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MEMORANDUM

Presentation of a third medical research programme on Chronic
Respiratory Diseases.

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Presentation of a third medical research programme on
Chronic Respiratory Diseases

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I. Introduction

Pursuant to Article 55, § 2 of the Treaty establishing the ECSC, a fresh initiative is proposed to promote research in the industrial medical sphere.

The principles guiding the Commission's policy and methods are described in the publication 'High Authority policy for the promotion of study and research on industrial health, medicine and safety' (1).

2.5 millions u.a. were allocated for the preceding research programme 'Chronic Respiratory Diseases II' which was authorized by the Commission on 13 October 1970. Following the accession of the United Kingdom, Ireland and Denmark and by a Commission decision of 21 December 1973, a further million u.a. were made available for the projects. 63 research projects were financed in this manner between 1971 and 1974.

Whereas the first research programme (1955) was mainly proposed by professional research institutes whose interests were geared largely to basic research, recent years have shown an increasing general trend towards clinical and practical studies. Occupational lung diseases in particular (pneumoconiosis from varying causes and also the chronic non-specific respiratory syndrome) have undergone intensive study in the form of function tests on lungs, heart and circulation. For this, research workers in the Member States needed standardized questionnaires and, to obtain comparable results, harmonized methods of study.

(1) Office for Official Publications of the European Communities, Luxembourg, 1966

One of the aims of the recent programme on chronic bronchitis caused by pulmonary emphysema was to determine the connection between these diseases and occupational noxae, especially dusts, the programme itself comprising the following aspects :

1. Basic research on pneumoconiosis
2. Epidemiological research
3. Physiopathology and standardization
4. Prevention and therapy
5. Rehabilitation.

This programme has now reached successful completion. Detailed scientific results were presented to interested professional circles and to labour and management at a two-day conference in Luxembourg on 2 and 3 July 1975.

The new programme 'Chronic Respiratory Diseases III' is based on these results and includes further epidemiological research, diagnostic studies for the early recognition of bronchopulmonary diseases and the development of therapeutic and rehabilitation measures. Furthermore, new drugs are to be developed for the prevention or treatment of pneumoconiosis (animal experiments) (see Annex 1).

The new programme is in accordance with the 'social action programme' (1) submitted by the Commission to the Council on 25 October 1973, one objective of which is an 'improvement of living and working conditions'. It also provides specific support for the 'programme

(1) Council Decision of 21 January 1974 concerning a 'social action programme', Official Journal of the European Communities C 13 of 12 February 1974.

of action on the environment' (1).

II. Current position

Summary of the results of the research programme 'Chronic Respiratory Diseases II' adopted by the Commission on 13 October 1970

Basic research on pneumoconiosis

The aim of basic research was to gain further knowledge permitting more specific preventive, diagnostic and therapeutic measures to be taken.

Basic research projects on pneumoconiosis are an extension of the work undertaken in the preceding programme. The importance of these results was illustrated by the great interest in and response to the symposium held in Florence in 1968 (2). The latest results were presented at the symposium held in July 1975 and have been published (March 1976).

Epidemiology

The drafting of a standard ECSC questionnaire (3) enabled 16 institutes in the Community countries to implement identical procedures in determining the effects of workplace or environmental pollution on chronic bronchitis. In general, comparisons were made between subjects

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- (1) Declaration of the Council of the European Communities and of the representatives of the Governments of the Member States meeting in the Council on the 'Programme of action of the European Communities on the environment', Official Journal of the European Communities C 112 of 20 December 1973.
 - (2) 'Basic research on pneumoconiosis (Florence 16 to 18 October 1968)', Commission of the European Communities (ECSC) Industrial Health and Medicine Series No. 10, Luxembourg, 1970.
 - (3) 'Commentary on the ECSC questionnaire for studies of chronic bronchitis and emphysema of the lung', Commission of the European Communities, Industrial Health and Medicine Series No. 14, Luxembourg 1972, p 5.

from the coal and steel industries and non-industrial subjects. The sample sizes of 500 to 6 000 people used in individual research projects made for satisfactory statistics.

Field surveys have produced interesting results, especially as regards the aetiological significance of the various biological parameters considered in the separate projects. They also showed, however, that the ECSC questionnaire will have to be more detailed for future research programmes. In particular, the current definition of the clinical symptoms of the chronic non-specific respiratory syndrome has proved to be unsuitable for epidemiological retrospective screening. The research workers have already submitted and discussed the requisite amendments to this definition. These problems have to be solved if comparability of the subjects under study is to be guaranteed. There would also seem to be a need to settle any outstanding terminology difficulties and include more modern study methods, suitably standardized, (1) (2) in the research projects.

As far as the etiopathogeny of chronic bronchitis is concerned, a final opinion would seem to be somewhat premature, despite the fact that the results already obtained show that dust exposure and smoking habits are determining factors.

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- (1) 'Aide-memoire of spirometric practice for examining ventilatory function', Commission of the European Communities, Industrial Health and Medicine Series No 11, second edition, Luxembourg 1973.
 - (2) 'Aide-memoire pour la pratique des épreuves d'exercices en médecine du travail', Commission of the European Communities, Industrial Health and Medicine Series No 12, Luxembourg 1971.

Physiopathology and standardization

Valuable results were also obtained in this sphere, which is equally useful for both hospitals and general practitioners. A wide range of specific pulmonary function tests were carried out on a large number of subjects. Comparisons were made with the measurements taken on healthy subjects of different age and sex, thus producing valuable information for the standardization of ergometry and spirometry.

Finally, the results produced by the working parties concerned with cardiac diseases show that heart and circulation dynamics depend considerably on bronchopulmonary function. There are still many points to be clarified on this subject and these must be tackled in the new research programme with a view to preventing early disablement.

Prevention and therapy

In the preceding programme two different types of project on prevention and therapy were subsidized, namely :

- tests on animals to prevent experimental pneumoconiosis using polyvinyl pyridine N oxide (PVNO), and
- tests on human subjects for the treatment of chronic bronchitis in its various stages.

The results of what at first seemed to be a promising project, i.e. PVNO prevention of mixed-dust silicosis, were questioned by various research workers; in particular, the secondary damage caused by the drug means that it cannot yet be used unhesitatingly on humans.

Following clarification of the effect of airborne irritants on bronchial obstruction, certain research teams carried out studies

on bronchodilatory drugs. The pharmacodynamic features established for medicines best suited to various groups made it possible to develop preparations with longer-lasting effects but without toxic side-effects. Immunologic methods designed to control bronchial infection by stimulation of bronchial resistance to respiratory infections were tested. Some of the hypotheses were confirmed.

An interesting experiment would appear to be pulmonary lavage for chronic bronchitis. This therapy, however, is only to be applied to patients who are seriously ill. Certain technical problems still have to be overcome.

Rehabilitation

In the general context of the rehabilitation of handicapped persons measures for patients suffering from bronchopulmonary diseases, and in particular the chronic non-specific respiratory syndrome, are of considerable importance since these patients form a sizeable social and medical group. National social insurance statistics show to what a high degree these diseases are responsible for the increase in early disablement, the economic and social cost of which is considerable.

The success achieved with the physical and functional rehabilitation of patients suffering from heart diseases augurs well for patients suffering from chronic bronchitis.

A programme for respiratory rehabilitation accompanied by a corresponding questionnaire has been developed by experts interested in these aspects. It is based mainly on clinical data obtained from the ECSC questionnaire. Social and economic aspects as well as attempts to motivate the patients are further parameters to be added to the list of positive results. The training programme hitherto adopted still has to be modified if the effect on respiratory function is to be further increased. General physical fitness, however, is improved from both objective and subjective angles.

In the future further techniques should be sought and new methods of rehabilitation developed on the basis of the knowledge acquired.

Opinion of the advisory committees on the continuity of the research programmes

In the last few months the Commission of the European Communities has submitted the results to the following committees responsible for the ECSC social research projects on respiratory diseases :

1. Producers' and Workers' Committee on Industrial Safety and Medicine.
2. Committee of Government Experts on Industrial Medicine and Rehabilitation.
3. Research Committee on Chronic Respiratory Diseases.

All three committees have taken great interest in the results achieved thus far and made the following comments :

- Agreement on all questions connected with bronchopulmonary diseases in ECSC industries : the effect of dust at the work-place, which has to be analysed in greater detail, smoke and fume, chemical gases, general air pollution and certain infections go together with individual life styles to cause the chronic respiratory non-specific syndrome.

The disease itself (in view of the great number of workers suffering from or threatened by it) continues to pose major and urgent problems in the form of the sociological and economic consequences early disablement can have.

- Seen from the standpoint of labour and management, future research projects must continue to be geared to practical needs, i.e. prevention, therapy and rehabilitation.
- The research programme should be extended beyond work on these diseases and their occurrence in the ECSC industries to include other industries. Additional measures of a general nature must be taken for air pollution in particular, a good opening being offered by the Commission's environmental action programme.
- The Committee thought that the programme completed had produced positive results although not all possibilities had been fully exploited. Certain aspects need to be completed and further work done on problems already embarked upon. They therefore stressed that it was urgently necessary to carry out a further four-year research programme on chronic respiratory insufficiency.

Action

Current research in the field of chronic respiratory diseases is pursued in accordance with the concrete suggestions, needs and priorities indicated by the advisory committees when they draw up research programmes, and it takes account of the types of action currently possible.

The Commission calls on the cooperation of research institutes or centres in the Community which cover the spheres corresponding to the objectives set by the Commission. The financial aid which it grants entitles it to require that the work should be orientated towards the priorities established by the Commission after consulting labour and management. The institutes cooperate closely with the Commission's departments throughout the programme.

This has the effect of considerably developing international cooperation in the scientific field and constitutes real stimulation of national bodies, both private and public.

The preparation of a new research programme was begun in July 1975 and has now been completed. The advisory committees took part in the work and approved this programme.

III. New research programme 'Chronic Respiratory Diseases III'

The new research programme concentrates on three aspects :

1. pneumoconiosis
2. other occupational bronchopulmonary diseases
3. treatment and rehabilitation of bronchopulmonary patients.

The subjects are summarized in Annex 1 according to the methods of research thought appropriate.

1. Pneumoconiosis

In the research on pneumoconiosis, both as regards prevention and treatment, experiments will be confined to animals. These involve experiments on the anthropoid ape with a view to clarifying further the effect of PVNO on mixed-dust pneumoconiosis and to studying the effects of soluble aluminium salts.

The aim of the tests on human subjects is to develop tests for the assessment of individual reactions to exposure to various types of dust. This is of particular importance for pre-employment medical examinations. Further standardization and coordination of radiological tests for pneumoconiosis would also appear to be necessary. Despite the international classification of the ILO subjective factors still combine to produce varying interpretations.

As part of the study of lesions associated with pneumoconiosis, a further promising field of research is offered by the pathological and anatomical study of pulmonary emphysema and the development of extensive X-ray shadows, based on the knowledge already acquired.

To examine the development and epidemiology of pneumoconiosis, statistical studies on the life expectancy of persons suffering from the disease are to be encouraged. These studies must be considered in close connection with the research carried out on the radiological and clinical development and manifestation of pneumoconiosis as a function of the composition of the dust and the length of exposure to it. It is hoped in particular that the most recent studies will allow the clinical data to be correlated with the results of X-rays on the basis of the technical documents collected for over ten years.

2. Other occupational bronchopulmonary diseases

Further epidemiological studies are needed on other occupational bronchopulmonary diseases. There are plans for more detailed aetiological studies of the various types of air pollutants, both particulate and gaseous. To this end, further prognostic studies extending over several years are absolutely essential.

However, implementation of such studies with a view to recognition of early forms, requires intensive standardization of the various methods of analysing lung functions (analysis of respiratory curves for helium, oxygen and carbon dioxide, alveolo-arterial gradients, CO transfer factor, mechanical aspects of ventilation and parameters of bronchial hyperreactivity). New measurement methods must therefore be devised. For these occupational bronchopulmonary diseases, it was proposed that individual proneness to infection and individual sensitivity should be determined, as in the case of pneumoconiosis. This calls for identification of aggressive factors, particularly new gaseous pollutants, determination of their effects on the respiratory system and development of methods of function measurement.

3. Treatment and rehabilitation of bronchopulmonary patients

The accent in treatment must be on the development of medicines for use in the early stages. However, functional rehabilitation and assessment thereof must be developed further after standardization of the latest tests. To this end, physical tolerance levels at the workplace must be studied before and after treatment. For this reason early diagnosis of the cardiovascular complications of chronic emphysema was added to the list of research subjects.

Implementation

The new research programme will be carried out by research centres and institutes invited directly by the Commission of the European Communities. The accession of the United Kingdom, Denmark and Ireland will certainly provide further invaluable aid, on account of the experience acquired by the highly specialized national institutes in these countries.

A list of research centres and institutes which could be called upon to take part in the programme was compiled with the help of the three above-mentioned committees (see Annex 2).

Representatives from these centres and institutes must be given the opportunity of examining jointly the individual projects planned and the breakdown of the work to be carried out under the programme. Research projects submitted to the Commission will be examined by the Research Committee and the appropriate advisory committees (1), who will give their opinions, criticisms and suggestions which the Commission will take into account to ensure satisfactory implementation of all aspects of the programme.

The final decision on each research project and financing will be taken by the Commission of the European Communities. Research projects finally approved will be governed by the usual type of contract.

(1) Producers' and Workers' Committee on Industrial Safety and Medicine.
Committee of Government Experts on Industrial Medicine and Rehabilitation.

The results will be circulated in accordance with the above-mentioned criteria :

- distribution of published articles, in the form of offprints, to those participating in projects;
- preparation of a biennial progress report, under the terms of the agreements to be concluded;
- summary of the results at the end of the programme in the form of conference and publication of the papers presented.

Depending on the progress made in each research subject, working party and information meetings should be held throughout the programme.

An up-to-date distribution list for documentation and information must be drawn up with the help of the Directorates-General concerned.

Financial aspects

Estimation of the funds required for this four-year programme is based on the following considerations :

- a) The proposed programme is a continuation of the previous programme, for which a total of 3.5 million units of account was provided (see page 2).
- b) The scope and scale of research into occupational safety and health, improvement of working conditions and rehabilitation will certainly increase in all sectors.
- c) Rising research costs and the enlargement of the Community necessitate strict selection and restriction of the number of subjects, so as to concentrate efforts towards the realization of certain practical aims within the framework of this research programme.

- d) The Commission has information on the number of research workers, equipment and research capacity of the research institutes and centres invited to take part in the programme.
- e) The funds to be provided must also cover administrative costs throughout the programme, particularly those for :
- coordination of scientific cooperation;
 - official trips by experts and research workers;
 - publication and circulation of reports;
 - bibliographical documentation, etc.

Taking all these factors into account, the total budget for the four-year research programme is 5 million european units of account. As in previous years, Community aid will form only a part of the total funds required for carrying out the various research projects.

Conclusions

For the reasons outlined above, there is an urgent need for the release of more funds for medical and social research. The aim of the new programme is twofold : to permit continuation of studies which have undisputed value and to tackle new problems with new research methods and objectives.

It may be expected that the programme will produce a considerable amount of new knowledge and that the research capacities of the new Member States will contribute very substantially to the realization of this expectation.

APPENDIX I

PROGRAMME ON
"CHRONIC RESPIRATORY DISEASES IIF"
(1976)

I. PNEUMOCONIOSIS

A. Research on the anthropoid ape

Prophylactic or therapeutic effects of aluminium salts or P 204
on mixed-dust pneumoconiosis

B. Tests on human subjects

1. Assessment of individual reactions to dust exposure
2. Coordination and standardization of radiological tests for pneumoconiosis
3. Pathogenesis of extensive fibrosis
4. Pathological and anatomical study of pulmonary emphysema
5. Epidemiology and development
 - a) Life expectancy of persons suffering from pneumoconiosis
 - b) Radiological and clinical manifestation and development of pneumoconiosis as a function of exposure to dust and the composition of the dust

II. OTHER OCCUPATIONAL BRONCHIAL AND LUNG DISEASES

A. Early forms

1. Analysis of lung function and standardization of methods

- a) Analysis of expiratory curves for He, O₂, CO₂ etc.
 - b) Alveolo-arterial gradients
 - c) Mechanical aspects of ventilation (including flow-volume diagram)
 - d) CO transfer factor
 - e) Parameters of bronchial hyperreactivity
 - f) New methods
2. Identification of aggressive factors and of their effects on the respiratory system
 3. Factors influencing individual proneness to infection.

B. Epidemiological studies

1. Significance of various types of air pollutants (particulate and gaseous)
2. Prognostic studies

III. TREATMENT AND REHABILITATION

1. Use of medicine in treating the early stages
2. Standardization of the exercise tests
3. Research into admissible physical loads at the workplace
4. Early diagnosis of cardiovascular beat
5. Methods of functional rehabilitation and their relative merits in the early stages.

ANNEXE II
ANLAGE II
APPENDIX II

Provisorische Liste
Provisional List
Liste Provisoire

FORSCHUNGSINSTITUTE

PROGRAMM "CHRONISCHE ERKRANKUNGEN DER ATEMWEGE IIF"

RESEARCH INSTITUTES

PROGRAMME "CHRONIC RESPIRATORY DISEASES IIF"

INSTITUTS DE RECHERCHE

PROGRAMME "AFFECTIONS RESPIRATOIRES CHRONIQUES IIF"

ALLEMAGNE

Medizinische Klinik und Poliklinik
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Pathologisches Institut der
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Prof. KOENIG
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Prof. ULMER
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Institute of Occupational Medicine
Mr. JACOBSEN
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Institute of Occupational Medicine
Dr. MUIR
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Physiology Unit
Dr. C. DAVIES
London

National Coal Board
Dr. HOLLIVOCK
London

Post-graduate Medical School
Hammersmith Hospital
Dr. N. PRYDE
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Institute of Diseases of the Chest
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Medical Research Council
Pneumoconiosis Unit
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