-advanced regions, as recommended by the White Paper on Growth, competitiveness, and employment.

With the launching of the biomedical and health research programme Biomed 1 within the third framework programme, more than 6 000 research teams are collaborating within 400 networks designed to encourage cooperation between teams from all EC and EEA countries and between complementary disciplines, with a view to tackling health-related problems not readily solved in a narrower context.

Within the fourth framework programme it is intended to go beyond concertation only and to participate in cost-sharing research where indicated only for specific task-oriented research. There are numerous priorities to establish taking into account the large variations in national health systems, research structures, health industries, clinical practices and therapeutic procedures. Only those proposals with a sound scientific

concept, a high likelihood of success, a clear Community added value and contributing to the health and wealth of the European citizen will be selected.

No support will be provided to projects which may contravene elementary principles of the European Convention on Human Rights, the Charter of the United Nations and the future Bioethics Convention of the Council of Europe, subject to its adoption.

RTD activities proposed

The programme should be focused on priorities but should avoid rigidity and retain some flexibility for the following reasons:

1. New challenging health problems may arise which demand a rapid research response.

2. New scientific opportunities may arise which offer interesting research possibilities which will lead to health benefits for the population of the Community, but which do not coincide exactly with the research priorities of the scientific and technical content.

I. SPECIFIC RESEARCH AREAS

1. ***Pharmaceuticals research***

The general objective is the development of the scientific and technical bases required for the evaluation of new drugs, notably for the treatment of neurological, mental, immunological and viral diseases. These actions should also underpin the activities of the European Medicines Evaluation Agency and provide it, at the international level, with the research-based background necessary to achieve harmonization of technical requirements for drug development. Research will be conducted through collaboration between industry, research centres, hospitals, universities, and the authorities responsible for verifying the efficacy, safety and quality of new drugs, while respecting the ethical, social and legal aspects of medical research.

The contribution of functional imaging to neuropharmacology research will also be explored.

Research will be conducted in particular in the following areas:

— Pharmacotoxicology: prevalidation research of *in vitro* alternative methods, possibly using human cells and tissues, and where unavoidable animal models, in the general aim of reducing, refining and replacing animal experimentation, progressively and each time it is scientifically possible, also making use of mathematical modelling systems. Preference will be given to those tests which have reached the most advanced stages towards validation as those developed within the Biotechnology programme. Prevalidation research on these tests should ideally provide the European Centre for the Validation of Alternative Methods with the best candidates for proper validation studies.

— Pharmacovigilance: development of systems for high performance surveillance networks for early detection of possible undesired effects of new drugs, in accord with the existing regulatory framework and with particular attention to the international harmonization efforts. It will include research on the exposure of patients to drugs, into harmonization of diagnostic terms and criteria, approaches to assess adverse drug reactions signals, use of health statistics for pharmaco-epidemiology, transnational case-control studies, transnational registers and cohort studies.

— Clinical Trials: to support intra-european collaboration in large, randomized clinical trials of high scientific quality, in order to stimulate better opportunities for improved diagnostic procedures, for therapies treatments as well as for their pharmaco-economic aspects.

The development of European multicentre clinical trials networks of high scientific standard would help an objective evaluation of new diagnostics or therapeutics in a shorter time while preserving its scientific value; modelling systems should also be taken as a basis.

Research in this field will be mainly directed towards the establishment of clinical trials registries, research into meta-analysis methodologies and randomized clinical trials for rare diseases, including a depository of orphan drugs available for clinical research at European level.

2. *Research on biomedical technology and engineering*

Health technology assessment and prenormative research become more important in a European-wide market with its directives concerning medical devices and accompanying standardization activities. For industry as well as for decision-makers at all levels, it is essential to have in addition to requirements for safety, timely access to objective information on efficacy and efficiency of medical devices, before introducing these on the health market.

Research and development will be conducted in particular in the following areas:

— Minimal intervention techniques and robotics: robotics, three-dimension imaging, micro structure technology and 'nanotechnology' to support surgical therapy, and widen the range of clinical indications for minimal medical interventions; new ergonomic approaches of the operating theatre for minimally invasive surgery.

— Imaging techniques: magnetic resonance, ultrasound, biomagnetism, positron emission tomography, etc., as well as microwave imaging and fluorescence and near infra-red spectroscopy and imaging; comparative and integrated evaluation of different biomedical imaging technologies.

— Research on biosensors, especially with regard to their clinical value, as among others is the case of glucose monitoring for diabetes, oxygen monitoring and ion sensing for critcal care.

— Meeting the needs of the increasing population of elderly and handicapped persons calls for more research on rehabilitation technology in coordination with the relevant parts in the Telematics programme. The powerful trend towards replacement in medicine requires more research on biomaterials, especially towards improved mechanical properties and biocompatibility of polymers, as well as on artificial organs, such as on artificial heart and artificial pancreas. Research aiming at the modelling of human functions, as well as in biomechanics, haemodynamics and biorheology, is also required in that respect.

— Cellular engineering: synergistic benefits would accrue by combining cell and molecular bilogy with chemical, mechanical and electrical engineering, opening new possibilities for clinical applications.

3. *Brain research*

The high prevalence of mental illnesses and the increasing incidence of neurodegenerative diseases represent an immense economic and social burden in the Member States:

The new opportunities created by molecular biology and genetics, novel instrumentation and information technology will contribute to major advances in neurosciences and improvement in prevention and treatmant. Research which integrates fundamental aspects with clinical applications and industrial development will be encouraged.

In the field of neurosciences, participation in the decade of brain research will be promoted, in particular in the following areas:

— Research on the physiopathology and basic mechanisms leading to nervous system diseases which should integrate molecular, cellular and clinical approaches with the aim to promote appropriate and effective treatment of neural diseases.

— Research on central nervous system damage, regeneration and plasticity, development of therapeutic strategies for damage limitation, re-growth promotion and repair.

— Transdisciplinary research on the understanding of the genetic and immunological basis of nervous system diseases, in close cooperation with activities under human genome analysis and biotechnology programmes.

— Establishment of cell cultures and where necessary animal models of the human diseases of the brain for pathogenicity and development of therapeutic agents.

— Contribute to the development of better methods of brain imaging which combined with computer science will allow a better understanding of brain structures, functions and metabolisms, to map the distribution of proteins and other structures throughout the brain and to characterize the anatomical structures and psychological mechanisms interacting with cognitive function and dysfunction.

This approach will integrate the contribution of several disciplines, together with biomedical engineering, and bring together the most advanced technologies and infrastructures scattered over Europe.

— Clinical research, mainly focused on clinical trials, treatment of neurological, neurosensory and psychiatric diseases, prognosis and progression of these diseases and the impact of therapeutic practices.

— Research into the mechanisms of pain including the development of new therapies and the conduction of clinical trials to evaluate the effectiveness of currently available therapies.

— Research on addiction behaviour which should integrate basic and clinical approaches, with the general aim of reducing drug demand.

— Development of combined epidemiologic and long-term prevention programmes to evaluate the impact of neurological and psychiatric diseases and the benefits of their treatment also in small groups and high risk groups.

— Research on cognitive sciences including development of models of neuronal behaviour, learning, memory and psycholinguistics.

4. ***Research on diseases with major socio-economic impact: from basic research into clinical practice***

From all horizontal activities such as molecular biology, physiology, genetics, statistics, epidemiology and generic technologies, the ultimate yardstick for the European citizen is the benefit for him as an individual. The population expects basic answers by integration of basic and clinical research to improve the prevention, diagnosis and treatment of these illnesses with major socio-economic impact and the around 5 000 'orphan' illnesses which can be tackled optimally at an international level.

4.1. *Cancer research*

Improvements in cancer diagnosis, therapy and prevention require integrated fundamental and clinical approaches to research. It is particularly important to bring new advances in cellular, molecular and developmental genetics into contact with oncology and epidemiology, in order that new biological insights into the underlying causes of cancer allow for the development of novel approaches. The study of host-tumour interaction in the context of immune response and of somatic gene therapy targeted at cancer cells are fundamental together with epidemiological studies for investigating possible causative factors in carcinogenesis. In the area of research into genetic factors that cause susceptibility to cancer, priority should be given to projects relating to therapeutic approaches.

Research will be conducted in particular in the following areas:

— Molecular mechanisms of tumorigenesis and metastasis, including characterization of the genes and proteins responsible. Together with human genome research, genetic factors of cancer predisposition.

— The control of normal cellular growth, differentiation and death, and abnormalities which can alter this to predispose to cancer, inlcuding the development of accurate cellular and transgenic models suitable for cancer research.

— Specific anti-tumour immune responses and possibilities for early detection, including making use of biological techniques and progress in medical imaging and curative intervention.

— Research to support the effectiveness of systemic treatment modalities including cytotoxic agents as well as biological response modifiers.

— Research to improve the therapeutic ratio of radiotherapy as well in the domain of ballistic selectivity, as in the manipulation of radiation response in tumours and normal tissues.

— Quality of life as a parameter for treatment assessment including terminal care and rehabilitation, while respecting individual freedom of choice and the ethical rules seeking to protect human dignity at the end of life and to ensure that pain is treated at a sufficiently early stage in incurable diseases.

— Research into the causal relationships between environmental factors and the development of cancer.

4.2. *Research on AIDS, tuberculosis and other infectious diseases*

Many advances have been made in AIDS research in recent years. The concertation of AIDS research at European Community level has contributed to this progress, but a decisive breakthrough has yet to be made. There is neither a vaccine nor a drug capable of curing the disease. The number of seropositive people continues to show an increase. The immunosuppression caused by HIV in infected people provides an opportunity for the occurrence of old diseases, already drug resistant in some areas, and for opportunistic cancers.

Research will be conducted in particular in the following areas, with emphasis on the integration of basic and clinical research:

— Viro-immunological research, the genetics, molecular and structural biology of HIV and its variability.

— Contribution to the development of a safe and effective vaccine against AIDS and the establishment of markers to evaluate vaccine efficiency and to follow up the evolution of disease.

— The identification, synthesis and evaluation of antiviral compounds and drugs against AIDS.

— Clinical research, mainly focused on clinical trials, treatment of AIDS and opportunistic diseases, prognostic and progression of these diseases and the impact of therapeutic practices.

— Studies on the host response, pathogenesis, experimental models and new pathologies such as infectious diseases, including those caused by unidentified infectious agents, prion induced diseases and resistance mechanisms to conventional therapy, including the problem of hospital infections.

— Disease prevention, using epidemiological methods, including the development of new specific monitoring systems to determine the distribution patterns of old and new infectious diseases, analysis of risk factors for the development of AIDS, opportunistic diseases and novel infectious agents.

— Socio-economic and health services research: requirements for caring and prevention, analysis of socio-economic consequences and forecasts in cooperation with public health research.

4.3. *Research on cardiovascular diseases*

In order to accelerate the pace of unravelling the physiopathological mechanisms leading to cardiovascular disease development, in particular arteriosclerosis and hypertensive disorders, and translate these findings into prevention and treatments, multidisciplinary research will be stimulated by combining the expertise of physicians and scientists with different backgrounds in basic and clinical cardiovascular research and in molecular genetics.

In the field of cardiovascular research mainly the following subjects will be addressed:

— Analysis of the cellular and molecular mechanisms leading to diseases of the heart and blood vessels, including research on cardiac and vascular cell growth, injury and repair; cardiovascular-associated inflammation.

— Development of clinically useful agents for injury or excessive growth prevention, damage limitation and repair.

— Research on the understanding of the genetic basis of cardiovascular diseases, in particular those of high prevalence such as atherosclerosis and hypertension, including identification and decoding of genes, research on expression pattern, gene function and modification; where unavoidable, development of animal models and therapeutic strategies.

— Clinical research including assessment, verification and definition of the exact contribution of current basic knowledge in order to understand the onset and development of clinical pathologies; validation of preclinical screening programmes as well as multi-centre clinical trials for testing devices and therapeutic procdures.

— Research on imaging and non- or minimally interventional techniques that will enable studies of the structure, metabolism, and function of the heart and blood vessels.

— Research on combined epidemiologic and long-term prevention programmes including evaluation of possible differences in risk factors, impact of psychosocial factors on incidence and prevalence of cardiovascular diseases and the benefits of their treatment in high risk groups.

4.4. *Research on chronic diseases, ageing and age-related problems*

Because of the demographic evolution in Europe and the enormous social and economic impact of age-related problems in general and chronic diseases, handicaps and dependency in particular, a focus research effort is needed in conjunction with the other parts of the programme.

Research will be conducted in particular in the following areas:

— Etiology, including environmental aspects, and treatment of chronic diseases such as chronic arthritis, diabetes mellitus, respiratory problems (including asthma). Particular attention will be given to auto-immune aspects, immuno-genetics and T-cell disorders.

— Development through a transdisciplinary approach of new rehabilitation methods, new devices (see bioengineering) and appropriate care provisions in order to diminish dependency of the elderly, the handicapped and those with chronic disorders, in conjunction with biomedical technology and engineering part of this programme and with the telematics programme.

— Etiology and pathogenesis of congenital and genetic diseases, including hemoglobinopathies and in particular thalassemia. Evaluation of new protocols and methods of risk estimation, genetic counselling and possible prevention. Evaluation of new therapeutic approaches.

— Study of morbidity and co-morbidity caused by mental, motoric and sensorial handicaps and disabilities as a bridge between basic research and clinical practice, and in conjunction with the brain research part of this programme.

4.5. *Research on occupational and environmental health*

The objectives are to improve the scientific knowledge needed to increase the safety and health protection of workers in order to avoid accidents at the workplace and prevent work-related diseases and to reduce environmental risks for the population.

Research will be conducted in particular in the following areas:

— Identification and control of risk factors at the workplace with an emphasis on biological and chemical hazards in short- and long-term effects.

— Health education and preventive measures to reduce accidents at work and exposure to risk factors.

— The interaction between risk factors at the workplace and in the environment, fundamental research on allergic diseases affecting public health, and the aetiology of occupation and environment related diseases. Connections between occupational and environmental risk factors (e.g. toxic agents) and the aetiology of diseases in general (e.g. cancer).

4.6. *Research on 'Orphan' illnesses*

'Orphan' illnesses are these rare diseases (some 5 000) where no country in itself can afford to spend the necessary resources and case mix to implement basic and clinical research at the low number of cases occurring at national level. Nevertheless at an EC level as well as at a general scientific level these 'exceptional' cases turn out to be quite similar and to offer exceptional experiments by nature to do in-depth research on the basic mechanisms of diseases and handicaps and to offer opportunities to link genetic research with biochemical and physical expression of disease. Examples are inborn metabolic diseases due to defective peroxisomes, etc. Actions will include an inventory of rare disorders and together with the section on pharmaceutical research a depository of orphan drugs for clinical research.

5. ***Human genome research***

The achievements, activities and infra-structure established in preceding programmes have to be consolidated and — where appropriate — to be modified, to serve future needs. Fundamental research, with its emphasis on functional studies in order to ensure that advances in genetics are used to enhance human health, will be supported. Development of appropriate technologies and applications which contribute to the well-being of patients will be stimulated. In particular, attempts will be made to develop somatic gene therapy where the conditions/acceptance in Europe justify a targeted effort, e.g. cystic fibrosis. Research will also be carried out for the development

of new diagnostic techniques for genetic diseases and of new therapies resulting from the most recent progress in molecular genetics and in particular gene analogues or gene expression regulators.

Sharing and harmonization of genetic databanks comprising European Community participation in the management of international databases of the human genome (e.g. GDB) will be promoted. Links will be maintained with appropriate international organizations or forums (e.g. the Human Genome Organization, HUGO).

The confidentiality of any personal information collected in the course of the research must conform to the best data protection practice. No research modifying, or seeking ot modify, the genetic constitution of human beings by alteration of germ cells or of any stage of embryo development which may make these alteration hereditary, will be carried out under this programme.

It has become clear in recent years that, while the possibility of diagnosing diseases with the aid of human genetics is developing rapidly, there is a therapeutic approach in only a few cases. Research should aim to prevent the gap between diagnosis and therapy from widening further.

Assistance provided under this programme should give priority to projects relating to therapeutic approaches.

Research will be conducted in particular in the following areas:

— Gene mapping and genome analysis, including construction of integrated transcriptional maps; sequencing of specific chromosomal regions; exploitation of comparative approaches.

— Analysis of gene regulation, including the improvement of techniques for gene targeting and the development of animal models (e.g. the mouse), if no equivalent alternatives are available.

— Analysis of gene function, including identification of regulatory sequences; analysis of mechanisms of regulation of expression of specific genes, notably those involved in disease.

— Pre- and postnatal diagnosis and understanding of the patho-physiology of genetic disease at DNA-level, including non-genectic factors and development of protocols for risk estimation and for genetic counselling, with an emphasis on possible prevention.

— Somatic gene therapy, including development of vectors to transfer genetic material into cells *in vitro*; development of methods to deliver corrected genes *in vivo* effectively and safely; coordination of clinical trials on somatic gene therapy.

— Databases, including experimental data collection, storage, analysis, and development of integrated genome databases, taking account of the specific measures for the protection of intellectual property.

— Technology development, including promotion of research aiming at the development of methods suitable for the achievement of any one of the abovementioned objectives, while respecting the ethical, social and legal aspects specific to research on the human genome.

6. ***Public health research, including health services research***

More than 110 000 deaths under age 65 from 21 common diseases would be avoided annually, if only each European region could attain the optimal death rates reported nationally for each of those diseases.

Traditions, practices and the legal and administrative organization of public health services and systems are so varied in Member States as to render impractical any harmonization of services in this domain. However, objectives of research should be to assist Member States in strengthening their coverage of public health issues, assist in the formulation and implementation of objectives, policies and strategies, and contribute to continuity of health protection provision across the Community.

Research will be conducted in particular in the following areas:

— Research on methods for evaluating health education and prevention, primary care, assessment of health needs, including the needs of emerging dependency groups, performance measurements of health policy initiatives and the evaluation of health technologies.

— Coordination and comparison of European health data, including nutritional data, from the various Member States of the Community,

— Standardization of methods for outcome measurement of health care.

— The impact of the internal market on supply of health care across internal frontiers; regulations and de-regulations as well as the balance between health systems financed by the private and public sectors.

— Health economics and methods of evaluation of the organization of health systems.

— Research on new health indicators and new techniques of modelling.

— Health technology assessment, including the assessment of the costs, effectiveness and broader impact of all methods used by health professionals to promote health, prevent and treat diseases and improve rehabilitation and long-term care.

— Defining a European approach for the introduction of new technologies in health systems.

7. *Research on biomedical ethics*

Research on biomedical ethics will address general standards for the respect of human dignity and the protection of the individual in the context of biomedical research and its clinical applications. The social impact and the public awareness of the problems associated with biomedical progress will be addressed.

Topics to be considered in particular are:

— Medically assisted procreation, including gender selection, preimplantation and prenatal diagnosis, research on embryo, use of foetal ovarian tissue, post-menopausal pregnancy, sperm and egg donation and their possible conservation.

— Human genome analysis and its clinical applications, including testing, screening and somatotherapy.

— End of life, including palliative care, euthanasia, artificial prolongation of life by advanced medical techniques, resuscitation.

— Resource allocation: ethical and social dimensions of the choices to be made in health budgets and resource allocation.

— Organ and tissue transplantation including the use of human cells, organs, tissues, and xeno-transplant as well as the functioning of tissue and organ banks.

— Patient's consent: imformed consent of the individual for diagnosis, therapy, prevention or research, including the consent of vulnerable populations like e.g. prisoners and cognitively impaired patients.

— Confidentiality and privacy considering medical data, genetic and non-genetic, with an emphasis on the specific problem raised by modern information systems such as computerization with automatic data transfer, including patentability and intellectual property rights in the context of legal protection of biotechnological inventions.

II. HORIZONTAL ACTIVITIES

Research activities on biomedical ethics carried out within biomedical and health research and the activities on the ethical, legal and social aspects carried out by the horizontal unit 'Legal and ethical aspects' will be performed jointly throughout the three life sciences and technologies programmes and activities in other frameworks in order to benefit from interdisciplinary competences.

Measures will be taken to encourage the participation of all partners active in this area (universities, hospitals, research centres, bioethics institutes, patient associations, etc.).

In order to improve dialogue and mutual understanding between the main national, sociopolitical and bioethical positions, whilst recognizing the cultural differences which exist in Member States, working groups will be organized to prepare reports and surveys of interest also to the European Parliament and the Council. Targeted workshops to identify and debate areas of national and international divergences

and, where appropriate, research activities with multidisciplinary approaches to such topics will be carried out. Public awareness activities on new biomedical technologies will also be funded. This horizontal activity takes into account the European Bioethics Convention and its draft Protocols, subject to their adoption.

Wherever possible, experimentation and testing on animals should be replaced by *in vitro* or other methods. No research modifying, or seeking to modify, the genetic constitution of human beings by alteration of germ cells or of any stage of embryo development which may make these alterations hereditary, nor research seeking to replace a nucleus of a cell of an embryo with a nucleus taken from a cell of any person, embryo or subsequent development of an embryo, known as cloning, will be carried out.

Demonstration activities within biomedical and health research will facilitate comparative European multi-centre trials of new drugs, new therapeutic approaches, and ready-for-testing prototypes of new medical devices. Special attention will be given to demonstration of the latest technologies in clinical diagnostics and imaging technologies, implantable sensors for the monitoring or rehabilitation of pathological conditions, artificial organs, biocompatible materials, new cancer therapies and irradiation technologies. A bottom-up approach will be used, in cooperation with other Life Sciences programmes, to identify the best opportunities for pre-competitive demonstration, in order to prove the technical viability of these new technologies, together with, as appropriate, their economic advantage at a pre-competitive level. The early involvement of hospitals and clinicians in these demonstrations will allow for an efficient dissemination of knowledge and a quick realization of the benefits to be derived from the adoption into practice of such innovative approaches, drugs and devices. While keeping as a first priority the benefits for patients, demonstrations in these areas will take into account the specific needs of the biomedical engineering and pharmaceutical industries and health care delivery organizations, and will be implemented by partnerships involving these manufacturing industries, the health profession, the health-care providers and health authorities.

ANNEX II

INDICATIVE BREAKDOWN OF THE AMOUNT DEEMED NECESSARY

Area	ECU million
1. Pharmaceuticals research	37
2. Research on biomedical technology and engineering	37
3. Brain research	40,5
4. Research on diseases with major socio-economic impact: from basic research into clinical practice	141
4.1. Cancer research	*33,5*
4.2. Research on AIDS, tuberculosis and other infectious diseases	*27*
4.3. Research on cardiovascular diseases	*27*
4.4. Research on chronic diseases, ageing and age-related problems	*33,5*
4.5. Research on occupational and environmental health	*13,5*
4.6. Research on 'orphan' illnesses	*6,5*
5. Human genome research	40,5
6. Public health research, including health services research	33,5
7. Research on biomedical ethics	6,5
Total	336 (1) (2)

(1) Of which:
— a maximum of 3,5 % for expenditure on staff and 5 % for administrative expenditure,
— ECU 3 million for the dissemination and optimization of results.

(2) Up to 5 % of the funds will be allocated to horizontal demonstration activities; up to 1 % of the funds will be allocated to horizontal activities on ethical, social and legal aspects; up to 5 % of the funds will be allocated to horizontal training activities. These funds also include the necessary support for specific measures in respect of SMEs.

This breakdown does not exclude the possibility that a project could relate to several areas.

ANNEX III

SPECIFIC RULES FOR IMPLEMENTING THE PROGRAMME

The programme will be executed through indirect action, whereby the Community makes a financial contribution to RTD activities carried out by third parties or by JRC institutes in association with third parties:

1. Shard-cost actions of the following types:

   (a) RTD projects (including demonstration projects) carried out by undertakings, research centres and universities, including, where appropriate, basic research of an industrial relevance.

   Demonstration activities, as defined in Annex III of the framework programme, are intended to overcome the obstacles hindering the utilization of new technologies and to build the bridge between technology producers and users. Feasibility studies and awards to those who get involved in these technologies may also be included.

   Community funding will normally not exceed 50 % of the cost of the project, with progressively lower participation the nearer the project is to the market place. Those universities and other institutions which do not have analytical budget accountancy will be reimbursed on the basis of 100 % of the additional costs.

   (b) Technology stimulation to encourage and facilitate participation of SMEs in RTD activities

   (i) by granting awards for carrying out the exploratory phase of an RTD activity, including the search for partners, during a period of up to 12 months. The award will be granted following the selection of an outline proposal to be submitted normally by at least two non-affiliated SMEs from two different Member States. The award will cover up to 75 % of the cost of the exploratory phase, without exceeding ECU 45 000 or ECU 22 500 in the exceptional case of a single applicant SME, and

   (ii) by supporting cooperative research projects, whereby SMEs having similar technical problems but not having adequate own research facilities, engage other legal entities to carry out RTD on their behalf. Community funding for cooperative research projects, involving normally at least four non-affiliated SME's from at least two different Member States, will normally cover 50 % of the cost of the research.

   Following an initial call, in both cases proposals may be submitted at any time during the period covered by the work programme being implemented.

2. Measures appropriate to this specific programme:

   — measures in support of standardization,

   — measures intended to set up general service tools for research centres, universities and undertakings,

   — support of financing infrastructures or facilities necessary for the performance of a coordination action (reinforced coordination activity).

   Community funding may cover up to 100 % of the costs of these measures.

3. Preparatory, accompanying and support measures, such as:

   — studies in support of this programme and in preparation for future activities,

   — support for exchanges of information, conferences, seminars, workshops or other scientific or technical meetings, including intersectoral or multidisciplinary coordination meetings,

   — use of external expertise, including access to scientific databases,

   — scientific publications and activities for the dissemination, promotion and exploitation of results, in coordination with the activities carried out under the third activity; the factors liable to encurage use of results will be taken into account from the outset and throughout the duration of RTD projects, the partners in which will constitute a key network for diffusion and exploitation of results,

— analysis of possible socio-economic consequences and technological risks associated with the programme, which will also contribute to the programme 'targeted socio-economic research',

— training actions related to research covered by this programme in order to enhance employment skills and to facilitate technology transfer to industry,

— independent evaluation of the management and execution of the proramme and of the implementation of the activities,

— measures in support of the operation of networks for increasing awareness and providing decentralized assistance to SMEs, in coordination with the Euromanagement auditing activity of RTD.

Community funding may cover up to 100 % of the costs of these measures.

4. Concerted actions, consisting of the coordination, in particular through concertation networks, of RTD projects funded by public authorities or private bodies. The Member States will help the Commission to identify relevant laboratories or institutes, in order to ensure that no major activities are left out of this concertation process.

Concerted actions may also serve as the necessary coordination for the operation of common interest groups which, through shared-cost RTD projects, bring together, around the same technological or industrial objective, manufacturers, network operators, service providers, users, universities and research centres.

The concerted action option can also be used under the programme as a way of establishing the feasibility and defining the content of proposals for shared-cost research activities.

Community funding will cover up to 100 % of the costs of the concertation.

5. Participation in this programme of international organizations may be financed, in exceptional cases, on the same basis as that of legal entities established in the Communtiy.