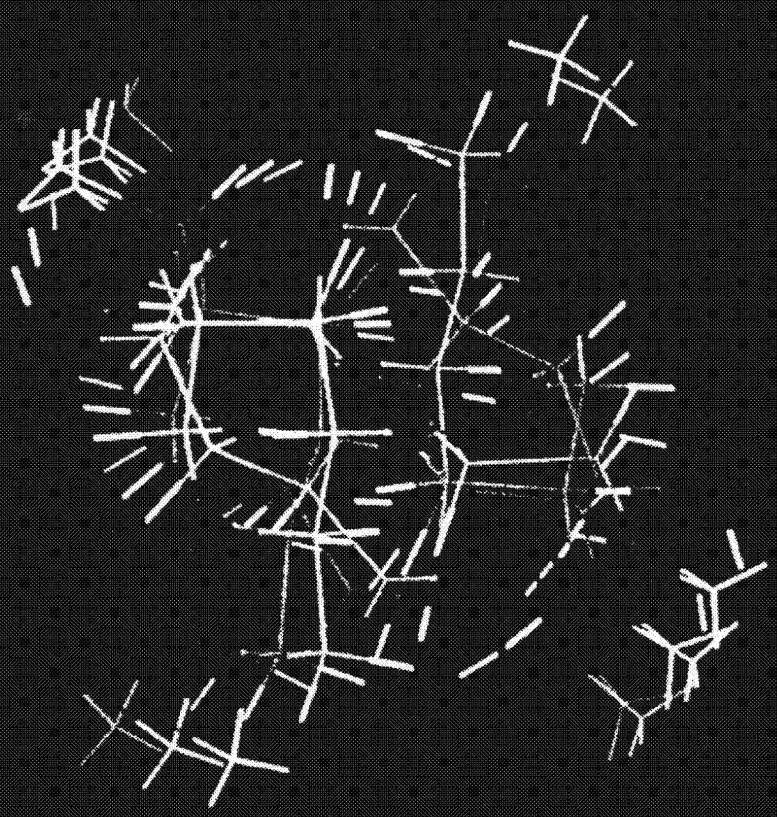
NIBSC

National Institute for Biological Standards and Control

Corporate Plan 1995-2000



A WHO INTERNATIONAL LABORATORY FOR BIOLOGICAL STANDARDS

NIBSC

National Institute for Biological Standards and Control

Corporate Plan 1995-2000

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Front cover illustration:
A computer generated molecular model of heparin

Preface

The National Institute for Biological Standards and Control (NIBSC) is managed by the National Biological Standards Board (NBSB – The Board). NBSB operates as a Non-Departmental Public Body of the UK Department of Health and was established as a body corporate by the Biological Standards Act 1975. The Board's functions are set out in Statutory Instrument (1976) No. 917 (The NBSB [Functions] Order). The Board fulfils these functions through its management of NIBSC.

This Corporate Plan sets out the Institute's aims, functions and strategy. NIBSC's work is set in the context of public health and the Institute's role as a national resource with the capability to respond to major public health issues is outlined. The Plan also indicates the criteria used in the selection of project and programme priorities, and gives a projection of the expected priorities over the next 5 years. Finally, the Plan outlines key features of programme implementation, including the Institute's multidisciplinary structure and approach, resource allocation, the development of quality systems and income generation.

1 Purpose and Functions

1.1 PURPOSE

The purpose of NIBSC is to safeguard and enhance public health through the standardisation and control of biologicals used in medicine.

NIBSC's multidisciplinary approach and depth of scientific expertise place it in a unique position within the UK to fulfil this purpose.

1.2 THE NATURE OF BIOLOGICALS

Biologicals are substances used in the prevention, treatment or diagnosis of human disease that cannot be adequately defined using chemical analysis alone, and thus require biological testing for their characterisation and quality assurance. In general, biologicals are derived from cells or animal tissues and are (in molecular terms) highly complex. They require special quality control procedures because of the biological nature (and intrinsic variability) of the starting materials and of manufacturing procedures. Some of the most complex biological medicines are living entities, such as the bacteria and viruses used as live attenuated vaccines. Many biological medicines are now prepared by recombinant DNA technology.

Because biological substances cannot be characterised chemically, their biological activity and thus potency has to be measured against that of a known standard of the same substance. The preparation and use of Biological Standards is fundamental to NIBSC's work. Well-characterised preparations of biological substances are used as actual physical standards against which to compare the properties of manufactured products. The authoritative, global reference materials for the majority of biological medicines are the International Standards produced at NIBSC on behalf of the World Health Organization (WHO).

1.3 FUNCTIONS

NIBSC has the following functions:

- **To control the purity and potency, and by implication the associated safety and efficacy, of biological substances used in preventative, therapeutic and diagnosis medicine and marketed or produced in the UK and other EU Member States by advising licensing authorities on scientific aspects of the licensing process and on the results of control tests.**
- **To prepare, test and make available nationally and internationally biological standards appropriate for the development and testing of biologicals used in medicine, by operating as a World Health Organization (WHO) International Laboratory for Biological Standardisation.**
- **To assist the efficiency and effectiveness of the licensing and control process, and to improve the quality of medicines available, by advising the pharmaceutical industry on the development, standardisation and quality control of biologicals.**
- **To develop strategies for the standardisation and control of novel medicinal substances, such as those derived from recombinant DNA technology and other new biological methodologies.**
- **To develop improved techniques for standardisation and control through an active programme of research and development.**
- **To provide scientific advice of the highest quality to the Department of Health and its associated bodies on all issues relating to biologicals used in medicine.**
- **To maintain the scientific/technical standards of control of biologicals available in the UK in the context of European licensing and control systems, by advising on specifications for manufacture and testing.**
- **To stimulate the exchange of information on the standardisation and control of biologicals used in medicine within the UK, and internationally through the WHO and other organisations including the European Commission, European Pharmacopoeia and the International Association for Biological Standardisation and other professional bodies.**

2 NIBSC Strategy

2.1 PUBLIC HEALTH

NIBSC safeguards and enhances public health by contributing to:

- The reduced incidence of communicable diseases by assuring the quality of preventative vaccines;
- The safety of immunisation programmes for healthy adults and children (incl. reducing the incidence of adverse drug reactions);
- The safety and quality of products derived from human blood;
- Improvements in the design of biological medicines by characterising changes in the organisms causing disease;
- Improvements in rates of recovery from illness;
- Improved and reliable diagnosis of disease;
- The safety of medicines used in long-term replacement therapy.

Certain biologicals are living entities and require special control procedures. For example, a single defective batch of a vaccine can have very serious public health consequences, both directly for individual recipients and potentially for their contacts, and for the effectiveness of, and public confidence in, immunisation programmes in general.

2.2 STRATEGY STATEMENT

NIBSC's strategy is to measure, characterise and understand biologicals used in medicine, so that their safety and efficacy can be effectively tested and biological standards developed and made available to key users.

2.3 STRATEGIC AIMS

Within the Functions outlined above, NIBSC has the following strategic AIMS:

- **To respond to and advise on public health problems involving biologicals;**
- **To provide a national scientific capacity in the field of biological medicine, and to maintain the flexibility, expertise and facilities needed to address new developments in science and medicine;**
- **To continue to operate, and be recognised, as a leading international authority on methods of assay such as those to quantify biological activity and characterisation of biologicals;**
- **To maintain a central role in the development of the scientific basis for control and standardisation of biologicals within Europe;**
- **To reduce, refine and/or replace animal testing where possible and appropriate;**
- **To achieve and maintain Quality Accreditation in key areas of control and standardisation.**

2.4 RESPONDING TO PUBLIC HEALTH REQUIREMENTS

NIBSC's Functions require the Institute to provide specialist advice and support in the event of public health threats and concerns, and to provide for customer needs in a number of areas. Where the demand for NIBSC activities and services exceeds its capacity to respond in a particular area, then the Institute makes choices by prioritising projects according to the criteria summarised in Section 2.6 below.

In its control activities, NIBSC supports and advises the appropriate licensing authorities, in particular the UK's Medicines Control Agency (MCA) and the European Medicines Evaluation Agency (EMEA). As a designated European Testing Laboratory, NIBSC carries out control work on behalf of the licensing authorities of other EU States. The Institute also advises the UK Department of Health on the control and standardisation of vaccines used in national immunisation programmes and in other areas of biological medicine not currently covered by the licensing procedures. By contributing to the development of testing procedures in the EU, NIBSC seeks to ensure that rigorously high standards are adopted in the interests of UK public health.

In the UK the Institute addresses the priority requirements of the National Health Service and the National Blood Authority and develops, processes and distributes British Standards.

Most of NIBSC's research and development work is targeted at the development of new techniques of control and standardisation. However, in specific areas, NIBSC addresses other areas of need as in relation to work on HIV and AIDS that is funded by the Department of Health and the UK's Medical Research Council. It is also NIBSC's strategy to carry out collaborative research and development projects that may be funded by external grant donors, such as the EC, the Medical Research Council, the Home Office, the Department of Trade and Industry, the WHO and others.

In its biological standardisation work, NIBSC develops, processes and distributes

International Standards identified as high priorities by the World Health Organisation (WHO).

2.5 MAINTAINING A CAPABILITY TO RESPOND

NIBSC aims to maintain a strong national capability for the standardisation and control of biologicals to enable it to provide scientific advice and services of the highest quality to the Department of Health and associated bodies. In so doing, it is part of its strategy to continue to be recognised as a leading authority in the field of biological medicines and biotechnology. This is effected through a range of international activities, including the provision of International Biological Standards, the co-ordination of quality assurance schemes and the stimulation of exchange of information relating to the standardisation and control of biologicals. NIBSC staff are also active and leading participants in international scientific meetings and on advisory bodies and committees, and make major scientific contributions through publications in leading scientific journals.

NIBSC's approach to research and development is to ensure that it has the capacity in future to deal with the control and standardisation of emerging new groups of biological products. In order to build future scientific capacity, it is part of NIBSC's strategy to collaborate closely with the pharmaceutical industry and other scientific groups, in order to keep abreast of all major scientific developments and to be able to anticipate the development of future biological products. In particular, we aim to develop and maintain leading expertise in the use of new techniques of molecular biology.

2.6 DEVELOPING PROGRAMME PRIORITIES

2.6.1 Criteria for Selection of Projects

NIBSC has developed a number of specific criteria which govern the selection of individual projects at the Institute. These criteria enable the Institute to prioritise activities to ensure the most effective and efficient use of resources and to ensure that the Institute's work is focused and targeted to the areas of greatest need.

In planning NIBSC's programme of work, Programme Areas and projects are prioritised using the following criteria:

- **Extent of actual/likely demand:** *Ratings against this criterion relate to both the existing and the potential demand for Control (e.g. batch testing and/or product monitoring), Standardisation (e.g. International Standards) and associated Development (e.g. need for new assays or techniques). This criterion is treated separately from those relating to the actual or potential medical importance of a group of products.*
- **Medical importance of products:** *Ratings relate to the existing or potential medical importance of the products covered or of the Programme Area in general. This is as distinct from the demand or market share of products, and as much as possible is treated separately from the specific public health risks that NIBSC's work seeks to avoid. It relates principally to the extent (incl. numbers of people affected) and severity of the illnesses to which the Programme Area or project refers.*
- **Extent of public health risks avoided:** *Ratings against this criterion reflect the extent of threats and risks to public health that are, or are likely to be, avoided by NIBSC's work in this area. Ratings relate to the nature of specific risks (e.g. viral contamination, adverse toxicity, neurovirulence, potency outside specifications) and the extent of the community (UK, EU, World) potentially affected.*
- **Special advantage of NIBSC:** *Ratings relate to the 'uniqueness' of NIBSC's role in this area and/or of the special facilities and expertise available at NIBSC. The highest rating may indicate that no other organisation is in a position to carry out this work as a result of the experience/expertise/mandate required for it.*

Similar criteria are also used to select those biologicals for which standards and reference reagents should be developed.

2.6.2 Health of the Nation

NIBSC's programme priorities contribute directly to the national health priorities and targets specified in the UK Government document 'The Health of the Nation'. The process of priority setting at NIBSC is informed by the knowledge and clear understanding of the public health implications of each area of work under consideration.

NIBSC's work supports two of the Target Areas specified in 'The Health of the Nation' as follows:

Action to Promote Health and Prevent Illness: NIBSC's work on the control and standardisation of viral and bacterial vaccines

is vital in maintaining the effectiveness and acceptability of national immunisation programmes.

Improved Diagnosis, Treatment and Rehabilitation: NIBSC's work on assuring the quality of hormones, immunologicals and blood products gives valuable support to this Target Area.

NIBSC also contributes directly to two of the five Key Areas identified in 'The Health of the Nation':

Coronary Heart Disease and Strokes – NIBSC's programme on thrombolytics and anti-thrombotics assures the quality of biological medicines used in this field.

HIV/AIDS and Sexual Health – NIBSC's work on HIV and AIDS, which is supported in part by the Department of Health, contributes to the safety of blood products and the development of vaccines against HIV and AIDS and the establishment of scientific principles for the standardisation and control of future products.

2.6.3 Research for Health

The research and development work carried out at NIBSC contributes to the Department of Health's research and development strategy outlined in the Department's document 'Research for Health'. This document highlights eight priority Themes of research, and NIBSC's work contributes principally to two of these:

Preventing Illness and Promoting Health – NIBSC's research and development work on immunisation and vaccination supports this area. Research and development is aimed primarily at the effective control and standardisation of biological medicines, and includes work on e.g. ensuring stability of vaccine products and effectiveness at the point of use, preventing reversion to virulence and minimising the occurrence of adverse reactions to vaccination.

Interventions and Services in Relation to Particular Conditions and Client Groups – NIBSC assists in developing the strategy for quality control and testing of novel medicines developed from new biotechnology / recombinant DNA methods, thus helping to assure the progression from development to effective and safe use.

2.6.4 Technology Foresight Programme

Where possible and appropriate, NIBSC's Scientific Programmes also aim to contribute to the UK Technology Foresight Programme in the 'health and life sciences' field. It is expected that NIBSC's work will make important contributions to the following priority areas identified under the Technology Foresight Programme:

- Research and development into new therapies;
- Development of gene therapy, protein / antibody drugs and cell or tissue-based therapies;
- Developments in pharmaceutical research;
- Development of improved laboratory procedures; and
- Use of information technology in health care and life sciences.

2.6.5 Consultation

NIBSC consults regularly with a range of external bodies (both national and international) as part of its process of priority setting. Particularly close and regular contacts are maintained in the UK with the Department of Health, and Medicines Control Agency and the Public Health Laboratory Service. Advice is sought on the needs for additional standards and reference materials, on any changes in the needs and priorities for control activities and on changes in epidemiological situations and emerging public health issues affecting the use of biologicals.

Bodies consulted include the following:

- World Health Organization
  - Expert Committee on Biological Standardisation (ECBS)
  - Biologicals Unit, WHO, Geneva
  - WHO Global Programme on Vaccines and Immunisation
  - WHO Global Programme on AIDS
- UK Department of Health
  - Senior professionals concerned with the UK Vaccination Programme and provision of blood products
  - The Office of the Director of Research and Development
  - Joint Committee on Vaccination and Immunisation
- UK Medicines Control Agency
  - Licensing Division
  - Biotechnology Unit
- The Committee on Safety of Medicines (UK)
  - Biologicals Sub Committee
- The Pharmaceutical Industry (in particular on the development of new products)
- UK National Blood Authority
- UK Public Health Laboratory Service

- European Union
  - European Medicines Evaluation Agency and its Working Party on Biotechnology/ Pharmacy
- European Pharmacopoeia (through UK Delegation to EP Commission and via Expert Groups)
- UK Medical Research Council
  - Committee on the Development of Vaccines and Immunological Procedures and its specialist sub committees

2.6.6 Role of NIBSC'S Board and Board Committees

Through the above channels, through the expertise and knowledge that NIBSC staff have on the development of biological medicines, and through staff contacts with both professional bodies and industry, priorities for future work in each scientific area are developed by the heads of NIBSC's scientific divisions. Proposed priorities are reviewed by the Director against the criteria given in Section 2.6.1 above, and presented to the Scientific Policy Advisory Committee (SPAC) of the National Biological Standards Board (NBSB). As the box below indicates, NBSB is responsible to the UK Secretary of State for Health for the management of NIBSC.

SPAC advises NBSB on NIBSC's programme priorities, and decisions on the allocation of resources to programmes are taken by NBSB, after also receiving the advice of the Board's Finance and General Purposes Committee on non-scientific matters and on resource availability (see Box).

SPAC co-ordinates peer reviews of the scientific programme and priorities of each NIBSC division on a rolling 4-year cycle. These SPAC reviews focus on the quality and productivity of the work as well as on project selection criteria listed in Section 2.6.1 above, and advise on the balance in a division's work between control, standards and research/development. The reviews rely on the involvement, recommendations and advice of specialist external reviewers who are selected after requesting nominations from relevant external organisations. SPAC reviews result in

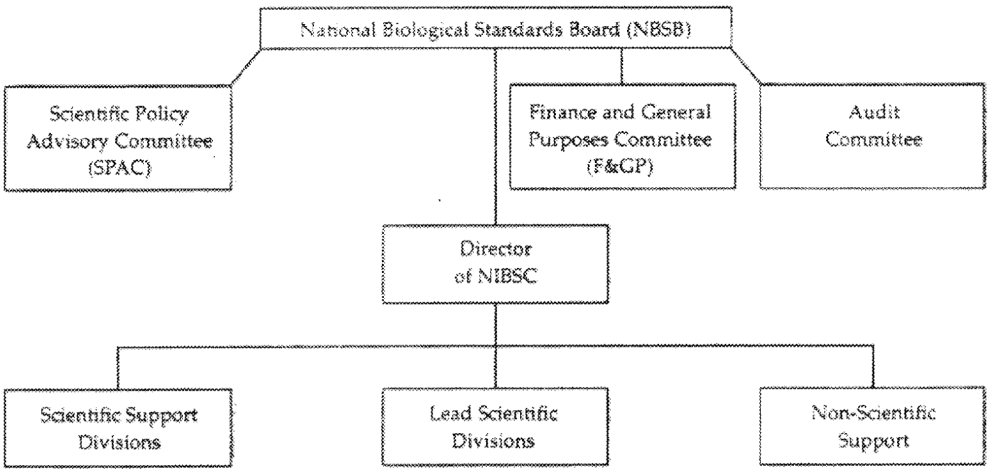
MANAGEMENT OF NIBSC

NIBSC is managed by the National Biological Standards Board (NBSB). The Board was established by the Biological Standards Act of 1975, with functions specified in the NBSB Functions Order of 1976.

The Board consists of up to 17 members appointed by the Secretary of State for Health. Board members include leading UK scientists in the field of biological medicine, as well as a number of management and finance specialists.

The Board is advised by three main committees:

- The Scientific Policy Advisory Committee (SPAC) includes all 'scientific' NBSB members plus several other highly experienced scientists in key areas; SPAC advises NBSB on the scientific programme of NIBSC and on priorities within it, and co-ordinates a regular programme of peer scientific reviews.
- The Finance and General Purposes Committee (F&GP) advises NBSB on all non-scientific matters, including resource availability and budgeting.
- The Audit Committee.



clear future priorities for a division's work. As part of the SPAC review programme, the Board also ensures that major areas of new work are subject to prior peer review before a decision is made to proceed.

SPAC also reviews the Director's recommendations for developments and changes in the balance of work between scientific divisions and in other Institute-wide scientific priorities. The recommendations of SPAC are further reviewed by NBSB before priorities for the future are finally agreed. It is also part of NIBSC's strategy to base its decisions on programme priorities against a background of clear budgetary information and costing data that is updated monthly.

The Director is required to report back to SPAC on the action taken as a result of the recommendations of a SPAC review. SPAC and the Board also regularly review progress against specific programme goals and targets.

3 Future Developments

3.1 SCIENTIFIC DEVELOPMENTS RELATING TO CONTROL AND STANDARDISATION

The rate of scientific progress in medicine and biology and in the industrial application of modern technologies is expected to gain further momentum over the next five years. New biological medicines derived from recombinant-DNA technology and monoclonal antibody methods are already coming forward for licensing at an increasing rate; this trend is expected to continue. Such new therapeutics present novel problems of standardisation and control. Radical new developments in therapy (such as gene therapy – see below) and in diagnostics are also expected to create new scientific and regulatory challenges in the area of control and standardisation. In turn, modern developments in biotechnology are leading to significant improvements in the technology available for the quality control and standardisation procedures themselves as applied to conventional and novel biological medicines - such improvements include reducing, wherever possible, the use of animals.

New vaccines: New international initiatives, such as the WHO Global Programme on Vaccines and Immunisation and the Childhood Vaccination Initiative, as well as work by the pharmaceutical industry, are aimed at enhancing progress towards the design of improved types of vaccines and extending the effective use of existing vaccines. In addition, new infectious disease threats continue to emerge, such as HIV infection and AIDS, new epidemic strains of cholera (0139) resistant to existing vaccines and rapid increases in the global impact of tuberculosis and malaria. Preliminary work on the standards required for new candidate malaria vaccines has recently begun.

The new approaches to vaccine design include the use of recombinant DNA technology for the precise genetic modification of infectious agents. This facilitates the production of stable attenuated strains as live vaccines and the design of live recombinant vectors such as vaccinia, avipox and salmonella strains. Slow release, single-dose vaccines are being designed that involve the techniques of microencapsulation of antigens. Such vaccines will hopefully avoid the necessity for multiple injections of the immunogen. Combined vaccines offering immunity to up to six diseases by a single series of injections are now being developed by industry. The standardisation and control of each set of vaccine combinations must be considered on a case by case basis since any one component may influence the immunogenicity of another. Over 20 different combinations of antigens are now possible. Very recently (1994) vaccines composed of DNA molecules alone have given strikingly successful results in laboratory tests and this technology holds out hope for the design of new and improved vaccines against infectious diseases. The regulatory issues concerning DNA vaccines will involve the development of the field of gene therapy, and their complexity will require a multidisciplinary approach by NIBSC.

New approaches for the standardisation and control of such products will also be required in order to ensure appropriate standards of quality, safety and efficacy. This includes the development of appropriate International Standards and test methods. Such work will represent a growing aspect of NIBSC's programme, and will be of considerable importance to public health.

Gene therapy: Only three years ago, many scientists would have considered human somatic gene therapy to be at an experimental stage, largely unproven, and a technology for the next millennium rather than for the 1990s. This field has, however, been subject to such rapid progress that the techniques that are now available for the delivery of specific genes into somatic cells are already being evaluated for therapeutic potential. Several inherited monogenic disorders are prime targets for gene therapy, and clinical trials are underway in the USA and Europe relating to adenosine deaminase deficiency and cystic fibrosis. It is widely believed that gene therapy potentially can be used to treat a broad spectrum of acquired, polygenic pathologies, including cancer and AIDS.

Gene therapy technology depends on the development and use of complex gene delivery systems such as replication-deficient retroviruses and adenoviruses, although simpler non-viral vectors, eg liposomes, are also currently under evaluation. It is anticipated that eventually a broad spectrum of products will be manufactured for use in gene therapy. Such 'gene-based' products will require new regulatory approaches and testing strategies, often necessitating a case-by-case assessment. At present, much more work is needed to develop safe and effective vectors for introducing genes into patients and NIBSC will

be in a position, with its wide expertise in the testing of medicinal biological products, to play a major role in providing advice and in meeting the new challenges involved in the testing of gene therapy products.

Based on an international symposium on Gene Therapy hosted by NIBSC, a set of guidelines on the quality aspects of potential future gene therapy products has been published by the EC.

Novel biological therapeutics: Cytokines and growth factors prepared by recombinant DNA technology, offer new opportunities for the treatment of disease. New molecules of this type are still being discovered at a fast rate. Some cytokines and growth factors are already licensed medicinal products, and many more are showing promising results in preclinical investigations.

Cytokines and growth factors show potential for the treatment of a wide range of clinical indications such as impaired wound healing, immunological dysfunction, haemopoetic reconstitution, viral hepatitis, cancers and neuropathies. They are complex molecules whose biological potency has to be assessed by appropriate bioassays with reference to standard preparations. In anticipation of the large numbers of these proteins which may become licensed medicinal products in the near future, NIBSC is increasing its activities in the development of bioassay techniques and the establishment of reference preparations. The Institute's expertise will be a valuable resource available to the pharmaceutical industry and regulatory authorities in developing these novel therapeutic agents.

3.2 EUROPE

Within Europe and within the context of the developing European legislation and procedures for the licensing and control of medicines, there is a need for the technical co-ordination of the scientific issues involved. Over the next five-year period, NIBSC aims to assist in the development of:

- Scientific and technical collaboration between European control authorities, leading to further strengthening of procedures for licensing and control;
- Harmonised technical guidelines for biological standardisation and control in the EU;
- European Pharmacopoeia monographs on biologicals specifying requirements for manufacturers and regulatory authorities alike;
- Specialist technical and scientific support to the European Commission, the European Medicines Evaluation Agency (EMEA) and other EC bodies;
- Scientific workshops within Europe on priority topics related to standardisation and control;
- European external quality assurance schemes to assure acceptable and consistent performance of control testing throughout the community;
- Specialised training in standardisation and control techniques for EC scientists and technologists;
- A European network to facilitate the exchange of information on the scientific and technical aspects of the standardisation and control of biologicals.

It is NIBSC's aim, in line with its role as a European Testing Laboratory, to carry out an increasing volume of testing for the EMEA and for national licensing authorities in the EU other than the MCA. In 1994 NIBSC achieved international quality accreditation for its European batch release work, covering 24 product areas and 91 tests. NIBSC plans to extend the scope of this accreditation, which is seen as an objective recognition of the high standard of the Institute's quality system in this area of work.

4 NIBSC's Programme Priorities, 1995 to 2000

The following outlines the expected developments in NIBSC's programme of work over the period 1995 to 2000.

4.1 VIRAL VACCINES (Division of Virology)

The programme over the next five years will see increases in work on measles, mumps and rubella vaccines, and on poliovaccines. Standards for the standardisation and control of safety testing of blood products will also be further developed. In line with our strategic aim to develop alternatives to animal usage, work on possible alternatives to the existing test for neurovirulence of oral poliovaccine will increase, while control work on these same vaccines is also likely to increase. Work on the virology of blood products, especially the molecular aspects, will change emphasis with an increase in use of gene amplification methods for testing products and plasma pools. Work on influenza will also address possible future DNA-based vaccines, slow release presentations of vaccines and the use of alternative cell substrates for the preparation of vaccines. However, demands for testing and standards in these two areas are expected to remain at current levels. There is a need to regularise the procedures for European batch release testing of vaccines and discussions on this matter are taking place with MCA.

4.2 BACTERIAL VACCINES (Division of Bacteriology)

The level of work on pertussis vaccines is expected to expand, mainly because of the renewed interest of the Industry in licensing acellular vaccines, both alone and in combination with other antigens. The work on encapsulated bacteria will also show some expansion. That on Hib vaccines will remain at present levels except where it is associated with new combination vaccines containing acellular pertussis, diphtheria, tetanus and viral components. However, increases are expected in the level of work on meningococcal conjugate and pneumococcal vaccines.

There is likely to be some overall increase in work on enteric vaccines, mainly in relation to cholera. It is anticipated that work on tuberculosis vaccine (BCG) and tuberculins will expand. The development of *in vitro* replacements for animal-based methods will continue. Following the successful development of *in vitro* and new *in vivo* assays for bacterial toxins and antitoxins, work in this area will continue with emphasis on the clostridial neurotoxins. Overall, the work on toxoids/toxins/antisera will continue to expand particularly with NIBSC's increasing involvement in the standardisation of single dose, slow release vaccines and the increasing use of low dose toxins in the treatment of certain neuro-muscular disorders.

4.3 IMMUNOLOGICALS (Division of Immunobiology)

Over the next 5 years, work on standard assays for cytokines will continue as a major aspect of the division's activities. Further development of work in the cellular immunology field and monoclonal antibodies (including those derived by rDNA procedures) are anticipated. Work with immunoglobulins will need to expand to cover the increased number of products undergoing clinical evaluation and licensing and increased testing to establish potency of specific immunoglobulin products. No work on allergens is planned, unless the rDNA-derived materials, which are presently early in development, progress to preclinical/clinical evaluation stages. There will continue to be a major emphasis on the development of International Standards and reference materials for cytokines and related molecules.

4.4 HORMONES (Division of Endocrinology)

Work on licensed products will continue to focus on developing improved assays and on selected product monitoring activities, with the highest priority areas likely to be licensed erythropoietin and gonadotrophin products. New products currently under development include genetically engineered gonadotrophins, tissue and bone growth factors and neurotrophic factors. Work relating to these products will concentrate on the development of standards and of *in vitro* bioassays, with particular emphasis on the application of molecular biology techniques. The Division will also continue to carry out all necessary pyrogen testing for the Institute.

4.5 BLOOD PRODUCTS AND RELATED SUBSTANCES (Division of Haematology)

In this area, in addition to work on blood clotting factors, a substantial increase in demand for work on anti-thrombotic drugs and

thrombolytic drugs is anticipated over the next 5 years, due to the introduction of new recombinant agents and other materials for diagnosis and treatment of thrombosis. The development of European batch release systems is expected to lead to an increased workload in the blood products area, because of the need to follow European guidelines and the increased volume of testing for Europe. Transfusion medicine work will continue at a level agreed with the National Blood Authority. The antigenic characteristics of Factor VIII derived from blood or prepared by recombinant DNA technology will require further study.

The need for biological standards and reference materials is expected to continue to expand with the introduction of more recombinant variants of existing molecules, as well as new agents. NIBSC will also be involved in the production of European working and reference standards, in collaboration with the European Pharmacopoeia and the Measurements and Testing Programme of the European Union.

4.6 AIDS (AIDS Collaborating Centre)

A major focus over the next five years will be the development of laboratory correlates of protection in order to develop strategies for vaccination against AIDS and to define methods for controlling the quality and efficacy of AIDS vaccines. Another major focus will be involvement in the WHO network for characterisation of HIV-1 isolates. Standards for PCR work will also continue to be provided, and there will be further development and application of quantitative PCR techniques.

4.7 MOLECULAR STRUCTURE (Laboratory for Molecular Structure)

The combined use of electrospray mass spectrometry, nuclear magnetic resonance (NMR) spectroscopy and optical spectroscopy will provide detailed structural and functional characterisation of a growing range of current and potential products and biological standards. These techniques will be especially relevant to the characterisation of recombinant proteins and glycoproteins, novel polysaccharide products and conjugate vaccines and are being increasingly used in the batch testing of products. Collaboration with lead scientific divisions within the Institute will improve our understanding of how small structural variations affect biological activity and clinical side-effects, and provide new control methods to monitor these variations. The physicochemical characterisation of existing Standards will also be further developed, thus enhancing their value as reference materials.

4.8 STANDARDS (Standards Division)

The Standards Division continually strives to improve the quality and stability of International Biological Standards and other reference materials by innovative approaches to their preparation, quality control and evalutation. An immediate development will be to install isolation technology appropriate for the preparation of new reference materials that are potentially infectious. It is also hoped to provide increased production capacity to meet the increasing quantity and variety of demand for new standards. The Division will also aim to reduce further freeze-drying times and processing costs for the preparation of biological reference materials without compromising product quality. As a consequence of its specialised expertise and facilities the Division undertakes a limited amount of contract work for industry and other organisations.

4.9 INFORMATICS (Informatics Laboratory)

Over the next five years, our networked information systems will be extended to cover other aspects of the Institute's work. The new database for monitoring control testing activities will be extended, and information databases on standards and reagents will be developed. NIBSC will also be involved in the development of global information systems on standards and reagents, particularly for use in the European Union. Statistical work on collaborative studies for standards will also have a high priority, particularly for recombinant products.

4.10 NIBSC TARGETS

Each year in its Annual Business Plan, NIBSC prepares a series of Targets which are demonstrable and/or quantifiable. These Targets relate to **Service Delivery** (Control and Standardisation), **Quality of Service** and the **Efficient Use of Resources.**

5 Programme Implementation

5.1 MODES OF OPERATION

Within the context of its overall strategy, and within the programme developed through NIBSC's planning process, the Institute and its Board have developed a number of operating principles or modes of operation. These modes of operation guide the Institute's approach in all areas of its Programme. These modes of operation can be summarised as follows:

Services

- **Provide accurate, timely and authoritative advice, information and results.**
- **Maintain, and where possible improve, the cost-effectiveness of performance to the benefit of all clients and customers.**
- **Maintain a high quality of performance and systems for the provision of services and materials, and where appropriate secure and maintain independent accreditation.**

Scientific

- **Act as a centre of scientific excellence in all matters relating to the control and standardisation of biologicals.**
- **Use available and relevant information networks and advice to formulate priorities.**
- **Adopt a multidisciplinary approach to studies, where appropriate.**
- **Maintain a standard of equipment and techniques that keeps NIBSC abreast of recent advances in research and development.**
- **Develop methods of control and standardisation of biologicals that render unnecessary or minimise the use of animals.**
- **In areas where the use of animals remains necessary, maintain the highest standards of animal husbandry and welfare under veterinary supervision.**

Impartiality

- **Provide impartial advice that is independent of commercial interest and that is consistent with the Board's statutory role in the UK and NIBSC's status as a WHO International Laboratory.**
- **Avoid any abuse of the Board's monopoly position while fostering the protection and exploitation of innovations by NBSB staff.**
- **Maintain the confidentiality of information and materials as appropriate.**
- **Pass on to the appropriate authority any information deemed significant to the protection of public health.**

5.2 ORGANISATIONAL DEVELOPMENTS

NIBSC's programme of control, standards and development/research is led by specialist scientific divisions, organised along disciplinary lines. These 'lead' divisions are responsible for the overall co-ordination and leadership of NIBSC's programme activities, and all other organisational units within NIBSC operate in support of these lead divisions in order to ensure maximum programme effectiveness and efficiency of use of resources. The work of each lead division is organised into Programme Areas that focus on groups of biologicals or products.

NIBSC separately identifies and costs its activities related to control testing, other control activities, international standards and national standards, and has identified senior scientists to assist in the scientific liaison with donors in each of these broad fields. NIBSC's new accounting system (installed during 1993/94) allows full costs to be allocated to projects.

5.3 MULTIDISCIPLINARY APPROACH

The structure of the Institute allows a multidisciplinary approach by several divisions to be adopted for the testing of individual products or groups of products, and for standardisation and development activities. The ability of the Institute to bring the expertise of a wide range of disciplines to bear on any area of biological medicine sets it apart from other testing laboratories and has resulted in the development of NIBSC's unique international role.

5.4 QUALITY SYSTEMS AND ACCREDITATION

NIBSC has developed standard operating procedures in its key statutory areas, and has a programme for attaining and maintaining internationally recognised quality assurance accreditation. NAMAS Accreditation (equivalent to European Standard EN 45001) for batch release testing involving 24 product areas and 91 separate tests was awarded in September 1994. EN ISO 9001 Accreditation of standards processing operations is scheduled for 1995.

5.5 FUNDING SOURCES AND ALLOCATIONS

NIBSC is funded principally through central

UK Government funding; the Institute also receives additional funding through External Grants, contracts and other sources. The Institute's projected funding in 1995/96 is as follows:

UK Government Funds	£9,724K
External Project Grants	£1,000K
Contracts and Other Income	£ 720K

The projected allocation of UK Government funds by group of biologicals for the period 1995/96 to 1999/2000 is shown in Figure 1.

Figure 1: *Projected Allocation of UK Government Funding to NIBSC by Group of Biologicals, over the period 1995/96 to 1999/2000.*

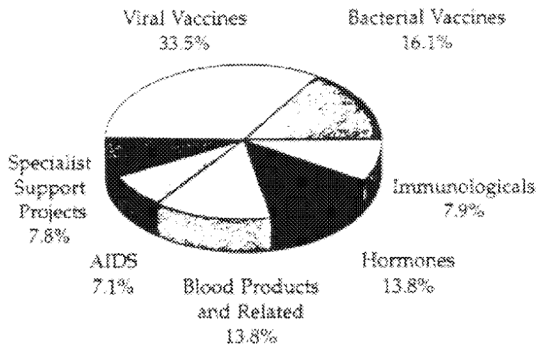
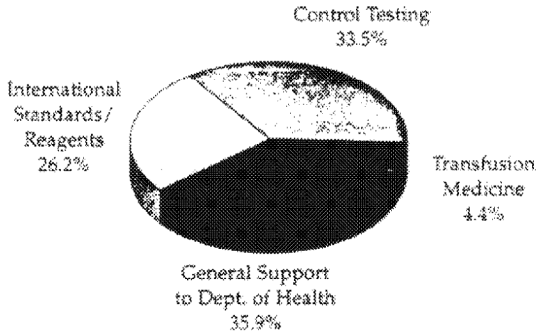


Figure 2: *The 1994/95 Allocation of NIBSC's UK Government Funding to Four Service Level Agreements.*



Service Level Agreements

NIBSC's central UK Government funds are associated with a number of Service Level Agreements (SLAs). These agreements specify the work and services to be provided by NIBSC during the year in question and indicate the allocation of funds to different Programme Areas and Projects. The nature and format of these SLAs is under review during 1995/96; in 1994/95, NIBSC's UK Government funding was associated with the four SLAs indicated in Figure 2.

External Grants

It is NIBSC policy to seek additional external funding for scientific development projects that support directly the Institute's statutory functions and complement its centrally funded activities. It is the Department of Health's current policy to limit the volume of such External Grant funding to no more than 15 per cent of total income. External Grant donors to NIBSC include the Medical Research Council, WHO, the European Commission, the Department of Trade and Industry and the Home Office.

Contracts and Other Income

It is NIBSC policy to provide certain specialised services on a contractual basis to paying clients. Service contract arrangements are only agreed where the work is in line with NIBSC's overall aim and functions, where it can be shown that no other work of the Institute would be adversely affected by the service contract commitment, and where such work would not involve NIBSC in any conflict of interest relating to its impartial and independent role in the control and standardisation of biologicals. NIBSC also makes handling charges for the distribution of biological standards and other reference materials resulting in further income to the Institute.

5.6 REVIEW OF RESOURCE ALLOCATION

NIBSC's programme activities are planned and reviewed annually within the broad context of this Corporate Plan (as described in Section 2.6 above). Annual plans of scientific activities within the following year are reviewed initially by the Board's Scientific Policy Advisory Committee. The allocation of resources to agreed scientific priorities is proposed by Management, reviewed by SPAC and the Board's Finance and General Purposes Committee (F&GP), and approved by the Board for submission to the Department of Health.

Each year, as part of the annual review by the Department of Health of NIBSC's progress and future plans, NIBSC identifies those areas of work where it is believed that additional resources will be needed over the coming 5 years. From now until the year 2000 and beyond, the role of biologicals in medicine is expected to increase, and new biological substances and medical approaches are continually emerging. While there remains an

important need for continued work on conventional products (such as vaccines used in childhood immunisation campaigns) the pressures for increased variety and quantity of work by NIBSC are expected to increase.

Areas where additional resources need to be considered over the next 5 years include blood microbiological safety and testing, the control of new bacterial vaccines, potency monitoring of vaccines at the point of use, gene therapy/cell biology and the control of DNA vaccines. A number of major items of equipment and plant needing replacement over the same period have also been identified.

5.7 MANAGEMENT OF RESOURCES

The NBSB is responsible for the overall management of use of resources by NIBSC. The Board, advised by its Finance and General Purposes Committee, is responsible for approving NIBSC annual budgets, and monitors expenditure at regular intervals throughout the year. The Board and its committees have access to the management information which allows NIBSC Management to monitor programme expenditure on a monthly basis. NIBSC's financial management information allows expenditure to be monitored according to expense headings under its statutory accounts, to organisational units, to Programme Area and to external grants and contracts.

5.8 PROGRAMME REPORTING

NIBSC reports on its activities annually to the Department of Health through an Accountability Review process. The Institute publishes each year an Annual Report summarising programme highlights. NIBSC publishes its scientific results through peer-reviewed scientific journals.

5.9 LINKS WITH CLIENTS

It is NIBSC's policy to maintain close links with all its clients and target groups, in order to ensure that its programme and activities are fully responsive to their needs. The balance between the activities that NIBSC carries out for different client groups is monitored through the Accountability Review process operated by the Department of Heath. In line with its Statutory Functions, NIBSC maintains close working relationships with the Medicines Control Agency (on both policy and technical issues), the World Health Organization, the European Commission, the European Pharmacopoeia and a number of other Government bodies within the UK. NIBSC also maintains close technical links with the pharmaceutical industry.

5.10 MARKET TESTING

NIBSC has a programme of market testing of operations and services in order to maximise their cost-effectiveness. Major contracts such as those for plant and equipment maintenance, energy, waste disposal, grounds, catering and cleaning are put out to competitive tender on a regular basis. Operations and Services valued at >£900K in the Administration and Estates areas are currently subject to competitive tendering.

NBSB Members

The National Biological Standards Board (NBSB) is accountable to the UK Secretary of State for Health for the management of NIBSC. The following were serving as members of NBSB on 1 April 1995:

Dr N J B Evans, CB FRCP FFPHM (Chairman)
Professor I Allen, MB BCh BOA MD DSc
Professor S R Bloom, MA DSc MD FRCP
Mr D F R Crofton, BComm FCA ACIS
Dr M Ferguson, BSc PhD
Professor K Gull, BSc PhD
Professor H S Jacobs, MD FRCP FRCOG
Professor F Y Lieuw, PhD DSc MRCPath
Mr P J S Lumsden, MA FCA FCT
Mrs N Morris, MA
Mr J B Pring, Dip.RCP Dip.RCS
Professor J G Ratcliffe, MSc DM BMBCh FRCP FRCPath
Dr G C Schild, CBE BSc PhD DSc FIBiol FRCPath Hon MRCP
Professor R A Weiss, BSc PhD Hon MRCP FRCPath

Senior NIBSC Staff

Director:	G C Schild, CBE BSc PhD DSc FIBiol FRCPath Hon MRCP
Assistant Director (Scientific):	M M Jordan, BSc MSc PhD CEng MBCS CStat
Assistant Director (Administration):	R A Stewart, BSc PhD

Heads of Department:

AIDS:	J Stott, BA PhD MRCPath
Bacteriology:	M J Corbel, BSc PhD DSc(Med) CBiol FIBiol MRCPath
Endocrinology:	A Bristow, BSc PhD
Haematology:	T W Barrowcliffe, MA Oxon PhD
Immunobiology:	R Thorpe, BSc PhD MRCPath
Informatics:	M M Jordan, BSc MSc PhD CEng MBCS CStat
Molecular Structure:	C Jones, BSc PhD ARCS
Standards:	P K Phillips, BA PhD FIQA
Virology:	P D Minor, BA PhD

for further information on NIBSC please contact:

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