

Long-term Programme for Pollution Monitoring and Research
in the Mediterranean Sea
(MED POL Phase II)

EVALUATION OF METHYLMERCURY IN MEDITERRANEAN POPULATIONS AND RELATED HEALTH HAZARDS

Report on a Consultation Meeting

Athens
13-17 September 1982



WORLD HEALTH ORGANIZATION
Regional Office for Europe
Copenhagen, 1982

Original: English

ICP/RCE 211(1)
07581

Note

This report contains the collective views of an international group of experts and does not necessarily represent the decision or the stated policy of either the World Health Organization or the United Nations Environment Programme.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the Secretariats of the World Health Organization or the United Nations Environment Programme concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization or by the United Nations Environment Programme in preference to others of a similar nature that are not mentioned.

CONTENTS

	<u>Page</u>
1. Introduction	1
2. Discussion of the outline of the epidemiological programme, including selection of areas in the Mediterranean where intakes of methylmercury are (or could be) relatively high, and identification of population groups which could be monitored	2
3. Outline of the monitoring programme, including methylmercury, other forms of mercury and selenium	2
4. Discussion on the detailed protocols for the dietary surveys . .	3
5. Sampling, storage and analysis of seafood for mercury and selenium	3
6. Discussion of the detailed protocols for the sampling and analysis of human hair	3
7. Discussion of the detailed protocol for the epidemiological studies	3
8. Identification within the participating countries of the institutions responsible for carrying out the different parts of the project	4
9. Discussion and approval of the detailed work plan, including institutional arrangements and timetable of the project	4
Annex 1 Protocol for dietary survey	5
Annex 2 Evaluation of methylmercury in Mediterranean populations and related health hazards	15
Annex 3 List of participants	21

1. Introduction

International activities organized during the last seven years, particularly by the Food and Agriculture Organization (FAO), the United Nations Environment Programme (UNEP), WHO and the International Atomic Energy Agency (IAEA), have revealed that, according to the best available data, most of the general Mediterranean population appeared to have a low methylmercury intake through consumption of seafood and could therefore be considered not at risk. On the other hand, it appeared equally evident that some population groups in the Mediterranean region may have an intake of methylmercury through seafood in excess of permissible levels. Results obtained during the course of the pilot phase of the Coordinated Mediterranean Pollution Monitoring and Research Programme (MED POL Phase I), which constitutes the scientific component of the UNEP-sponsored Mediterranean Action Plan, together with the recommendations of several meetings, lent further support to the carrying out of an integrated monitoring and epidemiological study of methylmercury in the Mediterranean to fill the gaps in existing knowledge. These gaps have so far made it difficult to undertake the proper assessment of hazards to health from the intake of methylmercury from Mediterranean seafood or to protect those sectors of the population that may be at risk.

Activities under the responsibility of WHO's Regional Office for Europe within the overall framework of the Long-term Programme for Pollution Monitoring and Research in the Mediterranean Sea (MED POL Phase II), designed to cover the period 1981-1990, include the performance of epidemiological studies directed at the finalization of environmental quality criteria for a number of parameters, including mercury in seafood. To this end, a comprehensive project was formulated on the evaluation of methylmercury intake in Mediterranean populations and related health hazards. This project is being implemented, both within the framework of MED POL Phase II and as part of the WHO Regional Office for Europe's programme on chemical safety.

The specific objectives of this project include the selection of population groups in the Mediterranean with a relatively high intake of methylmercury; the identification of those groups whose methylmercury intake exceeds the WHO Provisional Tolerable Weekly Intake (PTWI); an estimation of this group's size, its patterns of individual consumption of seafood, and its exposure to other forms of mercury, the actual concentrations of methylmercury in the various species consumed, the assessment of methylmercury exposure in the critical segments of the population, and the investigation of mercury-associated abnormalities in high-risk population groups as compared to control groups.

A Consultation Meeting on Evaluation of Methylmercury in Mediterranean Populations and Related Health Hazards was convened by the WHO Regional Office for Europe, in cooperation with the UNEP Coordinating Unit for the Mediterranean Action Plan, with the objectives of establishing criteria for selecting areas in the Mediterranean where intakes of methylmercury are (or may be) relatively high, taking into account the results of the monitoring exercise carried out in MED POL Phase I and the experience of the countries involved; of agreeing on the population groups to be monitored and on methods for estimating their exposure to methylmercury, their exposure to other forms of mercury, and their exposure to selenium wherever necessary; of agreeing on procedures for carrying out an epidemiological study on the relevant sectors of the sample populations, and of developing protocols for the dietary survey, the sampling and analysis of human hair, and epidemiological studies.

A number of experts from Mediterranean institutions which had shown an interest in the project were invited to participate in the Consultation Meeting. In addition, the following international organizations and agencies were invited to send representatives: FAO, IAEA and the European Community.

The Meeting took place at the seat of the Coordinating Unit for the Mediterranean Action Plan in Athens from 13 to 17 September 1982.

It was attended by eight participants from five Mediterranean countries, three representatives from UNEP, a representative from IAEA and three staff members of WHO headquarters and the Regional Office for Europe. A list of participants is given as Annex 3.

Dr L.J. Saliba, WHO Senior Scientist, Mediterranean Action Plan, WHO Regional Office for Europe, opened the Meeting and welcomed the participants on behalf of the Regional Director.

Mr A. Manos, Coordinator, Mediterranean Action Plan, welcomed the participants to the seat of the Coordinating Unit in Athens. Mr Manos stressed the importance of the project and the preparatory work already undertaken by FAO, UNEP and WHO. He described the main components of the Mediterranean Action Plan and their evolution since the Plan was first adopted by Mediterranean coastal states in February 1975. He also expressed his appreciation that the project was being

undertaken, both within the framework of MED POL and as part of the WHO Regional Office for Europe's programme on chemical safety. Mr Manos also welcomed the participants on behalf of the Executive Director of UNEP, Mr M.K. Tolba.

Dr L.J. Saliba explained the scope and purpose of the Consultation Meeting and its place within the overall project. He briefly explained the events leading to it as well as the expected output for further action.

Dr A. Cruzado, Senior Marine Scientist, UNEP Coordinating Unit for the Mediterranean Action Plan, explained the components of the Long-term Programme for Pollution Monitoring and Research in the Mediterranean Sea (MED POL Phase II), and particularly the various activities falling under the monitoring and research components. He also outlined the procedural matters involved and the role of the Working Group for Scientific and Technical Cooperation (WGSTC) for MED POL, which had to approve projects prior to their implementation. In view of the fact that MED POL funding was involved, a firm proposal would have to be prepared for submission to the next meeting of WGSTC (to be held in 1983) insofar as activities to be held from 1983 onwards were concerned.

Mr G. Vournas was elected Chairman of the Meeting, and Dr A. Grech was elected Vice-Chairman.

The provisional agenda was adopted by the Meeting without material change.

2. Discussion of the outline of the epidemiological programme, including selection of areas in the Mediterranean where intakes of methylmercury are (or could be) relatively high, and identification of population groups which could be monitored

Dr V. Silano introduced this item and also presented the paper prepared by Dr I. Farkas, "Protocol outline for monitoring and epidemiological studies on health effects of methylmercury" (ICP/RCE 211(1)/10). One of the important issues was the identification of those groups whose intake of methylmercury exceeded the Provisional Tolerable Weekly Intake (PTWI). There was reason to assume that such groups exist in the Mediterranean region.

The Meeting held a comprehensive discussion on the epidemiological criteria on which the protocol and studies would be based. Among the points mentioned by various participants were (a) the size of population groups, which should be large enough to allow adequate statistical analysis; (b) the investigation of the levels of dietary mercury intake; (c) the criteria for selecting control groups; and (d) the study of interference of other compounds (e.g. organolead). It was agreed that the protocol should cater for all these points. With regard to sample size, the Meeting considered it advisable not to attempt to fix a definite figure at this stage, but to leave the matter open, on the understanding that the relevant parts of Dr Farkas' paper would be taken into account when the sample size of each critical population group was eventually determined.

The Meeting also discussed the criteria for the selection of areas. These would obviously have to be localities where mercury levels in seafood were relatively high. Sociological patterns, such as season population movements, would also have to be considered. Matched control groups should be studied in parallel with the test groups. It was agreed that the selection of population groups for the epidemiological studies would have to be made on the basis of preliminary data collected.

During the discussion on this item, the matter of correlation with seafood analysis was raised, as the analysis conducted during the first phase of MED POL was for total mercury, and only a few laboratories had specifically analysed seafood for methylmercury. Following a comprehensive discussion on this, it was agreed that figures for total mercury would afford a reasonably accurate basis for the evaluation of methylmercury intake from the dietary survey. It was also suggested that a study on the relationship between the total mercury and methylmercury content of various species of seafood should be conducted. This would enable the MED POL data to be utilized with a greater degree of confidence.

3. Outline of the monitoring programme, including methylmercury, other forms of mercury and selenium

As this item mainly concerned the monitoring of population groups, most of the discussion on it was held conjointly with that on the preceding item. The importance of possible interference with results, both by other forms of mercury and by other elements, was underlined, and it was agreed that an assessment of other contaminating sources would be necessary. The available data from the pilot phase of MED POL were outlined, and a number of species of seafood that had a relatively high mercury content were noted. The importance of sediment analysis was also pointed out.

4. Discussion on the detailed protocols for the dietary surveys

Professor G. Tomassi introduced his paper "Protocol for dietary surveys" (ICP/RCE 211(1)/8) and explained the rationale behind the various items in the proposed questionnaires. During the ensuing discussion, one of the major points raised was whether it would be valid to assume that seafood was the only source of methylmercury intake by man. It was concluded that although this could be considered as the most important source and that other sources were probably not of significance, a multi-exposure study, even on a limited scale, should be carried out. As an example, information complementary to the dietary survey could take the form of the measurement of methylmercury in the air. It was agreed that arrangements could be made for one of the institutions participating in the project to carry out periodically such limited environmental monitoring.

Various amendments to the draft protocol were suggested, either for clarification or for the acquisition of more information. The protocol for the dietary survey, as finally adopted by the Meeting, is contained in Annex 1.

5. Sampling, storage and analysis of seafood for mercury and selenium

Dr A. Cruzado gave an account of the reference methods being prepared by UNEP's Regional Seas Programme Activity Centre, in collaboration with the relevant UN agencies, for pollution studies in the Mediterranean and other regional seas. These methods included the determination of (a) methylmercury and (b) selenium in seafood. Both were in preparation and would be available shortly. The Meeting also received information regarding the parameters laid down for the MED POL monitoring programme. It was agreed that, since sampling and analysis of seafood for methylmercury and selenium were not mandatory within the MED POL monitoring programme, arrangements would be made, with national coordinators for MED POL, for the relevant national monitoring programmes to cover the requirements of the project as much as possible. Moreover, any additional studies which could, at this stage, be considered as falling under the research component could be performed as part of the project.

6. Discussion of the detailed protocols for the sampling and analysis of human hair

Professor L. Kosta presented his paper, "Reference method for determination of methylmercury and selenium in human hair" (ICP/RCE 211(1)/9). He explained the various methods which could be used and underlined the importance of quality control and intercalibration between different laboratories. There was also a need to analyse other tissues, such as the placenta, for methylmercury. It was agreed that human hair constituted a good indicator tissue, although sometimes difficulties could be encountered in obtaining large amounts.

Professor L. Kosta agreed to submit detailed protocols for analysis of human hair based on up-to-date literature. Apart from the discussions at the Meeting, he would also take into account existing information (e.g. sample collection, pre-analytical treatment, etc.) from the IAEA programme on the subject. The representative of IAEA agreed to provide Professor Kosta with any necessary information for this purpose.

The role of selenium was discussed and, in view of the importance of measuring selenium and of allowing parallel determinations with mercury content, it was agreed that, since the first phase of the study would be limited to methylmercury, samples of seafood and human hair should be stored in order to allow their analysis for selenium at a later stage.

The Meeting also considered that more research was required on the interaction between mercury and selenium in order to achieve a better understanding of the toxic action of mercury and of the possible antagonistic effects of selenium. It was suggested that Mediterranean institutions should be encouraged to perform such research.

7. Discussion of the detailed protocol for the epidemiological studies

Following the discussion on the criteria for the epidemiological studies, based on document ICP/RCE 211(1)/10, the Meeting noted the exhaustive material submitted as an annex to this document. It was considered that this material could provide a sufficient basis for the formulation of a detailed protocol for the epidemiological studies, and it was recommended that such a protocol should be drawn up as early as possible.

8. Identification within the participating countries of the institutions responsible for carrying out the different parts of the project

Institutions from Algeria, France, Greece, Italy, Malta and Yugoslavia had already indicated an interest in participating in the project. It was agreed that although at this stage participation would have to be limited, it should remain open, allowing other institutions from Mediterranean countries to enter. National coordinators for MED POL would be among those approached.

Participants at the Meeting gave indications that their institutions, as well as others, would be interested in taking part in one or more aspects of the project. Emphasis was placed on the dietary survey, since it would be the first cooperative activity. Among institutions provisionally identified at this stage for participation in the survey were the Istituto Nazionale della Nutrizione (Italy), the Department of Health (Malta) and the Institute of Public Health (Zagreb, Yugoslavia). These would be confirmed. In addition, other participants stated that the necessary internal arrangements would be made in their respective countries to ensure appropriate participation.

Regarding the other aspects of the project, Dr M. Branica (Yugoslavia) and Dr C. Alzieu (France) indicated that, subject to confirmation, their respective institutions could participate in the sampling and analysis of seafood. Other institutions which had participated in the appropriate aspects of MED POL Phase I were also mentioned as possible participants. Professor C. Boudene (France) and Professor L. Kosta (Yugoslavia) gave similar indications with regard to the sampling and analysis of human hair. The Istituto Superiore di Sanità in Rome could also assist in analysis of other tissues. It was agreed that formal correspondence to finalize participation would commence immediately after the Consultation Meeting.

9. Discussion and approval of the detailed work plan, including institutional arrangements and timetable of the project

The Meeting discussed the draft project document (ICP/RCE 211(1)/6), as a result of which the document was updated and various amendments made. Among these, the Meeting recommended that before the commencement of the epidemiological studies, an ad hoc meeting of epidemiologists from the various participating institutions should be convened, and this was reflected in the budget proposals for 1983 in the project document. The Meeting noted the financial difficulties involved in the convening of this meeting. The final version of the project document as approved by the Meeting is given in Annex 2.

Annex 1

PROTOCOL FOR DIETARY SURVEY

Background

The considerations on which this protocol for a dietary survey in Mediterranean populations have been based are the following:

- (a) the majority of methylmercury intake comes from the consumption of seafood;
- (b) the seafood consumption levels are strictly related to their grade of availability;
- (c) the populations most involved in seafood consumption are those resident along the coasts, particularly where fishing activities and commerce are principally concentrated;
- (d) the biological effects of methylmercury are dependent, for the same level of intake, on the anthropometric (age, sex) and physiopathological (pregnancy, particular pathological conditions) characteristics of the consumer and on the intake of other elements, with particular emphasis on selenium.

On the basis of the above considerations, the areas where the dietary survey should be conducted can be defined and established. In these areas, large population groups with presumably high seafood consumption levels can be selected on the basis of existing data on population size and distribution (fishermen and their families, workers in fish restaurants, etc.).

Survey design

The dietary survey is divided into two phases. In the first phase (the interview phase), the composition of families and their seafood consumption habits, including any single species consumed throughout the year, are recorded on prepared model forms (see Appendix A).

This phase enables the individualization, among the families interviewed, of samples of a proper size, resulting in an inadequate representation of differing levels of consumption and family composition. Stratification according to the sex, age, pregnancy and occupation of family members can be made.

The second phase involves the registration of the seafood consumption patterns of selected population groups during those periods of time that are representative of different seafood availability (minimum one week, but usually three weeks).

The type and quantity of seafood consumed during the survey period by individuals within the family, both at home and outside, are registered in a properly prepared model (Appendix B).

The registration should be repeated according to the seasonal variation of the species available for consumption during the year (generally two or three times a year).

The family consumption values can be converted to individual values by the use of mathematical factors calculated on the basis of the energy requirements for the main age groups within the population, taking sex into consideration.

By multiplying the values of individual consumption of single seafood species by the values of methylmercury concentrations in the corresponding species, according to the most correct and valid data, the intake of total methylmercury per capita can be calculated.

Objective

The survey protocol provides seafood consumption data for each species of seafood consumed by individuals within the family differing by age, sex and other registered conditions. These data, together with actual levels of methylmercury in the seafood species consumed, enable the recognition, at different confidence levels, of small groups in the population who are critically exposed to methylmercury intake. On these individualized groups, it will be possible to carry out a dietary survey for selenium intake, which will take into consideration foods other than seafood taken as good sources of selenium, and to collect samples of hair or blood for analysis and/or to perform clinical studies.

Annex 1

Appendix A

DIETARY SURVEY

INTERVIEW ON FAMILY CONSUMPTION OF SEAFOOD

Registration No.

□□□□□□□□

Family

Location

FAMILY COMPOSITION

Total number of cohabiting members

□□□□

	Age	Sex	Weight	Height	Profession	Presence at meals
Family member No. 1	□□□□	□	□□□□	□□□□□□	_____	□
2	□□□□	□	□□□□	□□□□□□	_____	□
3	□□□□	□	□□□□	□□□□□□	_____	□
4	□□□□	□	□□□□	□□□□□□	_____	□
5	□□□□	□	□□□□	□□□□□□	_____	□
6	□□□□	□	□□□□	□□□□□□	_____	□
7	□□□□	□	□□□□	□□□□□□	_____	□
8	□□□□	□	□□□□	□□□□□□	_____	□
9	□□□□	□	□□□□	□□□□□□	_____	□
10	□□□□	□	□□□□	□□□□□□	_____	□

Date of interview: _____

Type of seafood	<input type="text"/>
Mode of conservation	<input type="text"/>
Quantity consumed per meal (g)	<input type="text"/>
Size (g or cm)	<input type="text"/>
Frequency	<input type="text"/>
Origin (local fishery, market)	<input type="text"/>
Type of seafood	<input type="text"/>
Mode of conservation	<input type="text"/>
Quantity consumed per meal (g)	<input type="text"/>
Size (g or cm)	<input type="text"/>
Frequency	<input type="text"/>
Origin (local fishery, market)	<input type="text"/>
Type of seafood	<input type="text"/>
Mode of conservation	<input type="text"/>
Quantity consumed per meal (g)	<input type="text"/>
Size (g or cm)	<input type="text"/>
Frequency	<input type="text"/>
Origin (local fishery, market)	<input type="text"/>
Type of seafood	<input type="text"/>
Mode of conservation	<input type="text"/>
Quantity consumed per meal (g)	<input type="text"/>
Size (g or cm)	<input type="text"/>
Frequency	<input type="text"/>
Origin (local fishery, market)	<input type="text"/>
Type of seafood	<input type="text"/>
Mode of conservation	<input type="text"/>
Quantity consumed per meal (g)	<input type="text"/>
Size (g or cm)	<input type="text"/>
Frequency	<input type="text"/>
Origin (local fishery, market)	<input type="text"/>

Annex 1

Appendix C

INSTRUCTIONS FOR COMPLETING THE DATA FORMS

The dietary survey should be carried out on families that are permanently resident in the selected area. The data forms are in two sections (Appendices A and B).

The first part (Appendix A) should be completed by a trained interviewer (ideally a local person, in order to facilitate introduction into families), who should fill in the appropriate boxes as follows.

Appendix A (first page)

Age: Number of years
Sex: M for male; F for female; P for pregnant woman
Weight: Figures in kilograms
Height: Figures in centimetres
Profession:^a Short description (which can also be codified (see box))
Presence at meals: 0, 1, 2, 3 according to presence at the three main daily meals
Registration No.: Progressive number given to help identification of the interviewed family

Appendix A (second page)

The interviewer should complete the central part of the form, leaving the boxes on the right which are designed for code numbers (which can be established for computerized records).

The same information is required for all the species consumed. This means that more than one page will be needed if the number of species consumed throughout the year exceeds the number appearing on the page (six).

Type of seafood: Species of seafood (fish or shellfish) consumed (in vernacular names)
Mode of conservation: Fresh or canned, frozen, salted, smoked or other
Quantity consumed: Average grams of species consumed per meal
Size: Approximate weight or length of the species consumed
Frequency: Number of times per year the species is consumed
Origin: Where the species consumed comes from (local fishery, market, etc.)

Appendix B (first page)

This part is left with the family for the duration of the survey. It should be filled in by a family member (generally the housewife), who will report all the required information on the species consumed at each meal. If, for example, two meals in the same day consist of the same species, it should be reported twice. Before leaving the forms with the family, the interviewer should note the starting date (and at the end of the survey period the closing date) and the registration number, which has to be the same as that appearing on Appendix A, page 1.

^a In describing professions, details should be given of any of those listed in Appendix D.

Date: Day, month and year of the actual consumption

Type of fish: Vernacular name of the species prepared for the meal

Indication of whether fresh or processed: Fresh or any kind of preservation

Quantity of each type prepared for meal: Amount in grams of the species prepared for all the family

Portion not consumed: Total portion left by the whole family

Name: Under 01, 02, etc., give the name of the family members - this helps the responsible person to avoid the confusion of using only numbers when registering presence at meals (which can simply be indicated by "X")

Fish identification code: This part should not be completed by the panelist. It can be done at the central level, as the vernacular names have to be translated into scientific names. To help the identification and comparison of seafood species reported with vernacular (local) names, reference can be made to Fischer, W., ed., FAO species identification sheets for fishery purposes, Mediterranean and Black Sea (fishing area 37), Vols. 1 and 2, Rome, FAO, 1973; and ASE - Mediterranean Sea, Black Sea, Teleostei, identification sheets - taxonomy, geographical distribution, fisheries, vernacular names.

Appendix B (second page)

To take into consideration the meals eaten outside the home during the survey period by some family members, those who eat out are requested to complete this form personally (it is left with the reporting family), giving the amount of each species (type) consumed (quantity in grams). The same registration number and the family member number as on page 1 of Appendix A should be given.

To break down the family meals into individual meals (subjects present), key factors derived from the energy requirement for the different age and sex groups can be used.

For example, according to the recommended levels of energy and nutrients required by different Italian population groups (Table 1), the factors calculated for Italy are as shown in Table 2.

Table 1. Recommended daily intake of nutrients for the Italian population

Age groups (years)	Energy MJ	Protein g	Lipids g	Calcium mg	Iron mg	Iodine µg	Magnesium mg	Zinc mg	Thiamine mg	Riboflavin mg	Nicotinic acid eq.	Folic acid µg	Vitamin B12 µg	Ascorbic acid mg	Vitamin A Retinol eq.	Vitamin D Calciferol	
Male and female																	
0-0.5	2.7	12	22	500	7	35	60	3	0.3	0.4	4	40	0.3	35	450	10 ^b	
0.5-1.0	4.0	25	32	600	7	40	70	5	0.4	0.5	6	60	0.3	35	450	10	
1-3	5.2	29	42	500	7	60	150	10	0.5	0.7	8	100	0.9	40	250	10	
4-6	7.2	38	57	500	9	60	200	10	0.7	0.9	11	100	1.5	40	300	10	
7-9	8.4	45	67	500	9	80	250	10	0.8	1.1	13	100	1.5	40	400	2.5 ^c	
Male																	
10-12	10.1	54	81	700	12	120	350	15	1.0	1.3	16	100	2.0	45	575	2.5	
13-15	11.6	66	93	700	12	120	350	15	1.1	1.5	18	200	2.0	45	725	2.5	
16-19	12.4	67	99	700	15	140	400	15	1.2	1.6	20	200	2.0	45	750	2.5	
20-39	12.6	64	83	600	10	140	350	15	1.2	1.6	20	200	2.0	45	750	2.5	
40-49	11.9	64	79	500	10	130	350	15	1.1	1.6	19	200	2.0	45	750	2.5	
50-59	11.3	64	75	500	10	130	350	15	1.1	1.5	18	200	2.0	45	750	2.5	
60-69	10.0	64	67	500	10	130	350	15	1.0	1.3	16	200	2.0	45	750	2.5	
70 and over	8.8	64	58	500	10	130	350	15	0.8	1.2	14	200	2.0	45	750	2.5	
Female																	
10-12	9.6	56	77	700	18	110	300	15	0.9	1.3	15	100	2.0	45	575	2.5	
13-15	10.5	59	83	700	18	110	300	15	1.0	1.4	16	200	2.0	45	725	2.5	
16-19	9.6	54	77	700	18	110	300	15	0.9	1.3	15	200	2.0	45	750	2.5	
20-39	9.0	53	60	600	18	110	300	15	0.9	1.2	14	200	2.0	45	750	2.5	
40-49	8.6	53	57	500	18	100	300	15	0.8	1.1	14	200	2.0	45	750	2.5	
50-59	8.1	53	54	500	10	100	300	15	0.8	1.1	13	200	2.0	45	750	2.5	
60-69	7.2	53	48	500	10	100	300	15	0.7	1.0	11	200	2.0	45	750	2.5	
70 and over	6.3	53	42	500	10	100	300	15	0.6	0.8	10	200	2.0	45	750	2.5	
Pregnant	+0.8	+13	+5	1200	18	125	450	20	+0.1	+0.1	+1	400	3.0	60	750	10	
Lactating	+2.1	+24	+14	1200	18	150	450	25	+0.2	+0.3	+3	300	2.5	60	1200	10	

^a Vitamin C
^b (400 international units)
^c (100 international units)

Table 2. Factors used to break down family meals into individual meals

Age (years)	Male	Female
1-6	0.51	0.51
7-12	0.76	0.74
13-19	0.98	0.82
20-49	1.00	0.72
50-69	0.87	0.63
≥ 70	0.72	0.52

Annex 1

Appendix D

In describing individual professions, full details should be collected of any that entail occupational exposure to the following:

- chlorine and caustic soda manufacture;
- felt hat manufacture;
- laboratory work involving the use of mercury;
- dentistry;
- mining;
- paint and paper manufacture;
- smelting;
- electrical apparatus production;
- manufacture of drugs containing mercury;

as well as general exposure, e.g. industrial emissions, coal burning and consumption of drugs containing mercury.

Information on unusual dietary factors capable of affecting the results, such as the consumption of frogs and/or mushrooms, should also be sought.

Annex 2

EVALUATION OF METHYLMERCURY IN MEDITERRANEAN POPULATIONS AND RELATED HEALTH HAZARDS

Project document

1. Objectives

The general objective of the proposed activity is the evaluation of the possible hazards to the health of selected population groups arising from the methylmercury content of Mediterranean seafood.

The specific objectives are the following:

- (1) the selection of populations in the Mediterranean that have a relatively high intake of methylmercury;
- (2) the identification of groups whose methylmercury intake exceeds the WHO Provisional Tolerable Weekly Intake (PTWI);
- (3) an estimation for the above groups of their:
 - (a) size;
 - (b) patterns of individual consumption of seafood;
 - (c) exposure to other forms of mercury;
 - (d) actual concentrations of methylmercury in the various species consumed;
- (4) an assessment of methylmercury exposure in the critical segments of the population;
- (5) an investigation of methylmercury-associated abnormalities in high-risk population groups as compared to control groups.

The attainment of these objectives will significantly assist the relevant government authorities in the Mediterranean in the selection and formulation of regulatory action to limit the intake of methylmercury through seafood.

As the human foetus is considered to be the most sensitive target, special attention will be given to the estimation of methylmercury intake by pregnant women.

2. Background

The First Meeting of the Contracting Parties to the Convention for the Protection of the Mediterranean Sea and its related Protocols, held in Geneva from 5 to 10 February 1979, endorsed the development of environmental quality criteria within the framework of the Mediterranean Action Plan, stating in particular that "work should be continued on the development of the scientific rationale for the criteria applicable to the quality of recreational waters, shellfish-growing areas, waters used for aquaculture, and seafood" (UNEP/IG.14/9, Annex V, paragraph 13).

The Bureau of the Contracting Parties, at their first meeting in Geneva on 26 and 27 June 1979, also considered the matter and urged the Secretariat to take steps to develop the environmental quality criteria for bathing waters and mercury in seafood.

The Second Meeting of the Contracting Parties, held in Cannes from 2 to 7 March 1981, approved the Long-term Programme for Pollution Monitoring and Research in the Mediterranean Sea (MED POL Phase II), including, under research and study topics, "Epidemiological studies related to the confirmation (or possible revision) of the proposed environmental quality criteria (standards of use) for bathing waters, shellfish-growing waters and edible marine organisms" as well as "Biogeochemical cycles of specific pollutants, particularly those relevant to human health" (including mercury) and "Development of sampling and analytical techniques for monitoring the sources and levels of pollutants" (UNEP/IG.23/11, Annex V, paragraph 42).

During the interim period, interagency consultations were held in November/December 1979 on the design and implementation of a cooperative programme on health-related aspects of mercury levels in edible marine organisms, with the following objectives:

- (1) to obtain reliable information on the mercury content of fish and shellfish in various parts of the Mediterranean region;
- (2) to establish patterns of consumption of fish and shellfish in selected communities around the Mediterranean and to identify high-risk groups;
- (3) to gather epidemiological information on the levels of exposure and the related possible effects on the health of high-risk groups and the general population;
- (4) to review the recommended national and international limits and guidelines for mercury levels and intake by man in the light of the latest available information and in relation to consumption patterns of fish and shellfish in the Mediterranean region;
- (5) to establish environmental and health monitoring systems and to recommend safeguards and measures for the reduction and control of exposure to mercury from the consumption of fish and shellfish.

It was also agreed that, in view of the necessity of providing the Contracting Parties with advice related to the consumption of mercury-contaminated seafood prior to the meeting on the long-term monitoring and research programme, the following preparatory activities would be undertaken:

- (1) the compilation and evaluation of data on the concentration of mercury in seafood;
- (2) the collection, evaluation and interpretation of available data on seafood consumption patterns, giving emphasis to high exposure groups, including the results of pilot studies in selected countries;
- (3) the collection of available data on mercury levels in the blood and other tissues and, if possible, the augmentation of these data by the biological monitoring of selected groups;
- (4) a review of the latest available data on the effects on health of mercury in seafood, with particular reference to dose-response relationships;
- (5) a review of national legislation and enforcement practices related to the subject;
- (6) the updating of the data profiles on mercury.

Most of these tasks were completed following the Consultation to Re-examine the WHO Environmental Health Criteria for Mercury, organized by WHO in Geneva from 21 to 25 April 1980 (WHO-ECE/EHC/80.22). The UNEP/FAO/WHO Meeting of Experts on Environmental Quality Criteria for Mercury in Mediterranean Seafood, held in Geneva from 3 to 8 November 1980 (UNEP/MED-HG/13), was also convened, in particular, to evaluate the hazards related to the intake of mercury by populations from seafood in the Mediterranean region and to develop recommendations on desirable environmental quality criteria for mercury in Mediterranean seafood.

In the light of available evidence and from evaluation of the hazards related to the intake of mercury from seafood by populations in the Mediterranean region, it is considered that part of the population in the region may have an intake of methylmercury which exceeds the WHO Provisional Tolerable Weekly Intake (PTWI), and it is therefore recommended that the total intake of methylmercury from seafood should be limited. In order to obtain a more accurate assessment of the situation and to enable governments to select from various possible options, additional information is required, and the main gaps in present knowledge can be summarized as follows:

- (1) anthropogenic sources of mercury and other selected pollutants and their contributions to the methylmercury content of seafood;
- (2) methylmercury concentrations in various types of seafood in certain areas of the Mediterranean Sea;
- (3) patterns of seafood consumption in various sectors of the Mediterranean area, including seasonal variations;

(4) identification of populations with a relatively high methylmercury intake and estimation of their size;

(5) biological monitoring data on mercury levels in populations with high methylmercury intakes.

The acquisition of this information is the scope of the present project.

3. Activities

Preparatory activities in connection with the project have consisted of the following:

(1) the preparation of a background paper reviewing international activities on the subject;

(2) the preliminary identification of the countries interested in participating in the project;

(3) the identification of a number of institutions (within the countries concerned) for carrying out the various components of the project, i.e. dietary surveys, sampling and analysis of edible seafood and human hair, and appropriate epidemiological studies on selected population groups; this identification was undertaken with the assistance of a number of national coordinators for MED POL;

(4) the preparation of protocols for:

- (a) the conduct of a dietary survey;
- (b) the determination of methylmercury in human hair;
- (c) the conduct of epidemiological studies with the assistance of various consultants;

(5) the convening of a Consultation Meeting of individual experts interested in participating in the project; this Consultation Meeting, held in Athens from 13 to 17 September 1982, achieved the following:

- (a) an indication of the criteria to be applied in determining "hot spots" to be used as sampling areas for the studies;
- (b) the development of a detailed work plan and the revision of the project document;
- (c) the development of the protocols for the dietary survey, sampling and analysis of human hair, and the principles underlying the epidemiological studies;
- (d) agreement on the target groups to be sampled;
- (e) agreement on the modalities of the project within the overall framework of UNEP's Coordinated Mediterranean Pollution Monitoring and Research Programme (MED POL), taking into account both the aspects being implemented by the WHO European Regional Office and the inputs from other parts of the programme, and also as part of the Regional Office's programme on chemical safety.

The project will consist essentially of parallel studies carried out in a number of Mediterranean countries. An attempt will be made to identify, in each country, one or more appropriate areas in the light of data resulting from the following studies:

- (1) the compilation of existing national data on the subject to facilitate the identification of suitable areas for the dietary survey;
- (2) a preliminary dietary survey on seafood consumption and an evaluation of methylmercury intake, based on the results of the survey and on available data on levels of mercury in seafood;
- (3) the sampling and analysis of human hair (and, whenever appropriate, of other tissues) for total mercury and methylmercury among the target population.

In order to obtain reliable figures on population exposure to methylmercury, the areas selected will consist of a number of representative villages with similar fishing patterns, local ecologies and lifestyles, and could include places where elevated mercury levels in seafood have been recorded in the MED POL monitoring programme.

In the identified communities, the number of families sampled will be determined by local conditions, but should be sufficient to allow adequate statistical analysis (on the lines indicated in document ICP/RCE 211(1)/10, "Protocol outline for monitoring and epidemiological studies on health effects of methylmercury"). Usually, all members of the family will be sampled. Should this not be possible, every effort will be made to sample the women of childbearing age. Employees of fish restaurants and their families who are believed to have a high level of seafood consumption should also be sampled, as should any other groups who have a high seafood consumption.

Activities throughout the course of the project would be the following:

- (1) the carrying out of dietary surveys in order to assess seafood consumption patterns in selected areas;
- (2) the sampling and analysis of edible seafood for total mercury and methylmercury;
- (3) the carrying out of sampling and analytical programmes on the determination of methylmercury in human hair and, whenever appropriate, in other tissues;
- (4) the carrying out of appropriate epidemiological studies on selected population groups within the sample.

An essential input into the project would be the carrying out of a sampling and analytical programme on levels of total mercury and methylmercury in seafood. Work already being undertaken within the framework of the monitoring component of MED POL should be used to the fullest extent possible, and arrangements made for that part of the work not at present covered to be performed.

Exposure to mercury may occur through the ingestion of water and food, through inhalation or through the dermal route. Available studies indicate that human exposure to methylmercury occurs almost exclusively via seafood consumption. A rapid assessment of the multi-media exposure situation might still be appropriate and, in the design of the epidemiological studies, it would be desirable to confirm that, for the selected study groups, exposure via other media is indeed negligible. Analysis of a limited number of drinking-water and air samples for mercury/methylmercury would probably be sufficient to meet requirements, together with information on any occupational exposure (e.g. chlorine and caustic soda manufacture, felt hat manufacture, laboratory work, dentistry, mining, paint and paper manufacture, smelting, electrical apparatus production and manufacture of drugs containing mercury), general exposure (e.g. industrial emissions, coal burning) and unusual dietary factors (e.g. consumption of frogs, mushrooms, canned seafood and drugs containing mercury).

The possible role of dietary selenium in antagonizing the toxic effects from methylmercury should be considered in the interpretation of results from the epidemiological studies. In order to enable parallel determinations of levels of selenium in the sample population, samples of seafood and human hair collected for methylmercury analysis will be stored for future analysis for selenium. If necessary, an appropriate dietary survey for selenium could be carried out.

The epidemiological studies on methylmercury-related abnormalities will be conducted on the indicated high-risk groups within the sample population as early as possible during the course of the project. Such studies will be based on the acquisition and evaluation of data from the above surveys to identify such high-risk groups and will entail a number of sophisticated clinical and laboratory analyses. This part of the project will have to be conducted in stages. The necessary details and timetabling will be decided at the earliest available opportunity in the light of results obtained.

Technical assistance

Available funds will be used to provide assistance to participating institutions to the extent possible to enable them to carry out the various surveys and sampling programmes. Such assistance will include the provision of technical documentation, basic equipment for the collection and analysis of samples, their storage and despatch, the financing of attendance by appropriate members of the institutions concerned at relevant WHO and UNEP training courses and the financing of the exchange of samples and appropriate personnel between participating institutions to ensure the comparability of results and the quality of data as well as the meeting of basic requirements for carrying out the epidemiological studies. In addition, those institutions carrying out the "centralized" work of analysis will also be provided with the necessary equipment and material.

Duration of project

Preparatory work on the project began on 1 May 1982, and development of the various protocols is expected to be completed by 31 December 1982. The dietary survey will start in late 1982. The sampling and analysis of seafood and human hair will begin in 1983. The epidemiological studies will begin at the earliest appropriate date. Consultation meetings should be convened (a) before the initiation of the epidemiological studies; and (b) in early 1984 to develop the successive stages of the project, which will include the monitoring of seafood and human hair in the selected areas and sample populations, as well as the continuation of the epidemiological studies. It is expected that the project will be completed by the end of 1985.

4. Output

The following output is expected:

- (1) an updated background paper on the present knowledge about hazards to human health arising from the intake of methylmercury through consumption of seafood in Mediterranean populations;
- (2) protocols for dietary surveys on seafood consumption patterns;
- (3) a reference method for the determination of methylmercury in human hair and other appropriate tissues;
- (4) a reference method for the determination of selenium in human subjects;
- (5) a protocol for epidemiological studies relating to methylmercury intake and its effects on health;
- (6) an indication of the upper range of daily intake of methylmercury, together with seasonal variations, peak level attained and those individuals or subgroups with the highest levels of mercury;
- (7) a better correlation between methylmercury intake and the consumption of mercury-contaminated seafood;
- (8) a better knowledge of the effects on health of methylmercury intake among population groups at risk in the Mediterranean, to provide a better basis for regulatory action by responsible governmental authorities.

5. Work plan and timetable, 1982-1983

<u>Activity</u>	<u>Period</u>
1. Preparation of background paper	1 May - 30 June 1982
2. Contracts with institutions	1 May - 30 June 1982
3. Preliminary identification of participants	1 May - 30 June 1982
4. Consultation Meeting	13-17 September 1982
5. Development of protocol for dietary survey	By 17 September 1982
6. Development of reference method for determination of methylmercury in human hair	By 31 December 1982
7. Development of protocol for epidemiological studies	By 31 December 1982
8. Formalization of arrangements for institutional participation	1 October - 31 December 1982
9. Performance of dietary survey	1 December 1982 - 30 September 1983
10. Sampling and analysis of seafood	1 January - 31 December 1983

- | | |
|-------------------------------------------------------------------------|----------------------------|
| 11. Sampling and analysis of human hair | 1 April - 31 December 1983 |
| 12. Consultation meeting on epidemiological programme | 1983 |
| 13. Initiation of epidemiological studies on selected population groups | 1983 |

Note: as far as possible, item 10 to be performed as part of the monitoring programme of MED POL Phase II.

6. Tentative budget (covering UN contribution)

	<u>1982</u>	<u>1983</u>
	\$	\$
1. Preparation of protocols	2 000	-
2. Consultation meeting	8 000	8 000
3. Dietary survey	18 000	-
4. Sampling and analysis of seafood	-	20 000
5. Sampling and analysis of human hair	-	20 000
6. Epidemiological studies (initial)	-	10 000
7. Training	-	6 000
8. Miscellaneous	3 000	1 000
	<hr/>	<hr/>
	31 000	65 000
	<hr/>	<hr/>

Recapitulation

	<u>1982</u>	<u>1983</u>
	\$	\$
Experts	2 000	-
Subcontracts	18 000	30 000
Equipment	-	20 000
Training	-	6 000
	<hr/>	<hr/>
Direct assistance	20 000	56 000
Meetings	8 000	8 000
Reporting costs	2 000	-
Miscellaneous	1 000	1 000
	<hr/>	<hr/>
TOTAL	31 000	65 000
WHO contribution in services	4 000	8 500
	<hr/>	<hr/>

The above budget covers the financial input from the Mediterranean Action Plan and the WHO Regional Office for Europe. It is estimated that this only represents 15-20% of the total project costs, the rest of which would be borne by participating institutions and other national sources.

Annex 3

LIST OF PARTICIPANTS

TEMPORARY ADVISERS

- Dr C. Alzieu
Institut scientifique et technique des Pêches maritimes (ISTPM), Nantes, France
- Professor C. Boudene
Laboratoire de Toxicologie, INSERM U 122, Université de Paris Sud, Chatenay-Malabry, France
- Dr M. Branica
Centre for Marine Research, Rudjer Boskovic Institute, Rovinj, Yugoslavia
- Dr A. Grech
Chief Government Medical Officer, Department of Health and Environment, Valletta, Malta
(Vice-Chairman)
- Professor L. Kosta
Department of Chemistry and Chemical Technology, University of Ljubljana, Yugoslavia
- Dr H. Lekehal^a
Direction de la Prévention, Ministère de la Santé publique, Algiers, Algeria
- Ms D. Spala^b
Biologist, Environmental Pollution Control Project, Ministry of Physical Planning, Housing and
Environment, Athens, Greece
- Professor G. Tomassi
Istituto Nazionale della Nutrizione, Rome, Italy
- Mr G. Vournas^b
Head of Sector, Environmental Pollution Control Project, Ministry of Physical Planning,
Housing and Environment, Athens, Greece (Chairman)

REPRESENTATIVES OF OTHER ORGANIZATIONS

United Nations Environment Programme (UNEP)

Coordinating Unit for the Mediterranean Action Plan, Athens

- Dr F.S. Civili
Marine Scientist
- Dr A. Cruzado
Senior Marine Scientist
- Ms Z.G. Yilmaz
Data Processor

^a unable to participate

^b participation expenses not paid by WHO

International Atomic Energy Agency (IAEA)

Dr S.B. M'Baku
Section of Radiation Biology and Health-Related Environmental Matters, Division of Life
Sciences, Vienna

WORLD HEALTH ORGANIZATION

Regional Office for Europe

Dr L.J. Saliba
WHO Senior Scientist, Coordinating Unit for the Mediterranean Action Plan, Athens (Secretary)

Dr V. Silano
Consultant, Promotion of Environmental Health

Headquarters

Dr H. Galal Gorchev
Environmental Hazards and Food Protection, Environmental Health Division

Dr J. Parisek^a
International Programme on Chemical Safety, Environmental Health Division

^a unable to participate