



## MEDICAL RESEARCH IN ESTONIA

An evaluation performed by  
the Swedish Medical  
Research Council 1992

---

**Medicinska forskningsrådet**

TELEFON 08 - 610 07 70 TELEFAX 08 - 610 07 77  
BOX 6713 • 113 85 STOCKHOLM  
BESÖKSADRESS: SVEAVÄGEN 166, 17 tr

**Swedish Medical Research Council**

TELEPHONE + 46 8 610 07 70 TELEFAX + 46 8 610 07 77  
BOX 6713 • S-113 85 STOCKHOLM  
SWEDEN

## INTRODUCTION

The Swedish Medical Research Council (SMRC) was requested by the Swedish Academy of Sciences to take care of an evaluation of Estonian scientific projects of a medical origin. The evaluation was initiated by the Estonian Academy of Sciences and the Estonian Research Council.

In order to fulfil the task requested, SMRC established a working group of five distinguished Swedish professors with a knowledge covering the more specialized areas represented in the documentary material received. The members of the working group are presented on p. 3.

The evaluation procedure used has been the following. All specialists have gone through the complete documentation and the comments given and conclusions drawn are those of the group in toto. In a few cases specialists outside the group have been consulted in order to improve the evaluation.

The working group decided to classify the reports/projects in three different groups

- 1) Projects of a reasonable scientific quality
- 2) Projects which could be further developed into scientifically sound projects
- 3) Projects of insufficient quality

Projects referred to group no 3 are either

- a) insufficient in terms of scientific quality,
- b) the material presented has been insufficient to such an extent that an evaluation has been impossible or
- c) being understood as clinical procedure of a routine character and lacking a scientific approach.

It has been noted by the SMRC-group that some of the Estonian research groups have reported data concerning their budget during the last few years. During the present rather unstable economical circumstances in Estonia the SMRC group has deemed it to be of limited value and in practice impossible to cover the financial aspects of ongoing medical research. It should be said however that the classification from a scientific point of view, which has been undertaken in this evaluation, could constitute a basis also for a prioritization from a financial point of view.

The evaluation has been restricted to the reported material in the form it has been delivered. The SMRC was not in a position to influence the protocol of the reports before they were finalized. Thus the possibility can not be excluded that the unfamiliarity to scientific evaluations by the reporting research groups and their habit to publish preferentially in Russian or Estonian scientific journals may have been unfavourable for the outcome of the evaluation in some cases. The evaluation has furthermore been a theoretical one, since the SMRC group did not have the opportunity to visit the various laboratories due to lack of time. Furthermore the unfamiliarity of the SMRC group to Estonian working conditions and limiting factors in terms of resources is therefore another factor which has to be taken into consideration by the readers of this evaluation document.

**List of members in the SMRC working group for evaluation:**

professor Tomas Albrektsson  
Dept of Handicap Research  
University of Gothenburg

professor Göran Bondjers  
Wallenberg Laboratory  
University of Gothenburg

professor Lars Jacobsson  
Dept of Psychiatry  
University of Umeå

professor Felix Mittelman  
Dept of Clinical Genetics  
University of Lund

professor Hans Olov Sjögren  
Dept of Tumour Immunology  
University of Lund

**Coordinator of the evaluation:**

Dr Ivar Vallin

administrative director of the SMRC

(to whom correspondence concerning the evaluation should be sent)

**Address:** Swedish Medical Research Council  
Box 6713  
S-113 85 STOCKHOLM  
Sweden

**Telefax:** +46-8-6100777

**ESTONIAN RESEARCH PROJECTS WHICH HAVE BEEN EVALUATED**

as originally numbered in the material received for evaluation

1. Lembit Mehilane, professor

Dept of Psychiatry, Tartu university

**Epidemiology, clinical variants and differentiated treatment of depressive states**

Reporter: Jacobsson

**Purpose:** 1) to study the prevalence of depressive disorder in Estonia, 2) to analyze the clinical structure of depression in the Estonian population and 3) to make comparative multinational studies of depressive disorders in cooperation with the university of Tampere (Finland), Hamburg (Germany), Uppsala (Sweden) and Nashville (USA). As a result of these studies the project group intends to work out methodological recommendations for diagnosis and differentiated treatment of depression and prevention of suicide.

**Methodology:** The methodology adapted in the study is traditional but adequate. The study group will use internationally established rating scales and they have also developed their own rating scales which will be assessed in the process of the international cooperation.

**Competence:** It is apparent that the research leader professor Mehilane has a good competence for conducting the studies. Furthermore the group has established cooperation with international groups in Tampere, Uppsala, Hamburg and Nashville, which all are well known research centres.

**Scientific report:** So far there is a limited number of internationally published papers and a great number of articles published in the Russian language.

**Usefulness of the project:** The area of research is important for many reasons. There are stable indications that depression is an increasing disorder in the western countries. It is reasonable to presuppose that depressive disorders will increase and might be rather high in Estonia. There are also clear evidence that the suicide rate is rather high in Estonia and it is of great interest to continue to study this phenomenon and to develop preventive strategies.

**Scientific value:** The project is well planned and should be quite possible to fulfil. Scientifically the project should contribute to the knowledge about epidemiology of depressive disorders which are of paramount importance in the mental health field.

**Conclusion:** The project has been considered to belong to the group number one projects.

2. A. Vain, assistant professor  
 Dept of Biomechanics and Microprocessor Technology, Tartu university  
**Myotonometric methods**  
 Reporter: Albrektsson

**Purpose:** To further develop a myometer based on microprocessor technology and to test muscle response in various groups of patients.

**Question at issue:** A clearly formulated question is lacking.

**Methodology:** The group itself has developed the so called myotonometer, based on the principle that a mechanical stimulus results in muscle oscillations which are registered and analyzed.

**Competence** of the group is good.

**Scientific report:** Only a few short abstracts in English accepted at international congresses are available for evaluation. Measurements of Parkinson patients before and after stereotactical operations imply that the myometer is practically functional.

**Usefulness of the project:** The idea to measure muscle oscillations as a response of a defined mechanical stimulus is interesting. Invasive methods used for registration of muscle tonus have obvious drawbacks. To our knowledge non invasive methods for measurement of muscle tonus are not used in Western Europe and the USA. The method in question seems thus to have a certain novelty value.

**Scientific value:** Provided that careful registrations and evaluations will be continued, the myotonometric method must be considered to be of interest and to have a clear scientific value. A parallel study where invasive methods are used in comparison would be an improvement.

**Conclusion:** The project has been considered to belong to group number two.

3. R. Teesalu

Laboratory of Clinical Physiology, Tartu university

**Study of the influence of home-produced prostaglandins in blood coagulation and cardiovascular system with the aim to introduce them into the treatment of cardiovascular disease**

Reporter: Bondjers

**Aim:** To reduce myocardial infarction and improve the results in bypass surgery.

**Procedure:** To study the balance of thromboxane and prostacyclin in its effect on thrombus formation and blood perfusion. Effects with various synthetic prostacyclin analogues would be performed. The studies in man would focus on the effects on platelet aggregation and those in animals on the effects during experimental myocardial infarction.

**Methodology:** Adequate in general although not really front-line.

**Scientific report:** No scientific papers in international, refereed journals concerning this project are included for evaluation.

**Scientific value:** The effects of prostacyclin on myocardial infarction have already been subject to a number of studies and using adequate controls, it has not been possible to demonstrate any benefits. We already have a simple way of achieving the desirable effects on the prostacyclin/thromboxane balance in patients, through treatment with ASA.

**Conclusion:** The studies planned would not be of major significance. The projects have therefore been considered to belong to group two.

4. Ain-Elmar Kaasik,

Cerebrovascular Research Laboratory, Dept of Neurology and Neurosurgery

Institute of General and Molecular Pathology, Tartu university

**Research of the mechanisms of development of focal brain damage**

Reporter: Jacobsson

**Purpose:** The purpose of this project is a complex evaluation of morphological, hemodynamic and biochemical signs and markers of vascular and traumatic brain damage. An investigation of the pathophysiological mechanisms of the local brain damage is included in the project, as well as the possibilities and efficiency of treatment. The investigation is using CSF enzymatic studies in stroke and craniocerebral injury as well as in newborn babies after prenatal hypoxia or injury. The cerebral blood flow and vascular reactivity is studied in experimental and clinical conditions.

**Methodology:** The methods used are relevant and adequate.

**Competence:** The competence of the researcher is high. (Professor Kaasik was appointed honorary doctor of the university of Uppsala in 1991).

**Scientific report:** In the project there has been published a number of papers in international journals and a great number in Estonian journals and publications. The investigators have also participated in a great number of international conferences presenting their work.

**Usefulness of the project:** The project is certainly possible to fulfil and has a clear scientific value.

**Scientific value:** Vascular and traumatic brain damage is an increasingly important topic in the modern society and the contribution of the research group is substantial.

**Conclusion:** The project has been considered to belong to the group number one projects.



5. Andres Piirsoo

Laboratory of Cell Biology,

Inst of General and Molecular Pathology, Tartu university

**Structural, functional and molecular changes of cells during induced differentiation and cell activation**

7. Erkki Juronen, head of institute et al

Dept of Genetics and Biotechnology

Inst of General and Molecular Pathology, Tartu university

**Biotechnology: Producing of monoclonal antibodies for using in qualitative detection of substances and in epitope analysis**

16. Jaanis Kasesalu,

Estonian Agribiocentre, Tartu university

**Monoclonal antibodies against neuron-specific enolase**

Reporter: Sjögren

**Purpose:** These projects are based on already developed monoclonal antibodies (mAb) or in some cases, mAb to be developed. In study 5) mAb to differentiated/undifferentiated human cells of myelomonocytic origin and to certain intracellular proteins (lactoferrin, ferritin and A1-antitrypsin) will be used to identify differentiation molecules that may be important for e.g. haematologic tumour diagnosis. In study 7) mAb to myoglobin, progesteron, the thyroid hormone complex and spermatozoid proteins are to be developed to be used for quantisation of the corresponding target molecules. In study 16) two established mAb to two different epitopes on neuron-specific enolase will be used to judge brain damage and small cell lung cancer by performing ELISA to quantize produced enolase.

**Methodology:** There seems to be no question about the capacity of the groups involved to produce mAb to a variety of protein molecules. The technology of ELISA assays also appears to be functioning well. In study 16) the epitopes of the two mAb have been exactly mapped on the protein molecule which indicates a good technical level.

**Feasibility:** The production of mAb with the wanted specificities is likely to function well. The indicated investigations are therefore likely to be carried out successfully.

**Scientific value:** The usefulness of the studied mAb is likely to vary greatly as they do in other similar studies performed in other laboratories. Although the clinical part of the intended investigations is much more difficult to judge because of the lack of details in the material supplied, these plans are felt to have merits. It is important that the clinical collaborators pay full attention to the planning of an appropriate evaluation of the various mAb together with actual groups.

**Conclusion:** These projects are considered to belong to group number one.

6. Hele Everaus, assistant professor

Laboratory of Haematology,

Inst of General and Molecular Pathology, Tartu university

**Interactions of the immune and endocrine systems in lymphoproliferative diseases**

Reporter: Sjögren

**Purpose:** The aim is to evaluate the importance of the immunological and hormonal reactivity defects in relation to progression of CLL and myeloma on the basis of previous own findings of a depressed T cell- (PHA and ConA) and B cell reactivity (LPS and dextran sulphate) and oestrogen/androgen imbalance associated with these diseases and the modulating effect of Cimetidine and vitamin A on these defects.

**Methodology:** The T-and B-cell analysis appears to be relatively superficial as judged by the material available. The depth of the analysis of the Cimetidine and vitamin A effects is not possible to judge from the material presented.

**Feasibility:** In view of the lacking description of the methodology to be used the feasibility cannot be finally judged. However, the kind of analysis required to yield interpretable results is quite demanding and may not be expected to be available.

**Scientific value:** The background material lacks in essential scientific information. This makes it impossible to judge it favourably. However, if a detailed investigation of the effects of Cimetidine and vitamin A has been competently performed, showing that the lymphocyte reactivity can be significantly augmented, then the merit may be good.

**Conclusion:** Under the present circumstances the project has been considered to belong to group number three.

7. Erkki Juronen, head of institute et al

Dept of Genetics and Biotechnology,

Inst of General and Molecular Pathology, Tartu university

**Biotechnology: Producing of monoclonal antibodies for using in qualitative detection of substances and in epitope analysis**

see group number 5

8. Aarvo-Valdur Mikelsaar, Dir of Institute  
Dept of Genetics and Biotechnology  
Inst of General and Molecular Pathology, Tartu university  
**Genetic characterization of Estonian population**  
Reporter: Mittelman

**Purpose:** To characterize the incidence of certain genetic disorders in the Estonian population, in particular congenital hypothyroidism, cystic fibrosis, alpha-1-antitrypsin polymorphism and chromosomal C-band heteromorphism.

**Methodology:** The methods are conventional and in some instances not entirely adequate. The use of modern molecular genetic techniques would have substantially increased the value of the study. According to the information supplied, plans to incorporate such techniques are in progress and should be encouraged.

**Scientific value:** Very little is obviously known about the incidence of genetic disorders in the Estonian population and the study is therefore of general interest. The project thus has a great potential for providing some answers to questions of scientific interest.

**Conclusion:** The project has been considered to belong to group number two.

9. Marika Mikelsaar and Anne Orminsson,

Inst of General and Molecular Pathology, Tartu university

**To reveal the etiological structure and mechanism of development of severe bacterial infections caused by some opportunistic microorganisms of the normal microflora of gastrointestinal tract**

Reporter: Sjögren

**Purpose:** The aim of the project is to clarify the mechanism of development of serious bacterial infections via opportunistic microorganisms from the bowel microflora of newborn infants, patients with serious traumata, malignant tumours and recipients of organ transplants.

**Methodology:** Broad bacterial routine investigations of the microflora of patients skin, mouth and rectal mucosa in relations to the actual infections.

**Feasibility:** This study can no doubt be carried out.

**Scientific value:** As a natural part of the care of these patient groups these tests should be performed. However, the scientific merit is low.

**Conclusion:** The project has been considered to belong to group number three.

10. Leo Päi, professor and Reinhold Birkenfeldt, professor,  
Dept of Hospital Therapy and Rheumatological laboratory, Inst of General and  
Molecular Pathology, Tartu university

**Principles of the disturbances in the immunological system function in the  
rheumatic diseases**

Reporter: Sjögren

**Purpose:** The specific aims are not clearly specified. The project is very broad and includes all aspects of rheumatology from genesis to therapy.

**Methodology:** The methodology is not specified in anything but very broad terms. It is said to include the study of "characteristics of the magnetoionosphere situation".

**Feasibility:** To perform meaningful investigations at any depth of all the indicated aspects is completely unrealistic.

**Scientific value:** This project lacks focus and has a very low priority.

**Conclusion:** This project has been considered to belong to the number three projects.

11. Paju Aili, professor

Laboratory of Adaptation and Neuroendocrine Processes,  
Inst of General and Molecular Pathology, Tartu university

Reporter: Bondjers

**a) Neuroendocrine status of human organism in extremal conditions**

**Purpose:** To evaluate the effects of asphyxia during birth and cerebral ischaemia on a number of variables including hormonal patterns. These are important subjects for research.

**Methodology:** Quite simplistic and simply includes quantisation of various hormones in blood.

**Scientific report:** No scientific papers in international, refereed journals concerning this project were included for evaluation.

**Conclusion:** We do not see how the approach would contribute to our understanding of the effects of the actual conditions. The scientists should try to define their working hypothesis for these studies better. The project is considered to belong to group number three.

**b) Ionic mechanisms of cardiac tissue depolarization developments**

**Purpose:** To study of the effects of myocardial ischemia on the electrolytic balance in the myocardium and in particular the effect of lysolecithin.

**Scientific value:** This is an important area of research as many of the complications during ischemia and reperfusion might be related to these effects.

**Methodology:** Appears to be adequate as evaluated from papers published by the group.

**Conclusions:** These studies appear far more interesting than those under a) and have already given results accepted for publications in international journals. We would encourage the group to concentrate on this line of research, which appears quite promising. This project is considered to belong to group number one.

12. A. Lenzner, prof. and H. Lenzner, doc.

Lab of Microbial Ecology, Inst of General and Mol. Pathology and  
Dept of Microbiology, Tartu university

**The search and selection of strains of lactobacilli needed for a correction of lactoflora**

Reporter: Sjögren

**Purpose:** The purpose is to clarify the mechanisms by which different strains of LACTOBACILLUS can protect a patient against microbes and to create a basis for its use against infections in the bowel and urogenitalia.

**Methodology:** The methodology is mainly traditional but applied to exceptional groups of individuals, i.e. cosmonauts and persons subject to overdoses of irradiation e.g. in connection with the Chernobyl accident. The preliminary result that LACTOBACILLUS per os enhances the antibody response to typhus vaccine is of interest.

**Feasibility:** The project can be done as described.

**Scientific value:** This project has merit and is potentially very important. What is lacking is depth in the analysis of the mechanisms involved. A sharp definition of the various issues in connection with the various possibilities to explain the effect of LACTOBACILLUS would be required in order to increase the depth of analysis.

**Conclusion:** The project has been considered to belong to group number two.



13. Raivo Ubio,

Lab of Immunology, Inst of General and Mol. Pathology, Tartu university.

**Autoimmune mechanisms in gastrointestinal and liver diseases**

Reporter: Sjögren

**Purpose:** The purpose is to characterize tissue specific autoantigenic molecules in chronic atrophic gastritis, choelic diseases and biliar cirrhosis and to clarify the B- and T- cell epitopes of these molecules.

**Methodology:** The methods to develop serological tests are traditional without any innovative aspects despite the fact that the project is well established clinically with collaboration with a Finnish group. We miss the use of monoclonal antibodies in this project, in which these reagents would seem to be very important tools to achieve the goals set. The aim of clarifying T-cell epitopes is very demanding and still there is no hint of a plan to really achieve it.

**Feasibility:** The feasibility of this project plan to achieve the ambitious goal set is doubted. There is no sign of a sharp, step-wise plan leading up to the aims.

**Scientific value:** The goals are very important and work on the problems involved should be stimulated. However, the scientific merit is diminished by the discrepancy between the ambitious specific aims and the lack of innovative technology. On the serological side it seems obvious that the project would benefit from the development of monoclonal antibodies, e.g. by involvement of the strong group working successfully with monoclonal antibodies at the Dept of General and Mol. Pathology. On the important T-cell aspect the analysis requires a set of instrumentation that might not be available at present. A sharper definition of what should be needed to achieve the goals is extremely important as a basis to get access to the instrumentation locally or by cooperation with other laboratories.

**Conclusion:** The project has been considered to belong to group number three in its present form.

14. Agu Tamm,

Lab of Enterology, Inst of General and Mol. Pathology, Tartu university.

**Hypolactasia: Epidemiology and Molecular Pathology.**

Reporter: Mittelman

**Purpose:** To determine the epidemiology of lactose deficiency, to determine individual clinical manifestations of lactose intolerance and to elucidate risk of myocardial infarction in relation to milk consumption. The prevalence of lactose deficiency or lactose intolerance varies substantially among different ethnic populations, as has been nicely demonstrated by this group to be the fact in several Finno-Ugric groups.

**Methodology:** The biochemical basis and the metabolic and clinical consequences of the disease has been extensively studied by researchers throughout the world during the last decade. It is therefore difficult to anticipate that important new knowledge may be obtained using the rather conventional approach proposed in the research program.

**Scientific value:** Continued epidemiological monitoring of the prevalence of lactose intolerance indifferent populations in Estonia will undoubtedly provide information of interest, but will not in principle add to our understanding of the disease. The proposed population study on milk consumption in relation to myocardial infarction would require a large collaborative international effort in order to produce meaningful results since obviously many environmental and predisposing genetic factors interact in the pathogenesis of myocardial infarction.

**Conclusion:** The project has been considered to belong to the group three projects.

15. Lembito Allikmets, professor, dean of faculty of medicine et al

Dept of Pharmacology, Lab. of Psychopharmacology, Inst of General and Mol Pathology, Tartu university.

Reporter: Fredholm

**Evaluation:** The documentation describes a conceptually well harmonized set of research using pharmaco-behavioural, in vitro-biochemical and receptor binding techniques. The issues at question in the work presented during the last three years concern long time effects of neuroleptica and anxiolytica research, questions of international actuality.

**Scientific reports:** Even if the scientific production to a large extent has been presented in Russian, a number of results has also been published in journals with a good reputation in the scientific circles concerned. The activity has furthermore been summed up in well written review articles in proceedings from symposia.

**Conclusion:** The aim of the research and the methodological competence at the department of pharmacology in Tartu makes the laboratory an interesting partner for cooperation for some Swedish neuropharmacologists. The research is considered to belong to group number one.

16. Jaanis Kasesalu, PhD.

Estonian Agrobiocentre, Tartu university.

**Monoclonal antibodies against neuron-specific enolase.**

see group number 5

17. Toomas Veidebaum,  
Inst of Exptl and Clinical Medicine, IECM, Tallin  
**Environmental mutagens and carcinogens in Estonia.**  
Reporter: Mittelman

**Purpose:** The main objective of this study is to determine the mutagenic and/or carcinogenic effects of different environmental exposures, including occupational exposure to a number of potentially mutagenic/carcinogenic agents.

**Methodology:** The program encompasses both in vivo carcinogenicity studies as well as a number of in vitro mutagenicity tests such as the AMES' assay, the micronucleus test and evaluation of sister chromatid exchange and chromosome aberration frequencies. All methodological approaches are relevant in relation to the aims of the study. The group seems to have very good competence to carry out the proposed studies as evidenced by the list of publications.

**Scientific value:** The proposed study is of interest and the results are of general significance.

**Conclusion:** The project is of a good international standard and has been considered to belong to group number one.

17. Toomas Veidebaum,

Inst of Exptl and Clinical Medicine, IECM, Tallin

**Environmental mutagens and carcinogens in Estonia.**

Reporter: Mittelman

**Purpose:** The main objective of this study is to determine the mutagenic and/or carcinogenic effects of different environmental exposures, including occupational exposure to a number of potentially mutagenic/carcinogenic agents.

**Methodology:** The program encompasses both in vivo carcinogenicity studies as well as a number of in vitro mutagenicity tests such as the AMES' assay, the micronucleus test and evaluation of sister chromatid exchange and chromosome aberration frequencies. All methodological approaches are relevant in relation to the aims of the study. The group seems to have very good competence to carry out the proposed studies as evidenced by the list of publications.

**Scientific value:** The proposed study is of interest and the results are of general significance.

**Conclusion:** The project is of a good international standard and has been considered to belong to group number one.

18. Hubert Kahn, head of dept

Dept of Occupational Medicine, IECM, Tallin

**Early Diagnosis of the Effects of Toxic Substances on the Organism.**

Reporter: Mittelman

**Purpose:** The main objectives of this project are to study: 1. the effect of toxic substances frequently used in Estonia, such as lead, aromatic hydrocarbons, organic solvents, shale oils and phenols; 2. individual sensitivity to toxic substances; 3. improvement of methods for the treatment of chronic intoxications; 4. toxicity threshold values; and 5. epidemiology of acute intoxications.

**Methodology:** The methodologies to be used are not described in sufficient detail to allow a proper evaluation.

**Scientific value:** The questions posed are in principle of general interest. The approach is not very original and similar studies are being pursued in a number of laboratories all over the world. Since, however, some of the questions are specifically related to conditions in Estonia, the results may have practical consequences for the health care system and in the evaluation of working conditions. Due to lack of information a proper priority rating as regards the different sub-projects has not been possible to perform.

**Conclusion:** The project in general has been considered to belong to the group number one projects.

19. Mati Rabu,

Dept of Biostatistics and Epidemiology, IECM, Tallin

**Cancer Registration, Statistics and Epidemiology**

Reporter: Mittelman

**Purpose:** To continuously update a population-based Cancer Registry covering the total population of Estonia and monitor time and regional trends in cancer incidence, mortality, prevalence and cancer survival. The general aims, which also include scientific treatment of data in order to develop and test hypotheses and offer explanations for cancer occurrence, are thus similar to those of other national cancer registries.

**Evaluation:** The Estonian Cancer Registry is obviously a very well functioning data base, staffed with competent researchers and every effort has been made to design the documentation and the information retrieval at a high level. The registry seems to serve its purpose well and the proposed projects and the methodology are clear, well presented and interesting. The scientific contribution in the past has been very good as evidenced by a number of publications in international scientific journals of high repute.

**Conclusion:** This has been considered to be a very good project that deserves funding with high priority. It belongs to the number one projects.



20. Vello Jaakmees

Lab of Industrial Hygiene and Physiology, Dept of Occupational Health, IECM, Tallin.

**Hygienic conditions in oil shale and furniture industries, risk factors and their influence on the worker's health.**

Reporter: Mittelman

**Purpose:** To determine harmful effects from occupational and environmental exposure to products from oil shale and wood processing industries. The studies include epidemiological as well as toxicological, biochemical, physiological, psychological and clinical investigations.

**Evaluation:** The oil shale industry in Estonia is the biggest in the world and obviously the elucidation of any harmful health effects of this industry is of great importance. The identification of any harmful substances offers a possibility for prevention and therefore the results may have important practical consequences. Such studies should therefore be pursued. However, neither the study design nor the methodology to be used are described in sufficient detail to allow a proper evaluation of the project. Actually there are instances where the method seems not to be entirely adequate. Therefore the project can not be assigned a high priority.

**Conclusion:** The project reported has been considered to belong to group number three.

21. Endel Veinpalu, head of dept  
Dept of Health Resort Treatment, IECM.

**Exptl and Clinical Investigation on the Effect of Estonian Curative Muds and their bioactive Compounds.**

Reporter: Albrektsson

**Purpose:** To investigate the Estonian muds and their effects on health. Muds from lakes and the sea are to be studied from a chemical and physical point of view and from its importance to cure various illnesses.

**Question at issue:** The effects of Estonian muds would primarily be of interest to what is usually referred to as alternative medicine.

**Methodology:** So called curative muds are abundant in Estonia. They can be administered in various ways. Mud baths in combination with NSAID and so called negative electro aerosols are popular forms of treatment. Injections of humisol, being a 0,01% solution of humic acid from sea mud, are recommended. No particular method is described in order to prove the clinically successful results which are implied.

**Competence:** Based on the report describing the so called pelotherapy and its curative effects, the competence of the group must be judged as doubtful.

**Scientific report:** It has not been possible to evaluate the scientific production in Russian and Estonian which has been referred to. The production in English contains either short abstracts or popularly kept reviews which lack real scientific value.

**Usefulness of the project and its scientific value:** Mud therapy in various forms is reported to give positive results in 80 - 90% of patients with various rheumatic and peripheral nervous illnesses. Patients with immunological, endocrine, neurovegetative and heart-lung functional conditions are reported as improved in 25% of the cases. A general improvement is reported for a large number of other illnesses. In all these claimed effects of treatment there is no documentation of the investigations behind the beneficial results reported and no control groups seem to have been used. The scientific value of the project must therefore be considered as very low.

**Conclusion:** The project has been considered to belong to group number three as being of insufficient quality.

22. Lii Janus, head of dept

Dept of Pulmonology, IECM

**Prevalence of Bronchial Estonian Asthma Diagnosis and Treatment.**

Reporter: Bondjers

**Purpose:** To map the prevalence and effects of bronchial asthma in different regions of Estonia and in addition to evaluate different treatment modalities.

**Scientific value:** The project would be of some significance if adequate data on the prevalence of bronchial asthma were obtained. In particular, this would be the case if the prevalence actually is changed and these changes could be related to environmental or other conditions.

**Methodology:** It is unclear from the report how the epidemiological study would be performed. The methodology described appears more suitable for smaller clinical studies and appears adequate for such studies even if it is not exciting or novel.

**Conclusion:** The studies suggested may provide clinical data of some value in the future. The project was considered to belong to group number two.

23. N. Elshstein, professor, head of dept  
Dept of gastroenterology, IECM

**Morbidity, Follow up and Risk-factors of Main Gastrointestinal Diseases.**

Reporter: Bondjers

**Purpose:** To follow the epidemiology of various gastrointestinal diseases in Estonia.

**Methodology:** Different treatments of patients have been evaluated and the longitudinal development of these diseases has been described. Since the report is rather restricted in volume and no English-spoken papers are included it is not easy to evaluate the methodology. Apart from simple clinical evaluations and questionnaires, ultrasound and endoscopy appears to have been available. These procedures would be adequate if not very exciting. The epidemiological methodology has not described and can therefore not be commented upon.

**Conclusions:** The scientific quality of the project is not possible to evaluate as no papers from international journals have been presented. The project has been considered to belong to group number two.

24. Väino Rätsep, professor, head of dept (minister of health 1975-88)

Dept of Clinical Oncology, IECM

**Immunological changes and hormonal responses in cancer diagnosis and adjuvant therapy.**

Reporter: Sjögren

**Purpose:** The material presented includes the whole clinic's development program for breast-, stomach- and lung cancer as well as melanoma research. The scientifically most interesting aspects concern investigations of variants of alfa2-macroglobulin complexed with various suppressive molecules and found to exert a T-cell suppressive effect in stomach cancer patients. The aim is to clarify the importance of this mechanism of immunosuppression in cancer.

**Methodology:** The innovative part concerns the alfa2-macroglobulin and particularly the CD2 molecule in soluble form. This is of considerable interest and a detailed analysis is clearly important. The members of the project are well informed in this field and are quite aware of the fact that also other active molecules such as TGF-beta create complexes with alfa2-macroglobulin. A sharp definition of the mechanisms involved in the T-cell suppression in the cancer patients related to alfa2-macroglobulin requires a simultaneous analysis of the various possible suppressive molecules that might be complexed with alfa2- macroglobulin. The plan does not detail on this but the group is likely to have the necessary technical competence.

**Feasibility:** The analysis and evaluation appear to be quite feasible.

**Scientific value:** Although the total project material presented lacks focusing, we feel that the T-cell suppression by alfa2-macroglobulin complexed with various other molecules has merit. This aspect is innovative and is likely to provide new basic information and might become clinically useful as well.

**Conclusion:** A restricted part of the material presented has been considered to belong to group number one.

25. Ludmilla Priimägi, dir of institute

The Institute of Preventive Medicine, Tallin

140 persons, working with Human ecology, Biomedicine, Drugs and Toxicology

Reporter: Mittelman

This programme consists of a number of projects, including studies of the Estonian population's health in relation to ecological factors, studies of heredity factors determining physical working capacity and sport abilities, health effects of environmental and occupational exposure to potential mutagenic/carcinogenic agents, toxicological evaluation of food products, sanitary evaluation of water and relationship between viral infections and environmental pollution.

**Evaluation:** The projects are extremely varied both quantitatively and qualitatively and it is extremely difficult to make an overall judgement of the total programme. In principle, the different projects may be grouped into three categories: 1. good quality with an interesting question and adequate methodology, 2. reasonable but not sufficiently good quality, either as regards originality or methodology, and 3. poor quality.

The projects dealing with the Estonian population's health in relation to ecological factors, in particular the development of systems for "physical education and hardening aimed at the promotion of health and development in children and adolescents", and the study of hereditary factors determining physical working capacity and sport abilities of children belong to category 3 above, i.e. the questions posed are scientifically uninteresting and the methodology is inadequate. These studies should absolutely not be pursued in the future.

The following projects belong to category 1, i.e., the quality is good and there is a clear potential for future development: the virology project, composed of a number of subprojects, is in general of very good quality. Some of the projects undoubtedly belong to routine clinical virology, but on the whole a number of interesting scientific questions are raised, the methodology is sound and the competence of the staff seems to be unquestionable. The toxicological evaluation of food products and the evaluation of bacterial water contamination are two other examples of solid studies using adequate methodology and where interesting results may be expected.

**Conclusions:** see above under evaluation.

26. Igor Shevchuk, project leader

Institute of Chemistry, Dept of Bioorganic Chemistry, Estonian Acad Sci  
**Chemistry and Biological Properties of Tetrapyrrole Compounds** (for laser photodynamic therapy)

Reporter: Mittelman

**Purpose:** The project is centred around the chemistry and biological properties of tetrapyrrole compounds used in laser photo dynamic therapy. The major aim is to develop and characterize new compounds with a strong photosensitizing effect and which have the capacity to accumulate in tumour tissue and induce cell death and subsequent tumour necrosis.

**Methodology:** The methods are not presented in sufficient detail to allow a proper evaluation, but the promising preliminary experimental results show that the group has a sufficient knowledge and methodological competence to successfully pursue this area of research.

**Evaluation:** The study is interesting and the results are of general interest and may also have practical clinical consequences. The project is considered to belong to group one.

27. Rein Raie, professor  
 Dept of Orthopaedics of the A. Seppo Clinic  
 Basal Metallosteosynthesis Research Laboratory  
**Scoliosis in children, adolescents and adults**  
 Reporter: Albrektsson

**Purpose:** To investigate differences in scoliosis treatment of children and adults, to describe indications for surgical corrections of scoliosis as it develops in relation to age, to judge indications for surgical treatment of scoliosis of adults, to investigate the cause of pain connected to scoliosis and to investigate the differences between surgically treated and non treated patients from various social aspects.

**Questions at issue** are important and of a clear clinical interest

**Methodology:** A series of questions related to spondylolisthes of children, youth and adults are presented. The methodology is however given in general terms. Clinical and roentgenological evaluations are to be done, neuro-muscular function to be estimated, effective methods for surgical treatment are to be evaluated etc.

**Competence:** The team seems to have a good clinical competence as the treatment of scoliosis is concerned. There is however no documentation in English from which the scientific competence can be judged.

**Scientific report:** Harrington stags have been used in a group of 230 patients as well as massive bone allografts. A per cent wise improvement is reported after various methods of corrections of scoliosis in 106 individuals in the ages between 11 and 16. A follow up was done after another five years. An animal study was performed where scoliosis was induced by rhizotomy and rods used for stabilization. The study showed that spine fusions are not necessary in order to prevent progress of the scoliosis symptoms. These data induced a clinical study of 42 children where Harrington stags were used without spine fusion in spite of damage of degrees III - IV. Finally a study indicates that scoliosis at adult ages should be treated surgically.

**Scientific value of the project:** The group has presented a good documentation of the follow up of earlier treatments. The purpose of future research and methods to be used is not conclusively described. The value of the project lies in the documented capacity of the group to follow up patient groups, which seems to be done objectively. This should constitute a good prognosis for the investigations of spondylolisthes.

**Conclusion:** The project is considered to belong to group number one, constituted of subprojects of a reasonable scientific quality.



28. Lembit Pihkva

The A Seppo Metalloplastic Osteosynthesis Laboratory and Clinic

**A complexed treatment of acute haematogenous osteomyelitis with Seppo system's needle**

Reporter: Albrektsson

**Purpose:** To evaluate methods for treatment of acute osteomyelitis in children

**Question at issue:** To evaluate results of clinical treatment of purulent infections in legs and joints of the hand. Different methods for treatment as performed at the clinic are described. Direct comparisons between controlled and matched groups are lacking. The question at issue is therefore somewhat unclear.

**Methodology:** Methods developed at the clinic earlier for treatment of osteopurulent infections are referred to, such as 1) administration of pharmaca to the infected bone tissue without restriction of the mobility of the patient, 2) a series of solutions of various oxidants for injection in the infected area, 3) various surgical techniques. Tissue samples may be taken in connection to such treatments in order to evaluate diagnosis and effect of treatment. Obviously techniques like roentgenology, scintigraphy and magnetic resonance are available to the group. No information is however given of experimental design, control groups etc.

**Scientific report:** In a follow up study involving 21 patients various surgical techniques such as closed external fixation and open stable osteosynthesis with external fixation are evaluated. The formation of patients into groups for the various treatments has been done on clinical criteria and the material presented does not allow a comparison between alternative treatments.

**Competence:** The clinical competence of the group seems to be good. The scientific competence is more difficult to evaluate since there are no scientific reports in English available. None in the group has a formal scientific education.

**Scientific value of the project:** Since the purpose of the project is unclear and with the lack of scientific schooling of the group, the scientific value of the project must be considered as doubtful.

**Conclusion:** The project has been considered to belong to group number two.

29. Jaan Môtus, MD

The A Seppo Clinic, Basal Metalloosteosynthesis Research Laboratory

**Surgical treatment of trochanteric fractures of the femur by means of Seppo device**

Reporter: Albrektsson

**Purpose:** The so called Seppo-stabilizer for treatment of pertocantheric fractures has been developed earlier at the clinic. The present aim is unclear but could possibly be a further evaluation of the Seppo system.

**Question at issue:** A specific question or hypothesis is not given.

**Methodology:** In earlier studies a clinical evaluation system based on Evans has been used.

**Competence:** The clinical competence seems to be good. The scientific competence to perform controlled studies is not sufficiently documented. Some ten publications are referred to but there is no evidence that the leader of the group has passed a formal dissertation.

**Scientific report:** Except for publications in Estonian, only a short description is available. The stability of various fixations in carcass bones has been evaluated. The more precise technique for that evaluation is not emerging. A group of 83 individuals with pertocantheric fractures, half of which was treated with a Seppo instrumentation was further evaluated. The selection of patients to form the two halves of the group is not described. Since only a few parameters like stability and "anatomic recovery" are covered, the conclusion that the Seppo instrumentation is superior for treatment of pertochantery fractures is not quite convincing.

**Scientific value of the project:** The evaluation of various fixation techniques may be of certain interest. The scientific value depends of cause on the quality of the protocol to be followed. Such a protocol is not sufficiently described. It is further doubtful if enough competence has been spent on the selection of patients to form groups so that an objective comparison may be made between various principles of treatment.

**Conclusion:** The project has been considered to belong to group number 3 as being of insufficient quality.

30. Maido M Uusküla

Lab of cardiology, Inst of General and Molecular Pathology, Tartu University

**Early pericarditis in the acute myocardial infection...**

Reporter: Bondjers

**Purpose:** To assess the prognostic significance of immune responses during acute myocardial infarction. In addition, the effects of thrombolytic treatment on the process will be evaluated.

**Methodology:** The investigators have established adequate methods to evaluate a restricted portion of the problem.

**Scientific value:** This is an interesting and timely programme. No publications in internationally recognized journals have been submitted. We still feel favourably disposed to this project, which delineates a specified problem, namely to evaluate this problem in depth. We would further suggest that the investigators refrain from splitting their resources by including the behaviour/infarction project, which is a very complicated as well as poorly defined problem.

**Conclusion:** The suggested project was considered to belong to group number two.

31. Peeter Laare et al

Estonian Institute of Cardiology, Tallin

**Various clinical forms of coronary active diseases**

Reporter: Bondjers

**Purpose:** To study morphological and physiological aspects of heart function in patients with coronary artery disease. Long-term prognosis of the patients has been related to risk factors for atherosclerosis and electrophysiological investigations.

**Methodology:** It should be emphasized that the methodology certainly is not in the international front-line. Contacts with leading laboratories in the west might improve the quality of these studies. The more pure clinical investigations appear to duplicate already available data in other countries, even if long-term follow up studies are important.

**Scientific value:** In the absence of data published in English, we feel unable to evaluate these studies in a fair way.

**Conclusion:** The project was considered to belong to group number three.

NS 22. M Epler et al

Lab of Biophysics, Inst of General and Mol Pathology, Tartu university

**Regulatory processes in human cardiovascular system in health and disease**

Reporter: Bondjers

**Purpose:** To study how the physiological characteristics of the cardiovascular system in the individual varies in response to various stimuli such as emotional stress, physical exercise etc.

**Scientific value:** The effects that various stimuli might have on blood pressure, heart rate, heart rate variability and peripheral blood flow are important to study. From the submitted papers, it is unclear however, how the investigators would transform actual measurements to computerized analysis, which probably is necessary for a meaningful evaluation of the information. We suggest that the scientists are encouraged in these studies. We do however doubt, whether it really would be worth-while or even possible to perform cross-sectional studies in the Estonian population as suggested in the report. The investigators do not appear to have published any data in international journals with referees.

**Conclusion:** The projects reported have been considered to partly belong to group number two (see comments above).

NS 47a. Ülo Lille et al

Inst of Chemistry, Dept of Bioorganic Chemistry, Estonian Acad of Sci

**Search for synthesis and action of polyenic acid metabolites and related compounds**

Reporter: Bondjers

**Purpose:** In order to test the possibility that prostaglandins as compounds of major significance in a number of different biological processes might modify several important disease processes pharmacologically, pure and preferentially stable prostaglandin species need to be purified or synthesized.

**Scientific value:** This research group has ventured into such isolation and/or synthesis. Within that field they are exposed to fierce competition both from other academic institutions and from the industry. Still they have been quite successful, with a number of publications in internationally recognized journals.

**Conclusion:** This appears to be a group of some substance which should be provided support also in the future. Even if it could be doubted that synthetic prostaglandins would have any pharmacological value in the future, these may be quite practical in experimental studies. The project is considered to belong to group number one and it is suggested that the investigators are provided adequate support also in the future.

NS 47b Margus Lopp, PhD, Head of Department  
Institute of Chemistry, Estonian Academy of Sciences, Department of Organic Synthesis  
and Technology

**Estonian Curative Muds**

Reporter: Albrektsson

**Purpose:** To investigate chemically the components of the humisol solution, as extracted from Estonian mud, and used for injection into patients (see report no 21).

**Question at issue:** Since the documentation of the curative effects of mud extracts is very poor, a chemical description of the muds will lack interest from a medical point of view.

**Methodology:** No methodology has been reported in the material presented.

**Competence:** The chemical competence of the group is difficult to estimate from the few data presented.

**Scientific report:** Some references are given, none however in English.

**Scientific value of the project:** Based on what has been considered as the scientific value of project no 21, being the medical counterpart of the present project, the scientific value of a chemical analysis of humisol is insignificant.

**Conclusion:** This project has been considered to belong to group number three as being of insufficient quality.

NS 50. Toomas Kööp,

Dept of Animal Physiology and Genetics, Inst of Exptl Biology, Estonian Acad

Sci

**Biologically active fractions of lymph tissue and their roles in the organisms affected by irradiation**

Reporter: Sjögren

**Purpose:** The purpose is to isolate peptides from Bursa Fabricius and to clarify their biological effects and on that basis use them clinically.

**Methodology:** The basic technique is to produce acetone extracts of Bursa Fabricius and to test their effects on antibody responses in Jerne type assays and effects on T-cell responses by assaying the "ecto-ATPase activity". The latter technique is very little used by immunologists so a spelled out reason why to use it and a detailed discussion on what it measures in relation to commonly used techniques are required in order to be acceptable.

**Feasibility:** The study as described is feasible.

**Scientific value:** The isolation and characterization of active peptides from Bursa Fabricius by the methods indicated appear to have only a small chance of success, particularly since the activity seems to be rather weak (40% stimulation of antibody production) and the T-cell stimulation has not been evaluated by any well known standard technique. A detailed plan with more powerful techniques including peptide synthesis and detailed mechanistic analysis is lacking. Furthermore, the clinical implications need to be judged in view of the fact that patients do not have Bursa Fabricii and that Bursa equivalents are only partially analogous.

**Conclusion:** The scientific merit of this project is questionable as judged from the material available. The project has been considered to belong to group number three.



## INDEX

Principal investigator	page
Aiiiili Paju	15
Allikmets Lembito	19
Birkenfeldt Reinhold	14
Elshtein N	27
Epler M	36
Evarus Herle	10
Jaakmets Vello	24
Janus Lii	26
Juronen Erkki	5(11)
Kaasik Ain-Elmar	8
Kahn Hubert	22
Kasesalu Jaanis	5(20)
Kööp Toomas	39
Laare Peeter	35
Lenzner A	16
Lenzner H	16
Lille Ülo	37
Lopp Margus	38
Mehilane Lembit	5
Mikelsaar Aarvo-Valdur	12
Mikelsaar Marika	13
Môtus Jaan	33
Orminsson Anne	13
Päi Leo	14
Pihkva Lembit	32
Piirsoo Andres	9
Primäägi Ludmilla	29
Rabu Mati	23
Raie Rein	31
Rätsep Väino	28
Shevchuk Igor	30
Tamm Agu	18
Teesalu R	7
Ubio Raivo	17
Uusküla Maido M	34
Vain A	6
Veidebaum Toomas	21
Veinpalu Endel	25