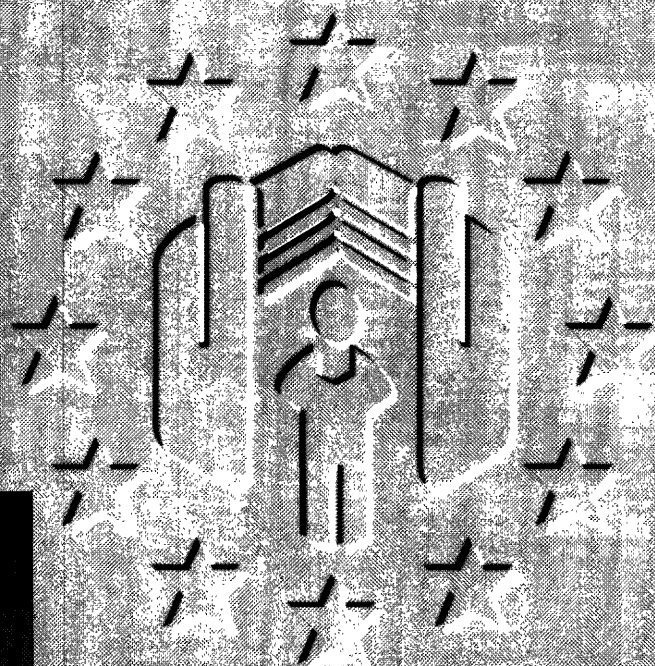




**COMMISSION  
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# **The formation and function of the Mesothelioma Panel of the Commission of the European Communities**



## **Health and safety**

**Report**

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The formation and function of the  
Mesothelioma Panel of the  
Commission of the European Communities

**Health and safety series**

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# **The formation and function of the Mesothelioma Panel of the Commission of the European Communities**

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THE FORMATION AND FUNCTION  
of the  
MESOTHELIOMA PANEL  
of the  
COMMISSION OF THE EUROPEAN COMMUNITIES

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## INTRODUCTION

A period of gradual evolution preceded the actual formation of the Mesothelioma Panel of the Commission of the European Communities (hereafter referred to as the CEC Mesothelioma Panel). After the publication in 1960 of the paper by Wagner, Sleggs and Marchand on the connection between asbestos exposure and mesothelioma formation, it became apparent over the succeeding decade that a potentially serious health problem existed. In 1974, at a meeting of the International Academy for Environmental Protection held in Vienna, Professor J. Clemessen (Denmark) proposed a scheme for the "Monitoring of Environmental Carcinogens through Employers' Records". Shortly before this, a similar proposal had been made to the International Labour Organisation (ILO) by Dr Robert Murray (United Kingdom). Professor Clemessen's recommendations were then made to a working group of the Committee on Medical Research and Public Health of the Commission of the European Communities.

In the period 1975-1976 the Health and Safety Directorate of the Commission of the European Communities organized meetings of a Working Group of experts, in order to agree for publication a report entitled "Public Health Risks of Exposure to Asbestos" (EUR 5653e). This report contained several conclusions and recommendations; one of the latter stated that "a mesothelioma register should be set up in those countries of the EEC where non exist, in accordance with criteria and procedures agreed upon by a panel of pathologists".

In this context, a meeting was convened in Luxembourg in 1976 under the Chairmanship of Dr W.J. Hunter of the Health and Safety Directorate of the Commission of the European Communities. The participants were pathologists and epidemiologists from a number of the Member Countries of the Community who had a special interest in asbestos-associated diseases. Asbestos was considered to be a first category pollutant requiring priority investigation within the Action Programme of the European Communities on the Environment.

The meeting was originally convened to discuss the feasibility of an EEC Cancer Register. In particular, consideration was to be given to two specific points:

- the role, if any, of a Mesothelioma Register within the broader context of a Cancer Register
- the basic information requirements for a workable Mesothelioma Register.

During the discussions that followed it was felt that the creation of a European Cancer Register would be impractical. The methods for verification of diagnosis and certification of death varied so much in different countries that the accuracy of such a generalised register would be open to doubt. In particular the different attitudes to post mortem examinations amongst the Member Countries could produce biased results. The concept of a general Cancer Register was therefore thought to be too cumbersome to contemplate. However Dr J C Wagner (United Kingdom) suggested that a Mesothelioma Register was a far more feasible target to aim for, and this proposal was accepted.

Professor J Bignon (France) considered that the only way to obtain accurate information for inclusion in the Mesothelioma Register was through pathologists. Dr Frentzel (W.Germany) suggested that a panel of pathologists be created to study the comparability of diagnosis, similar to that created in Germany to study primary bone tumours. Dr M Greenberg (United Kingdom), in supporting the proposal, suggested that the concept of the Mesothelioma Register should be limited to studies which could be performed in depth on a selective basis.

Dr H Planteydt (Netherlands) and Dr S Jones (United Kingdom) presented papers which illustrated the ways in which mesothelioma surveys had been carried out in their respective countries. They drew attention to the practical difficulties of obtaining accurate information. It was clearly essential that epidemiologists and statisticians would need to have the best diagnostic information available in order to study occupational



causation of disease and disease trends. This could only be provided by pathologically confirmed cases of mesothelioma.

It was agreed that from a practical point of view it would not be possible to create an EEC Mesothelioma Register that could from the beginning meet all the requirements. It was therefore suggested that a phased programme be instituted, as follows:-

1. A Mesothelioma Register be instituted in each individual Member Country based on general mortality statistics.
2. Pathologists in each Member Country be asked to report all cases of mesothelioma diagnosed by them to their own national Mesothelioma Registers.
3. Encouragement should be given to the creation of Mesothelioma Panels in each Member Country in order to standardize the histopathological diagnosis.
4. A Mesothelioma Panel of the Commission of the European Communities be established to develop standardized histopathological criteria for diagnosis.
5. Eventual integration of data from each Member Country be carried out.

As a general guidance, the type of information that should be sought in each individual case should be as follows:-

- a) The type of primary serosal tumour (pleura, peritoneum, pericardium, tunica vaginalis)
- b) Date of birth
- c) Date of death
- d) Sex
- e) Name
- f) Occupations throughout life of individual and of spouse
- g) Places of residence
- h) Identity numbers (eg social security, health service or pathology specimen numbers).

## TERMS OF REFERENCE OF THE CEC MESOTHELIOMA PANEL

These were formulated at a meeting held in Middelburg (Netherlands) in May 1977. They were as follows:-

1. The Panel has as one of its basic objectives the standardization of the pathological diagnosis of mesothelioma by exchange of information between Members of National Panels.
2. The Panel should provide data which, when combined with information from clinical and epidemiological sources, can be used for the compiling of the EEC Mesothelioma Register.
3. The Panel should consist of one pathologist from each Member State, who has experience of primary tumours of the serosal cavities and of asbestosis.
4. The Panel should be able to co-opt pathologists with specialized knowledge, eg of gastro-intestinal tumours, or tumours of the female genital tract.
5. The Panel should have statistical advice for the planning of its function.
6. The Panel should consider the amount of biopsy material required to make a definitive diagnosis, especially in relation to needle biopsies.
7. The Panel should determine whether or not deleterious effects follow the practice of taking biopsies by open thoracotomy.

8. The Panel should attempt to establish the dose/response relationship between asbestos exposure and mesothelioma formation. This should be considered in cases subjected to post mortem examination when tumour tissue can be examined histologically and when mineral analysis (concentrations of fibres and typing of fibres) can be performed on samples taken from a sagittal section of lung tissue.

9. The Panel should agree on a classification scheme for mesotheliomas and a voting system concerning the confidence of diagnosis.

10. The Panel should agree on a classification scheme for assessing the degree of severity of asbestosis in the lung tissue of patients in whom mesothelioma has been diagnosed.

## **VOTING PROCEDURE FOR THE DEGREE OF CONFIDENCE IN DIAGNOSING DIFFUSE MALIGNANT MESOTHELIOMA**

It was accepted that in some cases it was possible for a pathologist to come to a positive conclusion on both macroscopic and microscopic grounds that a given tumour definitely **was** a mesothelioma, or that another tumour definitely **was not** a mesothelioma. It was also accepted that there remained areas of uncertainty in many cases as to a definite diagnosis. It was regarded as being essential that the system to be used for recording the diagnoses of the various members of the Mesothelioma Panel should be as simple as possible.

It was therefore decided to adopt the scheme used by McCaughey and Oldham (1973), by the Netherlands Mesothelioma Panel (Planteydt, 1980) and by the IARC Mesothelioma Panel of the United Kingdom (Jones et al, 1980). This scheme determined the degree of certainty of diagnosis, and it was agreed that it should be carried out on a trial basis to test its effectiveness. Five categories of opinion were defined, as follows:-

### **OPINION**

- A. Definite mesothelioma** - No doubt about the diagnosis, ie both macroscopic and microscopic criteria were fulfilled.
- B. Probable mesothelioma** - Some reservations about the diagnosis, ie not all the diagnostic criteria were fulfilled, possibly due to sampling limitations, but there was reasonable evidence present to support the diagnosis.
- C. Possible mesothelioma** - The diagnosis can neither be fully supported nor excluded.
- D. Probably not a mesothelioma** - The diagnosis could not entirely be excluded.

**E. Definitely not a mesothelioma** - Some tumours could mimic a mesothelioma macroscopically, but histologically the diagnosis could be positively rejected. The lesions could be reactive, or be neoplasms which were not of mesothelial origin.

## **PROGRESS OF THE CEC MESOTHELIOMA PANEL**

At a meeting in Alessandria and Turin, Italy, in September 1978, Dr W Hunter explained the action programme that had been devised by the Health and Safety Directorate of the European Commissioners relating to asbestos. It was intended that there should be a continuing existence of the CEC Mesothelioma Panel and plans were proposed for it to meet on a more regular and formal basis.

Since the meeting in Middelburg, a number of tumour sections had been circulated to Members on an informal basis. Members also presented further diagnostic problems which were discussed in a round table microscopic session. Attempts were made to classify these under a coding system prepared by Professor J Clemmeson. Consideration was given to the use of the term "mesodermoma" rather than mesothelioma, as proposed by Professor A Donna (Italy). This related to mesothelial neoplastic lesions based on their embryonic origin. The name "mesodermoma" was intended to embrace all primary tumours arising in the pleura, not only mesotheliomas. While the embryological concept could undoubtedly explain some of the variants of the primary serosal tumours, from a practical point of view it was thought that most pathologists were developing a clear idea of the diagnostic criteria for mesotheliomas, and that this term should be adhered to.

It was noted that in many countries the number of autopsies that were carried out were very few and this factor alone would limit the diagnostic opportunities and distort the statistics. Every encouragement should be given to increase the number of autopsies, particularly in those cases where an occupationally-related disease might be a contributory factor to death.

## **DIRECTIVE ON ASBESTOS WITHIN THE EEC**

At the Dortmund meeting in 1979 Dr Hunter informed the Panel members that the European Commission had issued a "Proposal for a Council Directive on the protection of workers from harmful exposure to chemical, physical and biological agents at work". This envisaged an individual Directive on asbestos.

Dr Wagner presented a report prepared by himself and Dr P C Elmes (United Kingdom) on "The Establishment of a Mesothelioma Register in the E.E.C." If it could be implemented it would help health authorities in the Member Countries to determine:-

- a) the extent of the problem
- b) the association with asbestos exposure, or other pollutants
- c) future trends

The report detailed the different ways in which the Member Countries could collect information, and it emphasised that some uniform method would be advantageous. The following suggestions were discussed:-

1. That a Mesothelioma Register be set up in the EEC.
2. That information for this Register would depend on efficient Registers being established in Member Countries.
3. That the Registers in these Countries should be under the control of the Government departments which were responsible for Health and Safety.
4. That those running the Register should be advised by a panel of epidemiologists supported by a panel of clinicians/radiologists, and the panel of pathologists.
5. That it was essential that detailed information should be recorded on the Death Certificates as issued now in all Member Countries. This

information should be made available to responsible people engaged in epidemiological studies.

6. That the information on individuals be kept confidential.

7. That autopsies should be undertaken on all those who have died from, or were suspected of having died from diffuse malignant mesothelioma of the pleura and/or peritoneum, whether there has been a history of occupational exposure to fibrous minerals, or not.

8. That initially it may be advisable to undertake pilot studies in an industrial and a rural area in all countries which are Members of the European Community. Later, the scheme may be enlarged to cover the whole of each Country.

9. That wherever possible, the dust content of the lungs removed at autopsy should be analysed, both to confirm histories of exposure and to see if fibrous dusts other than asbestos are present.

10. That it would be of great importance that the Register was to be set up by a competent epidemiologist who has experience in this type of organisation.

The work of the CEC Mesothelioma Panel was underlined by the Council of Ministers in a Directive in 1983 on the protection of workers from the risks related to asbestos at work. This required Member Countries to keep a Register of recognized cases of mesothelioma. The accuracy of the Registers would naturally be dependent on reliable diagnostic information. It was therefore essential that pathologists supply reliable data. The CEC Mesothelioma Panel therefore embarked on two major projects:-

1. To write a book, primarily intended for pathologists, which illustrated the macroscopic and microscopic criteria for the diagnosis of mesotheliomas. This was prepared by Drs Lund, Jones and Planteydt.



It was entitled "A Colour Atlas of Mesothelioma" and it was published in 1985 by MTP Press Ltd under the sponsorship of The Commission of the European Communities.

2. To devise a programme to explore new diagnostic methods, particularly of histochemical and immunohistochemical techniques which might assist pathologists in coming to concise conclusions, particularly with respect to small biopsy samples taken during life.

## **ESTABLISHMENT OF A FORMAL POSTAL CIRCULATION SYSTEM**

At the meeting of the CEC Mesothelioma Panel in Dortmund, Germany in May 1979 it was agreed that members should submit cases of interest, or of particular diagnostic difficulty, for postal circulation around the Panel. A system was to be devised for correlating the various opinions, and for the maintenance of a tumour registry. The Department of Histopathology at the City Hospital, Nottingham was contracted to provide the technical and secretarial support for the scheme which would be co-ordinated by Dr Jones.

Members were asked to submit paraffin-embedded blocks of formalin-fixed tissues, together with occupational, clinical and pathological details for each case. Sections would be cut ( 1 haematoxylin and eosin-stained, and three unstained spares ) at the co-ordinating centre, and the sets would be sent to each member of the CEC Mesothelioma Panel. Members would carry out additional stains of their own choice in their own laboratories. A summary of the clinical and occupational details would also be sent to each member in a sealed envelope. The member would examine the sections microscopically and form a preliminary opinion before opening the envelope. A further, and possibly a modified opinion would be given, after consideration of all the factors.

Each member's opinion was to be recorded on a standard form (Appendix III) which would be sent to the Nottingham Centre. When all the opinions on a particular case had been received, a composite report - giving the results of each member - would be sent to all members of the Panel. Cases of particular interest or diagnostic difficulty would be earmarked for discussion at the next meeting of the Panel.

## CRITERIA FOR THE DIAGNOSIS OF DIFFUSE MALIGNANT MESOTHELIOMA

As a result of the study of many cases by the CEC Mesothelioma Panel the following criteria have been established:-

**Macroscopic** The neoplasm should have the appearance of a primary tumour involving either the pleura (figure 1), peritoneum (figure 2), pericardium or tunica vaginalis. There should be no obvious primary site in any other organ which might suggest that the tumour of the serosal membrane was metastatic.

**Microscopic** The classical diagnostic features require the tumour to have a dimorphic structure, with both "epithelial" and "connective" tissue neoplastic elements present (figures 3 & 4). The tumour essentially has a marked variability in different parts of the neoplasm. In some areas the "epithelial" element may predominate; in others, the "connective tissue" element may predominate; while in other zones there is a mixture of "epithelial" and "connective tissue" components. The wide spectrum of appearances is depicted in Figure 5, which shows how some mesotheliomas can mimic carcinomas at the "epithelial" end, while others can mimic sarcomas at the "connective tissue" end.

The histopathologist should not be surprised to find differentiation of elements in the connective tissue type of mesothelioma, such as cartilage, bone, muscle and even occasionally fat. Very rarely, areas of squamous metaplastic change are seen in the epithelial type of mesothelioma.

While most diagnostic information can be gained by the microscopic study of haematoxylin and eosin-stained sections, it may be necessary to use additional staining techniques to confirm the nature of the tumour.

The most useful additional stain is the **diastase-PAS stain** which usually is able to distinguish "epithelial" types of mesotheliomas from secondary adenocarcinomas. This stain is negative for mesotheliomas, but is usually positive in mucin-secreting adenocarcinomas. If epithelial mucin is seen, the diagnosis of mesothelioma must be rejected in favour of adenocarcinoma.

### **New Diagnostic Methods**

The diagnostic value of immunohistochemical stains has been evaluated by the CEC Mesothelioma Panel over the years.

**Carcino-Embryonic Antigen (CEA) stain** This reaction may vary with the used antibody. However most of the antibodies give negative results for mesotheliomas and positive results for adenocarcinomas.

**Cytokeratin stain** This is usually strongly positive in mesotheliomas, but may be weakly positive in adenocarcinomas. Certainly a negative cytokeratin stain would make the diagnosis of mesothelioma extremely dubious. Cytokeratin is also useful in distinguishing a connective tissue type of mesothelioma (positive) from a secondary sarcoma (usually negative).

**Vimentin** This is usually strongly positive in the connective tissue type of mesothelioma. It may also be positive in the epithelial element of mesotheliomas. However some pulmonary adenocarcinomas and pleural metastases from other primary sources may also react with vimentin antibodies.

Two techniques have been introduced at various meetings of the CEC Mesothelioma Panel by Professor Donna.

1. He has developed an **immunohistochemical stain** which is designed to identify positively cells of mesothelial origin, whether they are of benign or malignant type. In testing out the antibody in his laboratory

Professor Donna has achieved a high level of correlation with the histological diagnosis of many tumours submitted to the CEC Panel. However it has not been possible so far to achieve such a correlation when the stain was used by Panel members in their own laboratories. Professor Donna has carried out further research on his stain and has found that the freshness of the tissue and the mode of fixation is critical in order to obtain consistent results. Because of the importance of trying to establish a stain which would **positively** and **selectively** identify mesothelial cells, further work will be carried out in an endeavour to improve the reproducibility of the technique.

2. Morphometric (planimetry) techniques (an assessment of geometrical features of structures in a two-dimensional plane) have been shown to differentiate between benign and malignant cells. In contrast to this, ploidy studies which have been carried out using either flow cytometry (Burmer et al, 1984) or static cytometry (Tierney et al, 1990) were unable to produce such an effective distinction. Clearly, this is another area where further work needs to be carried out.

## **OBSERVER VARIATION**

At the meeting of the CEC Mesothelioma Panel in Athens in December, 1988, Professor G Delides (Greece) presented an analysis of the performance of the Panel members in relation to the opinions expressed in the "A" to "E" postal voting system. He reported that there was greater agreement among the Panel members when considering the earlier cases, rather than the more recent ones. While it might be expected that the increased experience gained by members would lead to a greater measure of agreement, it was pointed out in discussion that simple, classical examples of mesothelioma were included in the early series, but only cases of great diagnostic difficulty had been circulated in the latter part of the series. While the postal circulation of cases was a very valuable means of sharing difficult diagnostic problems, it was felt to be essential for all members of the Panel to meet at intervals to discuss the problem cases around a table at which individual microscopes were provided. After such discussions it was possible to obtain a consensus agreement on a diagnosis in the majority of cases.

Over the years a great deal of experience had been gained in seeing the wide ranging variants of this tumour. The difficulties in differentiating between some neoplastic and reactive lesions - especially in the peritoneum - were still recognised, and expertise was still being acquired, particularly on the basis of follow-up studies.

The challenge of interpreting small biopsy specimens had been taken up. In general terms the larger the sample of tissue submitted, the greater was the possibility of a definite diagnosis.

## **CAUSAL RELATIONSHIPS**

The quality of the occupational histories which have accompanied the cases submitted to the Panel, and the limited number of cases that have been studied, have not made it possible to come to a valid conclusion on the causal relationship of the mesothelioms. However individual members of the Panel, in collecting cases within their own Countries, have indicated that approximately 85% of mesotheliomas are asbestos-related. While the Panel is aware that in various parts of the world there are cases of mesothelioma which have been related to the inhalation of non-asbestos fibres, none of these have been submitted to the CEC Mesothelioma Panel.

## EDUCATIONAL ROLE OF THE PANEL

The exchange of information on asbestos-induced diseases between the Member Countries was one of the fundamental concepts of the Panel. As new Countries have joined the European Community, so it was deemed to be important that they had access to the knowledge and experience of those already in the Community. When Professor Delides joined the Panel as the representative of Greece, he invited Professor Jones to address the Hellenic Society of Anatomic Pathology at a national meeting in Halkis in 1987. The problems of asbestos-induced diseases were broadly covered, together with an update of diagnostic methods, epidemiology and the mineralogical association with tumours of the mesothelium. This preliminary presentation was followed in December 1988 by a joint meeting in Athens between the full CEC Mesothelioma Panel and the Hellenic Society of Anatomic Pathology.

At the Athens meeting the members of the Mesothelioma Panel presented the merits of various pathological investigative techniques. Dr Lund and Professor Jones outlined the gross, histological and cytological criteria. Dr Planteydt emphasised the value of the diastase-PAS stain in distinguishing the epithelial component of mesotheliomas from secondary deposits of adenocarcinomas. Further differentiation using immunohistochemical stains, especially CEA, Keratin and Vimentin were discussed.

Dr Nebut (France) cited the value of electron microscopy.

Professor Otto (Germany) described the techniques for identification and quantification of asbestos bodies and fibres by light microscopy, using the millipore filtration method.

Professor Donna presented further results of his mesothelial cell-specific stain and of his morphometric studies.



An important additional contribution to the joint meeting in Athens was made by experts who presented some non-pathological aspects of the problems associated with asbestos and other mineral fibre-induced diseases.

Professor J Corbett Macdonald (United Kingdom) discussed the Epidemiology of Diseases due to Asbestos and other Mineral Fibres.

Professor F D Pooley (United Kingdom) discussed the Mineralogy of Fibrous Particles which are Harmful to Man. He described his techniques for measuring the fibre concentration and the type of minerals in lung tissue.

Dr S Raucan (Turkey) presented studies of Mesothelioma and other Pleural Diseases in Turkey.

Dr Planteydt described the Organisation and Working of the Netherlands Mesothelioma Panel.

Dr Wagner presented an update on the Biological Effects of Mineral and Man-made Fibres.

The meeting ended with a slide seminar when discussions took place on the pre-circulated cases which had been sent to pathologists in Greece from the Nottingham centre.

The meeting in Athens thus provided not only a useful review opportunity for the Members of the Mesothelioma Panel, but also a comprehensive coverage of the subject of diseases associated with mineral fibre inhalation for the Hellenic Society of Anatomic Pathology.

## ACHIEVEMENTS AND THE FUTURE

1. By exchanging information and diagnostic problems over the years, the CEC Mesothelioma Panel has fulfilled one of its basic objectives - that of standardizing the diagnostic criteria for this tumour. This information has been made available throughout the European Community in the publication "A Colour Atlas of Mesothelioma", sponsored by the Commission.
2. Although no direct links have been created between Panel members and their own National Mesothelioma Registers, the quality of diagnosis of pathologists generally has improved so that the information on Death Certificates is now more reliable. However there is still room for improvement, particularly in recording the **site** of the primary mesothelioma - an omission which is unnecessarily often prevalent. It is recommended that the acceptance for registration of a Death Certificate should depend on this information being provided.

At the Panel Meeting in Dublin in 1991 three new members were welcomed:-

Dr F Borderas (Spain)

Dr D Jacobovitz (Belgium)

Dr M Ramalhinho (Portugal)

The Panel was also pleased to welcome Professor J Sugar (Hungary) and Dr M Brockman (Germany) as observers.

By appointing a pathologist from each Member Country to serve on the Panel, it is hoped that Registers of Mesothelioma cases in each Member Country are being established on a basis of good diagnostic information.

3. A good channel of communication between pathologists from all the Member Countries of the European Community has been established through

the medium of the Panel representatives. It is hoped that the joint testing of new techniques of diagnosis will continue, that detailed mineralogical evaluation can be carried out on lung tissue to increase the knowledge of causation of mesotheliomas. To this end it is essential that autopsies are carried out on all those who die of occupationally-related diseases. This aspect is worrying, as all the information we have concerning autopsy rates in the Member Countries indicates that there is a progressive decline in this essential field of investigation. The Panel recommends that this trend be reversed in the future.

4. In order to make the best use of material already available, a bank of formalin-fixed pleural and peritoneal tumours and lung tissue has been established. This consists of over 360 autopsy samples which have been collected by Professor Jones over a ten year period (1977 - 1987). These, and subsequent specimens (1987 onwards) are being added to the large collection of mesotheliomas stored in Penarth by Dr Wagner and Dr Gibbs. All this material is available to those working on specific research projects within the European Community.

5. With regard to the amount of biopsy material required to make a definite diagnosis of mesothelioma (or a definite rejection of the diagnosis), the Panel note that in general, the more material that is available for examination, the greater is the chance of a diagnosis. Because of the variability of the tumour appearance in different parts, sampling assumes great importance. Because it is desirable to make the smallest surgical incision to obtain biopsy material, it is recommended that thoracoscopy or peritoneoscopy examinations are carried out, with multiple small biopsies taken from different sites. While open thoracotomy or laparotomy will give a wider opportunity of collecting larger amounts of biopsy material,

there is a tendency for tumour to spread through the chest or abdominal wall during succeeding months. While the same complication may follow at thoracoscopy/peritoneoscopy or simple needle biopsy sites, the tendency for this procedure to lead to distressing symptoms for the patient is minimised

6. Further work is to be carried out on the establishment of the dose/response relationship between asbestos exposure and mesothelioma formation. This work is in progress, using those cases which are available in individual Member Countries in whom post mortem mineral analyses have taken place. The degree of severity of asbestosis is also being evaluated in these cases. The cases which have been submitted for diagnostic opinion to the Panel have not been suitable for this type of evaluation.

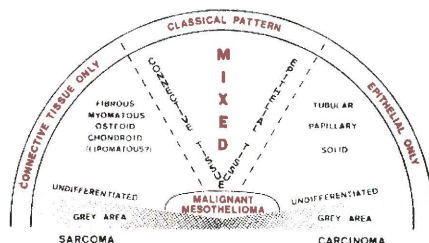
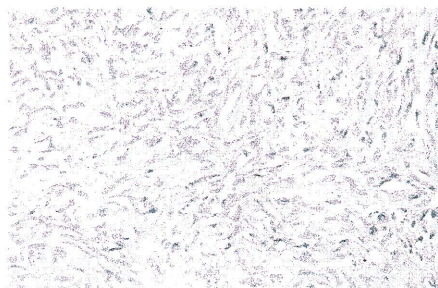
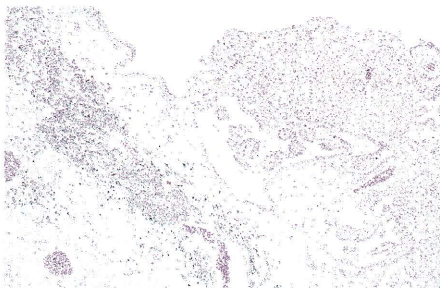
7. The Panel has achieved considerable progress in defining the diagnostic criteria for mesotheliomas, for devising a classification system and a voting system concerning the confidence of diagnosis. There remains much to be done in the future, particularly in developing a positive selective stain for mesothelial cells, in pursuing morphometric studies, and in evaluating dose/response information. The establishment of a communications system throughout the European Community via the Members of the Mesothelioma Panel has been a most rewarding experience.

8. It is hoped that the information in this publication will be of help to all those who have an interest in diseases associated with occupational or environmental factors (especially asbestos), and that it will encourage pathologists throughout the European Community to refer cases of diagnostic difficulty or interest to their national representative for consideration by the CEC Mesothelioma Panel.

Illustrations for the article  
on the

FORMATION & FUNCTION OF THE MESOTHELIOMA PANEL  
OF THE  
COMMISSION OF THE EUROPEAN COMMUNITIES

1. Cross section of a lung and pleura to show the selective spread of pleural mesothelioma along the serosal surfaces.
2. Cross section of the intestines to show the selective spread of a peritoneal mesothelioma along the serosal surfaces.
3. Microscopic structure of a mesothelioma to show the epithelial component of the tumour.
4. Microscopic structure of a mesothelioma to show the connective tissue component of the tumour.
5. Spectrum of histological variation of diffuse malignant mesothelioma.



## APPENDIX I

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APPENDIX II

C.E.C. No.

CASE FOR REFERRAL TO THE C.E.C. MESOTHELIOMA PANEL

Source of material ..... Ref. no. ....

Name ..... Sex Male / Female

Date of birth ..... Date of death .....

Occupational history .....  
.....  
.....  
.....

Asbestos exposure Yes / No / Unknown

If yes, length of exposure in months .....

Clinical history (including duration in months) .....  
.....  
.....  
.....  
.....  
.....

Cigarette smoker Yes / No / Unknown

Pleural plaques Yes / No / Unknown

Autopsy Yes / No

If yes, Autopsy findings .....  
.....  
.....

Mineral Analysis Yes / No

If yes, results .....  
.....

Signature..... Date .....

APPENDIX III

C.E.C. MESOTHELIOMA PANEL

C.E.C. Code No: \_\_\_\_\_

Pathologist: \_\_\_\_\_

DIAGNOSIS

1. DIFFUSE MALIGNANT MESOTHELIOMA

<input type="checkbox"/> A	Definite mesothelioma	<input type="checkbox"/>
<input type="checkbox"/> B	Probable mesothelioma	<input type="checkbox"/>
<input type="checkbox"/> C	Possible mesothelioma	<input type="checkbox"/>
<input type="checkbox"/> D	Probably not mesothelioma	<input type="checkbox"/>
<input type="checkbox"/> E	Definitely not mesothelioma	<input type="checkbox"/>
<input type="checkbox"/> F	Unsuitable material	<input type="checkbox"/>

2. NOT A DIFFUSE MALIGNANT MESOTHELIOMIA

Suggested alternative diagnosis.....  
.....  
.....

3. COMMENTS

4. Do you consider this case to be of special interest to be discussed  
at a future meeting.      YES / NO

DATE. .... SIGNED .....

APPENDIX IV

OPINIONS

C.E.C. 187 (Ireland T.11.A. 58.86)

---

A A A A A A A A A B C

Suggested alternative diagnosis

--

COMMENTS

CEA negative  
Diffuse epithelial well differentiated mesothelioma  
D-PAS negative  
Peripheral lung adenocarcinoma cannot be 100% excluded.

JSPJ/VGB  
20.2.87

## APPENDIX V

### SUMMARY OF RESULTS OF THE FIRST 200 CASES SUBMITTED TO THE CEC MESOTHELIOMA PANEL

Number of cases with sufficient diagnostic material	194
Number of cases with insufficient diagnostic material	6
Number of cases on which an agreed diagnosis was made	184
Number of cases on which an agreed diagnosis could not be made	10

#### Agreed diagnosis

Diffuse Malignant Mesothelioma of pleura	90
Diffuse Malignant Mesothelioma of peritoneum	19
Serosal tumours other than mesothelioma	64
Reactive lesions	11

Serosal tumours other than diffuse malignant mesothelioma were mainly metastatic carcinomas, the majority which were derived from primary lung tumours.

Other primary tumour sites were:-

- Kidney
- Pancreas
- Testis
- Ovary
- Malignant melanoma of skin

Other lesions of the pleura were:-

- Primary sarcomas
- Anaplastic tumours of unclassifiable type
- Benign localised mesothelioma of pleura
- Adenosquamous carcinoma of pleura

Benign mesothelioma of pleura with malignant transformation to adenocarcinoma

Benign adenocarcinomatoid tumour of peritoneum

Benign papillary mesothelioma of peritoneum

Benign cystic mesothelioma of peritoneum

Reactive hyperplasia of peritoneum

Retroperitoneal cyst

Thymoma

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*J.S.P. Jones*

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The Panel has achieved considerable progress in defining the diagnostic criteria for mesotheliomas, for devising a classification system and a scoring system concerning the confidence of diagnosis. Further work is required, particularly in developing a positive selective stain for mesothelial cells, in pursuing morphometric studies, and in evaluating dose/response information. The establishment of a communications system throughout the European Community via the Members of the Mesothelioma Panel has been a valuable contribution to progress.

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