# EVALUATION OF THE NATIONAL PUBLIC HEALTH INSTITUTE OF FINLAND -KANSANTERVEYSLAITOS

REPORT OF THE EVALUATION PANEL



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Members of the Evaluation Panel: Dr David Evered (Chairman) Professor Philippe Grandjean Dr Bernhard Hirt Professor J.H. Koeman Professor Daan Kromhout Professor Ulf Pettersson Sir Joseph Smith Professor Dag Thelle

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# FOREWORD

I am happy to present the Report of the Evaluation Panel which was appointed to evaluate the National Public Health Institute of Finland (Kansanterveyslaitos). The conclusions and recommendations contained within this Report have been agreed by all members of the Panel. I was honoured to be invited to chair the Panel and privileged to work with such distinguished and committed colleagues whose objective and perceptive judgements form the basis of this Report.

We vould all wish to record our gratitude to Professor Karma, the members of the Steering Group and the staff of the Academy of Finland, particularly Mrs Anna-Liisa Kauppila and Dr Sakari Karjalainen, for their support and assistance throughout. We also wish to express our appreciation of the substantial volume of work which was undertaken so willingly by Professor Jussi Huttunen and his colleagues which provided us with the information necessary for the evaluation.

DAVID EVERED

# PREFACE

In March 1994, the Medical Research Council of the Academy of Finland, in response to a proposal put to it by the National Public Health Institute of Finland (KTL), decided to carry out an evaluation of the research activities of the KTL.

A Steering Group was established by the Academy under the Chairmanship of Professor Pekka Karma (University of Helsinki). The other members were Dr Jarkko Eskola (Ministry of Social Affairs and Health), Professor Jussi Huttunen (KTL), Professor Olli Jänne (University of Helsinki), Professor Aulikki Nissinen (University of Kuopio), Dr Elisabeth Helander (Academy of Finland), Dr Terttu Luukkonen (Academy of Finland), and, the Secretary to the Group, Mrs Anna-Liisa Kauppila (Academy of Finland). Dr Sakari Karjalainen (Academy of Finland) was appointed to serve as Scientific Secretary to the Evaluation Panel.

In June 1994, Dr David Evered of the UK Medical Research Council was invited and agreed to serve as Chairman of the Evaluation Panel. The terms of reference for the Panel and evaluation methodology were prepared by him in consultation with the Steering Group. The other members appointed to the Panel were: Professor Philippe Grandjean (University of Odense, Denmark); Dr Bernhard Hirt (**ISREC**, Switzerland); Professor J.H. Koeman (Agricultural University Wageningen, The Netherlands); Professor Daan Kromhout (Public Health Research Division/RIVM, the Netherlands); Professor Ulf Pettersson (Department of Medical Genetics, Biomedical Center, Uppsala, Sweden); Sir Joseph Smith (U.K.); Professor Dag Thelle (University of Oslo, Norway).

The KTL prepared a report for the Evaluation Panel which provided (i) a brief history and account of the mission, roles and responsibilities of the Institute; (ii) details of the public health monitoring and surveillance activities; (iii) a report on progress in research over the period 1989-1994 and research plans for the period 1994-1999 and (iv) information on the contribution which the Institute makes to meeting the national need for highly trained research personnel and the development of skills in the disciplines of public health. The KTL was also asked to provide information on (i) the arrangements for setting and modifying the scientific strategy of the Institute taking due account of national public health needs; (ii) the role of the Institute in the dissemination of research results and knowledge and technology transfer; (iii) the interface between the Institute and other ministries and agencies with related and overlapping interests; (iv) the interface between the Institute and other research providers (eg the universities); (v) the arrangements for governance and management and (vi) allocation staff and resources.

The Panel met on three occasions. The purpose of the first meeting in April 1995 was to receive the Report from the KTL, receive briefing from the Academy, Ministry of Social Affairs and Health, the KTL and other relevant bodies, and to identify othe information needs and the key scientific and strategic issues which would require discussion and exploration. The Panel made site visits to the three divisions of the KTL during June 1995 and met once more in August 1995 to discuss the draft of the evaluation report and agree their conclusions and recommendations. The evaluation Report was presented to the Academy during October 1995.

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# SUMMARY AND PRINCIPAL RECOMMENDATIONS

The mission of the National Public Health Institute of Finland (KTL) is to: (i) survey and monitor the health of the Finnish people; (ii) conduct basic and applied research which contributes to the development of public health policy and the improvement of the health of the Finnish population through health promotion and prevention of disease; (iii) identify priority areas for public health research and prosecute research in those areas; (iv) develop national and international collaborations in public health research; (v) promote and contribute to the training of researchers in the disciplines of public health.

The KTL has undergone a major transformation from public health laboratory to research institute over the last twenty years. The majority of the service responsibilities have been transferred to major hospitals and municipal health centres and the principal research activities of the Institute have been developed during this period. Much of the research which has been carried out at the KTL has been of the highest quality and has been of considerable public health importance. The high international standing of the KTL reflects the outstanding contributions which have been made by the best of the staff and this has been facilitated by the unique opportunities for public health research which the Institute offers. The Panel applauds the success of the Director-General in building a major public health research institute on the foundations of a public health laboratory over the course of the last 15 years.

The KTL also carries responsibility for a number of public health surveillance and monitoring functions (some of which are statutory responsibilities). The major current statutory responsibilities are (i) infectious diseases surveillance, (ii) production and procurement of vaccines, (iii) blood alcohol and drug testing, (iv) paternity testing and (v) screening for neonatal hypothyroidism. The KTL also assumes responsibility for a wide range of other public health responsibilities. These include the monitoring of major chronic health problems (excluding cancer), risk factors and health behaviour, maintenance of the food composition database and the provision of advice on environmental matters.

### The Panel's principal conclusions and recommendations are:

### 1. Development of policy and strategy.

The Panel considers that the current arrangements for the formulation of policy and strategy for the KTL in the medium and longer term should be strengthened. A more clearly defined strategy would provide an improved framework for the annual agreements

between the KTL and the Ministry and a more secure basis for longer term planning. The strengthening of current mechanisms will require more broadly based arrangements for strategic planning on the part of the KTL, the establishment of mechanisms through which the Ministry can clearly identify and articulate its research needs, and the development of satisfactory channels of communication between the KTL, the Ministry and the municipalities (which carry the responsibility for the delivery of health care and the development of the system).

### The Panel recommends that:

(i) a Director-General's strategy group should be established. The purpose of this group would be to advise the Director-General and Board on the development of the research strategy, public health role and the training and career development responsibilities of the Institute. The group should have no more than eight to ten members serving under an independent chairman with a suitable scientific or professional background. The membership would comprise the Director-General, a representative of the Ministry of Social Affairs and Health, a number of leading members of the scientific or professional background. The group should each be appointed for a four year term (with the possibility of renewal for a further single four year term) and that at least one member should be recruited from outside Finland;

(ii) the Ministry of Social Affairs and Health should take steps to strengthen its own capacity to identify and articulate its own policy and operational research needs;

(iii) a national public health forum should be established by the Ministry and the KTL to provide a framework for the exchange of information about the research and public health strategies of the public sector bodies and for consideration of major issues of policy and strategy for the future. This should also include senior representatives of the other sectoral research institutes, the Centre for Health Education, the universities with faculties of public health and representatives of the municipal health authorities who would be able to indicate the research needs of those who have the responsibility for health care delivery.

### 2. Interface with other sectoral research institutes - NAWH and FIOH.

There is frequent contact between the KTL and these agencies for the conduct of business on a day to day basis and the Ministry also convenes two meetings each year which bring together the Directors of all three Institutes for the exchange of information and the coordination of activities. There are, however, areas in which a greater degree of coordination of effort between the Institutes would be desirable and these are highlighted in the reports on the individual divisions and departments. The Panel recommends that:

(i) the Ministry should clarify the relative responsibilities of the KTL and the National Research and Development Centre for Welfare and Health (NAWH);
(ii) the NAWH and Finnish Institute of Occupational Health (FIOH) should be represented on the proposed broadly based national public health forum to ensure better alignment of the strategic planning mechanisms of both Institutes, to improve the transfer of information and provide a more secure basis for the development of joint activities in areas which fall within the sphere of responsibility of both Institutes.

### 3. Meeting the needs of users.

The KTL has three particular roles to play in relation to the municipalities: (i) the conduct of research which will underpin the development of public health policies and contribute to the planning and development of the health care delivery system, (ii) the provision of advice and on occasions assistance in addressing specific problems (eg control of outbreaks of infectious disease, environmental problems etc) and (iii) the training of public health personnel The KTL represents a major resource which can contribute to meeting these needs.

### The Panel recommends that:

(i) the municipal health authorities should be represented on the national public health forum proposed above;

(ii) the role the KTL in the investigation and control of outbreaks of infections and the investigation of environmental problems should be extended and strengthened and its formal responsibilities should be more clearly defined;

(iii) the Ministry of Social Affairs and Health should examine and clarify the individual responsibilities of the Ministry, the KTL, the NAWH and the municipal authorities in the dissemination and application of research results and in the provision of training in the disciplines of public health.

### 4. Interface with the universities.

Links between the KTL and the universities are limited in number but increasing and collaborations on specific projects exist between scientists within all three divisions in the KTL and colleagues in the Universities. These have been developed through the identification of shared or complementary interests. Members of the staff of the KTL also contribute to teaching programmes in a number of the universities. The Panel was pleased to note the increasing level of collaboration between the KTL and the universities and would wishes to see these links evolve and strengthen in the future.

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### 5. International collaboration.

International collaborations offer some particular advantages for public health research. The KTL has a substantial record of research carried out with a wide range of partners elsewhere in Europe and in North America. Members of the staff of the KTL have a particularly successful record in playing a leading role in EU funded research (largely but not exclusively through the BIOMED programme). The KTL staff also have a substantial record of work carried out in collaboration with developing countries and have played an significant role in a number of WHO programmes. The Panel wish to commend the commitment of the staff in setting up, and in many instances leading, these collaborations.

### 6. Training and career development.

The KTL is a valuable training resource for those who plan to pursue a career in public health research and potentially for those who will follow a service career in public health. The number of graduate students is increasing. Responsibility for ensuring that there is appropriate supervision and mentoring rests with the individual heads of departments and supervisors. There is no system in place at present for ensuring that the overall needs of postgraduates are met and the quality of the research training assured. It was also noted that current arrangements are entirely demand driven and there is no established mechanism through which the national manpower needs for public health professionals can be systematically assessed. It is essential that there should be close links between the training and career development programmes for those who intend to pursue a career in public health research and those who will primarily follow a service career track.

### The Panel recommends that:

(i) the KTL should designate a senior member of staff as postgraduate tutor who would be charged with the responsibility for ensuring that the overall training programmes and environment properly meet the needs of the graduate students;

(ii) the Ministry of Social Affairs and Health should conduct a review of the national needs for professionals trained in the disciplines of public health and, in the light of their findings consider how these needs might best be met in consultation with the KTL and the universities building on the strengths created by the recently created graduate schools.

### 7. Dissemination of research results.

The dissemination and implementation of research results is achieved through the Ministry but its role is limited following devolution of responsibility to municipalities. The major responsibility currently lies with non-governmental organisations working through the Centre for Health Education. The Panel was concerned at the apparent absence of a coherent structure for the dissemination of research results to public health and health care professionals and at the limited scale of the arrangements for health promotion in Finland.

The Panel recommends that:

(i) the Ministry should undertake a review of the current arrangements for the dissemination and implementation of research results with a view to clarifying further the responsibilities of all the parties concerned (the Ministry, the municipal health authorities, NAWH, KTL and the Centre for Health Education) and ensuring that effective mechanisms are in place;

(ii) the mechanisms which are developed following this review should not be limited to the dissemination of research results which have been generated in Finland but they should have the capacity for systematically feeding information (originating in Finland or elsewhere) through to those who have responsibility for formulating public health policies and planning health care delivery at national and local level.

8. Exploitation of research results.

The major products of the research effort of the KTL feed directly into public health and clinical practice without the need for development within a commercial environment and thus the issue of the protection and exploitation of intellectual property does not arise. There is, however, a small but significant proportion of the research portfolio of the Institute which has and will continue to lead to the generation of novel products and processes which should properly be protected and exploited in the name of the KTL. Current arrangements (the majority of which relate to the Division of Infectious Diseases) have been put in place on an ad hoc basis and the Panel does not consider that these are satisfactory for these purposes.

The Panel recommends that the KTL should commission a suitably qualified professional to review its current arrangements for technology transfer and for the patenting and licensing of the products of its research and advise on the establishment of suitable mechanisms for the protection and exploitation of its intellectual property.

9. Current public health activities and responsibilities.

These have been summarised above

The Panel's recommendations are:

(i) the KTL should continue to carry formal responsibility for the monitoring and control of infectious disease in Finland and steps should be taken to ensure that effective interfaces are maintained with the Ministry of Social Affairs and Health and the municipal authorities;

(ii) the KTL should undertake a review of the role, responsibilities and research strategy of the Department of Alcohol, Drugs and Traffic (see also below);

(iii) the KTL should discontinue the provision of paternity testing and screening for congenital hypothyroidism as soon as alternative arrangements can be put in place.

10. Overview of current research activities and responsibilities.

The research role and responsibilities of the KTL have been described above.

The major recommendations of the Panel are:

**Division of Chronic Diseases** 

(i) the Director-General should undertake an overall review of the research strategy of the Division. This review should include a detailed reappraisal of the role of the KTL in research in cardiovascular disease covering the Departments of Epidemiology and Health Promotion, Nutrition, Biochemistry and Human Molecular Genetics. The future research strategy should be based upon the development of hypothesis driven epidemiological studies and the evaluation of interventions exploiting the well characterised populations deriving from past, current and future epidemiological studies;

(ii) there should be further investment in human genetics and new programmes should be developed in collaboration with staff in other Departments within the framework of the overall Divisional strategy;

(iii) the programmes in the genetics and determinants of mental illness should continue to be developed;

(iv) the activities of the disparate groups working on aspects of health behaviour should be brought together, strengthened and focused to form an integral component of the principal research themes of the Division;

(v) the future of the Departments of Immunobiology and Alcohol, Drugs and Traffic should be subject to a fundamental reappraisal.

**Division of Infectious Diseases.** 

(i) the current research strategy, the major objective of which is to improve the diagnosis, control and prevention of infections, has led to the development of programmes in which the public health surveillance and research activities are well integrated and effective internal and external collaborations are in place. These should

be strengthened and developed. A greater degree of focus should be achieved through the discontinuation of projects which are of low priority and do not contribute to the overall Divisional strategy;

(ii) the assumption of an increasing range of public health responsibilities by this Division merits greater investment but this should be met by the reallocation of resources released through the discontinuation of activities of low priority;

(iii) further investment in the development of improved diagnostic methods should be more clearly justified by public health and research needs;

(iv) the Division should be reconfigured in the light of this review to concentrate expertise in a smaller number of larger Departments. Particular attention should be paid to the need to ensure that the existing expertise in bacteriology is used to best effect and to strengthen immunology within the KTL;

(v) the future role of the Laboratory in Oulu should be reviewed by the proposed Director-General's strategy group in the light of this review.

Division of Environmental Health.

(i) the overall strategy for the Division should be reviewed as a matter of urgency by an expert group which would report to the Director-General and the proposed Director-General's strategy group;

(ii) the Division should develop a more structured and co-ordinated approach to studies to enable it to carry these through in a systematic manner from hazard identification, to epidemiological association, to assessment of exposure and its consequences, to study of mechanisms of toxicity and evaluation of factors which might modify the impact of exposure;

(iii) major research themes for the future should include air pollution and other programmes which have a particular relevance to Finland (eg relating to the timber processing industries). Other major targeted programmes might be developed in neurotoxicology, immunotoxicology or reproductive/developmental toxicology - (it is recognised that the establishment of a strong programme in one or more of these fields will require considerable strengthening of the limited number of current staff members with expertise in these areas);

(iv) a critical strategic review of the Division should be carried out in the context of its relationships with the University and the FIOH (ideally in collaboration with these other bodies). The possibility that these might be drawn together into an Institute of Environmental Health to develop a major resource and research centre in the field with a clearly defined strategy should be explored;

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(v) the contribution which staff of the Division make to the maintenance of bacteriological expertise within the KTL should be considered in the reappraisal proposed in the review of the Division of Infectious Diseases;

(vi) the Division should not continue to provide a toxicity testing service on a contractual basis.

11. Management issues.

The Panel recommends that:

(i) each department of the KTL should be reviewed every four years by an external peer review team. The review should report on the research performance and future proposals of each department using accepted criteria (similar to those developed for this evaluation). The proposed Director-General's strategy Group should be charged with responsibility for oversight of the peer review process;

(ii) a broad institutional review should be carried out each five years;

(iii) a staff audit should be carried out in the light of the Panel's recommendations to ensure that the human resources available to the KTL are used in the most effective manner;

(iv) consideration should be given to developing and introducing terms and conditions of employment which will provide the necessary flexibility which is essential for a major research organisation.

## INTRODUCTION

The Institute was established in 1910 as a serum laboratory. Its primary responsibility, in its early years, was the diagnosis of infectious diseases and the production of vaccines and antisera. The laboratory developed over the course of the next 60 years to provide a wide and comprehensive range of microbiological, immunological and biochemical diagnostic services for hospitals and health centres throughout the country through its central laboratory in Helsinki and seven regional laboratories. It was designated the Public Health Laboratory in 1969. A major change in the mission of the Laboratory occurred in the 1970s as a result of growing public concern over the high prevalence and mortality associated with a number of non-communicable diseases in Finland. This led to the establishment of a state committee in 1974 which recommended that the Public Health Laboratory should be developed as a research institute with responsibility for monitoring health and for research necessary for promoting the health of the nation. The National Public Health Institute of Finland (KTL) was formally established in 1982. The transformation from public health laboratory to research institute has taken place over a considerable period of time as the majority of the service responsibilities have been transferred to major hospitals and municipal health centres. The principal research themes of the KTL have been developed during the last seventeen years. Research into the epidemiology and prevention of cardiovascular diseases (followed by studies of other chronic non-communicable diseases) commenced in 1978, nutrition research followed in 1982, research into environmental factors and health in 1983, mental health research in 1985 and human genetics in 1988. The KTL has also developed a major research programme into the epidemiology, pathogenesis and prevention of infectious disease building on the established public health strengths of the Institute.

The mission of the KTL is to:

- survey and monitor the health of the Finnish people;
- conduct basic and applied research which contributes to the development of public health policy and the improvement of the health of the Finnish population through prevention of disease and health promotion;
- identify priority areas for public health research and prosecute research in those areas;
- develop national and international collaborations in public health research;
- promote and contribute to the training of researchers in the disciplines of public health;
- implement the objectives set by the Ministry of Social Affairs and Health.

The KTL is one of four research institutes which are funded directly from the budget of the Ministry of Social Affairs and Health. The others being the Finnish Institute of Occupational Health (FIOSH), the National Research and Development Centre for Welfare and Health (NAWH) and the Finnish Centre for Radiation and Nuclear Safety. Research relevant to the Ministry is also carried out by the State Alcohol Monopoly (these research functions were transferred to the KTL and NAWH subsequent to the evaluation) and the Social Insurance Institution. The Ministry is responsible for defining the aims of research and development in its own sector to meet its own policy needs. The research institutes translate these objectives into their work plans which are agreed annually with the Ministry.

The KTL operates under a Board of Directors (eight members) which has responsibility for overall strategy, financial planning and accountability, and the recruitment of the most senior members of staff. The Director-General is the chief executive officer and carries responsibility for all aspects of management of the Institute and also for the development of strategy. The Institute operates through three divisions (chronic diseases and health, infectious diseases and environmental health) which comprise 18 departments. In December 1994 there were 592 staff (557 full-time equivalents) of whom 375 were on permanent staff contracts and 217 on short term contracts (88 of these were graduate students whose stipends were paid by the KTL). There are currently 225 graduate students in total at the KTL. The Institute's operating costs in 1994 were 158 million FIM and the cost of the vaccination programme was a further 24.5 million FIM. 26 million FIM (16.5%) was derived from extra-budgetary sources. 46% of the operating costs were spent on infectious diseases, 39% on chronic diseases and 15% on environmental health.

# **BACKGROUND TO THE EVALUATION**

The objective of this wide ranging review was to provide an evaluation for the Academy of Finland and the Ministry of Social Affairs and Health of the public health functions, strategic importance, scientific merit and value for money of the scientific work undertaken and the proposals for future work. The review covered all the activities of the Institute (apart from the vaccine production and procurement programme). In particular the review was set up to determine to what extent the Institute has succeeded in meeting its scientific and research objectives, to evaluate the strategic importance and scientific merit of the proposed future programmes in the context of its public health responsibilities and to make recommendations to the Academy of Finland and the Ministry of Social Affairs and Health on the strategic development, organisation and resourcing of the KTL. Full details of the evaluation methodology, the terms of reference and membership of the Panel are to be found in Annexes A, B and C. A list of those interviewed by the Panel is at Annex D.

It is important, however, to emphasise a number of points.

1. A comprehensive evaluation has been completed by the Panel (supported by written opinions from expert referees in a number of areas). However, the panel reviewed 90 major research programmes (many of which included a number of individual projects) during the site visits - and thus the Panel's judgements are of an overarching and strategic nature. This review thus provides an assessment of the overall scientific achievements and future proposals of the KTL, the effectiveness of the management of resources, and the success of the KTL in meeting its objectives through programmes within the Institute and through scientific interactions and collaborations nationally and internationally.

2. The Panel has reached broad judgements on the pattern of resource allocation within the Institute (and has made some recommendations for reallocation of resources) but it was not possible for the group to undertake a detailed audit of human and financial resources within the KTL within the time available.

3. The Panel has been conscious, throughout the course of its work, that the activities of the KTL cannot be evaluated in isolation and of the need to make its judgements in the context of national public health needs and taking due account of the responsibilities of other sectoral research institutes. The effective discharge of the mission of the KTL demands that satisfactory arrangements are in place for operating the interfaces between the Institute and the Ministry and a wide range of other public sector agencies within Finland. The panel has explored these interfaces and has identified a number of instances in which they do not appear to be operating wholly satisfactorily. It has made a number of recommendations but in some cases these highlight the need for further work since they raise questions relating to the role and responsibilities of other agencies which were beyond the scope of this review.

# **REVIEW OF INSTITUTIONAL OBJECTIVES AND RESPONSIBILITIES**

## **OVERALL MISSION OF THE INSTITUTE**

The agreed mission and principal objectives of the KTL are listed above and in the Institute report - section 2/2 (p12). These objectives are formulated in broad terms and in the view of the Panel this is appropriate and provides the flexible framework within which the Institute can properly discharge its public health and research responsibilities.

# ARRANGEMENTS FOR THE DEVELOPMENT OF POLICY AND STRATEGY

The KTL operates under a Board of Directors (eight members) which has responsibility for overall strategy, financial planning and accountability, and the recruitment of the most senior members of staff. The Director-General is the chief executive officer and carries responsibility for all aspects of management of the Institute and also for the development of strategy. The Board comprises four representatives of the Ministry of Social Affairs and Health (one of whom chairs the Board), representatives of the Ministries of Environment and Education, the Director-General of the KTL and a staff representative of the Institute. The Board meets four to six times each year. It was put to the Panel that the role of the Board was less significant than in previous years since most strategic decisions are taken during the course of the annual planning cycle (see below).

The effective discharge of the mission of the KTL requires that satisfactory mechanisms should be in place for the development of policy and strategy. The key characteristics of these arrangements defined by the Panel should be:

- clarity and transparency in the formulation of policy and strategy based upon scientific opportunity and health need;
- satisfactory mechanisms through which the objectives and needs of the sponsors and users are given due weight in the process of strategic planning;
- robust mechanisms for prioritisation and determining which activities merit new or increased investment and which should be reduced or discontinued to achieve an appropriate balance in the research portfolio;
- arrangements which ensure that investment is fully maximised through collaborations and partnerships nationally and internationally.

The present arrangements for the development of policy and strategy for the KTL were reviewed by the Panel. Strategic planning and review of the programme of the KTL is currently carried out on an annual cycle. The key stages are:

- March annual planning meeting with Ministry;
- May agreement of objectives with Ministry;
- September plans put forward by individual departments;
- October-November internal review of plans by Director-General and Divisional heads;
- December internal agreement on detailed objectives and resources.

The KTL prepares detailed plans for the following year and an overall strategy document for the coming quinquennium each autumn. These plans are based on discussions within the three divisions and the document is finalised by the Director-General's Advisory Group (the Director-General, the Heads and Deputy Heads of each Division and the Head of Administration). These plans and objectives are submitted to the Board of Directors for approval and to the Ministry in February each year as an annex to the budget proposal. The objectives for the coming year and the longer term objectives for the KTL are discussed at the principal meeting which takes place with the Ministry in March. This provides the forum for the review of the activities of the previous year, the discussion of objectives for the coming year, the consideration of longer term plans for the following quinquennium and the presentation of budget proposals. This process leads to the production of a formal agreement which defines the objectives and agrees the budget for the Institute for the coming twelve months. The current agreement lists 21 key objectives and 169 detailed objectives for the current year. The participants include the Permanent Secretary of the Ministry, three Directors-General and key officers from the Departments of Health Promotion and Prevention, and Planning and Finance of the Ministry. The representatives of the KTL include the Director-General and the Heads and Deputy Heads of the Divisions. Interim reviews are carried out by the Ministry in March and September each year.

The Panel was pleased to note that established arrangements were in place for the conduct of business and strategic planning between the Ministry of Social Affairs and Health and the KTL. They take the view, however, that these could be strengthened in a number of respects.

• The current process is largely driven by the KTL which plays the major role in setting the research agenda for the Institute. The Panel was concerned, however, that the process is dominated by the current interests and activities of the senior members of staff and that there are no established mechanisms for the conduct of a regular more broadly based review of the overall strategy of the KTL with expert inputs from the wider scientific community.

- The Panel is aware that there is a great deal of interaction between the KTL and the Ministry on a day to day basis but is concerned that the Ministry does not appear to have well developed mechanisms for identifying and articulating its own research needs and setting appropriate research targets. Such mechanisms are essential to ensure that the information needs which are required to underpin the development of public health policy are met.
- A further difficulty identified by the Panel was the absence of any mechanism for th end users of the KTL's research to contribute to the shaping of the research agenda ( the Institute. The National Board of Health was formerly responsible for providing a interface between the KTL and the municipal health authorities but this body wa abolished in the recent health reforms (1991) and the municipalities now have th primary responsibility for the provision of health care and other services for the loca population within their area. Two specific difficulties were reported to the pane. First, there is no established channel of communication between the municipalities and the KTL and second, many do not have adequate numbers of trained public health professionals to identify their research needs.
- A consequence of the difficulties noted above is that there is no forum in which research strategy can be developed for the KTL which will allow priorities to be se and which achieves appropriate balances within the research portfolio (ie between investigator initiated work exploiting scientific ideas and opportunities and work designed to address specific health problems, between basic, clinical and public health research, and between work requiring long term investment and that requiring shor term support etc). Such a mechanism is necessary if the undoubted strengths of the Institute are to be deployed as effectively as possible to meet its objectives.
- The KTL has an outstanding record in establishing and leading a wide range of collaborative activities both within Finland and internationally. It is clear that the KTL is playing an ever increasing role in European Union activities and is actively extending the range of its collaborative activities with the universities and other research agencies in research and research training. The evidence presented to the Panel indicated a limited number of areas where these interactions could be exploited further particularly with other research agencies and these are discussed below.

The Panel recommends that mechanisms for the formulation of an overall strategy for the KTL with a five year time horizon (which would be updated on an annual basis) should be strengthened. This will be essential to provide the framework for setting priorities and making the difficult choices between competing programmes which are worthy of support. The strategic plan must relate scientific opportunities to health and user needs and be based upon the support of scientific excellence (since only research of the highest quality will be of value to users). A strategy is not a directory of prescribed routes - it is a commentary by the scientific and user communities on the most productive directions for research in the foreseeable future which will contribute to the improvement of the health of

the Finnish people in the short, medium and long term. A more broadly based strategy will provide a more secure framework for the annual agreement (business plan) between the KTL and the Ministry - and for resource allocation within the KTL.

The introduction of improved mechanisms for strategic planning will require more broadly based arrangements for medium and long term strategic planning on the part of the KTL, the establishment of better mechanisms through which the Ministry can clearly identify and articulate its research needs (not unnecessarily duplicating expertise already available), and the development of satisfactory channels of communication between the KTL and Ministry, and the municipalities (which carry the responsibility for the delivery of health care and the development of the system).

The Panel, therefore, recommends that :

(i) a Director-General's strategy group should be established. The purpose of this group would be to advise the Director-General and Board on the development of the research strategy, public health role and the training and career development responsibilities of the Institute. The group should have no more than eight to ten members serving under an independent chairman with a suitable scientific or professional background. The membership would comprise the Director-General, a representative of the Ministry of Social Affairs and Health, a number of leading members of the scientific or professional background. The Panel further recommends that the independent members of the group should each be appointed for a four year term (with the possibility of renewal for a further single four year term) and that at least one member should be recruited from outside Finland;

(ii) the Ministry of Social Affairs and Health should take steps to strengthen its own capacity to identify and articulate its own policy and operational research needs;

(iii) a national public health forum should be established by the Ministry and the KTL to provide a framework for the exchange of information about the research and public health strategies of the public sector bodies and for consideration of major issues of policy and strategy for the future. This should also include senior representatives of the other sectoral research institutes, the Centre for Health Education, the universities with faculties of public health and representatives of the municipal health authorities who would be able to indicate the research needs of those who have the responsibility for health care delivery.

### THE INTERFACE WITH THE MINISTRY OF SOCIAL AFFAIRS AND HEALTH AND THE OTHER SECTORAL RESEARCH INSTITUTES

The Ministry of Social Affairs and Health has overall responsibility for research a development in its sector. This encompasses the activities of the sectoral reseau institutes which are its direct responsibility - the KTL, the NAWH, the Finnish Institute Occupational Health and the Finnish Centre for Radiation and Nuclear Safety. There important interfaces between the first three of these. This is recognised by the Minis which convenes two meetings each year which bring together the Permanent Secreta senior officials of the Ministry and the Heads of each of the institutes.

**Relationships between the KTL and the Ministry.** The operation of the interfa between the KTL and the Ministry in the formulation of policy and development strategy has been discussed above. The Panel is aware that there are frequent conta between senior staff in the conduct of day to day business. The arrangements at this le appear to work well and the Panel does not propose any change.

Relationships between the KTL and the National Research and Development Cen for Welfare and Health. The NAWH was created at the start of 1991 from the merger two boards (Health and Social Welfare) and was in December 1993 further developed in an expert body - the National Research and Development Centre for Welfare and Heal The defined responsibilities of the agency are a) research and development, b) collect and collation of national and international information and its transmission to users, statutory databases, registers and statistics (although some of these responsibilities discharged by the central statistical office), d) assessment of services and th development, e) promotion and implementation of educational and training programm f) initiation of action for welfare and health care development. It is understood that programme will include policy evaluation, health technology assessment, econor evaluations and health services research. It is clear that this is an important interface a that there are a number of areas of common interest between the KTL and the NAW These include the roles of the two bodies in the evaluation of interventions (includi economic evaluations and quality-of-life studies), mental health and the disseminatior research results. The Panel takes the view that the relative roles and responsibilities each agency requires further clarification.

The relationships between the KTL and the Finnish Institute of Occupational Heal The Institute of Occupational Health was established in 1945. Its mission is to "produ compile and disseminate scientific information on the relationship between work a health and promote its utilisation" so that "working conditions can be made healthy a safe" It has four main functions - research, the provision of expert occupational hea safety services, training and the dissemination of information. The Institute operates fr a centre in Helsinki and through six regional institutes. Active research programmes en within each of the individual departments and in addition the Institute has develope number of initiatives ("action programmes") some of which are research based and some are intervention oriented. The current programmes are focused on a) allergy and work, b) prevention of work-related musculo-skeletal disorders, c) development of occupational health services, d) noise-induced hearing loss, e) ageing, f) healthy and productive work organisation and g) the workplace. The KTL and the FIOH have closely related but complementary responsibilities in a number of areas.

There is frequent contact between the KTL and these other two agencies (and the Ministry) for the conduct of business on a day to day basis and the Ministry of Social Affairs and Health also convenes two meetings each year which bring together the Directors of all three Institutes for the exchange of information and the co-ordination of activities. The Panel did, however, identify a number of specific areas in which a greater degree of co-ordination of effort between the Institutes would be desirable - in particular between the KTL and the NAWH and these are highlighted in the reports on the individual divisions and departments.

### The Panel recommends that:

(i) the Ministry should clarify the relative responsibilities of the KTL and the NAWH;

(ii) the NAWH and FIOH should be represented on the proposed broadly based national public health forum to ensure better alignment of the strategic planning mechanisms of all three Institutes, to improve the transfer of information and provide a more secure basis for the development of joint activities in areas which fall within the sphere of responsibility of both Institutes.

### **MEETING THE NEEDS OF THE USERS**

The major users of the research and public health outputs of the KTL are the Ministry of Social Affairs and Health (which has been discussed above) and the municipalities which are responsible for the promotion of public health and the provision of health care at a local level. The administrative and fiscal reforms which took place in 1991 have led to a considerable devolution of responsibility for health care to the municipalities (which have limited numbers of skilled personnel) and this change was accompanied by the abolition of the National Board of Health and the establishment of the National Research and Development Centre for Welfare and Health. The need to assume new responsibilities and to develop new working relationships between the Ministry and other bodies involved has inevitably been associated with considerable perturbation to the system.

The Panel took the view that the KTL had three particular roles to play in relation to the municipalities.

1. The conduct of research which will underpin the development of public health policies and contribute to the planning and development of the health care delivery system. Evidence presented to the Panel indicates that much of the research activity of the KTL is of direct relevance to the health of the Finnish population (detailed comments on the individual programmes and projects are provided below). It is, however, concerned that no satisfactory means exist through which the municipalities can feed into the strategic planning processes of the KTL (see above) and that there are only limited mechanisms for disseminating the results of the research conducted at the KTL to the municipalities.

2. The provision of advice and, on occasions assistance, in addressing specific problems (eg control of outbreaks of infectious disease, environmental problems). The KTL provides only limited advice and assistance to help in problem resolution by the municipalities at present. The principal responsibilities relate to the monitoring and control of infectious diseases and these arrangements appear to work well - although these responsibilities are limited in scale. The Panel noted that the public health duties of the other divisions have not been so clearly defined. The Panel is concerned that the current limited role of the KTL does not represent the best use of scarce expertise and that it might result in unfortunate delays in the containment and management of major events of public health importance.

3. The training of public health personnel (see below). The Panel noted that the health reforms have placed significant additional duties upon the municipalities. A concern was expressed to the panel that some of the municipal authorities did not have sufficient personnel trained in the disciplines of public health to discharge these responsibilities effectively. It was beyond the terms of reference of the Panel to test the validity of these assertions. The Panel did, however, take the view that the KTL was an important national resource for research training and postgraduate education in the disciplines of public health and we comment further on this below.

### The Panel recommends that:

(i) the municipal health authorities should be represented on the national public health forum proposed above;

(ii) the role the KTL in the investigation and control of outbreaks of infections and the investigation of environmental problems should be extended and strengthened and its formal responsibilities should be more clearly defined;

(iii) the Ministry of Social Affairs and Health should examine and clarify the individual responsibilities of the Ministry, the KTL, the NAWH and the municipal authorities in the dissemination and application of research results and in the provision of training in the disciplines of public health.

### **INTERFACE WITH THE UNIVERSITIES**

There are five universities in Finland with medical faculties and departments of public health (Helsinki, Turku, Oulu, Kuopio and Tampere). The last two of these were founded in 1970 and these have the largest departments of public health. The university departments do not have any formal public health duties within the Finnish health care system (with the exception of Helsinki) although they do have a major responsibility for postgraduate education in the disciplines of public health and for the award of higher degrees. Links between the KTL and relevant university departments are limited in The most important links are with the Departments of number but increasing. Epidemiology and Health Promotion in Helsinki and Kuopio, the Department of Nutrition in Helsinki and the Department of Mental Health in Tampere. A number of other collaborations on specific projects exist between scientists within all three divisions in the KTL and colleagues in the universities which have been developed through the identification of shared or complementary interests. Members of the staff of the KTL also contribute to teaching programmes in a number of the universities. The Panel was pleased to note the increasing level of collaboration between the KTL and the universities and would wish to see these links evolve and strengthen in the future. The establishment of five joint professorships between the KTL and the universities was particularly welcomed.

### INTERNATIONAL COLLABORATIONS

International collaboration in research is not an end in itself but a mechanism for the better attainment of national objectives. International collaborations offer some particular advantages for public health research. These include access to the large populations and cohorts necessary for some studies and also the opportunity to exploit the ethnic, environmental, social and cultural differences which exist between (and within) countries for research purposes. The KTL has a substantial record of research carried out with a wide range of colleagues elsewhere in Europe and in North America. Members of the staff of the KTL have a particularly successful record in playing a leading role in EU funded research (largely but not exclusively through the BIOMED programme). The Panel wishes to commend the commitment of the staff in setting up, and in many instances leading, these collaborations.

The KTL staff also have a substantial record of work carried out in collaboration with developing countries and have played a significant role in a number of WHO programmes. These programmes make an important contribution to helping the developing world with specific health problems (eg infectious disease). They are also of increasing and direct importance to industrialised countries for two reasons. First, with increased ease of travel, disorders which were at one time limited to specific geographic areas may now be encountered in medical and public health practice in any part of the world (eg AIDS). Second, a major change in the pattern of disease is emerging as conditions in the developing world improve and these countries are increasingly faced by the problems

which continue to pose a major public health challenge in industrialised societies. Research carried out in collaboration with developing countries offers some unique insights into a range of global problems. The Panel commends the efforts of the staff of the KTL in the establishment of such projects. In addition, members of staff of the Institute have played a major role in the establishment of demonstration projects, in the provision of training for health personnel from outside Finland and as advisers for WHO and other international organisations.

### TRAINING AND CAREER DEVELOPMENT

The KTL plays a significant role in the provision of research training in the disciplines of public health - a responsibility which it shares with the universities. Members of the staff of the KTL act as supervisors for a number of graduate students (leading to 93 awards of PhD degrees over the five year period 1990-1994) - the degrees being awarded by the universities (principally the University of Helsinki). The numbers of graduate students is increasing and the total undergoing training at the time of the evaluation was 225. Responsibility for ensuring that there is appropriate supervision and mentoring of graduate students rests with the individual heads of departments and supervisors. There is, however, currently no system in place for ensuring that the overall needs of postgraduates are met and the quality of the research training assured. The Panel also expressed concern that some of the programmes relied over heavily on graduate students for their prosecution and that this might not be in the best interests of their research training and career development.

It is recognised that the KTL is a valuable training resource both for those who plan to pursue a career in public health research and potentially also for those who will follow a service career in public health. Recently the universities have been charged with establishing collaborative multi-centre postgraduate training programmes ("graduate schools") in order to encourage the effective use of resources for training purposes. The KTL is a partner in a numbers of these programmes. These are the Graduate School of Public Health (with the Universities of Helsinki and Tampere, FIOH and NAWH), the Helsinki University Programme of Research Training in Medicine (with the University of Helsinki) and the Kuopio Graduate School of Public Health. The current arrangements, however, are entirely demand driven and there is no established mechanism through which the national manpower needs for public health professionals can be systematically assessed. The Panel was informed that a review of policy was currently being undertaken.

The Panel took the view that there should be close links between the training and career development programmes for those who intend to pursue a career in public health research and those who will primarily follow a service career track. Such links are essential for the conduct of research in community care settings, for the identification of research needs, for audit and for effective implementation. The Panel welcomes the creation of graduate schools in public health.

### The Panel recommends that:

(i) the KTL should designate a senior member of staff as postgraduate tutor who would be charged with the responsibility for ensuring that the overall training programmes and environment properly meet the needs of the graduate students;

(ii) the Ministry of Social Affairs and Health should conduct a review of the national needs for professionals trained in the disciplines of public health and, in the light of their findings consider how these needs might best be met in consultation with the KTL and the universities building on the strengths created by the recently created graduate schools.

### DISSEMINATION AND EXPLOITATION OF RESEARCH

### Dissemination

The dissemination and implementation of research results is achieved through the Ministry but its role is limited following devolution of responsibility to municipalities. It has little power to encourage implementation except in a limited number of instances. Some dissemination occurs through non-governmental organisations (NGOs) - principally through the Centre for Health Education. The Centre is a coalition of about 100 NGOs working in the health field (eg the Finnish Cancer Society, Finnish Heart Association, Finnish Red Cross etc). Its goal is to promote health education and promotion in Finland in collaboration with its member organisations through seminars, publications, health promotion campaigns and demonstration projects. The Centre has been strengthened in recent years following the closure of the former National Board of Health's Office for Health Education. There are good informal contacts between the Centre and the KTL. We were informed, however, that its influence upon the municipalities is very limited. The NAWH also has a responsibility to "produce and acquire the necessary national and international information and expertise and forward them to users". The KTL also produces a newsletter Kansanterveys which was first produced in 1993 and is published 10 times a year. It is primarily targeted at health care professionals and has a wide circulation (approximately 6500). The KTL has, in addition, a series of occasional publications (eg The Vaccinators Manual, International Travel and Health and The Parents' Guide to Vaccinations). Certain research results are made available through the World Wide Web.

The Panel is conscious that (in all countries) the impact of a number of major health problems could be significantly diminished by the better application of existing knowledge. The Panel was concerned at the apparent absence of a coherent structure for the dissemination of research results to public health and health care professionals and at the limited scale of the arrangements for health promotion in Finland.

### The Panel recommends that:

(i) the Ministry should undertake a review of the current arrangements for the dissemination and implementation of research results with a view to clarifying further the responsibilities of all the parties concerned (the Ministry, the municipal health authorities, NAWH, KTL and the Centre for Health Education) and ensuring that effective mechanisms are in place;

(ii) the mechanisms which are developed following this review should not be limited to the dissemination of research results which have been generated in Finland but they should have the capacity for systematically feeding information (originating in Finland or elsewhere) through to those who have responsibility for formulating public health policies and planning health care delivery at national and local level.

### Exploitation

The major products of the research effort of the KTL feed directly into public health and clinical practice without the need for development within a commercial environment and in these instances, the issue of the protection and exploitation of intellectual property does not arise. There is, however, a small but significant proportion of the research portfolio of the Institute which has and will continue to lead to the generation of novel products and processes which should properly be protected and exploited in the name of the KTL and its principal sponsor (the Ministry of Social Affairs and Health). Current arrangements (the majority of which relate to the Division of Infectious Diseases) have been put in place or an ad hoc basis. The Panel recognises that the primary responsibility of the KTL is to prosecute research which will lead to improvements in the health of the Finnish people. It also takes the view that, when in the discharge of its mission, research results in inventions which have a potential commercial value the Institute has a responsibility to ensure that these are protected and exploited for the benefit of the KTL and the Ministry. The Panel does not consider that the present arrangements are satisfactory for these purposes.

The Panel recommends that the KTL should commission a suitably qualified professional to review its current arrangements for technology transfer and for the patenting and licensing of the products of its research and advise on the establishment of suitable mechanisms for the protection and exploitation of its intellectual property.

### CURRENT PUBLIC HEALTH ACTIVITIES AND RESPONSIBILITIES

The KTL has undergone a major transformation from public health laboratory to research institute over the last twenty years. During this period the majority of the service responsibilities have been transferred to major hospitals and municipal health centres and the major research themes of the KTL have been developed. The KTL also carries responsibility for a number of public health surveillance and monitoring functions (some of which are statutory responsibilities).

The major statutory current responsibilities are:

1. Infectious diseases surveillance. The KTL has had a formal responsibility (under the terms of the Infectious Diseases Act) for the management of the statutory national infectious diseases surveillance system since 1992 (this was formerly the responsibility of the National Board of Health). This responsibility is discharged by the Department of Infectious Disease Epidemiology. The system requires notification of 32 infectious diseases and the detection of some 40 other micro-organisms by microbiological laboratories. A new system for the collection, collation and analysis of this information has been established recently. The Department also takes responsibility for training the personnel for the 22 regional registers in the health care districts in the implementation of surveillance programmes and in data management and analysis.

The Department has also undertaken a range of additional public health responsibilities. These include:

- quality assurance of clinical microbiology laboratories (also a statutory responsibility);
- surveillance of certain other infections (sexually transmitted diseases and common respiratory and gastrointestinal disorders);
- screening for prenatal infections;
- the provision of reference laboratory functions;
- surveillance of the national childhood vaccination programmes;
- the regular publication of information on communicable diseases (through Kansanterveys);
- control of epidemics (through the provision of advice, developing guidelines for control measures and the performance of epidemiological investigations);
- liaison with other national and international authorities.

2. *The production and procurement of vaccines.* This is a long standing statutory responsibility which dates back to the earliest days of the Institute. The procurement of vaccines is funded separately by the Ministry of Social Affairs and Health while the costs of production, quality control and distribution are funded from the regular budget of the KTL.

3. *Blood alcohol and drug testing*. The Department of Alcohol, Drugs and Traffic has a statutory responsibility for blood alcohol measurements on all suspected drivers and also for determination of drug (licit and illicit) levels in drivers at the request of the police. A similar service is provided for facilities caring for alcoholics and drug abusers and for the prison service. The number of blood alcohol estimations amounts to about 22 000 per annum. This has declined during the recession and is expected to decline further as breath alcohol estimations are accepted as evidence by the courts.

4. *Paternity testing*. This carried out by the Department of Immunobiology and about 2 500 estimations per annum are carried out.

5. Screening for congenital hypothyroidism. The screening is carried out by the Department of Biochemistry and about 40 000 estimations a year are performed. The number is declining as a number of large hospitals have started to perform their own analyses.

The most substantial routine public health responsibilities are those relating to the monitoring and control of infectious disease (1 and 2 above). These are largely statutory responsibilities which have been assigned to the KTL by the Infectious Diseases Act. The KTL has developed a number of other public health functions which are related to its formal responsibilities. These are all closely related to research programmes of the Division - particularly those in infectious diseases epidemiology, vaccine development and viral and bacterial pathogens.

The Panel was impressed by the high level of professionalism of the staff who meet the public health responsibilities in this field and who have improved the arrangements for infectious disease surveillance very substantially. The assumption of added responsibilities for the monitoring and control of infectious diseases in Finland represents a valid and cost-effective use of KTL resources. The Panel was also impressed by the close integration of the public health and research functions of this Division which exploits this interface particularly effectively.

The Panel noted that the responsibility for testing for alcohol and drugs was also a formal responsibility of the KTL but that the need for such estimations was likely to decline in the near future. A substantial reduction in these statutory responsibilities raises questions about the future structure and strategic direction of the Department of Drugs, Alcohol and Traffic and we consider this issue further below.

The Panel takes the view that the remaining service responsibilities (paternity testing and screening for congenital hypothyroidism) are no longer appropriate for the KTL. These services are unrelated to the research programmes of the departments in which they are carried out and the competent use of these techniques is now within the scope of many laboratories.

The KTL also assumes responsibility for a wide range of other public health responsibilities. These include the monitoring of major chronic health problems (excluding cancer), risk factors and health behaviour, maintenance of the food composition database and the provision of advice on environmental matters. The Panel's analysis and judgements on these activities are reported in the sections on the activities of the individual Divisions.

### The Panel recommends that :

(i) the KTL should continue to carry formal responsibility for the monitoring and control of infectious disease in Finland and that steps should be taken to ensure that effective interfaces are maintained with the Ministry of Social Affairs and Health and the municipal authorities;

(ii) the KTL should undertake a review of the role, responsibilities and research strategy of the Department of Alcohol, Drugs and Traffic (see also below);

(iii) the KTL should discontinue the provision of paternity testing and screening for congenital hypothyroidism as soon as alternative arrangements can be put in place.

# **OVERVIEW OF CURRENT RESEARCH ACTIVITIES AND RESPONSIBILITIES**

The Director-General emphasised to the Panel the importance which he attaches to developing a research programme of the highest quality. He made the point that public health research must meet particularly high standards since the results were potentially applicable to large population groups. The Panel welcomed this clear emphasis on quality. The Panel recognises that much of the research which has been carried out at the KTL has met this criterion and has been of considerable public health importance. The high international standing of the KTL reflects the outstanding contributions which have been made by the best of the staff and this has been facilitated by the unique opportunities for public health research which the Institute offers. The Panel also wishes to acknowledge the success of the Director-General in building a major public health research institute on the foundations of a public health laboratory over the course of the last 15 years. The Panel's evaluation of the activities of each Division is to be found the following sections of this report.

### Overall comments on the Division of Chronic Diseases and Health

The Division has a wide range of important public health responsibilities including the monitoring of major chronic health problems (excluding cancer), risk factors and health behaviour, the maintenance of the food composition database and the provision of support for the police and courts in relation to substance abuse and traffic offences. The Division has a well-deserved international reputation in a number of fields for its research - most notably in the epidemiology of cardiovascular diseases and through the ATBC trial. The research in the newly created Department of Human Genetics is also internationally highly competitive and this is strongly supported by the Panel. Some of the projects in the Departments of Mental Health and Biochemistry are also of high quality and of considerable public health importance and these were also strongly supported by the

Panel. The Division is, however, at a cross-roads and important strategic decisions need to be taken. The majority of the studies in the epidemiology of cardiovascular disease and related investigations which have dominated much of the work of the Division have been completed and there are relatively few clear ideas for future work in these areas. The well characterised cohorts generated by these studies are a unique resource - but it is not clear that they are necessarily a valuable resource - and the Panel was conscious that they might constrain thinking in the development of future research plans. The future plans for the departments which were most involved in these studies largely comprise a number of studies of limited scientific interest and mix of small scale and unrelated projects. An overarching review of the strategy of this Division should be undertaken with a particular emphasis on its future role in cardiovascular research covering the Departments of Epidemiology and Health Promotion, Nutrition, Biochemistry and Human Molecular Genetics. Consideration should be given to some reconfiguration of departmental boundaries to meet the needs of the strategy more effectively and enhance critical mass in key areas. The future of the Departments of Immunobiology and Alcohol, Drugs and Traffic should also be subject to a fundamental reappraisal.

The major recommendations of the Panel for the Division of Chronic Diseases are:

(i) the Director-General should undertake an overall review of the research strategy of the Division. This review should include a detailed reappraisal of the role of the KTL in research in cardiovascular disease covering the Departments of Epidemiology and Health Promotion, Nutrition, Biochemistry and Human Molecular Genetics. The future research strategy should be based upon the development of hypothesis driven epidemiological studies and the evaluation of interventions exploiting the well characterised populations deriving from past, current and future epidemiological studies;

(ii) there should be further investment in human genetics and new programmes should be developed in collaboration with staff in other Departments within the framework of the overall Divisional strategy;

(iii) the programmes in the genetics and determinants of mental illness should continue to be developed;

(iv) the activities of the disparate groups working on aspects of health behaviour should be brought together, strengthened and focused to form an integral component of the principal research themes of the Division;

(v) the future of the Departments of Immunobiology and Alcohol, Drugs and Traffic should be subject to a fundamental reappraisal.

### General comments on the Division of Infectious Diseases

The overall strategy for the Division was clearly described in the KTL report and the additional papers which were presented to the Panel. The Division has major (and increasing) public health responsibilities - some of which are statutory and others rational extensions of current activities using the undoubted skills of the professional staff. The public health surveillance responsibilities and research activities of the Division are generally well integrated - each deriving strength from the other. The development of productive international research collaborations is commended by the Panel. A limited number of the activities do not fit within the current strategic framework - and some of these are of limited scientific value and should be discontinued. The plans for the reconfiguration of the Division were regarded as sensible by the Panel but these should be examined again in the light of this review. The Panel, in general, favours movement towards a structure with fewer individual Departments. It would wish to draw particular attention to the need to ensure that there should be a review of the disposition of bacterial expertise within the KTL (taking due account of skills available elsewhere in Finland) to ensure that it meets its public health and research responsibilities in the most cost-effective manner. The Panel was also concerned at the limited expertise in molecular and cellular immunology available within the Institute and current and likely future needs in this discipline should also be an integral component of this review. It is the view of the Panel that immunology should be strengthened and that this can only be achieved through the recruitment of a senior immunologist to the KTL to provide the necessary scientific leadership. The Panel considers it essential that the proposed Director-General's strategy group should review options for the future role of the small laboratory in Oulu. The Panel wishes to commend the strong and effective scientific leadership of Dr Mäkela who retires next year.

The major recommendations of the Panel are:

(i) the current research strategy (the major objective of which is to improve the diagnosis, control and prevention of infections) has led to the development of programmes in which the public health surveillance and research activities are well integrated and effective internal and external collaborations are in place. These should be strengthened and developed. A greater degree of focus should be achieved through the discontinuation of projects which are of low priority and do not contribute to the overall Divisional strategy;

(ii) the assumption of an increasing range of public health responsibilities by this Division merits greater investment but this should be met by the reallocation of resources released through the discontinuation of activities of low priority;

(iii) further investment in the development of improved diagnostic methods should be more clearly justified by public health and research needs; (iv) the Division should be reconfigured in the light of this review to concentrate expertise in a smaller number of larger Departments. Particular attention should be paid to the need to ensure that the existing expertise in bacteriology is used to best effect and to strengthen immunology (particularly cellular immunology) within the KTL;

(v) the future role of the Laboratory in Oulu should be reviewed by the proposed Director-General's strategy group in the light of this review.

### General comments on the Division of Environmental Health

The Division has a series of public health responsibilities (although these do not include regulatory responsibilities). It is currently in a state of transition (programmes are being terminated and significant senior staff movements are taking place) and without a clearly defined strategy for future. The Panel considers that the KTL should review its overall strategy for the Division as a matter of urgency establishing an expert group for this purpose which would report to the Director-General and the proposed Director-General's strategy group. The Panel also considers that the public health role of the Division in the provision of expert advice and the investigation of environmental problems should be more clearly specified. It would strongly support the development of major programmes on air pollution and microbial exposures and health in buildings and would recommend that a strategic review of the skills and expertise needed for the effective prosecution of such a programme should be given to the development of other programmes which have a particular relevance to Finland (eg relating to the timber processing industries).

The Panel also took the view that the Division should develop a more structured and coordinated approach to studies. This will enable the Division to carry these through in a systematic manner from hazard identification to epidemiological association, to exposure assessment (with development of appropriate biomarkers), to assessment of the consequences of exposure, to study of mechanisms of toxicity, to the evaluation of factors (intrinsic and extrinsic) which might modify the impact of exposure. The Panel further recommends that the Division should consider the development of other major targeted programmes designed to improve understanding of mechanisms in human toxicity and the consequences of exposure to hazardous agents - these might be in the fields of neurotoxicology, immunotoxicology or reproductive/developmental toxicology. The establishment of a strong programme in one or more of these fields will require considerable strengthening of the limited number of current staff members with expertise in these areas. The range of activities within the Division does not appear to offer good value for money at present.

The Panel was also concerned at the small (and in some cases very small) numbers of staff in some of the groups which are well below critical mass. The disadvantages which result from this are in part mitigated by the development of collaborative activities. The Panel
remains concerned, however, that many of the research programmes are small in scale and scope and of limited scientific value. The Panel gained the clear impression that a number of the collaborating groups were also probably operating below critical mass and thus the potential gains from proximity with those in the University and FIOH have not been realised. This is not in the interests of the KTL or its partners. The Panel would propose that a critical strategic review of the Division should be carried out in the context of its relationships with the University and the FIOH. There is a strong case for the review being carried out jointly with these other bodies. The Panel took the view that there might be advantages if the key elements in Kuopio were to be drawn together into an Institute of Environmental Health with a clearly defined strategy - but the possible advantages and disadvantages would have to be explored with considerable care. (We recognise that such a recommendation takes us beyond our terms of reference). The achievement of this objective would permit the development of a major research centre in the field. It would also require considerable reconfiguration of the skills base of the Division with recruitment of staff with additional complementary skills. It is probable that the substantial changes which would strengthen the Division could be achieved without additional investment taking advantage of this transitional period. The Panel recommends that the Division should not continue to provide a toxicity testing service on a contractual basis to outside bodies.

#### The Panel recommends that:

(i) the overall strategy for the Division should be reviewed as a matter of urgency by an expert group which would report to the Director-General and the proposed Director-General's strategy group;

(ii) the Division should develop a more structured and co-ordinated approach to studies to enable it to carry these through in a systematic manner from hazard identification, to epidemiological association, to assessment of exposure and its consequences, to study of mechanisms of toxicity and evaluation of factors which might modify the impact of exposure;

(iii) major research themes for the future should include air pollution and other programmes which have a particular relevance to Finland (eg relating to the timber processing industries). Other major targeted programmes might be developed in neurotoxicology, immunotoxicology or reproductive/developmental toxicology - (it is recognised that the establishment of a strong programme in one or more of these fields will require considerable strengthening of the limited number of current staff members with expertise in these areas);

(iv) a critical strategic review of the Division should be carried out in the context of its relationships with the University and the FIOH (ideally in collaboration with these other bodies). The possibility that these might be drawn together into an Institute of Environmental Health to develop a major resource and research centre in the field

with a clearly defined strategy should be explored;

(v) the contribution which staff of the Division make to the maintenance of bacteriological expertise within the KTL should be considered in the reappraisal proposed in the review of the Division of Infectious Diseases;

(vi) the Division should not continue to provide a toxicity testing service on a contractual basis.

#### MANAGEMENT ISSUES

The panel was not mandated, nor did it have the time, to undertake a detailed review of the management arrangements of the Institute. It would, however, wish to highlight a number of points which became evident during the course of the evaluation which require further consideration.

1. The Panel was clear that much of the overall success of the KTL derives from the abilities and leadership qualities of the Director-General. The Panel was concerned that the KTL might be very vulnerable if the Director-General were to leave. It was noted that the current management structure is very flat and broad and, although this has certain advantages, it is not ideal in management terms and undoubtedly carries certain disadvantages. The Panel takes the view that it would be desirable to review the scientific leadership and managerial arrangements (accompanied by a review of the organisational structure) in the light of this evaluation. A significant reduction in the number of individual departments would be desirable (and the Panel recognises that the Director-General and his colleagues already plan to take steps in this direction). The Panel also recommends that proper consideration should be given to succession planning for the most senior positions at the appropriate time.

2. The point has been made above (p11) that this Institutional review covered 18 departments and 90 individual research programmes and thus the Panel's judgements have been of a broad strategic nature. We were informed that Departments are reviewed on a triennial basis by groups comprising staff from other departments within the Institute and some external (usually but not exclusively Finnish) evaluators and the report of one such evaluation was made available to us. The Panel considers that such evaluations do not provide a satisfactory mechanism for evaluating the scientific programmes with the necessary degree of rigour. The Panel also takes the view that regular and detailed review of the individual scientific programmes should be complemented by a regular overarching strategic review of the Institute. It is anticipated that this would be less detailed than the current evaluation since it would be conducted against the background of regular external peer review based upon each major programme area. An institutional review of this nature is also necessary since it permits an assessment of the overall scientific achievements and future proposals of the KTL, the effectiveness of the management of resources, the extent

to which the KTL has met its objectives and the possibility of exploring how the KTL provides added value by developing scientific interactions and collaborations.

The Panel recommends that:

(i) each major programme area of the KTL should be reviewed every four years by an external peer review team. The review should report on the research performance and future proposals of each department using accepted criteria (similar to those developed for this evaluation). The proposed Director-General's strategy Group should be charged with responsibility for oversight of the peer review process;

(ii) a broad institutional review (similar to the present evaluation) should be carried out each five years.

3. The Panel has undertaken an overall review of the scientific achievements and future proposals of the KTL and has reached broad judgements on the merits of the scientific programmes presented. It was not possible within the time available to the Panel to conduct a detailed audit of human and financial resources.

# The Panel, therefore, recommends that a staff audit should be carried out in the light of the Panel's recommendations to ensure that the human resources available to the KTL are used in the most effective manner.

4. The Panel understands that the terms and conditions of service of the permanent staff members of the KTL impose considerable limitations on the ability of the Director-General to deploy staff in the most effective manner. The Director-General reported to the Panel that he was working towards achieving a greater degree of flexibility by increasing the proportion of staff on limited term contracts when making new appointments (a process which can only achieve change in the medium to long term). These are considerable constraints for a research organisation - particularly one which is in a state of transition as a number of major programmes of research are reaching their final stages and there will necessarily some reorientation of the Institute.

The Panel recommends that consideration should be given to developing and introducing terms and conditions of employment which will provide the flexibility that is essential for a major research organisation.

# **REVIEWS OF DIVISIONS AND DEPARTMENTS**

# DIVISION OF HEALTH AND CHRONIC DISEASES

# INTRODUCTION

The overall objective of the Division is to develop strategies for the promotion of health and the reduction of morbidity and mortality from chronic diseases among the Finnish people. The Division aims to provide a focal point for the monitoring of, and expertise in, the major chronic diseases and the general health of the population. The research programme is directed towards a better understanding of the fundamental causes and factors which predispose to the development of chronic disease and the evaluation of preventive strategies through randomised clinical trials and community based interventions.

The specific principal objectives of the division are:

- monitoring of the major chronic diseases and their determinants in the Finnish population;
- high quality basic and applied research into the causes and determinants of chronic diseases and health;
- training of experts, professionals and researchers in public health;
- dissemination of information on public health;
- provision of centralised public health services.

The Division has substantial public health responsibilities. It monitors the incidence, mortality and risk factors for a number of chronic diseases and the general health of the population through:

- analysis of disease-specific mortality rates in various subgroups using national mortality register data;
- monitoring trends in cardiovascular disease using acute myocardial infarction and stroke registers;
- monitoring suicide mortality and the rate of attempted suicides in conjunction with the national suicide prevention project;
- surveying the prevalence of major chronic disease risk factors in selected target populations at 5 year intervals (FINRISKI project).
- surveying health behaviour in random samples of the adult population;
- developing measures of functional capacity;
- monitoring rates of drinking and driving and drug use.

The main focus of research activities within the Division are:

- aetiology and prevention of major chronic diseases (atherosclerotic cardiovascular disease, diabetes, chronic arthritis, self-destructive behaviour and multiple sclerosis);
- genetic background to monogenic disorders and common disorders;
- risk factors for major chronic diseases;
- diet and nutrition;
- smoking alcohol and drugs;
- general health of the population;
- evaluation of preventive interventions.

#### DEPARTMENT OF EPIDEMIOLOGY AND HEALTH PROMOTION

The principal objectives of the Department are the monitoring of major chronic diseases and the study of the risk factors involved. Members of the staff of the Department are also involved in the development of national strategies for health promotion and disease prevention. The principal focus is on cardiovascular disease and diabetes with a particular emphasis upon risk factors.

The Department receives more than half of its funding from extra-budgetary sources. In 1994 this amounted to 5.0 million FIM (of a total of 9.7 million FIM). The most important sources are the Academy of Finland, the National Institutes of Health (NIH) in the USA. and private Finnish foundations. Twelve of the 45 members of the staff (26 professional and 19 technical) are supported by the core budget. Many of the programmes of the Department involve large scale collaborations (national and international) and staff of the Department act as the co-ordinators for a number of these. The Department with its large cohort studies and intervention trials is regarded as a flagship of the Division and its programmes involve substantial collaboration with, and to an extent dominate, the activities of certain other departments.

The Department has a number of major public health responsibilities (listed above) and these are of considerable potential value for the development of strategies for public health and the planning of health care delivery. These functions (ie monitoring the incidence of major non-communicable diseases and national health behaviour surveys) provide a basis for the research activities of the Department, and the public health responsibilities and the research are, in general, well integrated. The data generated by this Department will be of fundamental importance in the near future when the KTL assumes responsibility for preparing a report for the Finnish government on the state of the public health in Finland.

Epidemiology of cardiovascular diseases. Work carried out in this field within the Department has been of the highest quality and of major international importance. The

FINMONICA acute myocardial infarction (AMI) register has been established as a part of the WHO MONICA project. The data collected have been invaluable in charting the changing pattern of morbidity and mortality from AMI (eg the incidence of AMI is declining overall more rapidly than the mortality from AMI). The stroke register has operated in parallel and has charted trends - although over a shorter period of time. There are plans to repeat the monitoring every five years and also to extend the studies to musculoskeletal disorders and mental health. The data collected during the course of these studies represents an important resource for monitoring future trends in the incidence of cardiovascular disease in the context of changes in health behaviour and they should also provide a unique framework for a range of primary and secondary intervention studies. The Panel was, however, concerned at the limited scale of the plans for future activities. These are largely limited to the continuation of the public health surveillance and monitoring activities and no significant plans for future major hypothesis based studies or evaluations of interventions were presented to the Panel. It is recommended that further consideration be given to possible future uses of these unique resources which represent a considerable investment of KTL resources.

WHO MONICA data centre. The Department maintains the WHO MONICA data centre. The analysis of the data from the principal elements of the MONICA study is now well under way and WHO funding will probably be discontinued after 1998. The study is now being extended to gain further information on subsets of the study population as they age by monitoring coronary events and congestive heart failure. The Panel takes the view that the maintenance of the data centre should be regarded as a high priority for the future but would wish to see further detailed consideration given to ways in which these data might be exploited for future research purposes.

Studies of risk factors. The population surveys of risk factors and health behaviour commenced in 1972 and have been carried out subsequently every five years in three or four areas of the country (the FINRISKI study). The range of factors observed has been increased in recent years and these studies are now contributing to the development of health policies and are also providing the basis for some intervention studies (eg the evaluation of the effectiveness of some health education programmes). There are plans for more comprehensive surveys every ten or fifteen years and these will also include a physical examination and the development of a bank of biological materials. This project is commended by the Panel.

**Diabetes mellitus.** Diabetes is an important public health issue in Finland which has the highest incidence of insulin dependent diabetes mellitus (IDDM) in the world and non-insulin dependent diabetes mellitus (NIDDM) is an important risk factor for cardiovascular disease. The studies on IDDM are directed towards identifying the genetic and environmental factors which predispose to the development of the disease. The department serves as co-ordinator for an international study on the incidence of IDDM. The incidence data are being collected over the period 1990-1999. The Finnish national register has been in place since 1987. This work is of high, but not outstanding, quality.

These studies are being carried out by one permanent member of the staff and the Panel was concerned by the isolated (and potentially non-competitive) position of the scientist concerned and that only very limited collaborations had been established with the others with related interests in the KTL (in the departments of Molecular Genetics and Acute and Chronic Viral Diseases). The collaboration with the National Center for Human Genome Research, while valuable, is limited to the provision of family material for an NIH study.

Health behaviour. This programme was established at the request of the Ministry of Social Affairs and Health. The purpose of the programme is to generate an integrated approach to health promotion and education. The work of the group is largely of an observational nature comprising a number of limited scale studies focusing on a range of behavioural and life style variables (particularly smoking). The Panel recognises the importance of developing programmes in this area to complement current activities within the Department and future studies of interventions. It was not clear, however, from the current range of studies, that there was an effective overall strategy for this group or that its activities formed a coherent part of the research programme of the Department as a whole. The Panel noted that there was relatively little interaction with those engaged in related activities in the Departments of Mental Health and Alcohol, Drugs and Traffic.

## **Conclusions and recommendations**

The Department has an outstanding reputation for the conduct of large scale epidemiological studies and these have made important contributions to knowledge and been invaluable for the development of public health policies. A number of these studies have been concluded in recent years and most of the others will be completed over the course of the coming quinquennium. The Department retains important public health monitoring and surveillance responsibilities. A satisfactory balance has been achieved between the research and the public health responsibilities and these have been well integrated. The Department, however, is at a cross-roads and this is a time for strategic reappraisal and consideration of future directions. It is recognised that past and current work has generated unique collections of data - but these can only be regarded as valuable if they are exploited to provide the framework for a range of hypothesis based studies of importance for human health. It is essential, therefore, in formulating a strategy for the Department that the importance of these are recognised but that they do not unduly constrain planning for the future .

# The Panel recommends that:

(i) the Director-General and his colleagues should develop a strategic plan for the Department building on existing strengths - taking due account of the need to achieve an appropriate balance between, and integration of, the public health and research activities. The major themes of this plan should be the development of hypothesis based epidemiological studies and evaluation of interventions exploiting the well characterised populations derived from past, current and future epidemiological studies;

(ii) the work on diabetes mellitus should be strengthened by incorporating this programme within the overall strategy for the Department and through the development of collaborations with those in other Departments with related interests;

(iii) the programme on health behaviour should be developed as an integral component of the strategy of the Department and steps should be taken to enhance interactions with behavioural scientists in other departments within the KTL.

#### DEPARTMENT OF HUMAN MOLECULAR GENETICS

The genetic isolation of Finland offers unique opportunities to analyse the genetic background of human disease. The Department exploits these to dissect the molecular background of the Finnish heritage and to identify those genes which predispose to certain common multi-factorial disorders. The Department of Human Molecular Genetics, which was founded in 1988, is one of the newest departments within the the KTL. The Department carries out fundamental and applied research into human genetics.

The major research themes of the Department are to (i) develop specific DNA tests of disease mutations based on research findings for population based studies and the development of diagnostics for large scale screening programmes and (ii) carry out fundamental studies of the genetic and molecular processes involved in human disease to provide a basis for prevention and treatment, not only of the monogenic disorders, but also of the complex common multi-factorial diseases which increase in frequency with age. Both within the KTL and nationally, the Department serves as a resource and knowledge centre for molecular biology techniques. The scientists of the Department play an active role in informing health care professionals and the general public of issues relating to genetic analysis and DNA technology. Nationwide surveys on population attitudes have been carried out to optimise the content and form of presentation of this information.

The Department had a total staff of 46 (35 professional and 11 technical) in 1994. The budget in that year was was 8.7 million FIM of which 40 per cent was derived from extrabudgetary sources. The major sources of extrabudgetary funds are the Academy of Finland and private Finnish foundations. The Department has extensive collaborations in Finland and also with groups in the US and other European countries. The main foreign collaborators are the National Center for Human Genome Research at NIH and Genethon in France. The main focus of the Department of Human Molecular Genetics is research and it has no direct public health responsibilities.

Finnish disease heritage. The focus of work in this group has been on the eight specifically Finnish disorders (and a limited number of other monogenic diseases). The group has been successful in assigning a chromosomal location to the genes responsible for all of these. Specific mutations have been characterised in Marfan's syndrome,

amyloidosis of the Finnish type and aspartylglucosaminuria (AGU), and the AGU enzyme has been crystallised. Good progress has been achieved through work on disease genes already identified by positional cloning or a candidate gene approach. This project has exploited effectively the Finnish disease heritage and is commended by the Panel.

**Predisposing loci of complex disease.** The gene mapping unit has developed a programme to study genetic loci predisposing to complex disorders with a high prevalence in the population. The Department is developing major programmes in molecular epidemiology using the twin register, regional isolates and population samples to study the genetic background of multiple sclerosis (MS) and bipolar disease. The group has been successful in identifying linkage to two loci predisposing to MS - the gene encoding for myelin basic protein on chromosome 18 and the HLADQ region on chromosome 6. Similarly a predisposing locus for severe bipolar disease has been identified on Xq25. The homogeneity of the Finnish population facilitates the identification of genetic predisposition to such disorders. There are good collaborations with the FINRISKI study and the Department of Mental Health. These studies are of the highest standard and have made an important contribution to the study of MS and bipolar disease are strongly supported by the Panel.

Molecular pathogenesis of disease. This programme is of limited scale at present. It has mainly focused on AGU, amyloidosis of the Finnish type and Marfan's disease. The group is mainly studying the cellular consequences of mutations. There is, at present, relatively little work in the Department correlating changes in the genotype with those in the phenotype - other than that at the cellular level. This work is strongly commended by the Panel which notes the importance of the establishment of facilities for transgenic animals for its future development.

**Future.** The future plans of the Department are directed to continuing existing studies and assigning chromosomal locations for a number of other Finnish diseases for which no molecular information is available at present. Research will be carried forward from linkage studies to the identification of disease genes. The group is participating in a positional cloning consortium with the Universities of Helsinki and Tampere.

#### **Conclusions and recommendations**

The Panel was impressed by the quality and volume of the work produced by the group comprising five scientific staff, three post-doctoral scientists and about 25 graduate students. The work was regarded as being of high international standing and the group are to be commended for the effective exploitation of the opportunities offered by the Finnish population. Research in human genetics is of major potential significance for public health. The development of reliable and cost-effective tests suitable for population wide screening for gene carriers could substantially reduce the number of children with major disabling genetic disorders. The identification of the predisposing loci for complex disorders common at the population level will make it possible to identify those at risk and

plan appropriate interventions and health education programmes. The group also has effective international collaborations in place.

The Panel recommends that:

(i) there should be further investment in this group in view of the potential public health importance of research in human genetics;

(ii) the KTL should consider developing mechanisms through further investment and collaboration to extend the range of studies on the structure and function of gene products - including the use of transgenic animals;

(iii) these studies should be developed further through the development of screening and other programmes - particularly through collaborations with other groups within the KTL which have the necessary skills in epidemiology and the behavioural sciences.

# DEPARTMENT OF NUTRITION

The Department of Nutrition was founded very recently (in 1992) by combining the nutritional expertise within the former Departments of Epidemiology and Biochemistry. The Department has recently carried responsibility for the largest study ever carried out by the KTL, namely, the Alpha-tocopherol, Beta-carotene Cancer Prevention Study (the ATBC study). The principal activities of the Department centre on nutritional epidemiology and surveillance, nutritional biochemistry and some selected topics related to nutrition.

The Department had a total staff of 27 (21 professional and six technical) in 1994. Eleven held permanent contracts paid from the core budget and 16 other staff members had short-term contracts met from extrabudgetary sources. Half of the total budget of 7.4 million FIM was derived from external sources. The most important source of extrabudgetary funding has been the National Cancer Institute of the US (the ATBC study). This funding will extend to the year 2001 with a reduced budget.

**Nutritional epidemiology.** Research is closely related to the public health responsibilities of the Division and much of the work is carried out as part of the MONICA and FINRISKI studies. The Division (mainly the Department of Epidemiology and Health Promotion) carries out a large risk factor survey (the FINRISKI project) at five year intervals which includes an extensive review of diet and nutrition with three-day food records. Other research activities in nutritional epidemiology include a case control study on dietary risk factors for breast cancer. This study is co-ordinated by the International Agency for Research on Cancer (IARC) and the Department plays a significant role in the project. The group also plays an active part in the work of the National Nutrition Council which brings together a range of constituencies and plays an important advisory role in making

nutritional recommendations for the population. A food composition database, run by the Department, is used, for example, to calculate the nutrition intakes in the FINRISKI survey. The links between the research and public health responsibilities of this group are very good. The maintenance of a food compositon database is of particular public health importance. The Department has plans to carry out a number of studies exploring the possible associations between dietary factors and cardiovascular disease and cancer.

**ATBC study.** The ATBC study has dominated the activites of this Department in recent years. The study was designed to explore the relationship between dietary factors and disease risk - and in particular to determine if alpha-tocopherol or beta-carotene reduce the risk of lung or other cancers. The first phase of this large collaborative study between the KTL and the US National Cancer Institute (NCI) was completed in 1994. This phase has generated a considerable volume of information of considerable public health importance - and a number of other publications are currently in preparation. The contract with the NCI has been renewed until the year 2001 to allow monitoring of the long term effects of antioxidant supplementation and to carry out cohort analyses on possible associations between dietary factors and the risk of cancer and cardiovascular disease. Detailed information on the dietary habits of the subjects in the study and the finding that AT and BC supplements may have harmful effects opens up the possibility of generating new hypotheses which might be explored within the Department.

The Department is not carrying out any controlled clinical nutrition trials at the present time. The latest trial on the effects of dietary sterols was completed in December 1994. The group has applied for money from the EU BIOMED programme for a study of levels of fatty acids and naturally occurring antioxidants.

Nutritional biochemistry. The aim of the nutritional biochemistry unit has been to develop, validate and use biomarkers of dietary exposure. The main focus of the work of the unit has been on selenium, because the Finnish diet has been characterised by a low selenium content. A series of studies of selenium supplementation have been carried out and these have led to nationwide supplementation of fertilizers with selenium. This work has now been completed. The current work of the group is directed towards the provision of support for other studies - notably the ATBC study. Future work is planned on other methodological developments. These include biomarkers of lipid peroxidation for use in epidemiological studies, methods for the determination of bioflavonoids and carotenoids and for better separation of isomeric trans fatty acids. Much of the work of this group has been directed to supporting the ATBC trial and some redirection of activity will be required following the completion of the major phase of this study. The Panel recognises the importance of the development of new biomarkers but is concerned that the eforts of this group might be dissipated into a series of small scale studies which are unrelated to the major research themes of the Division.

#### **Conclusions and recommendations**

The ATBC study has been of the highest quality and importance, and it is essential that the follow-up studies are completed over the course of the next quinquennium. The Department's involvement in the multi-centre breast cancer study is also of considerable importance and it has played a valuable role in the MONICA and FINRISKI projects. The public health activities are of high quality and importance and these have been well integrated with the research activities of the Department. Much of the other work presented to the Panel has derived from these major studies and has been no more than competitive at the national level in research terms. The Panel was impressed by the number of further studies deriving from earlier work and the public health surveillance activities of the Department which are planned, but was concerned at an apparent lack of challenging new hypotheses as the basis of possible future studies. It was, however, recognised that the Department and the Division as a whole is in a state of transition as a number of large scale studies have come to or are close to their end (this particularly applies to epidemiology and nutrition - the programmes have been strongly interlinked in the past) and that one key member of the Department was absent on sabbatical leave at the time of the evaluation. The Panel also recognises that the responsibilities of the staff of the Department as key collaborators in a number of major KTL studies have made it difficult for them to develop major independent research programmes in nutrition. There is a need for strategic reappraisal.

The Panel recommends that:

(i) the future roles and direction of the research carried out in the Department should be the subject of a detailed reappraisal and this should be carried out in the context of the proposed strategic review of the activities of the Departments of Epidemiology and Health Promotion, Nutrition and Biochemistry;

(ii) the major research theme of the Department should be in the role of nutritional factors in the susceptibility of individuals to acute and chronic disease in collaboration with other groups within the KTL and elsewhere - in particular the Department should seek to exploit the opportunities deriving from major recent investigations and its public health responsibilities to generate and test novel and challenging hypotheses;

(iii) resources should be made available to maintain and update the food composition database at regular intervals. It is of fundamental value for public health and research purposes.

#### DEPARTMENT OF MENTAL HEALTH

The Department was established in 1992, although research into mental health has been carried out at the KTL since 1986 as a part of the national suicide prevention programme.

The major focus of the activity of the Department has been on suicide epidemiology and prevention. The range of research themes has been extended in recent years to other areas including depression, the genetics of psychiatric disease, mental health in childhood and adolescence and health psychology.

The total staff of the Department was 16 (9 professional and 7 technical) in 1994. Eleven of these were paid from the core budget of the KTL. The budget in 1994 was 4.3 million FIM of which 30% was derived from extrabudgetary sources. The most important sources of extrabudgetary funding were the Academy of Finland, the National Institutes of Health and private Finnish foundations. The Department has established a wide range of collaborative programmes - the most important collaborators in Finland being the Universities of Helsinki and Tampere. International collaborators include the NIH and a number of universities in the US.

Self destructive behaviour and depression. Suicidal behaviour is a major public health problem in Finland and suicide prevention has been one of the principal targets of Finnish public health policy since the late 1980s. Databases on suicide and parasuicide have been established. Studies have focused on psychological autopsy (the limitations of this technique are clearly understood by the staff involved) and the influence of antecedent mental illness, quality of life, lifestyle and behavioural and environmental factors in depression. The databases have also made it possible to monitor trends and carry out intervention studies directed towards suicide prevention. These studies have shown the importance of a variety of factors in the onset of depressive illness and the importance and cost-effectiveness of the treatment of depression. These have led to the establishment of a national programme for the recognition and treament of depression. A case-control study is now planned to study the role of treatment related factors in the prevention of suicide. There is good collaboration with the NAWH in the national suicide prevention programme. These studies are of high quality and of public health importance.

Genetic studies. Major collaborative studies have been developed with the Department of Human Molecular Genetics and international partners into schizophrenia, bipolar disease and the behavioural precursors of alcoholism. These studies involve the application of established techniques to the study of these disorders including studies of familial distribution, testing of candidate genes and suggested gene loci in representative samples and the use of linkage, sib-pair and association analyses to locate major predisposing genes. These approaches exploit the unique opportunities offered within Finland (in particular the Finnish twin and other national registers) to study the genetics of mental health and the interaction between genetic and environmenal factors and disease. These studies are of high quality and potentially of international importance and are commended by the Panel. The work on a possible association between ante-natal infection and schizophrenia was noted by the Panel but was regarded as of low priority.

Mental health in childhood and adolescence. The Department is participating in three major studies dealing with the development of temperament, the relationship between

stress and protective factors and mental health during childhood, and risk and protective factors for later mental health from adolescence and early adulthood. The first two of these are longitudinal cohort studies and are led by KTL staff and the third is part of a collaborative study of subjects selected from an earlier cross-sectional study. The Panel commended these studies which will require continued commitment for their succesful completion.

**Health psychology.** The health psychology group is small and is conducting a series of small scale unrelated studies. These include (i) perceptions of health and health risks, (ii) determinants and processes of health behaviour, (iii) coping with health threats, (iv) psychological impact of mammography and (v) psycho-social aspects of genetic screening. The Panel was concerned at the lack of coherence of the programme. The studies which it did regard as of particular importance were those on the psychological impact of the screening for breast cancer and aspects of genetic screening. The group are planning to focus to a substantial extent on the psycho-social aspects of genetic screening and the Panel was strongly supportive of this intention and would recommend that the programme should be developed alongside those deriving from the work of the Department of Human Molecular Genetics. The Panel would also wish to encourage a greater degree of interaction between the members of this group and those with an interest in health behaviour in the Departments of Epidemiology and Health Promotion and Drugs, Alcohol and Traffic.

#### **Conclusions and recommendations**

Much of the work carried out by the Department of Mental Health is of high quality and of considerable public health importance. The staff of the Department have established excellent collaborative links with the Department of Human Genetics and are developing programmes which exploit the unique opportunities available in Finland and these studies are potentially of international importance. The Department has wide ranging and generally well focused plans for the future. The one proposed area of study which was not supported by the Panel was that on the possible viral origin of schizophrenia.

#### The Panel recommends that:

(i) the programme should be focused further and directed primarily at developing the programmes in a) the genetics of mental disorders, b) the long term studies of the determinants of mental illness in adults and in childhood and adolescence, and c) on the psycho-social aspects of genetic screening;

(ii) studies in health psychology should be more directly focused and form an integral component of the principal research themes of the Division and that the other projects should be allowed to lapse in due course;

(iii) the work on the possible viral origin of schizophrenia should not be undertaken.

# DEPARTMENT OF BIOCHEMISTRY

The activities of the Department fall into three categories: (i) its own basic research, (ii) collaborative research in which the Department is responsible for biochemical analyses and (iii) diagnostic services. Historically, the Department has been service oriented, supporting the research projects of other departments with its biochemical expertise and laboratory facilities. Considerable effort has been invested to develop an independent research programme within the Department in recent years.

The Department had a total staff of 30 (10 professional and 20 technical) in 1994. Twenty-five of these were paid from the KTL core budget. The overall budget of the Department was 6.6 million FIM of which about 15 per cent was derived from extrabudgetary sources. The most important sources of extrabudgetary funding have been the private Finnish foundations and the Academy of Finland. The most important and extensive collaborative activities take place within the Institute with the Departments of Epidemiology and Health Promotion, Nutrition and Human Molecular Genetics. Staff of the Department have established a number of international collaborations with colleagues in universities elsewhere in Europe and North America.

Lipoprotein metabolism. The research programme of the Department has concentrated on lipoprotein metabolism and genetic factors influencing the risk of cardiovascular disease. The main programmes of this group have been directed towards HDL transformation and reverse cholesterol transport, the role of lipoprotein(a) as a risk factor for coronary artery disease and lipoprotein metabolism. The main emphasis, in future, will be on characterising the structure and functions of lipid transfer proteins and their role in lipoprotein metabolism. This work is of high quality and properly exploits opportunities which derive from or are related to the major research themes of the Division. Future opportunities to collaborate in broadly based epidemiological and intervention studies will be dependent upon the development of plans for such studies within the Division as a whole and particularly within the Department of Epidemiology and Health Promotion (see comments above).

Lipoprotein genetics. The main goal of the studies in lipoprotein genetics is to determine the relationship between genetic variation and the risk of disease. Recent studies have explored the effects of genetic variation in the lipoprotein lipase and hepatic lipase genes. These will be studied further in a number of clinical contexts. The work has been of good but not outstanding quality. There are opportunities for developing more broadly based programmes of major strength building on existing internal collaborations.

Cell biology. Cell biological skills have only recently been established at the KTL. Current research is directed to the study of intracellular membrane traffic and microsomal triglyceride transfer. These are important studies focusing on intracellular mechanisms which have been neglected by many other groups and relate closely to other research interests which are being developed in the Department. There are some collaborations with the university and it it important that these should be developed (particularly drawing on the strengths in cell biology which exist within the country). The Panel was impressed by the quality of the work but concerned by the very small size of the group. This group will need to be strengthened if it is to remain competitive.

Other projects. The staff of the Department are active partners in many major collaborative studies within the Institute. The principal responsibility of the Department has been to carry out biochemical analyses and provide other services. The list of these collaborative studies includes the ATBC study, the diabetes atherosclerosis intervention study, the European atherosclerosis research study and the FINMONICA project. The staff of the Department have contributed actively to the planning of these studies and they have in some instances played a major role. The majority of these studies have been completed.

Neonatal hypothyroidism screening. A screening programme for neonatal hypothyroidism has covered the majority of all neonates in Finland since 1980. It was initially considered necessary to centralise the analysis of the samples and that responsibility was undertaken by the Department. The number of samples has dropped since that time as a number of hospital laboratories now carry out these analyses independently of the KTL. This is a purely service function and quite unrelated to any of the research programmes of the KTL. Current analytical methods are well within the competence of all hospital biochemistry laboratories. The Panel, considers that this is no longer an appropriate responsibility and that it should be devolved to the hospital laboratories as soon as arrangements for a smooth transfer of responsibility can be put in place.

#### **Conclusions and recommendations**

The Panel was impressed with the work carried out by the staff of the Department who have developed a programme of high quality which derives from or relates clearly to the major research themes of the KTL. However, the completion of a number of major projects in which staff collaborated has left a void and there is no clear sense how this will be filled and this must be the subject of a strategic reappraisal.

# The Panel recommends that:

(i) a strategic reappraisal of the role of the KTL in cardiovascular research should be undertaken covering particularly the Departments of Epidemiology and Health Promotion, Human Molecular Genetics, Nutrition and Biochemistry with possibly some reconfiguration of departmental boundaries to meet the needs of the strategy more effectively and enhance critical mass in the key areas;

(ii) the professional staff of the Department be encouraged to continue to develop their own high quality research programmes within an overall stratgeic framework;

(iii) the cell biology group should be strengthened;

(iv) the KTL should no longer continue to carry responsibility for screening for congenital hypothyroidism.

#### DEPARTMENT OF IMMUNOBIOLOGY

Historically the main function of the Department has been to carry out routine immunological examinations for hospitals and health centres. Responsibility for the provision of these diagnostic and analytical services was devolved to regional and local laboratories in 1991. The Department retains one service function only - paternity testing which is carried out using DNA based technology. There are currently three research programmes being pursued within the Department: (i) pathogenesis of rheumatoid arthritis, (ii) immunology of atherosclerosis and (iii) thrombosis and immunological mechanisms in allergy. The Department has recently established a tissue culture laboratory to study cell-mediated immunity in type I diabetes together with the Department of Acute Viral Diseases.

The Department had a total of 17 staff (5 professional and 12 technical) in 1994. Fifteen of these posts were supported by the core budget. The total budget of the Department was 3.7 million FIM of which 11 per cent was derived from extrabudgetary sources. The Department has established a number of collaborative projects involving other Departments within the KTL and other groups in Finland.

Pathogenesis of rheumatoid disease. The commitment to these studies is very small indeed involving little more than half the time of one member of the professional staff and one member of the support staff. The work is of an observational nature examining the timing of the appearance of certain disease markers (particularly rheumatoid factor) in relation to the onset of clinical disease. The plans are to extend these observations to look at other immunological variables (eg antikeratin and antiperinuclear factors) and other possible markers. The Panel took the view that the initial observation was of interest but it was not impressed by the quality of the current work. It is all of an observational nature and it is far from certain that it will generate additional insights into the pathogenesis of the disease. In particular, it is not clear that simply measuring a wider range of variables and establishing a further range of correlations will improve understanding of the pathological processes involved in rheumatoid disease.

Atherosclerosis and thrombosis. The commitment to these studies is also small involving little more than half the time of one member of the professional staff and two members of the support staff. The research is directed towards the identification of immunological factors associated with atherosclerosis and thrombosis. These studies are largely observational in nature and focused on the identification of antibodies against oxidised low density lipoprotein and cardiolipin. Plans for the future are poorly formulated and there are no plans to link these to more fundamental work on the pathogenesis of atherosclerotic heart disease.

Allergy. The principal focus in allergy studies is on allergy to latex. It is acknowledged that this is of importance and the work is of a more fundamental nature than that of the other studies in this Department. The Panel was, however, concerned by the small size and isolation of the group and it was not clear why this work was not being carried out in the Finnish Institute of Occupational Health which supports work in related areas or in a university laboratory with an established interest in allergy.

**Paternity testing.** The Department has been responsible for the conduct of paternity testing in Finland for historical reasons. The Panel recommends that this should be discontinued at the KTL.

## **Conclusions and recommendations**

The Panel was concerned by the small size of this Department (which is below critical mass), the heterogeneity of the projects which were being conducted on a range of unrelated topics (which are not clearly linked to the current main research themes of the KTL) and the limited quality of the work. There appears to be little justification for an independent Department of Immunobiology within the Division. It was noted that there was only limited immunological expertise within other Divisions in the KTL. The Panel was also concerned at the isolation of one new recruit (a young cellular immunologist) who was judged to have considerable potential but works in considerable isolation. They take the view that she would be better located in a university environment in which there were significant strengths in immunology.

#### The Panel recommends that:

(i) the future of the immunobiology group as a whole should be reviewed by the Director-General and it should only be maintained if it can be strengthened considerably and its programme developed in such a way that it makes a significant contribution to the main research themes of the KTL;

(ii) the research on rheumatoid arthritis and atherosclerosis should be accorded a low priority and be discontinued.

(iii) consideration should be given to transferring the work on latex allergy which is of higher quality, but unrelated to other research activities within the KTL, to the Finnish Institute of Occupational Health or in a university laboratory with an established interest in allergy; (iv) the Director-General should take steps to make appropriate arrangements for the future career development of the recently recruited cellular immunologist;

(v) the KTL should discontinue the provision of a paternity testing service as soon as alternative arrangements can be put in place.

# DEPARTMENT OF ALCOHOL, DRUGS AND TRAFFIC

The Department comprises two laboratories which currently have a range of service responsibilities and are pursuing six research projects. It was established in 1992 by combining two laboratories which had previously been a part of the Department of Biochemistry. The blood alcohol laboratory is almost entirely a service laboratory. It is responsible for blood alcohol determinations from all living drivers suspected of driving with blood alcohol levels above the legally permissible limit in Finland. This service will be scaled down substantially as breath alcohol analyses become accepted by the courts although the laboratory will from 1996 be engaged in implementing a new computer-based breath analyser system. The laboratory of pharmacology and toxicology is more research-oriented although it also has some forensic responsibilities (being responsible for determination of the levels of licit and illicit drugs at the request of the police). The majority of the research projects are related to the statutory service responsibilities of the Department. The main aim of the research is to contribute to the development of policies and programmes designed to reduce traffic accidents resulting from the use of alcohol and drugs.

The total staff was 32 (12 professional and 20 technical) in 1994. Twenty-seven of these were in posts paid from the core budget. Only a small fraction (2 per cent) of the 6.3 million FIM budget in 1994 was derived from extrabudgetary sources. It should, however, be noted that much of the core budget allocation has been specifically voted to fund the statutory service responsibilities of the Department and cannot be vired and used for other purposes by the Director-General. There are extensive collaborations between members of staff of the Department and others in Finland.

The six research areas of the Department are (i) alcohol and traffic, (ii) drugs and traffic, (iii) drug and narcotic abuse, (iv) mechanisms of addiction, (v) safe use of drugs and (vi) abuse of anabolic steroids. The majority of the research projects are closely linked to the service functions. The overall research strategy of the Department is to establish a clear picture of the extent of the alcohol and drug problems in traffic accidents and identify the major determinants which lead to substance abuse and hazardous behaviour. The epidemiology of drug and narcotic abuse is studied to help plan rational preventive and educational measures. Research on addiction is also being developed using an animal model. The laboratory of pharmacology and toxicology collaborates with the Finnish anti-doping committee and represents the major expert resource in this field in Finland.

Alcohol and traffic. Much of the work related to alcohol, drugs and traffic is carried out to meet statutory responsibilities or is of a routine public health surveillance nature. The collection, collation and analysis of data on the sociological, behavioural and demographic background to drinking and driving feeds into legislation, the planning of control measures and the development of policies in relation to alcohol. Similar studies are carried out in relation to drug taking and driving - and these are mainly of an epidemiological nature. These are valuable studies in the Finnish context. There would be opportunities to extend these to improve understanding of the biological and psychological antecedents of these forms of antisocial behaviour but the group would need to be strengthened with inputs from the behavioural and social sciences to achieve these.

**Drug and narcotic abuse.** In the field of drug and narcotic abuse the group carries out analyses of a wide range of drugs (mainly by GMS). These include opiates, benzodiazepines, amphetamine and tetrahydrocannabinol. This is largely a service and public health surveillance activity. These studies have provided the basis for the development of withdrawal, rehabilitation and therapy programmes and have also contributed to the planning of educational and preventive measures.

Mechanisms of addiction. The group studying mechanisms of addiction is very small and isolated in the context of other activities within the Department. It is focused on the evaluation of the impact of various illicit drugs on neurotransmitter (DA and serotonin) levels in the freely mobile rat using an in vivo microdialysis technique. These studies are of an observational nature and are not linked through collaborations to more detailed studies of the precise neuropsychological and neurochemical consequences of exposure to these agents nor to parallel studies using non-invasive techniques in man. The Panel took the view that, while the study of the biological basis of drug dependence is an important area of study, this group did not have the critical mass to extend these studies and that it was not in a location in which it could build the necessary collaborative links with high calibre neurobiologists to establish a competitive programme.

**Safe use of drugs.** Safe use of drugs is an activity of very small scale (involving only half the time of one member of professional staff) and is directed towards assessing a range of physiological and lifestyle factors which might alter the pharmacokinetics of a range of drugs. The Panel was concerned that this activity was isolated and of limited quality and took the view that this would more properly be carried out within a mainstream university department of pharmacology.

Anabolic steroids. The laboratory doing the analysis of anabolic steroids is the only one in Finland working in this area. The work is largely of an analytical nature and is not closely related to the activities of the other staff in the Department.

#### **Conclusions and recommendations**

The activities of the Department have been dominated by the need to provide a range of statutory services to meet the requirements of the police and the courts. The majority of the public health surveillance activities and current research programmes relate directly to and derive from the analytical services which are provided. These have proved to be of considerable value in the development of public policy and the planning of health education and promotion programmes. The Department, however, is at something of a cross-roads - a number of changes will have a considerable impact on the Department: (i) the service load in blood alcohol testing will decline as the courts accept evidence deriving from breath testing, (ii) two senior members of the Department retire in the near future and (iii) the Panel was informed at a late stage in their discussions that the research group from the State Alcohol Monopoly was to be transferred to the KTL and the NAWH (the Panel was not provided with sufficient details of this transfer to make a judgement on the potential implications). The development of a strategy for the future development of the Department will need to consider (i) the nature and extent of its residual service responsibilities, (ii) if the KTL should develop a significant research presence in the field of drug dependence and (iii) if so what the focus of that presence should be (ie in the biological or in the psychological basis of dependence). The establishment of an internationally competitive research group in the field of drug dependence will require the allocation of significant resources and facilities;

#### The Panel recommends that:

(i) a detailed and radical appraisal of opportunities for the future should be undertaken in the light of impending changes and the transfer of research staff from the State Alcohol Monopoly to the KTL;

(ii) those small scale research activities which do not relate directly to the main research themes of the Department (ie the studies on mechanisms of addiction and those on the pharmocokinetics and safe use of drugs) should be accorded a low priority and discontinued.

# **OVERALL COMMENTS ON THE DIVISION**

The Division has a wide range of important public health responsibilities including the monitoring of major chronic health problems (excluding cancer), risk factors and health behaviour, the maintenance of the food composition database and the provision of support for the police and courts in relation to substance abuse and traffic offences. The Division has a well-deserved international reputation in a number of fields for its research - most notably in the epidemiology of cardiovascular disease and through the ATBC trial. The research in the newly created Department of Human Genetics is internationally highly competitive and this is strongly supported by the Panel. Some of the projects in the

Departments of Mental Health and Biochemistry are also of high quality and of considerable public health importance and these were also strongly supported by the Panel. The Division is, however, at a cross-roads and important strategic decisions need to be taken. The majority of the studies in the epidemiology of cardiovascular disease and related investigations which have dominated much of the work of the Division have been completed and there are relatively few clear ideas for future work in these areas. The well characterised cohorts generated by these studies are a unique resource - but it is not clear that they are necessarily a valuable resource - and the Panel was conscious that they might constrain thinking in the development of future research plans. The future plans for the departments which were most involved in these studies largely comprise a number of studies of limited scientific interest and a mix of small scale and unrelated projects. An overarching review of the strategy of this Division should be undertaken with a particular emphasis on its future role in cardiovascular research covering the Departments of Epidemiology and Health Promotion, Nutrition, Biochemistry and Human Molecular Genetics. Consideration should be given to some reconfiguration of departmental boundaries to meet the needs of the strategy more effectively and enhance critical mass in key areas. The future of the Departments of Immunobiology and Alcohol, Drugs and Traffic should also be subject to a fundamental reappraisal.

The major recommendations of the Panel for the Division of Chronic Diseases are:

(i) the Director-General should undertake an overall review of the research strategy of the Division. This review should include a detailed reappraisal of the role of the KTL in research in cardiovascular disease covering the Departments of Epidemiology and Health Promotion, Nutrition, Biochemistry and Human Molecular Genetics. The major themes of the future research strategy should be the development of hypothesis based epidemiological studies and the evaluation of interventions exploiting the well characterised populations deriving from past, current and future epidemiological studies;

(ii) there should be further investment in human genetics and new programmes should be developed in collaboration with staff in other Departments within the framework of the overall Divisional strategy;

(iii) the programmes in the genetics and determinants of mental illness should continue to be developed;

(iv) the activities of the disparate groups working on aspects of health behaviour should be brought together, strengthened and focused to form an integral component of the principal research themes of the Division;

(v) the future of the Departments of Immunobiology and Alcohol, Drugs and Traffic should be subject to a fundamental reappraisal.

# **DIVISION OF INFECTIOUS DISEASES**

## INTRODUCTION

One of the principal objectives of the KTL is to reduce the incidence of infectious diseases and to minimise their harmful effects on the health of the population. The Division of Infectious Diseases is responsible for carrying out the tasks assigned to KTL as they relate to infectious diseases. This includes a number of responsibilities specified by the Infectious Diseases Act. It also has assumed a range of additional responsibilities for surveillance of infections, outbreak control and the promotion of preventive measures, supported by research into the epidemiology, pathogenesis, control and prevention of infectious diseases.

The main functions of the Division include:

- surveillance of diseases, their causative agents and risk factors;
- expert advice and help in analysis and control of outbreaks and epidemics;
- reference laboratory services;
- support for the national vaccination programme;
- strategic research to support these activities, to broaden the base of knowledge and skills and to generate new knowledge;
- provision of expertise and advice to the Ministry of Social Affairs and Health, municipal authorities, the medical profession and other health care professionals.

The activities of the Division fall into three broad categories: (i) infectious disease epidemiology, (ii) national vaccination programme and (iii) strategic research which has been developed around three principal themes - microbe-host interactions, intervention strategies and associations between infectious and non-infectious disease. The aim of the strategic research programmes is to strengthen the methology and understanding necessary for the two other functions.

#### DEPARTMENT OF INFECTIOUS DISEASE EPIDEMIOLOGY

The activities of the Department fall into three categories: (i) national surveillance of infectious diseases and prevention of epidemics, (ii) expert functions (including information and training) connected with surveillance and prevention of infectious diseases and (iii) research on prevention of infectious diseases. The Department functions as the national expert institute in the field of infectious diseases as specified by the

Infectious Diseases Act and has responsibility for the maintenance of the Infectious Diseases Register covering 32 infectious diseases of national or international importance. The KTL has undertaken responsibility for the maintenance and development of this system since 1992 and a novel surveillance system was introduced in 1994. Data are gathered from regional registries. Information is disseminated to the regional registries both electronically and through the monthly KTL newsletter KANSANTERVEYS. The newsletter, for which the Department is responsible, has a circulation of 6500 copies and is distributed to all health centres and hospitals and to other interested groups.

The Department is also responsible for the quality control of vaccines used in Finland, the evaluation of new vaccines and for monitoring, evaluation and further development of the national vaccination programme. The Department monitors the coverage of childhood vaccination programmes, subsequent adverse events and the immune status of the population. It also participates in the control of epidemics by the timely provision of information to regional and local infection control authorities, by providing guidelines for control measures, and by consulting with local authorities in epidemic management. In its research programme, the Department concentrates on the occurrence and prevention of infectious diseases and on the evaluation of new vaccines and optimisation of vaccination programmes.

The Department had a total staff of 39 (15 professional and 24 technical) in 1994. Eleven of these were in posts provided by the core budget. The overall budget of the Department in 1994 was 9.7 million FIM, of which more than half was derived from extrabudgetary sources, the most important being the Academy of Finland, the European Union and vaccine manufacturers. It is estimated that approximately one third of the time of the staff is committed to surveillance functions. Two thirds of the total resources are used for vaccine research.

The Department has established contacts with infectious disease epidemiologists in other Nordic countries, Russia and Estonia. These collaborations include the exchange of epidemiological information and contingency planning for outbreak control. Major collaborative vaccine research programmes have been established, in Finland with research groups at Tampere and Helsinki Universities and also with workers in a number of other countries. The Department has had a substantial collaboration since 1984 with the Research Institute for Tropical Medicine in the Philippines. Other current programmes include groups from Oxford, Johns Hopkins University and Houston. There is also active collaboration and exchange of information with the research groups of major vaccine manufacturers (Pasteur-Merieux; Lederle-Praxis, Connaught Laboratories, Merck Research Laboratories and SmithKline Beecham).

There are four main areas of research: (i) new vaccines and the development of vaccination programmes, (ii) prevention of acute otitis media, (iii) research on prevention of childhood pneumonia in developing countries and (iv) mathematical models for infectious diseases (including prevention and vaccination).

New vaccines and vaccine programme. Recent and current vaccination research programmes include immunogenicity studies and efficacy trials on vaccines against Haemophilus influenzae type b infection, pneumococcal infections (using polyvalent vaccines), pertussis (using an acellular vaccine) and rotavirus infections. Much of this work has been of a developmental nature - but it has been of the highest quality and is of considerable public health importance. The studies have been designed to determine the most effective mechanisms for achieving protective immunity in the community. For example, the focus in 1983-1993 was on Haemophilus influenzae type b (Hib) diseases and evaluation of Hib conjugate vaccines. These studies have led to the implementation of an immunisation programme and Hib infections have now been largely eliminated in Finland. The Panel would, however, wish to see the inclusion of cost-benefit analyses included in future evaluations.

Acute otitis media. A pilot study has just been completed as a prelminary to the development of a major trial of a pneumococcal vaccine to prevent the development of acute otitis media. This will start during 1995. Data on the epidemiology, pathogenesis and immune responses have already been collected to provide background for the trial. This study is of major public health importance and is strongly supported by the Panel.

**Childhood pneumonia in the developing world.** The aim of this study in the Philippines is to evaluate the use of both pneumococcal and Hib vaccines in the prevention of childhood pneumonia. The study is a logical extension of other work in the Department and builds on existing links in the Philippines. This is an important study, though one of a number being carried out around the world, and should continue to be supported.

Mathematical modelling. The mathematical modelling project has applied a stochastic approach to modelling Hib infections and the evaluation of Hib vaccination strategies. These approaches are widely applicable and there are plans to develop these in the context of other infections and vaccination programmes. The stochastic approach can also be developed for application at the "micro" level (ie individual and household level). The Panel was strongly supportive of this programme and was pleased to note that the programme was being built up through collaborations with the Department of Mathematics in the University of Helsinki and also with the Department of Computer Science. The Panel's view is that this is potentially an important resource for the KTL (and not only for this Division) and would recommend that it should be strengthened further. The Panel would encourage the group to extend and strengthen established links with other European groups in the field.

#### **Conclusions and recommendations**

The current and future plans of the Department were well articulated and described. They comprise a coherent package of activity which strikes a good balance between service, development and research with each drawing strengths from the others. The public health

responsibilities of the group (some of which have only recently been placed upon them) are being developed in a highly effective manner. The Panel, however, wishes to highlight a number of specifc points;

(i) the Panel did not review the vaccine production activities in detail. It assumes that the responsibility for quality assurance is properly carried by an independent group which does not have responsibility for production;

(ii) the Panel was concerned that there was an artificial division of responsibility between this Division which has responsibility for food borne pathogens and the Division of Environmental Health which has responsibility for water borne pathogens;

(iii) the Panel noted that the Department plays only a limited role in the investigation and control of outbreaks of infections and expressed some concern that the failure to use fully the expertise of the KTL for these purposes might not represent the best use of limited expert resources within Finland. Moreover, the investigation of outbreaks by research personnel can lead to the identification of important research needs and opportunities.

The Panel recommends that:

(i) the public health and research activities of this Department should continue to be strongly supported - the major programme of vaccine trials is of the highest standard and of great public health importance;

(ii) future trials should, when appropriate, include cost-benefit analyses;

(iii) the programme in mathematical modelling should be strengthened with the long term aim of developing a group which will contribute to a range of research activities within the KTL;

(iv) consideration should be given to expanding the responsibilities of the Department for outbreak investigation and control.

# DEPARTMENT OF SPECIAL BACTERIAL PATHOGENS

The Department of Special Bacterial Pathogens derives from the former Department of Bacteriology, some of the staff of which have been reallocated to other Departments in the KTL. The reshaped Department is the national reference laboratory for bacteria of public health importance apart from those assigned to other Departments. The Department is also the WHO National Reference Centre for Salmonella, Shigella, E. coli and Staphylococci. The Department primarily concentrates on enteric bacteria, gram positive bacteria and anaerobes, while some other important bacteria, are assigned to other Departments (e.g. Mycobacteria, Borrelia, Chlamydia, Haemophilus and pneumococci). The overall

objectives of the Department are the prevention of infection and illness from these organisms, the provision of advice and support and contributions to the quality assurance schemes of clinical microbiology laboratories. The research programme of the Department is closely associated with its reference laboratory functions. It is directed towards the improvement of methodologies used in reference laboratory activities, a better understanding of mechanisms of pathogenesis and spread of infection, and of the role of normal microflora in host resistance. The research and surveillance activities are now substantially based on the use of molecular techniques and involve active collaboration with other laboratories (including veterinary laboratories) and clinicians.

The Department had a total staff of 24 (9 professional and 15 technical) in 1994. Seventeen of these were in posts supported by the core budget. The budget in 1994 was 4.4 million FIM, of which about 15 per cent was derived from extrabudgetary sources. Extrabudgetary funds were obtained from a number of sources including the Academy of Finland, Nordic and EU funds and industry. The reference laboratory tasks have led to active collaborations with other microbiology laboratories in Finland and abroad and with WHO. International collaborations include laboratories and institutes in Estonia, Russia, Sweden, Bangladesh, Australia and the US. The Department also participates in a number of Nordic, European and international networks.

The four principal areas of research within the Department are: (i) epidemiology of diarrhea-associated bacteria, (ii) virulence associated characteristics of E. coli, (iii) oral bacterial flora and (iv) hospital-acquired infections.

Epidemiology of diarrhoea associated bacteria and virulence characteristics of E. coli. The programme is designed to lead to a reduction in the incidence of infection resulting from diarrhoea associated bacteria. Finland has extensive control systems in place for the minimising the contamination of foods (particularly with Salmonella) within the country but traveller's diarrhoea is a considerable public health problem in Finnish people travelling abroad with an estimated 100,000 cases each year. The main approach has been detailed typing of isolates from patients, carriers and animal sources. A large clinical trial with a new oral B subunit/whole cell cholera vaccine against traveller's diarrhea has just been completed. The group has planned studies in which it will use an enterotoxigenic E coli (ETEC) vaccine. This work is of good quality and competitive at the national level and should continue to be supported.

Virulence associated characteristics of E. coli. E. coli infections represent a major public health problem leading to infections of the gastro-intestinal and the urinary tracts and to bacteraemia in some instances. These studies aim to identify molecular characteristics associated with virulence. The approach has focused on bacterial fimbriae and adhesins, hemolysin and serotyping. The significance of specific characteristics is assessed through the use of statistical modelling techniques. These methods have led to the identification of factors which individually and in combination are associated with virulence and the persistence of infections with E. coli. The work of this group is of high quality and competitive at the national level.

**Oral bacterial flora.** The studies on oral bacterial flora aim to characterise the bacteria composition of the flora within a healthy oral cavity and those changes which are associated with dental and peri-odontal disease. The specific objectives are to (i) improve understanding of juvenile and adult peri-odontal disease, (ii) describe the pattern or bacterial colonisation of the oral cavity in health and disease and (iii) identify the pathogens associated with severe disease. The major current effort is on peri-odontal disease. The group is examining a range of potential pathogens and works in close collaboration with the Institute of Dentistry (Helsinki University). The work is valuable ir an area of considerable public health importance and is of high quality and competitive a the national level.

Hospital acquired infections. "Hospital-acquired infections" are of major public health importance and their human and economic costs are substantial. The incidence could be reduced if effective control measures were in place. The Department is establishing a database for hospital acquired infections. The aim of the programme is to identify the sources of infection and their mode of spread in order to provide guidance for the control and prevention of outbreaks. This has been set up in collaboration with hospital laboratories. These collaborations have been established on an informal basis, but appear to be effective. The Department is developing the database through detailed molecular typing of bacterial strains associated with hospital infections and this provides a framework for the investigation of outbreaks. The Panel commended these initiatives bu noted that their successful further development will depend upon the maintenance of excellent links with those in the hospitals since the investigation of outbreaks must take place in those environments. Future plans include the identification and molecular analysis of organisms capable of existing within a hospital environment, studies of the mechanisms involved and of the host response, and economic evaluations of the costs o: hospital infections and the benefits of control programmes. The Panel was concerned tha in the development of this programme there should be a clarification of the roles of the various players in routine monitoring and outbreak investigation. The Panel would wish to see a greater level of collaboration with the group working on antibiotic resistance in the KTL.

#### **Conclusions and recommendations**

The Department carries responsibility for the performance of a wide range of reference functions and these are of considerable public health importance. The Panel noted that the current Department did not carry as wide a range of microbiological reponsibilities as the former Department of Bacteriology and expressed some concern at the dispersion of bacteriological expertise to Departments in Helsinki, Turku, Oulu and Kuopio. It takes the view that it would be timely to review the disposition of bacteriological skills within the KTL (taking due account of skills available elsewhere in Finland) with a view to ensuring that limited expertise is deployed in the most effective manner. The research activities of the Department are, in general, closely linked to the public health responsibilities. The work overall is of high quality and competitive at the national level.

## The Panel recommends that:

(i) the work of the Department should continue to be supported;

(ii) the need for a co-ordinated approach to the investigation and control of hospitalacquired infections should be developed in a more systematic manner and the role of the KTL more clearly defined;

(iii) the Director-General should undertake, in the light of this evaluation, a review of the disposition of bacterial expertise within the KTL (taking due account of skills available elsewhere in Finland) to ensure that it meets the public health and research responsibilities in the most cost-effective manner.

# DEPARTMENT OF BACTERIAL VACCINE RESEARCH AND MOLECULAR BACTERIOLOGY

The Department is mainly committed to strategic research. The major goals of the principal research projects are: (i) to develop novel bacterial vaccines and diagnostic measures, (ii) to develop novel production systems for vaccines and other medically useful proteins and (iii) to evaluate new bacterial vaccines. The Department exploits recent developments in cell biology, immunology and immunochemistry, which make it possible to carry out detailed analyses of microbial antigens and structures involved in protective immune responses and virulence. Molecular biotechnological techniques are increasingly used to produce a range of potential immunogens.

The Department had a total staff of 28 (18 professional and 10 technical) in 1994. The budget of the Department was 3.8 million FIM in that year, of which about 25 per cent was from extrabudgetary sources. The most important sources of extrabudgetary funding were the Ministry of Commerce and Industry and the Academy of Finland.

The Department has established a number of national and international collaborations. These involve research workers at Pasteur-Merieux Serum and Vaccines (France), Biozentrum (Switzerland), Forschungsinstitut Borstel (Germany), and universities and institutes within Finland and abroad (US, Gothenburg, Oxford, Moscow and Amsterdam). The Department participates in one consortium in the EU BIOTECH programme.

The research programme has two main areas (vaccine development and immunogenicity of vaccines) and consists of six projects:

- development of a prototype vaccine against Neisseria meningitidis group B,
- expression of heterologous proteins in B. subtilis,
- development of a vaccine for Chlamydia pneumoniae,
- bacterial lipopolysaccharide (LPS, endotoxin),
- mouse salmonellosis as a model for intracellular pathogenesis,
- immunogenicity of vaccines against encapsulated bacteria.

The Department has substantial skills and experience in molecular genetics and heterologous gene expression in Bacillus subtilis. and also in research on intracellular bacterial pathogens using animal model and cell envelope studies.

**Prototype vaccine against Neisseria meningitidis.** The Department has been developing a prototype vaccine against N. meningitidis group B. The work to date has shown that monoclonal antibodies to the membrane protein porin P1 provide protection against infection in an animal model (a passive immunisation approach). Further studies have shown that this protein (when delivered in liposomes) is immunogenic in mice. Plans are in hand to set up a phase 1 human trial using a similar approach and applying it to high risk volunteers (army recruits). The Panel considers the work to be of high quality but of high risk and would recommend continuation but with a further review in three years. The work is being carried out in collaboration with Pasteur Merieux.

**Expression of heterologous proteins in B. subtilis.** The aim of the study is to use B. subtilis as a host for producing proteins (ie possible immunogens) for medical use. The principal approach has been to explore the cellular mechanism of protein secretion to improve production of a range of bacterial proteins. These studies have led to the identification of a novel cellular component of the secretory system - an extracellular chaperon - the presence of which enhances the secretion of a number of proteins. The Group have succeeded in producing high levels of outer membrane proteins of gramnegative bacteria using this technique. It was put to the Panel that this would have advantages over an E. coli system. The work is also part of a European collaborative programme. The Panel was strongly supportive of this work. Some aspects of the system have been patented and two patents are held by the KTL.

Vaccine for Chlamydia pneumoniae. This work has been generated by the observation that on serological grounds in epidemiological studies there is an association between infection with this organism and coronary artery disease. Organisms have also been identified in aortic aneurysms and (subsequent to the site visit) in the coronary vessels. There is, however, no direct evidence that this organism, or that an immune response to it, are implicated directly in the pathogenesis of coronary artery disease. The development of a vaccine to Chlamydia pneumoniae cannot at present be regarded as a high priority on public health grounds and there is insufficient evidence to indicate that this is a programme which should command further support. More conclusive, and ideally direct, evidence of the involvement of Chlamydia pneumoniae in the pathogenesis of coronary artery disease is required before further investment in this project could be justified. Mouse salmonellosis. The work on mouse salmonellosis has been completed.

Study on the biosynthesis of bacterial LPS. The principal purpose of these studies is to improve understanding of the function of the gram-negative bacterial cell envelope and its role in bacterial pathogenicity. The studies have been focused on the investigation of structural changes in the LPS molecule in mutants and the effects of these on outer membrane permeability. The work in this project has identified a number LPS biosynthesis genes which regulate the structure of LPS. The genes responsible are found in E coli and S typhimurium. This work is carried out in collaboration with others who carry out the associated structural studies. The quality of the science is high but this project is not closely related to other activities in the Division and the Panel recommends that it should continue to be funded at a modest level only.

**Immunogenicity of vaccines against encapsulated bacteria.** This work focuses on the immune responses to capsular polysaccharide (PS) and PS-protein conjugate vaccines. The work is focused on the local immune responses in animal and human vaccine studies to N. meningitidis, H. influenzae and Streptococcus pneumoniae vaccines. It is carried out in collaboration with the Department of Infectious Disease Epidemiology. The quality of the science is high and the programme makes a significant contribution to one of the major research themes of the Division.

#### **Conclusions and recommendations**

The work of this Department is in an area of considerable importance and it represents a coherent and well integrated package of activities (with the exception of the work on chlamydia vaccine development). The projects contribute to the overall Divisional strategy and the staff have established effective internal and external collaborative programmes (the links with the field trials carried out by the Department of Infectious Disease Epidemiology are particularly commended). The quality of the science is high. The Panel noted that the EU (DGXII) had recently launched a task force on vaccine research and that this might offer further opportunities for strengthening international collaboration.

# The Panel recommends that:

# (i) the major research programmes of the Department should continue to be supported;

(ii) the chlamydia vaccine project should be discontinued.

## DEPARTMENT OF ACUTE VIRAL DISEASES

The Department of Acute Viral Diseases is responsible for surveillance and reference functions for enteric and respiratory viral infections, especially those caused by influenza and polioviruses. It carries out primary screening of selected sets of specimens for respiratory or polioviruses and, in collaboration with the Department of Infectious Disease Epidemiology, analyses related information from diagnostic laboratories. The immunity of the population to these viruses is monitored at regular intervals. The national enterovirus reference laboratory acts as a WHO Collaborating Centre for Reference and Research on Poliomyelitis and the inflenza laboratory serves as the WHO National Influenza Centre. The research programme covers the epidemiology, pathogenesis, diagnostic methods and the prevention of infections caused by enteric and respiratory viruses and Mycoplasma pneumoniae.

The Department had a total staff of 32 (13 professional and 19 technical) in 1994, of whom 21 were in posts supported by the core budget. The budget in 1994 was 6.5 million FIM, of which 12 percent was from extrabudgetary sources. The most important sources of extrabudgetary funding were the Academy of Finland and a private Finnish foundation. External collaborators include the Universities of Helsinki and Turku, and groups in the UK and the US

The research programme comprises four main themes:

- monitoring, diagnosis and prevention of enteroviral diseases,
- structure, replication and genetics of enteroviruses,
- sero-epidemiology and molecular epidemiology of influenza,
- diagnostic methods for acute respiratory infections.

**Enteroviral diseases.** The aim of the group studying enteroviral diseases is to develop mechanisms to improve the monitoring, diagnosis and prevention of poliomyelitis and other enteroviral diseases. The group have made particular contributions to the improvement of methods for strain identification and diagnosis of poliovirus infections which have been of considerable value in the study of transmission and have the potential for application in the developing world. The group have also developed a new vaccine to poliovirus type 3 and this is currently undergoing Phase III clinical trials. This work has been of the highest quality and is strongly commended by the Panel and it should continue to be supported.

The most speculative element of the future plans relates to the putative relationship between Coxsackie B infection and diabetes mellitus. It is planned to isolate and identify diabetogenic virus strains over the course of the next few years. It was noted that this work could be linked to other work on diabetes within the KTL. The Panel would recommend the development of this project for a limited period only and in collaboration with other groups within the KTL but that a judgement should be made within the next two years whether this was a potentially productive line to pursue.

Structure, replication and genetics of enteroviruses. The basis of these studies is the examination of the molecular characteristics of the viruses and the host-virus interaction to improve understanding of transmission and pathogenesis. Much of the current and future work focuses on the factors which determine cell receptor sensitivity and tissue tropism in virus infections with particular reference to Coxsackievirus A9. This has identified two distinct receptor molecules in a range of cell lines. The work carried out by this group is of high quality and should continue to be supported. Plans for future work, however, were not entirely clear and the Panel would recommend that this work should be reviewed again after a further three years.

**Influenza.** The work on influenza falls into two categories - monitoring and surveillance of influenza outbreaks in Finland and research. The surveillance and monitoring functions are met by the use of sero-epidemiological techniques and the analysis of vaccine-induced antibody responses, and by the use of molecular techniques based upon partial genomic sequencing and use of an established virus collection. The research programmes of the group are focused on structural studies on the virus and its evolutionary origin. The tracking of antigenic variation has been carried out drawing upon the data collected for surveillance purposes. This work is of good quality and represents an example of the effective exploitation of the public health function to provide better understanding of the molecular basis of virulence. The Panel would, however, wish to see a progressive redirection of effort away from the evolutionary and purely descriptive structural work to studies of a more functional nature which will lead to a better understanding of the features which determine the virulence of the organism.

**Diagnostic methods for acute respiratory infections.** The work on diagnostic methods for acute respiratory infections is focused on Mycoplasma pneumoniae, adenoviruses and respiratory syncytial virus using molecular techniques. The work is largely of a developmental nature and in the view of the Panel has a considerably lower priority for continued support than other programmes in this Department.

#### **Conclusions and recommendations**

The Department has a strong record in poliovirus research and continues to make important contributions in this field and the public health and research functions are well integrated. The record in other areas has been more variable although interesting observations have been made on other enteroviruses and influenza. The work on the development and improvement of methods for the diagnosis of respiratory disease have provided useful support for other studies carried out by staff in the Division. The Panel was concerned by the lack of detailed plans for future research. The Panel recommends that:

(i) work on the enteroviruses and enteroviral diseases should continue to be supported;

(ii) the planned study of the putative relationship between Coxsackie B infection and diabetes mellitus should be supported for a limited period and linked to other work on diabetes within the KTL. A judgement should be made within the next two years whether this was a potentially productive line to pursue further;

(iii) the studies on influenza should be continued but there should be an increasingly greater focus on the relationship between structure and virulence;

(iv) the development of diagnostic methods should only continue to command support if justified by public health and research needs.

# DEPARTMENT OF CHRONIC VIRAL INFECTIONS

The Department was established in 1994 by combining the Department of Human Immunodeficiency Viruses (HIV), and the Department of Viral Vaccines and Interferon Research and it comprises four laboratories. The HIV laboratory is the national reference laboratory and has established surveillance systems for monitoring HIV and AIDS in Finland. The laboratory of viral vaccines is the control authority for viral vaccines. Research activities are mainly focused on the effects of MMR (mumps, measles, rubella), influenza, and hepatitis A and B vaccines. The interferon laboratory has studied the interferons since the late 1950s and has made important contributions to basic and clinical research and clinical applications. The laboratory of viral and molecular immunology works mainly on the molecular pathogenesis of viral infections and cytokine mediated host defence mechanisms with special emphasis on interferons. In addition, the laboratory has wide experience of viral and other recombinant protein expression systems and functions as a support laboratory inside and outside KTL.

The Department had a total staff of 24 (13 professional and 11 technical staff) in 1994, of whom 23 were in posts supported by the core budget. The budget of the Department in 1994 was 6.7 million FIM, of which only a very small fraction was derived from extrabudgetary sources. The Department has extensive collaborations with other laboratories, and with hospitals and non-governmental organizations. International activities in collaboration with WHO include rabies surveillance in the Baltic countries. Collaboration with EU is mainly through the AIDS surveillance centre in Paris.

The research programmes of the Department are focused in three main areas (HIV, viral vaccines, and cytokines and molecular pathogenesis of viral infections) and some smaller areas (role of viruses in cancer and in juvenile-onset diabetes).

**HIV.** The work of the HIV study group is directed towards surveillance of HIV infection (which is not a major public health problem at present in Finland) with monitoring being directed towards those groups which are at particular risk. The group plays an important role in the committee on HIV control (previously a responsibility of the National Board of Health) and maintains the national HIV register. The group has a very limited commitment to research. The Panel considers, however, that it should be maintained for public health purposes but considers the research programme to be of low priority.

Viral vaccines. The major responsibility of this group is the surveillance of the MMR immunisation programme. MMR diseases are monitored both on a cohort basis and through clinically suspected cases. There is concern that the antibody titres in immunised children is lower than previously - possibly due to diminished exposure to natural "booster infections". The work comprises mainly surveillance and monitoring. The group has a small research component. The Panel recognises the importance of maintaining this group for public health purposes. Collaboration with the mathematical modelling group could be of value in the planning of follow-up programmes.

Cytokines and molecular pathogenesis of infections. The programme presented to the Panel is ambitious. The scientist concerned spends a substantial proportion of his time carrying out expression work for other staff within the Institute - although the need for this is likely to diminish. The planned programme comprises the examination of cytokine profiles in disease as part of a more extensive programme of research into mechanisms of host defences using influenza and Puumala viruses. It is hoped that the identification of differences in individual cytokine responses could explain differential susceptibility to infections. It is also hoped to extend the programme through studies in cytokine knockout transgenic animals. The programme was considered to be highly ambitious although it was recognised that the group leader was a scientist with an excellent research record. The Panel was, however, concerned that the planned programme was not based upon clearly expressed hypotheses and that the programme was likely to be beyond the capacity of a group of this size. It was also noted that this was a highly competitive field and that a number of key studies had already been carried out elsewhere (eg on cytokine knockout transgenic animals). The Panel, therefore, recommends that a more focused programme should be developed directed towards testing a limited number of clearly formulated hypotheses. The Panel also recognised the need to build up strengths in immunology (particularly in cellular immunology) and molecular biology in the Division and recommend that the Director-General together with the Head of the Division review the level of expertise in these disciplines.

**Other studies.** (i) viruses and cancer - the proposed study which was described to the Panel is part of an international study into the role of the HPV in childhood cancer. This was regarded as highly speculative and was not accorded a high priority by the Panel. (ii) viruses in Type 1 diabetes - it is proposed to study the role of enteroviruses in the initiation of B-cell destructive auto-immune processes. The Panel would only recommend the

development of this project if carried out in collaboration with other groups within the KTL and that a judgement should be made within the next two years whether this was a potentially productive line to pursue further.

#### **Conclusions and recommendations**

The Department overall is small and a number of the groups are currently below critical mass. The Head of the Division indicated that it was her intention that this Department should be wound up and that the staff should be reallocated to the Departments of Acute Viral Diseases to form a unified Department of Virology and to the Department of Infectious Disease Epidemiology. The Panel supports these planned changes. It is important that the surveillance and monitoring of HIV and the impact of the MMR immunisation programme is maintained for public health reasons. The planned studies on cytokine profiles in disease should be developed although on a more limited scale than is proposed. The Panel commented on the limited level of immunological expertise available within the Division and the KTL as a whole (see below).

#### The Panel recommends that;

(i) the current Department of Chronic Viral Diseases should be wound up and the staff reallocated to the Departments of Acute Viral Diseases and Infectious Disease Epidemiology in accordance with the plans of the Head of Division;

(ii) the skills and expertise in the HIV and viral vaccines laboratories should be maintained in view of their public health importance;

(iii) the proposed programme on cytokine profiles in disease should be reduced in scale and focused;

(iv) the project on viruses and childhood cancer should be discontinued as soon as the current collaborative programme has been completed;

(v) the proposed programme on the role of enteroviruses in the initiation of Type 1 Diabetes should only be supported if carried out in collaboration with other groups within the KTL and should be reviewed after two years.

#### DEPARTMENT IN TURKU

The Department in Turku was formerly a service medical microbiology laboratory. It was reorganized in 1990-1991 and subsequently it has assumed a range of public health surveillance and research activities which mirror those in other Departments within the Division. The major activities are the surveillance and control of mycobacterial infections and resistance to antimicrobial agents. The mycobacterial laboratory has established a
nationwide surveillance system for monitoring the incidence of infections and drug resistance to these organisms. The principal task of the antimicrobial research laboratory is to control the emergence and spread of bacterial resistance to antimicrobial agents in Finland.

The Department had a total staff of 67 (34 professional and 33 technical) in 1994. Thirtyeight of these were in posts supported by the core budget which was 11.1 million FIM in 1994. Forty-six per cent of the budget was derived from extrabudgetary sources, the most important of which were the Academy of Finland, private Finnish foundations, industry and the Technology Development Centre of Finland. There is close collaboration with Departments in the University of Turku which have considerable strengths in infectious diseases. The research projects of the Department form integral components of two programmes carried out by a network involving the local universities, the Turku University Hospital, the Biotechnology Centre, the pharmaceutical industry, and KTL. The Department also collaborates with laboratories in the US, Germany, Belgium, Sweden and Russia.

The research programme comprises six projects:

- mucosal immunity,
- pathogenesis of reactive arthritis,
- leukocyte-endothelial cell interactions,
- mycobacteria,
- borrelia and pertussis,
- antimicrobial resistance.

**Mucosal immunity.** The work of this group is designed to improve understanding of gut permeability and mucosal defence mechanisms with a focus on gut infections and food (milk) allergy. Current studies observe the immune responses to oral (attenuated) salmonella vaccination. The studies focus on the properties of antibody secreting cells and analyse the role of cytokines in the antibody response (to the O antigen). Similar studies have been carried out in rotavirus diarrhoea and urinary tract infections in children and adults. The studies do not include any direct measures of mucosal immunity. The research on milk allergy was being discontinued. The Panel considered that this work was of limited scientific value and recommends that it should be discontinued.

**Pathogenesis of reactive arthritis.** These studies are based on the observation that structural elements similar to features of yersinia and salmonella can be found in the joints of those with reactive arthritis long after exposure to the pathogen. It was suggested to the Panel that this implied the continued presence of these organisms somewhere in the body - although there is no direct evidence that this is the case. It was argued that these micro-organisms cannot be eliminated effectively in B27 positive patients and that the prospects for such patients would be improved by antibiotic therapy at an early stage. The Panel considered that these observations and the lack of adequate overall understanding of the

pathogenetic mechanisms involved in reactive arthritis did not provide a basis for such an approach to treatment and that it was difficult to support more than a small scale trial in the absence of a better understanding of the pathogenesis. The Panel accorded this project a low priority, although it receives funding from external sources, and it should be subject to critical review after two years.

Leukocyte-endothelial interactions. The objective of this programme is to develop methods for the treatment of inflammatory disease by reducing cell adhesion. Much of the work is focused on the identification of the factors which promote the binding of leukocytes to vascular endothelium in the synovium and other tissues (skin, bowel, etc) and the group have developed a good animal (dog) model of skin inflammation. The group have been successful in identifying two lymphocyte vascular adhesion molecules. The importance of these studies is substantial since they provide fundamental insights into the processes of inflammation. The quality of the science is high and the Panel supports continued investment in this group.

**Mycobacteria.** The mycobacterial work is currently focused on the gene coding for the 32kD secreted protein of mycobacteria (which appears to be specific to mycobacteria). The clinically most important mycobacteria can be differentiated by sequencing a 60 base segment of the gene. These studies are providing the basis for better specification of mycobacteria by PCR. They are also of value in assessing potential drug resistance which is likely to be a growing problem in Finland - multiple drug resistance is a major problem in Russia (approximately 20% of cases). The quality of the science is high and this work merits continued support on public health and scientific grounds.

**Borrelia and pertussis.** The work carried out by this group is directed to the establishment of better diagnostic tests for these organisms. Infections with borrelia are an important public health problem in the south western part of Finland and it is planned that improved serological tests should be be used in epidemiological studies. The aim of the work on Bordetella pertussis is to develop PCR based and serological techniques to identify the organism and to detect antibodies (particularly against filamentous haemagglutinin) which indicate a high degree of protection against infection. These will be of value in the assessment of the efficacy of acellular vaccines. The work is of good quality and underpins the public health and other research responsibilities of the KTL. It should continue to be supported.

Antibiotic resistance. The KTL has taken responsibility for the development of policies on antibiotic use in Finland. The co-ordinated approach is being developed through the programme to provide an action plan. The scientist leading the programme is developing mechanisms for advice, education, surveillance and research. The research programmes are targeted to explore various characteristics of antibiotic use. The Panel considered this to be an imaginative well organised programme which effectively integrates public health functions and research responsibilities of the KTL and commends it strongly.

## **Conclusions and recommendations**

The laboratory in Turku was originally established to provide a microbiological laboratory service. The Director-General and the staff have successfully reoriented the laboratory and current programmes make a significant contribution to the overall public health surveillance and research responsibilities of the KTL. There are excellent links between staff within the laboratory and those in the University of Turku. Much of the research is of high quality but the Panel considers the programmes on mucosal immunity and pathogenesis of reactive arthritis to be of limited value and of low priority.

## The Panel recommends that:

(i) the laboratory in Turku should be maintained and the existing good relationships with the University strengthened;

(ii) the current scientific programmes on leukocyte-endothelial interactions, mycobacteria, borrelia and pertussis and antibiotic resistance should continue to be supported;

(iii) the programme on the pathogenesis of reactive arthritis is of lower priority and should be subject to critical review after two years;

(iv) the programme on mucosal immunity should be discontinued.

# **DEPARTMENT IN OULU**

The Department in Oulu was established in 1993. It was previously a clinical bacteriological laboratory serving the university and other hospitals and health care centres in the area. There has been a major change in the pattern of activity over the course of the last four years. The laboratory has carried responsibility for screening of prenatal infections (since 1991), research on the efficiency and cost-effectiveness of influenza and pneumococcal vaccines in the elderly (since 1992) and certain reference laboratory functions. At the beginning of 1994, the functions and some staff of the former Department of Respiratory Bacterial Infections at the KTL were transferred from Helsinki to Oulu, and the new chlamydia laboratory was founded in the same year.

The Department has a number of functions including the prevention of pneumococcal and chlamydial infections and their chronic sequelae. The Department is the national reference laboratory for Streptococcus pneumoniae Haemophilus influenzae, Chlamydia pneumoniae, and C. trachomatis. It is also a reference laboratory for prenatal infections and responsible for the maternal screening for hepatitis B and syphilis in Finland. The research programme is closely associated with the reference laboratory functions, and includes the development of new diagnostic methods for respiratory bacteria, studies on

the association of chlamydial and other infections with chronic diseases, and intervention trials for preventing pneumococcal and chlamydial infections using vaccines and antibiotics.

The Department had a total staff of 40 (14 professional and 26 technical) in 1994. Twenty-six of these were in posts supported by the core budget. The budget of the Department in 1994 was 8.4 million FIM, of which 32 per cent was from extrabudgetary sources. The most important source of extrabudgetary funding was the Academy of Finland. The Department collaborates with clinicians in Finnish hospitals and research groups in Finland, Europe, US, Australia and the Philippines.

The research programme of the Oulu Department has three principal themes:

- bacterial respiratory infections;
- acute and chronic chlamydial infections;
- prenatal infections.

**Bacterial respiratory infections.** Current work is concentrating on the development of immunological approaches to the diagnosis of pneumonia - mainly pneumococcal. The aim of these studies is to support the planning of preventive measures in children and the elderly. The major developments have been the improvement of immunological methods and the development of a rapid diagnostic method based upon the PCR detection of pneumolysin DNA. A study on the efficacy of immunisation against pneumococcal pneumonia and influenza - particularly in the elderly (in whom there appears to be a limited response to pneumococcal vaccines) has been completed and is currently being analysed. Cost-effectiveness studies are also being carried out and will be completed in 1996. The work is competent and warrants continued support. The Panel recommends that current epidemiological work should continue with a view to providing the framework for intervention studies in due course. All the current studies will be completed over the course of the next three years.

**Chlamydial infections.** These studies are based on the observed association between chlamydial infection and cardiac or pulmonary disease. The limited evidence for a significant role of chlamydia in the pathogenesis of coronary artery disease has been referred to above. The conceptual basis and research plans for this work have not been satisfactorily developed. The only clear plan at present is for a trial of doxycycline prior to coronary artery bypass surgery to see if this clears organisms from coronary arteries - although there is no evidence that they play a role in the pathogenesis. The Panel considers that this very limited study should be accorded a low priority.

**Prenatal infections.** This is mainly routine work. There are research plans based upon routine screening for prenatal infections. The group intends to look at markers from these samples and correlate these with later pathologies. No clear hypotheses have been formulated. The Panel accords a low priority to these planned studies in the absence of any clearly defined hypotheses.

# **Conclusions and recommendations**

The Panel considers that the range of current activities and proposals for future work are limited in scale and disappointing in nature and is concerned that the research plans were not based upon clearly formulated hypotheses. The current work on bacterial respiratory infections (all of which will be completed within the next three years) is of value and makes a contribution to the overall research strategy of the Division but no clear plans have been formulated for future work. The work based on the putative aetiological relationship between chlamydial infection and coronary artery disease was considered to be of low priority in the light of present knowledge. The collection of antenatal samples constitutes a unique resource - but the Panel was concerned that no clear thought had been given to the use which might be made of this - nor if this was the right location for such a collection to be held. A clear case for the maintenance of the laboratory in Oulu was not made.

## The Panel recommends that;

(i) continued support should be given to the improvement of diagnostic methods for pneumococcal disease;

(ii) the planned work on the putative role of chlamydial infection in the development of coronary artery disease should be discontinued after completion of the planned three month trial;

(iii) a working group should be set up to consider the future of the prenatal infection screening service and the potential uses to which the material might be put for research;

(iv) the future role of the Laboratory in Oulu should be reviewed by the proposed Director-General's strategy group in the light of this evaluation.

# **OVERALL COMMENTS ON THE DIVISION**

The overall strategy for the Division was clearly described in the KTL report and the additional papers which were presented to the Panel. The Division has major (and increasing) public health responsibilities - some of which are statutory and others rational extensions of current activities using the undoubted skills of the professional staff. The public health surveillance responsibilities and research activities of the Division are generally well integrated - each deriving strength from the other and these have led to the development of a number of research programmes of the highest quality (although the breadth of the public health responsibilities was also the cause of some concern to the Panel). The development of productive international research collaborations is commended by the Panel. A limited number of the activities do not fit within the current strategic framework - and some of these are of limited scientific value and should be discontinued. The plans for the reconfiguration of the Division were regarded as sensible by the Panel but these should be examined again in the light of this review. The Panel

supports the view of the Head of the Division that a structure with fewer individual departments would be more effective.

The wide range of the KTL's responsibilities for the surveillance of infectious diseases and their causative agents has provided the basis for major research programmes - but it has also resulted in a failure to achieve critical mass in a number of laboratories and this has resulted in the development of a number of research programmes which are not of high quality This problem has been exacerbated by the geographical spread of available microbiological expertise. The Panel strongly recommends a review of the disposition of bacterial expertise within the KTL (taking due account of expertise available elsewhere in Finland) to ensure that it meets its public health and research responsibilities in the most cost-effective manner. The Panel was also concerned at the limited expertise in molecular and cellular immunology available within the Institute and current and likely future needs in this discipline should also be an integral component of this review. It is the view of the Panel that immunology should be strengthened and that this can only be achieved through the recruitment of a senior immunologist to the KTL to provide the necessary scientific leadership. The panel considers that the future role of the small laboratory in Oulu should be reviewed. The Panel wishes to commend the strong and effective scientific leadership of Dr Makela who retires next year.

## The major recommendations of the Panel are:

(i) the current research strategy, the major objective of which is to improve the diagnosis, control and prevention of infections, has led to the development of programmes in which the public health surveillance and research activities are well integrated with effective internal and external collaborations and these should be strengthened and developed. A greater degree of focus should be achieved through the discontinuation of projects which are of low priority and do not contribute to the overall Divisional stratgey;

(ii) the assumption of an increasing range of public health responsibilities by this Division merits greater investment but this should be met by the reallocation of resources released through the discontinuation of activities of low priority;

(iii) further investment in the development of improved diagnostic methods should be more clearly justified by public health and research needs;

(iv) the Division should be reconfigured in the light of this review to concentrate expertise in a smaller number of larger Departments. Particular attention should be paid to the need to ensure that the existing expertise in bacteriology is used to best effect and to strengthen immunology (particularly in cellular immunology) within the KTL;

(v) the future role of the Laboratory in Oulu should be reviewed by the proposed Director-General's strategy group in the light of this evaluation.

# **DIVISION OF ENVIRONMENTAL HEALTH**

# INTRODUCTION

The goals of the Division of Environmental Health are to (i) improve public health, (ii) achieve healthier indoor and outdoor, urban and rural environments, and (iii) improve understanding of environmental factors which are of significance for health. These goals are pursued through research, risk assessment, dialogue with decision makers, and public education. The strategy of the Division is based on the analysis of the changing challenges concerning environment and health. Such challenges include climate change and the environmental effects of the socio-political transformations of the former socialist countries in Eastern and Central Europe which pose an increased risk of serious environmental accidents in short term. The main national and local health concerns are:

- sources and health effects of indoor air pollutants,
- exposure and health effects of combustion products,
- drinking water and food contaminants.

The Division implements its strategy in the following ways:

- high quality basic research and applied research on environmental health,
- monitoring of environmental exposures with known or potential health effects,
- advising health authorities and municipalities on environmental health problems,
- training of experts, health and environment professionals and researchers in environmental health,
- dissemination of information relevant to environmental health to the competent authorities and to the public.

Expert and advisory functions play an important role in the activities of the Division. The staff of the Division serve as experts for two ministries - the Ministry of Social Affairs and Health and the Ministry of the Environment. Members of staff participate in regulatory and expert committees of the two ministries. The international expert functions of the Division are discharged through key positions in scientific societies, organising committees for scientific meetings and the assumption of leading roles in EU and WHO programmes.

The strategy of the Division is based upon the following approaches: (i) an expertise based Departmental structure; (ii) project based research management and (iii) promotion of intra- and extramural collaborations. The Division also has very close links with certain Departments in the University of Kuopio and the Regional Institute of Occupational Health. The four departments work closely together. The research has been focused in nine areas and two or more of the Departments contribute to each - frequently with the collaboration of Departments in the University. Much of the research attracts extramural funding and is carried out through national and international collaborations.

The evaluation of the activities of this Division are presented in a somewhat different manner from that of the other two Divisions taking due account of its structure and small overall size. Background information on each of the the four individual Departments is presented briefly and this is followed by the Panel's analysis and evaluation of each of the research projects presented.

## DEPARTMENT OF ENVIRONMENTAL HYGIENE

The mission of the Department of Environmental Hygiene is to prevent or reduce exposures to agents which are hazardous for health. The Department investigates water, soil, food, and human samples, as well as indoor and outdoor, man-made and natural environments to identify potentially harmful environmental agents and assess human exposure to them. The group studies the sources, environmental distribution and extent of human exposure (routes, levels and distributions within the population) of known harmful chemical and physical agents. Much of the work is carried out through collaborative research programmes involving other institutions, often in other countries and increasingly in the context of the European Union. Recent and current research in the Department has been focused on the accumulation of pollutants in the environment, on air pollution, and on by-products of the chlorination of drinking water (their health effects and methods to prevent their formation).

The Department had a total staff of 24 (6 professional and 18 technical) in 1994, of whom 12 were in posts supported by the core budget. The budget in 1994 was 6.8 million FIM, of which 25 per cent was derived from extrabudgetary sources. The most important sources of extrabudgetary funding were the Academy of Finland, the Finnish Food Office, the National Board of Waters and the Environment, and the Ministry of Trade and Industry.

**Comments.** The principal research activities are studies of chlorinated compounds and air pollution - and in the past these have not always been focused on areas which are of greatest importance for Finland. The future plans of the Department include the development of better methods of risk assessment and markers of the biological consequences of exposure to underpin studies of public health and research importance.

## DEPARTMENT OF ENVIROMENTAL EPIDEMIOLOGY

The aim of the Department is to respond to the growing public health need to investigate environmental incidents and for epidemiological studies on the health effects of environmental contamination. The Department is developing the capacity to respond to such concerns as they arise in the community. Examples include instances of groundwater pollution and exposure to airborne pollutants. The Department is also the WHO Collaborating Centre in Finland on Emergency Preparedness and Response (FINNPREP). The research strategy has been to accumulate expertise through research on respiratory disease and cancer.

The Department had a total staff of 8 (7 professional and 1 technical staff) in 1994, of whom 3 were supported by the core budget. The budget in 1994 was 2.0 million FIM, of which 40 per cent was derived from extrabudgetary sources. The most important sources were the Academy of Finland, and the Ministries of Social Affairs and Health, and the Environment. The Department has actively participated in the work of the EC Concerted Action in Air Pollution Epidemiology. The EC funded collaborative study Pollution Effects on Asthmatic Children in Europe (PEACE), involving fourteen centres, grew out of this collaboration. The Department also participates in another large collaborative project - the International Study of Asthma and Allergies in Childhood (ISAAC). The indoor air research group collaborates with research groups in the Netherlands, Poland, Lithuania, Denmark, Great Britain and the US.

**Comments.** The leader of this group has a strong background in cardiovascular disease, but is now planning to focus on respiratory disease, particularly on indoor and outdoor air pollution, and the prevalence of asthma. The Panel strongly supports this reorientation. It is also planned to develop a small area health statistics system. The Panel was supportive of this in principle recognising the value of such systems but recommend that it should only be used to address clearly defined questions. There are also links between this group and those at the Finnish Cancer Registry.

# DEPARTMENT OF ENVIRONMENTAL MICROBIOLOGY

Environmental micro-organisms, both in the built environment and in nature, are of significance for human health. Organisms in buildings, water and soil have a considerable impact on environmental quality and can cause human disease. The principal responsibility of the Department is to study these organisms and the prevention of human exposure to them, and to provide data which will underpin the development of policies and practices which will contribute to the enhancement of the quality of these environments. Key research areas have included the study of organisms in building materials (which might lead to respiratory disorders among the occupants of homes, offices and schools), legionella and mycobacteria, and water borne organisms which may cause environmentally derived infections. The staff of the Department are currently committing

significant periods of time to the improvement of methods for the identification of specific strains of micro-organisms.

The Department had a total staff of 21 (13 professional and 8 technical) in 1994, of whom 11 were supported from the core budget. The overall budget in 1994 was 2.5 million FIM, of which 20 per cent was derived from extrabudgetary sources. The most important sources were the Academy of Finland, the Ministry of Health and Social Welfare, the Ministry of the Environment, TELE Oy, and Imatran Voima Oy. The Department has collaborators in a number of universities in Finland, and in the University of Cincinnati and the Institute of Physics, Lithuania. A collaborative network within the field of microbial ecology includes scientists and institutes in the US, Canada, the Scandinavian countries, Netherlands, Germany and the UK.

**Comments.** The Panel supports the growing focus on air pollution and its respiratory consequences. The development of effective programmes will require substantial refocusing of the activities of the Department and the Division as a whole. The Panel commented on the artificial separation of responsibility for food and water borne infections during the course of the review of the Division of Infectious Diseases.

# DEPARTMENT OF TOXICOLOGY

The purpose of the Department is to serve as a national centre of expertise for the evaluation of the human health risks of chemical, biological and physical factors. The Department carries out basic and applied toxicological research. The Department also provides a toxicity testing service in Finland, for the pharmaceutical and chemical industries on a contract basis in accordance with Good Laboratory Practice (GLP) standards.

The research strategy of the Department has been to devise research programmes which explore the health effects of selected environmental contaminants: eg dioxins, heavy metals, air pollutants, wood preservatives, drinking water mutagens and non-ionizing radiation. The dominant activities have been the mechanism of action of dioxins and the study of their potential risk at the population level, mechanisms of neurotoxicity of environmental chemicals, toxicity of inhaled inorganic and organic particles and drinking water mutagenicity.

The Department had a total staff of 41 (17 professional and 24 technical) in 1994, of whom 12 were in posts supported by the core budget. The overall budget in 1994 was 6.7 million FIM, of which 40 per cent was derived from extrabudgetary sources. The major sources of extrabudgetary funding were the Academy of Finland, the Finnish Work Environment Fund, the Ministry of the Environment, the Ministry of Education, the Finnish Ice Hockey Foundation, the MOBILE Research Programme (co-ordinated by the Technical Research Centre) and the International Research Programme on Toxic Oil

Syndrome (WHO and the Government of Spain). The department collaborates with other Departments within KTL, the Universities of Kuopio, Oulu, and Jyväskylä and the Finnish Institute of Occupational Health. Internationally, the Department collaborates with groups in the United States, Sweden, Norway, Germany, the United Kingdom and Spain.

**Comments.** This Department is in need of reorientation in the context of a new strategy for the Division. Staff within the Department have a significant role to play in the programme on air pollution. There are also several minor projects being carried out by the group (which were not included in the main report to the Panel). These are - (i) the toxicity of wood preservatives, (ii) terato- and carcinogenecity of electromagnetic fields, (iii) pulmonary toxicity of radioactive particles, (iv) engine exhausts in ice arenas and (v) toxic oil syndrome. The Panel was concerned at the lack of focus of the activities in this Department.

The Department also has a programme of toxicity testing which is carried out on contract for the pharmaceutical industry and others. The Panel was concerned that this carried the risk of potential conflicts of interest bearing in mind the public health responsibilities of the KTL (although it was recognised that the KTL does not carry responsibility for drug regulation). It appears that the principal reason for engaging in contract work was that there was not sufficient volume of work generated by the research programmes to occupy the staff and maintain their expertise. The Panel did not consider this a satisfactory justification for engaging in contract work and would recommend that this be discontinued and further consideration given to establishing other mechanisms for the achievement of critical mass (see below). The Panel also noted the range of small projects which were being undertaken but were not in a position to evaluate these since details had not been provided in the report.

# **EVALUATION OF THE RESEARCH PROJECTS**

**Dioxins and PCBs (Departments of Environmental Hygiene and Toxicology).** The major focus of the work has been on the dioxins (in foods and the environment) although exposure to these compounds has not been a significant problem in Finland. The studies have been focused on the mechanisms by which the dioxins affect energy metabolism - probably through peripheral metabolic effects and also through effects on central regulatory functions. There has also been some concern about the developmental consequences of exposure to PCDD/Fs in Finland and a study is currently in hand to examine the consequences of exposure in a high exposure area (Åland). It was acknowledged that PCBs are a greater problem in Finland and the focus of this work has also been on the contamination of foods - particularly fish. The Panel noted that little work had been carried out on exposure to chlorinated compounds from the timber processing industries in Finland. The Panel recommends that work of a general nature on the mechanisms of toxicity of the dioxins and furans should be discontinued and that further

studies should have a clearer focus on problems specific to Finland - eg PCBs and exposure to chlorinated compounds from the timber processing industries.

Neurotoxicity of environmental chemicals (Department of Toxicology). These studies have been led by a scientist who has now taken up a post in the University of Kuopio. No detailed plans for further work in this area were presented to the Panel. The development of a significant programme in neurotoxicology would require significant additional investment.

Toxicity of inhaled particles (Departements of Toxicology, Environmental Microbiology and Environmental Epidemiology). There have been several strands to this area of work which focuses on specific characteristics of Finnish environments (mainly indoor environments). The contribution of the Department of Toxicology to this area has been on the effects of bioaerosols and this has now relocated to the university with the member of staff concerned. Other components of this programme include the identification of inorganic (particularly minerals) and biological components (bacteria and fungi) of inhaled particulates. Recent studies have been directed to the study of the role of cellular signalling and oxidative stress in the toxicity of inhaled particles. Future plans include an intention to develop biomarkers for use on nasal lavage material. These studies are carried out with the collaboration of staff of the University of Kuopio and link to the project on microbial growth in buildings (see below). The Panel was supportive of the development of a programme in this area with a particular focus on indoor air quality since this addresses a specifically Finnish problem.

Drinking water mutagenicity (Departments of Environmental Hygiene, Toxicology and Environmental Epidemiology). These studies were focused on a chlorination byproduct (MX), which was found in processed surface waters with high levels of organic matter. This compound has been shown to be mutagenic and carcinogenic and, as a result, water purification mechanisms have been modified. These studies, which are almost complete, were carried out in collaboration with staff in the University. A case control study of cancer incidence based upon lifetime exposure estimates remains to be analysed and then work on this topic will be discontinued as planned.

Chernobyl fallout (Department of Environmental Hygiene). The Department has been responsible for monitoring the fallout from this accident. This work has now been completed.

**Outdoor air pollution (Departments of Environmental Epidemiology, Environmental Hygiene and Toxicology).** The incidence of asthma is increasing in school pupils and military recruits. The Departments are planning studies in collaboration with the regional laboratory of FIOH which has responsibility for measuring bioaerosols and there are good links with the staff concerned. Epidemiological studies are planned to establish the current extent of respiratory health problems on a regional basis and examine these in relation to exposure to outdoor environmental pollutants. The Panel was supportive of the

development of these studies which address a major international health problem. It would wish to see these studies more fully integrated with those on indoor air pollution and also the inclusion of other observations which might be relevant in Finland (eg the role of air temperature in sensitising the respiratory tract to environmental pollutants).

Microbial growth in buildings (Departments of Environmental Microbiology, Environmental Epidemiology and Toxicology). The major objective of this programme is to identify the factors which contribute to "mouldy buildings" in Finland and limit their harmful effects on human health. The staff of the Department currently carry out a limited range of studies examining bacterial and fungal flora, and the impact of these on macrophage function in vitro with some limited studies on IgG levels in vivo. The group has plans to examine factors which will alter the microbial profile and load, improve understanding of molecular consquences of exposure and carry out intervention studies. The project is heavily reliant on collaborations (the group is not able to carry out its own serology) and the Panel was concerned at the limited resource available for addressing this important problem. The successful prosecution of this project will depend upon the enhancement of links with groups within the KTL, the University of Kuopio and other groups in Finland (including those in other disciplines - eg building studies in the Technical University in Helsinki). The Panel supports the development of major programmes in this area but would recommend that an overarching strategic plan be drawn up (with external advice) and that steps are taken to ensure that the necessary scientific expertise is available within the KTL or through collaborations.

Water and soil microbiology. (Departments of Environmental Microbiology and Environmental Hygiene) There is limited investment in this programme which has a number of components (i) water and food borne enteric pathogens, (ii) legionella, (iii) atypical mycobacteria and (iv) microbial processes and climate. Much of this work is either of a routine public health nature (the expertise of the group being available for incident investigation) or contributes to studies of microbial ecology which are part of major collaborative programmes in which the KTL plays a relatively small role. No clearly defined research plans were presented to the Panel.

## **OVERALL COMMENTS ON THE DIVISION**

**Public health responsibilities.** The Division has a series of public health responsibilities (although these do not include regulatory responsibilities). These include the provision of advice on environmental matters to the Ministries of Social Affairs and Health and the Environment and to the municipalities, the issue of statements on environmental health matters and the investigation of environmental problems. It should be noted that these responsibilities do place a significant load on the staff of the Division. The need to maintain the capacity to respond with advice, or to investigate environmental incidents, covering the wide range of possible environmental health problems is reflected in the small (and in some instances very small) numbers of staff in some of the laboratories and these

are below critical mass. This problem has been alleviated to an extent by drawing upon the expertise of staff in the University of Kuopio and the regional Institute of Occupational Health.

Links to University of Kuopio and FIOH. There are substantial links to a number of Departments in the University which, in general, are in close proximity. These include environmental sciences (air and environmental chemistry, water and soil hygiene and toxicology), chemistry (which provides expertise in structural studies, synthesis, modelling and some analyses) and community health (shared training programmes). They have teams working on allergy and the environment and mouldy homes - with a major theme of indoor air quality in residential and working environments. Links with the FIOH are in programmes related to pesticides, endotoxins and microbiology, The main interactions at present are in the provision of serological services and studies of the physical environment (air, surfaces, building materials etc). The KTL staff and those in the University and FIOH meet four times a year to discuss collaborative programmes and there are more frequent discussions between individuals in specific laboratories.

Management of Division. The Division is managed through an open matrix arrangement with an expertise based Departmental structure, project based research management and strong support for intramural collaborations.

#### Conclusions and recommendations.

The general framework for the management of the Division has much to commend it. The Panel, however, is concerned that the Division is currently in a state of transition (programmes are being terminated and significant senior staff movements are taking place) and without a clearly defined strategy for future activities. The Panel considers that the KTL should review its overall strategy for the Division as a matter of urgency, establishing an expert group for this purpose which would report to the Director-General and the proposed Director-General's strategy Group. The Panel considers that the public health role of the Division in the provision of expert advice and the investigation of environmental problems should be more clearly specified. It would strongly support the development of major programmes on air pollution and microbial exposures and health in buildings and would recommend that a strategic view of the skills and expertise needed for the effective prosecution of such programmes should be given to the development of other programmes which have a particular relevance to Finland (eg relating to the timber processing industries).

The Panel also took the view that the Division should develop a more structured and coordinated approach to studies. This will enable the Division to carry these through in a systematic manner from hazard identification, to epidemiological association, to exposure assessment (with development of appropriate biomarkers), to assessment of the consequences of exposure, to study of mechanisms of toxicity, to the evaluation of factors (intrinsic and extrinsic) which might modify the impact of exposure. The Panel further recommends that the Division should consider the development of other major targeted programmes designed to improve understanding of mechanisms in human toxicity and the consequences of exposure to hazardous agents - these might be in the fields of neurotoxicology, immunotoxicology or reproductive/developmental toxicology. The establishment of a strong programme in one or more of these fields will require considerable strengthening of the limited number of current staff members with expertise in these areas. The range of activities within the Division does not appear to offer good value for money at present.

The small (and in some cases very small) numbers of staff in some of the groups has been commented upon above and this has clearly led to the development of a number of research programmes which are small in scale and scope and of limited scientific value. The Panel gained the clear impression that a number of the collaborating groups was also probably operating below critical mass and thus not all the potential gains from proximity with those in the University and FIOH have been realised. This is not in the interests of the KTL or its partners. The Panel would propose that a critical strategic review of the Division should be carried out in the context of its relationships with the University and the FIOH. There is a strong case for the review being carried out jointly with these other bodies. The Panel took the view that there might be advantages if the key elements in Kuopio were to be drawn together into an Institute of Environmental Health with a clearly defined strategy - but the possible advantages and disadvantages would have to be explored with considerable care. (We recognise that such a recommendation takes us beyond our terms of reference). The achievement of this objective would permit the development of a major resource and research centre in the field. It would require considerable reconfiguration of the skills base of the Division with recruitment of staff with additional complementary skills. It is probable that the substantial changes which would strengthen the Division could be achieved without additional investment taking advantage of this transitional priod. The Panel recommend that the Division should not continue to provide a toxicity testing service on a contractual basis to outside bodies.

# The Panel recommends that:

## (i) the overall strategy for the Division should be reviewed as a matter of urgency by an expert group which would report to the Director-General and the proposed Director-General's strategy group;

(ii) the Division should develop a more structured and co-ordinated approach to studies to enable it to carry these through in a systematic manner from hazard identification, to epidemiological association, to assessment of exposure and its consequences, to study of mechanisms of toxicity and evaluation of factors which might modify the impact of exposure;

(iii) major research themes for the future should include air pollution and other programmes which have a particular relevance to Finland (eg relating to the timber processing industries). Other major targeted programmes might be developed in neurotoxicology, immunotoxicology or reproductive/developmental toxicology - (it is recognised that the establishment of a strong programme in one or more of these fields will require considerable strengthening of the limited number of current staff members with expertise in these areas);

(iv) a critical strategic review of the Division should be carried out in the context of its relationships with the University and the FIOH (ideally in collaboration with these other bodies). The possibility that these might be drawn together into an Institute of Environmental Health to develop a major resource and research centre in the field with a clearly defined strategy should be explored;

(v) the contribution which staff of the Division make to the maintenance of bacteriological expertise within the KTL should be considered in the reappraisal proposed in the review of the Division of Infectious Dieases;

(vi) the Division should not continue to provide a toxicity testing service on a contractual basis.

# ANNEX A

# EVALUATION OF THE NATIONAL PUBLIC HEALTH INSTITUTE OF FINLAND

## BACKGROUND AND PURPOSE

The National Public Health Institute of Finland carries the responsibility for researching, promoting and monitoring the health of the Finnish people. Activities of the Institute include basic research, ranging from the detailed analysis of the molecular mechanisms of pathogenesis to large scale epidemiological studies of disease incidence and specific research into factors influencing health. This work aims at developing better methods of preventive health care in the country. The ultimate goal is to reduce the human suffering and economic costs caused by illness and to help people enhance the quality of their lives.

The evaluation of the Institute has been carried out by the Academy of Finland, in collaboration with the Ministry of Social Affairs and Health. The purpose of the evaluation has been to provide an assessment of the scientific level of the Institute in the performance of its public health functions and in conducting and promoting public health research in Finland. The evaluation will contribute to the formulation of the scientific strategy and further development of the Institute.

## **OBJECTIVES AND SCOPE OF THE REVIEW**

The objective of the review has been to provide an evaluation for the Academy and the Ministry of Social Affairs and Health of the public health functions, strategic importance, scientific merit and value for money of the scientific work undertaken and the proposals for future work. The review has covered all the activities of the Institute.

In particular the review has judged to what extent the Institute has succeeded in meeting its objectives in the following areas:

- surveillance and monitoring of the health of the Finnish people;
- basic and applied research which contributes to the development of public health policy and the improvement of the health of the Finnish population through prevention of disease and health promotion;
- identifying priority areas for public health research and prosecuting research in those areas;

- developing national and international collaborations in public health research;
- promoting and contributing to the training of researchers in the disciplines of public health;
- implementing the objectives set by the Ministry of Social Affairs and Health.

## **EVALUATION METHOD**

#### 1. Terms of reference.

The terms of reference of the panel are attached at Annex B.

#### 2. Evaluation criteria.

The following evaluation criteria have been employed:

#### a. Scientific objectives and strategy

What progress has been made against agreed objectives? Are the objectives still appropriate? Are the future objectives clear, realistic and set out in a way which will allow progress to be monitored and reviewed? Do they satisfy the public health responsibilities and does the research programme properly exploit scientific opportunities and reflect health needs? Do they contribute appropriately to meeting the objectives set by the Ministry of Social Affairs and Health and other sponsors? Are there appropriate mechanisms in place for determining and reviewing the overall scientific strategy of the Institute? What is the relationship between the current and planned future individual research programmes and the Institute's overall scientific strategy?

#### b. Public health surveillance and monitoring

Is the range of public health surveillance and monitoring activities appropriate? Do these meet the national needs? Which of these activities are provided to satisfy statutory requirements and which for other purposes? Are these functions performed in the most cost-effective manner? Could some of these services be provided more effectively by other means?

#### c. Quality of science

The scientific programmes and proposals for future work were reviewed. The following classification provided the framework for the Panel's evaluation of the programmes:

1. Work of the highest quality which is at the forefront internationally and which, it is judged, has the potential to make an important and substantial contribution to knowledge and the improvement of human health.

2. Work of high quality which is at the forefront of the Finnish effort in the field, is internationally competitive and which is likely to make a significant contribution to knowledge and the improvement of human health.

3. Work which is competitive, will add to understanding and will make a contribution to knowledge but is at a lower priority.

4. Work which is flawed in the scientific and/or technical approach or repetitious of other work and judged not to be worth pursuing.

# d. Originality

Does the work address new problems or use novel techniques or approaches to address problems which have been identified previously?

# e. Appropriateness of approach/design

Are the methods appropriate to the problems being addressed? Is the experimental design appropriate ? Is it the most resource effective method of addressing the problem?

# f. Timeliness

Is the research scientifically opportune because it exploits recent advances in the field (or in related fields) or because it addresses a significant current public health problem?

# g. Applicability and exploitability

Is the research applicable to disease prevention, health promotion or the development of public health policy? Are appropriate arrangements in place for knowledge and technology transfer and dissemination of results?

# h. Balance

Is there an appropriate balance within the research portfolio (ie between investigator initiated work exploiting scientific ideas and opportunities and work designed to address specific health problems; between basic, clinical and health services research, between work requiring long term investment and that requiring short term support etc.)? Are the research strengths of the Institute properly supported and exploited?

## i. Local, national and international collaboration

Are appropriate arrangements in place for maximising the opportunities for collaboration and multi-disciplinary research within the Institute (ie is the whole greater than the sum of its parts)? Do the routine public health and research functions interface satisfactorily to the benefit of both? Are there satisfactory mechanisms for establishing collaborative research programmes (national and international) which will contribute to meeting the scientific and public health objectives of the Institute and attaining the national goals of the major sponsors of its research? What are those goals and what is the policy framework within which they have been set? What is the role and significance of those activities which are carried out in less developed countries?

## j. Training and career development

Is the contribution to research training appropriate in terms of numbers undergoing training, supervision of trainees, level of training provided and balance between disciplines and outcomes? What is the strategy of the Institute for training and career development? How is this strategy aligned with national needs?

## k. Value for money

Is the scale and quality of the science commensurate with the level of investment in the Institute?

## **l.** Organisation

Are the structure and organisational arrangements appropriate to meet the public health responsibilities and provide the optimum environment for the research programme of the Institute?

## 3. Evaluation plan

## a. Constitution of the evaluation panel

The evaluation has been carried out by a panel comprising a Chairman and seven members. The panel was constituted to ensure that there were two or three highly qualified experts in each of the areas of science covered by the three major divisions of the Institute. The members of the panel were appointed by the Academy after consultation with the chairman.

## b. Approach to be adopted by the panel

The panel has formulated its judgements using the agreed evaluation criteria on the basis of the following inputs:

(i) a progress report, strategic plan and proposals for future work prepared by the Institute;

(ii) opinions on the scientific programme provided in writing by expert referees;

(iii) site visits and discussions with the Director-General and senior staff of the Institute;

(iv) background briefing provided by the Academy and the Ministry.

(v) evidence submitted by other relevant agencies (eg National Research and Development Centre for Welfare and Health, Institute of Occupational Health etc), other government departments, the higher education sector and research users.

# c. Meetings of the panel

There were three meetings of the panel overall. The first was held April 4 and 5 1995. The purpose of this meeting was to:

- receive the written submissions from the Institute,
- receive briefing from the Academy, the Ministry and other relevant bodies through written material supplemented by discussion and interview,
- select expert referees from whom they would wish to receive opinions in writing on the scientific programmes within the Institute,
- identify other information needs,
- identify strategic and scientific issues which would require discussion and exploration during the course of the site visits,
- discuss and agree (in consultation with the Director-General of the Institute) the approaches to be adopted and the format of the site visits,
- agree a timetable for the conduct and completion of the review process.

The second meetings of the panel were the site visits. These took place between 19 and 27 June 1995. Each of the three divisions of the Institute was visited separately. Each of these visits took two full days and was conducted by a subgroup drawn from the panel comprising the Chairman together with the relevant experts. The panel was constituted in such a way that there was some overlap between the members of the subgroups. The responsibility of the members of each subgroup was to evaluate the scientific performance and the plans of each division in the light of the evaluation criteria. The site visits were organised to provide adequate time for presentations and for discussion between the

members of the panel and the scientific staff. The deliberations of the subgroups were informed by the written reports of the expert referees.

The third meeting of the panel took place on 14 and 15 August 1995. The members of the panel received the reports of the three subgroups and in the light of these and taking due account of broader strategic considerations has formulated its final judgements on the quality of the individual programmes of the Institute and on the scientific quality of its current and planned future work. The panel members also discussed and agreed the form of their final report and the recommendations which they wished to make to the Academy.

# d. Report of the panel

The report and the recommendations of the panel were completed following the final meeting of the panel and this was presented to the Academy during October 1995. The report includes the judgements of the panel on the scientific performance of the Institute in meeting its agreed objectives and the potential and relevance of its scientific strategy and research plans. These judgements have been made at scientific programme, divisional and Institute level and set in the context of other national and international efforts in the field. The recommendations of the panel are formulated in such a way that they will contribute to the development of the scientific strategy of the Institute. They indicate those areas which would justify additional investment to meet public health needs, further the development of public health policy or exploit new research opportunities (and those areas in which the level of investment might be reduced). The report also makes recommendations on the role and responsibilities in providing opportunities for research training and career development and the effectiveness of the arrangements for the dissemination of the results of research and knowledge and technology transfer.

## e. Timetable

The timetable for the evaluation was as follows:

August 1994 - first visit of Chairman to Helsinki. The purpose of the visit was to:-

- meet the relevant officers of the Academy of Finland and the Ministry of Social Affairs and Health,
- meet the Director and senior staff of the Institute,
- discuss and agree the evaluation procedure and terms of reference for the panel,
- discuss and agree the format and content of the report and other information to be provided by the Institute with the Director,
- discuss and agree the membership of the panel after consultation with the Director,
- discuss and agree the timetable for the evaluation,
- receive briefing from Officers of the Academy, Ministry and other relevant agencies
- make a preliminary visit to the Institute for familiarisation purposes,
- discuss and agree the arrangements for scientific and administrative support for the Chairman and panel.

# August 1994 to March 1995 -

- invitations sent to panel members,
- preparation of report and collection and collation of other relevant information by the Director of the Institute and senior colleagues,
- collection and collation of background information and preparation of briefing material by Officers of the Academy and Ministry and other relevant bodies for the panel,
- preliminary consideration of the names of possible expert referees from whom written opinions would be sought,
- establishment of scientific and administrative support arrangements for the evaluation procedure,

# March 1995 -

- receipt of documentation from Institute, Academy and Ministry,
- circulation of agenda, papers and other details for first meeting of panel to members,

April 1995 - first meeting of the panel - 4 & 5 April 1995. The objectives were to:

- receive and consider the written submissions from the Institute,
- receive briefing from the Academy and the Ministry (through discussion at interview supplemented by relevant written material),
- preliminary visit to the Institute to meet the Director and senior members of staff,
- select expert referees from whom they would wish to receive opinions in writing on the scientific programmes within the Institute,
- agree approach to referees,
- identify other information needs,
- identify strategic and scientific issues which would require discussion and exploration during the course of the site visits,
- discuss and agree (in consultation with the Director of the Institute) the approaches to be adopted and the format of the site visits,
- agree a detailed timetable for the conduct and completion of the review process.

# April to May 1995 -

- prepare and send letters to referees,
- submit the Institute's report to referees with suitable deadline for response,
- circulate details of arrangements for site visits together with additional information requested and referees reports to panel members no later that three weeks before the first site visit.

June 1995 - site visits by subgroups to each division allowing two days for the review of each division divisions of the Institute,

• agree content of evaluation report.

#### June to July 1995 -

- preparation of evaluation reports on each of the divisions of the Institute,
- circulation of agenda, details and draft reports to members of the panel.

August 1995 - final meeting of the panel - 14 and 15 August. The objectives were to:

- discuss the reports from the three subgroups,
- discuss and evaluate the Institute as a whole in the light of the subgroup reports and taking due account of broader strategic considerations applying evaluation criteria a, g, h, i j and k,
- discuss and agree the form of the final report and recommendations to the Academy
- engage in further discussions and clarify issues with the Director-General and senior staff (if necessary),
- engage in further discussions and clarify issues with Officers of the Academy and Ministry (if necessary).

#### August to October 1995 -

- finalisation of report by Chairman in consultation with other members of the panel,
- submission and presentation of report to academy,
- consideration of the plans for a seminar to discuss the results of the evaluation.

#### December 1995

- Seminar to discuss the results of the evaluation
- circulate details of arrangements for site visits together with additional information

# ANNEX B

# **TERMS OF REFERENCE**

1. To evaluate the public health functions, strategic importance, scientific merit, and effectiveness in the use of resources (human and financial) of the work of the KTL in relation to its objectives:

- the surveillance and monitoring of the health of the Finnish people;
- the conduct of basic and applied research which contributes to the development of public health policy and the improvement of the health of the Finnish population through prevention of disease and health promotion;
- the identification of priority areas for public health research and the prosecution of research in these areas;
- the development of national and international collaborations;
- the training of researchers in the disciplines of public health;
- implementation of the objectives set by the Ministry of Social Affairs and Health.

2. To evaluate the strategic importance and scientific merit of the proposed future programme for the KTL in relation to its objectives.

3. To provide the Academy of Finland and the Ministry of Social Affairs and Health with an evaluation of the current and planned future work and make recommendations on the strategic development, organisation and resourcing of the KTL.

#### ANNEX C

#### MEMBERS OF THE EVALUATION PANEL

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#### ANNEX D

#### LIST OF PEOPLE WHOM THE PANEL MET

Steering group of the evaluation

Professor Pekka Karma (Chairman), University of Helsinki Dr Jarkko Eskola, Ministry of Social Affairs and Health Professor Olli Jänne, University of Helsinki Mrs Anna-Liisa Kauppila, Academy of Finland Professor Aulikki Nissinen, University of Kuopio

#### Academy of Finland

Dr Elisabeth Helander, Director of Research Mrs Kristiina Helansuo, Secretary, Medical Research Council Dr Sakari Karjalainen (Scientific Secretary of the Evaluation Group), Secretary General, Medical Research Council Dr Terttu Luukkonen, Senior Researcher, Department of Science Policy Professor Leena Peltonen-Palotie, Chairperson, Medical Research Council

#### Science and Technology Policy Council Mr Esko-Olavi Seppälä, Chief Planning Officer

Council for Higher Education Professor Reijo Vihko, Chairman

#### Ministry of Social Affairs and Health

Dr Kimmo Leppo, Director, Department for Social and Health Services Dr Tapani Melkas, Senior Medical Officer, Department for Promotion and Preven tion

- National Research and Development Centre for Welfare and Health Dr Vappu Taipale, Director General
- Finnish Institute of Occupational Health Dr Jorma Rantanen, Director General
- City of Turku, Department of Health Services Dr Ilmo Parvinen, Director
- University of Kuopio Professor Pentti Kalliokoski, Dean, Faculty of Environmental Sciences
- Kuopio Regional Institute of Occupational Health Dr Juhani Kangas, Director Dr Kaj Husman, Chief Physician

## NATIONAL INSTITUTE OF PUBLIC HEALTH (KTL)

#### **Director General**

Dr Jussi Huttunen

#### **Division of Health and Chronic Diseases**

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Department of Nutrition Dr Antti Aro (Head), Dr Georg Alftan, Dr Jarmo Virtamo

Department of Mental Health Dr Jouko Lönnqvist (Head), Dr Anja Aro, Dr Hillevi Aro, Dr Erkki Isometsä, Dr Kari Poikolainen

Department of Biochemistry Dr Christian Enholm (Head), Dr Marjatta Antikainen, Dr Matti Jauhiainen, Dr Vesa Olkkonen

Department of Immunobiology Dr Kimmo Aho (Head), Dr Timo Palosuo, Dr Outi Vaarala

Department of Alcohol, Drugs and Traffic Dr Jarmo Pikkarainen (Head), Dr Pirjo Lillsunde, Dr Ralph Lindbohm, Dr Timo Seppälä

#### **Division of Infectious Diseases**

<u>Department of Infectious Disease Epidemiology</u> Dr Juhani Eskola (Head), Dr Olli Haikala, Dr Hanna Nohynek, Dr Aino Takala, Dr Rose-Marie Ölander

Department of Special Bacterial Pathogenes Dr Helena Mäkelä (Head), Dr Hannele Jousimies-Somer, Dr Anja Siitonen, Dr Jaana Vuopio-Varkila Department of Bacterial Vaccine Research and Molecular Bacteriology Dr Matti Sarvas (Head), Dr Ilkka Helander, Dr Helena Käyhty, Dr Nina Rautonen, Dr Kirsi Saukkonen

Department of Acute Viral Diseases Dr Tapani Hovi (Head), Dr Marjaana Kleemola, Dr Reijo Pyhälä, Dr Merja Roivainen

Department of Chronic Viral Diseases Dr Pauli Leinikki (Head), Dr Ilkka Julkunen, Dr Marja-Leena Kantanen, Dr Martti Valle

Department in Turku Dr Heikki Arvilommi (Head), Dr Kaisa Granfors, Dr Pentti Huovinen, Dr Sirpa Jalkanen, Dr Matti Viljanen

Department in Oulu Dr Maija Leinonen (Head), Dr Pentti Koskela, Dr Pekka Saikku

#### **Division of Environmental Health**

Department of Environmental Hygiene Dr Matti Jantunen (Head), Dr Hannu Komulainen, Dr Jorma Mäki-Paakkanen, Dr Matti Vartiainen, Dr Terttu Vartiainen

Department of Environmental Epidemiology Dr Juha Pekkanen (Head), Dr Mikko Holopainen, Dr Kirsi Timonen

Department of Environmental Microbiology Dr Aino Nevalainen (Head), Dr Maija-Riitta Hirvonen, Dr Tuula Husman, Dr Pertti Martikainen

#### Department of Toxicology

Dr Kai Savolainen (Head), Dr Hannele Huuskonen, Dr Hannu Komulainen, Dr Jorma Mäki-Paakkanen, Dr Raimo Salonen, Dr Kai Savolainen, Dr Jouko Tuomisto



In 1994, the Academy of Finland, in response to a proposal put to it by the national Public Health Institute of Finland (KTL), decided to carry out an evaluation of the research activities of the KTL. The terms of reference were:

- to evaluate the public health function, strategic importance, scientific merit, and effectiveness in the use of resources

- to evaluate the strategic importance and scientific merit of the proposed future programme for the KTL in relation to its objectives.

- to provide the Academy of Finland and the Ministry of Social Affairs and Health with an evaluation of the current and planned work and make recommendationon the strategic development, organisation and resourcing of the KTL.

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