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EUROPEAN REGIONAL PROGRAMME ON CHEMICAL SAFETY

STUDIES ON HEALTH EFFECTS OF OCCUPATIONAL EXPOSURE OF WELDERS TO CHROMIUM AND NICKEL

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1. Introduction

In November 1980, the Consultation of Priority Problems in Toxic Chemicals Control in Europe, held in Baden, Austria, highlighted the importance of internationally coordinated epidemiological studies capable of generating comparable data on high priority chemicals, inter alia, cadmium, lead and chromium, and recommended that such studies be implemented. As a first step in putting these recommendations into action, the Planning Meeting on Monitoring and Epidemiological Studies for Toxic Chemicals Control was held in Copenhagen in May 1981. The Planning Meeting supported the preparation of detailed protocols for these studies in order to improve the comparability of monitoring data and data produced or used by epidemiological studies. To ensure that such data are indeed comparable, the Planning Meeting recommended the standardization of procedures and the use of quality assurance. The Planning Meeting further recommended the use of biological monitoring as a valuable tool for assessing the health effects of chemical exposure. In 1982, a series of planning meetings was held to review outline protocols on epidemiological studies on cadmium, lead, chromium and nickel and further develop them into draft protocols.

In May 1982, the Planning Meeting on Health Effects of Occupational Exposure of Welders to chromium, held in Copenhagen, reviewed current knowledge concerning possible health effects, in particular lung cancer and chronic respiratory diseases, associated with welding fumes. It was noted that few epidemiological studies had been designed around welders and none had ideal control populations. Of particular concern are fumes from stainless steel welding, which are characterized by high concentrations of chromium and nickel. With about 200 000 stainless steel welders in Europe potentially at increased risk and no technologically simple solution currently available to the welding industry, an internationally coordinated epidemiological study on this population would seem appropriate.

The Planning Meeting revised an outline protocol submitted to it. Historical prospective mortality and cancer incidence studies of stainless steel welders were considered essential components. The Planning Meeting stressed the need to obtain adequately large cohorts of stainless steel welders with at least 25 years of follow-up from first exposure. The general opinion of the Planning Meeting was that by careful use of mild steel welding and nonwelding cohorts as internal and external reference groups, the effects of welding, and especially the effects of welders' exposure to chromium could be established, provided that several countries participated. The Planning Meeting agreed that there was a need to present all aspects of the problem of chronic health effects in welders at an international meeting.

In December 1982, the draft protocols on epidemiological studies on cadmium, lead, chromium and nickel were reviewed at the Consultation on Monitoring of Exposure to Selected Chemicals and their Health Effects, held in Berlin (West), and published in 1984 in the WHO/EURO Chemical Safety Interim Document No. 15.

During the International Conference on Health Hazards and Biological Effects of Welding Fumes and Gases, held in Copenhagen in February 1985, a meeting of potential principal investigators in the epidemiological study was organized with the purpose of evaluating the feasibility of the preliminary core protocol and to propose a minimum core protocol agreeable to all participants. It was also agreed that pooling of mortality data should be conducted by IARC, Lyon, while coordination of morbidity studies, occupational and biological monitoring, etc., should be undertaken on behalf of WHO/EURO by the Joint Coordinating Institutes in Copenhagen (Occupational Health Clinic of the National Hospital and the Danish Welding Institute). In order to share experience among principle investigators, it was agreed to convene a joint meeting of project participants at IARC, Lyon, in November 1986. The prime aim of this meeting was to review the progress and assess future needs of the mortality studies, and at the same time to establish firm interactions between the groups performing occupational monitoring and dose estimation, and the epidemiological projects. Further details of mortality studies can be found in Part 2 of the summary report of the Lyon consultancy (Annex 1). Principal investigators in mortality and morbidity studies agreed to the need for common core protocols to be followed in Occupational Exposure Monitoring and Biological Monitoring for both classes of studies. These two activities give information on external and internal dose, necessary for selecting and or stratifying individuals for morbidity studies, and in associating job classification with degree of exposure for use in mortality studies.

In order to achieve maximum coordination of the development and use of these (and other) core protocols, it was agreed to convene a meeting of interested project participants, at WHO/EURO, on 9-10 February 1987.

This Consultation was attended by 19 participants and 3 observers from nine european countries and the United States (Annex 3). Dr D. Kello opened the meeting and welcomed participants on behalf of the Regional Office.

Dr K.H. Kilburn was elected Chairman, and Professor R. Stern Rapporteur. Discussion leaders of four subgroups were chosen in order to focus on essential points in common, and to establish areas of potential conflict where certain studies could not be made to conform to a core protocol: occupational monitoring (Beck Hansen), biological monitoring (Hemmingsen), pulmonary function studies (Kilburn), and non-respiratory effects (Gyntelberg).

2. Scope and purpose

Based on discussions at the Working Group on Health Hazards and Biological Effects of Welding Fumes and Gases, Lyon, 17-18 November 1986, it was proposed that a meeting be held in Copenhagen, 9-10 February 1987, to harmonize the protocols currently being used in various ongoing morbidity studies. This meeting would ensure that these Protocols contain elements of a minimum core protocol for clinical studies of the health effects of welding. The results of the morbidity studies currently being undertaken will be reviewed.

It was expected that the meeting would agree on such a minimum core protocol, which will contain the following four elements:

- occupational exposure monitoring;
- biological monitoring;
- respiratory effects;
- nonrespiratory effects.

It would also be necessary to agree on further work on quality control measurements, which will be the responsibility of the selected reference centres for each area of the study, as well as on practical aspects concerning the analysis of collected data, timetable of the studies and publication of results.

3. Review of ongoing studies

In order to establish a practical reference framework for the study protocols, a brief review of ongoing morbidity studies was given by each of the participating investigators. In addition, some recent observations of health status of welders were presented by Professor Kilburn. An important recent observation was that all shipyard workers, regardless of job classification, exhibited reduced respiratory functional capacity with welders suffering no more or no less impairment than did members of other shipyard trades. This implies that either:

1. (a) all shipyard workers are exposed to welding fumes and gases (wherein one considers on-ship activity as the source of exposure, the ship acting as a container exposing all workers to the same atmosphere); (b) there might be other non-welding sources of toxic fumes and gases (bystander exposures);

2. shipyard employment preselects for reduced lung function.

This observation suggests that shipyard welders and controls (non-welding shipyard workers) should be studied separately from other welding populations. Shipyards, in fact, represented a special case for study because of the variable nature of exposure which shifts with the seasons and with activity (new-buildings, repair, refitting and ship-breaking). In principle, it was necessary to have access to activity registers, especially when measuring acute effects or cross-shift functional changes.

The participants were reminded that occupational monitoring yields information on external exposures, biological monitoring giving information on internal exposures, and respiratory tract studies provide a measure of effects. One must, however, decide on the "size" of the respiratory tract, i.e., if it should include the nose, mouth, larynx and pharynx. Furthermore, any effects found will reflect both recent and historical exposures, while the biological and exposure monitoring studies give information most relevant for recent exposures. In addition, although emphasis has traditionally been on respiratory effects, non-respiratory effects should be studied as well, provided that they can be examined with "standard instruments".

Although the protocols under consideration concern studies of welders; it would appear that 26% of nonexposed reference populations report some exposure to welding fumes. This means that, for practical reasons, only professional welding experience shall permit entry into exposed cohorts: it is probably impossible to exclude all non-professional welding exposures from control groups.

The importance of control groups cannot be over emphasized, especially with respect to eventual pooling of data from multi-centre studies. Fortunately, there is some preliminary evidence that, with only a few ethnic exceptions, reference populations are equal with respect to respiratory function parameters, provided that one uses a standard regression relation for body height. As a recent example, lung function parameters for nonsmoking

Michigan (USA) men agree very well with those for Danish nonsmoking shipyard electricians, indicating a much higher degree of reliability for the values of the Danish control group than would otherwise have been attributed to it because of small size (34 men).

For exposed cohorts, it should be realized that there may be significant differences in exposure levels between different categories of enterprises: shipyard welders (5–10 mg/m^3), assembly welders (2–3 mg/m^3), etc.

Finally, effects of dropout, self-selection (especially if there are early health effects of welding), and smoking must be considered. The respiratory effects of welding exposure may only be significant among nonsmoking populations, although nonsmoking populations may contain a disproportionately high number of atypicals when used in the study of some other health effects.

In order to explain the expected structure of the meeting, the Rapporteur presented an outline of a typical protocol, and described the requirements which must be met in order to make such protocols harmonizable, and to justify a pooling of the data and combined analysis. Stress was placed on the requirement that, in cases where the common core protocol could not be followed, a technique for calibration for these exceptional cases should be established so that the data could be made comparable.

The summary of ongoing studies (Table 1) indicates 11 programmes, some of which contain completed elements (e.g., Finland, the USA), several of which are well underway (e.g., German Democratic Republic, Norway,), and many of

Table 1. SUMMARY DATA SHEET - MORBIDITY STUDIES

	Sector	quality control wf	quality control pm	cohorts ss	cohorts ms	cohorts shipy.	control	fraction of cohort b	fraction of cohort bio. mon. u	fraction of cohort bio. mon. cyt	lung function	other studies	schedule start	schedule stop	report
ITA	military & shipyard	+	+									exposure m.			
FRA	military	+	+	500	500	70	500	100%	100%		100%	radio. cytogen.			12/89
FIN	construction pipe container	+	+	140 tot	50	-	int.	10%	10%		100%		1976	1987	1988
NOR	ship	+	+			55 (55)	20 match. local	100%	100%	100%	-	sce/- c.a. (grinders)	8/85	8/88	12/88
NOR	ship					25		100	100			stable cyt change			
DEN	food equip boiler weld.			90 (60)	100 30	30	160 300		20%		-	semen qual y body hormone	2/87	12/87	5/88
DEN	90 factories			2200	1200	-	2200	-	-		-	fertility rep outcome	1987	1988	1989
DEN	factory work	+	+	100		-	100 age match smoking	100	100		-	ca.sce uds mutagenic activ. semen qual. immunoglobulins	2/87	9/87	
USA	military & nuclear reactor vessels			200			40 cross shift*	100	100		100%	'Sat Sun *Monday	3/87	3/87	7/87
HUN	shipyard assembly Al (50)	+	+			150(ms) 150(ss)	350 age m.	100	100	-	100	Ni, Cr, Al Mn, F kidn (Al)	1987	1989	1990
GDR	shipyard chemical	+	+	150		150 ms	50	100	100	100	100%	Cr scalphair dose-effect select exp	1985	1987	12/88

Additional studies: Australia, United States (Ams), Germany (Schaller), Belgium (Leonard) which are about to begin (e.g., Denmark, France, Hungary, Italy, USA). For practical purposes, studies completed or underway (e.g., Finland, German Democratic Republic, Norway, USA) were to be considered as "pilot studies" and the experiences gained therein are to be used in developing the final version of the minimum core protocols in this consultancy. There was general agreement with respect to including elements of the common minimum core protocols found in all studies, with few exceptions. Each participating country had been involved in the quality control programme for welding fume analysis (conducted by Professor Stern), and all were planning to participate in the quality control programme for analysis of chromium and nickel in biological fluids. A brief description of the participating projects follows.

Denmark

1. A cross-sectional and follow-up study of semen quality among stainless steel, mild steel and alloy-steel welders, and controls (Aalborg).

2. A study of carcinogenic and mutagenic load in several selected groups (Hellerup).

3. A cohort study on male reproductive disorders, e.g., infertility, negative pregnancy outcome among welder wives, chromosomal abnormalities among children. Data by questionnaire/register linkage (Aalborg).

4. (Indirectly reported) a) health status and exposure study by questionnaire with selected lung function studies in a selected cohort of stainless steel welders (1987-1989); b) 5-year follow-up of health status,

exposure, and lung function study of heavily exposed shipyard welders (1988-1989) (Odense).

Finland (Helsinki)

1. Study of the correlation of respiratory symptoms, lung function reduction, effects on nasal mucosa, results of biological monitoring, exposure to stainless steel welding fumes, and other possible hazards. Measurement of lung-retained magnetic dusts and correlation to exposure times and possible hazards among mild and stainless steel welders and controls.

2. Follow-up of study of respiratory symptoms, pulmonary function and magnetic lung burden on MMA, TIG welders and grinders of stainless steel.

3. Study of the effects on the upper respiratory tract including nasal biopsy, cilliary function, and nasal status of stainless steel welding fumes in nonsmoking welders.

4. Evaluation of biological monitoring among stainless steel welders.

5. Follow-up study of shipyard welders for respiratory symptoms, pulmonary function, thorax X-ray, magnetic dust burden.

6. Study of excretion of chromium into urine and blood of stainless steel welders during summer vacation.

7. Study of kinetics of chromium after short (30 min) high-level exposure to stainless steel welding fumes.

France

1. Study of correlations between chromium and nickel exposure among stainless steel welders and pathological effects, and the effects of smoking, and non-welding exposures in welding and non-welding control groups (Nancy, Lille).

German Democratic Republic

1. Determination of the effects of welding fumes containing chromium and nickel on upper and lower airways, by comparison of signs and symptoms of respiratory disease among stainless steel welders with welders of mild steel. Determination of relationship between severity and type of symptoms and lung function parameter variation, and welding fume dose.

Hungary

1. Correlation between morbidity and CARD.

2. Effect of early changes in renal function through measurement of urinary enzymes.

3. Correlation between exposure levels of chromium, nickel, manganese, aluminium, fluoride and biological monitoring.

Italy

1. A study of mortality and morbidity among welders (Genoa).

Norway

1. Correlation between biological monitoring of chromium and nickel concentrations, cytogenetic damage and welding exposure among shipyard stainless steel (electrode) welders by means of daily measurements over a full work week, and the proceeding Friday and following Monday, using TIG/SS welders as a (negative) control (Porsgrunn)

2. Follow-up study of morbidity and mortality, especially cancer, of a long-term cohort of stainless steel welders with cytogenetic measurements looking for stable chromosome aberrations (Porsgrunn, Oslo).

USA

1. Does respiratory function decrease from years of exposure to stainless steel welding fumes, and are the effects cigarette smoking specific?

2. Can cross-shift respiratory effects of welding on respiratory function be detected in the field?

In addition, a study in Denmark (Brondby) and one in Norway (Oslo) are examining the solubility of welding fumes in appropriate biological fluids and tissue homogenate, to describe the dissolution and formation of metabolites of welding fumes, in vitro, as expected over long term in vivo.

3.1 Review of occupational exposure monitoring

In the general introductory discussion, it was agreed that all participants would engage in occupational monitoring of breathing zone concentrations of fumes. Some would measure O_3, NO_x and CO either by continuous instruments or sampling tubes. Of prime concern was the need to distinguish between background fume and direct fume since the composition could differ significantly. In particular, placement of the sampling cassette in front of the mask or helmet provides high exposure to direct fumes, while placement behind the helmet raises the relative contribution of background fume levels. The importance of handedness was noted with a general agreement to place lapel-mounted cassettes on the same side as the welding hand. The need for two filters was emphasized: one for total fume (usually cellulose acetate) and one for chromium speciation (usually polyvinyl chloride). Problems arose in certain countries (e.g., German Democratic Republic) because of worker reluctance to wear monitoring equipment, preventing more than one sample from being obtained. There was agreement to run the pumps over the lunch break except where it was certain to have them restarted after lunch, or where a separate afternoon sample was needed for specific reasons. Other questions raised were:

- the possibility of using alveolar CO (measure of carboxy haemoglobin in a 20-sec. breath-holding experiment) as an exposure indicator; probably useful among nonsmokers, except in the case of CO_2 shield gas welding where CO levels can reach 50 ppm in confined spaces;

- the validity of exposure questionnaires as predictive for actual exposures (see discussion at Lyon meeting and proposal to compare values measured with those predicted using the Danish database).

In addition to a cross calibration based on the database, it was agreed to eventually perform a single set of quality control measurements using mild steel manual metal arc welding under controlled conditions. Each participating laboratory would in the first instance find an available set of data for comparison (based on a given task with comparable electrodes under the same welding parameters). Should there be serious discrepancies between measured exposure levels, a laboratory experiment would be performed with new measurements taken under carefully controlled conditions. It was felt, however, that there would not be significant national differences between the average values currently measured. This activity would be supervised by the Danish Welding Institute.

The specific characteristics of occupational exposure monitoring for each project follow:

Denmark

Two pumps, PVC and CA filters for Cr (VI) and total fume. 8 h measurement on one day, stop for lunch. Afternoon sample correlates with after-shift urine. Analysis for Fe, Zn, Cr, Ni, Pb, Al, total fume.

Finland

Stainless steel welders (15), fumes monitored for 7 h during one week, cassette placed behind the mask. Analysed for total fume: Cr, Ni, Fe, Mn. Magnetic dust burden. No gases.

France

Behind mask collection for 4 h after lunch. Analysis of total fume, Ni, Cr, Cr (VI), Fe, Mn, but no gas monitoring.

German Democratic Republic

Lapel-mounted single cassette monitoring for 6-8 h of fume. Sample is cut in half for separate Cr (VI) analysis. Screening for gas exposure with sampling tubes.

Hungary

Active and passive sampling of NO_x and CO (personal samplers), passive O_3 monitoring. Total Cr. Total fume during 5+ h with personal and stationary samplers. PVC (polyvinyl chloride) sampling of Cr (VI), CA (cellulose acetate) sampling of Ni, Cr, Mn - both behind the mask.

Italy

Personal (lapel-mounted) and stationary sampling of fume for 7 h. Total dust and total Cr. Several sequential filters.

Norway

Lapel-mounted (in front of shield). Two pumps, two filter cassettes, CA for total fume, PVC for Cr (VI). Polycarbonate (3rd pump) in some cases for electron microscopy. 4-5 persons for 5 consecutive days MS/SS and MMA/SS with 10 MIG/SS (in 14 days) as control. Analysis for total fume, Cr, Ni, Fe, Cr (VI) soluble and insoluble.

USA

Stationary and personal samplers. Filters to be ent to Denmark (SVC) for analysis.

3.2 Review of biological monitoring

In the general discussion of details of biological monitoring, a number of points were agreed upon, with exceptions noted, as follows: Extreme care must be taken to account for chromium and nickel dynamics when choosing a protocol for biological monitoring. This is necessary because it is now evident that, based on the results of the pilot studies (Finland, Norway), there are several storage compartments for body burden, each with a characteristic time constant for clearance. Thus, monitoring will reflect the time between exposure and clearance for each compartment, and the monitoring protocol must be properly designed. Measurements after a long vacation should establish baseline levels, which can vary widely among individuals. These levels reflect a storage compartment with a half-time for clearance of 1-2 years. The presence of compartments with clearance half-times of from 1 h to 20 d leads to wide variation in clearance after exposure stops, e.g., over a weekend. There is preliminary evidence that the first void on Monday morning is misleading, even when corrected for density or creatinine, but that the second void on Monday morning is a good indicator of the exposure for the previous two weeks, and can also be used for measurement of cross-shift changes, by comparison with the first after-work void. Recent studies have also shown that the erythrocyte chromium is a good indicator of cumulative exposure during the previous 60 days. The model is not yet complete, but as long as the capacity for serum to reduce Cr (VI) to Cr (III) is not saturated, Cr (VI) uptake by erythrocytes should linearly integrate serum Cr (VI) concentration over the cell lifetime (120 d). The effect of a work week is generally to raise the base level by 20 to 40%. Work week measurements should also be accompanied by measurements on the previous Friday and following Monday, so that the baseline can be established if one is interested in measuring the effects of current exposures.

Technique for venous blood sampling received considerable discussion. In particular, contamination from needles was a major confounder in establishing baseline levels for nonexposed individuals. Several techniques were proposed, either use of a venflow or of a catheter to introduce the sampling tube or use only of later samples for chemical analysis (e.g., the 7th sample of 5 ml in a series), early samples being discarded or used for other purposes, e.g. morphology.

The question of choice of exposed cohorts and controls deserved careful consideration. In particular, some jobs, e.g., TIG/SS, provided such low exposures that TIG/SS welders should not be considered as exposed, but used for control measurements. Since biological monitoring was time consuming and expensive, it was strongly suggested that studies be designed around the most highly exposed individuals available since then one might find a correlation with exposure. If these correlations were absent, they would not be found in lower exposed groups either. Because of wide variations in individual uptake, it was strongly recommended to follow the response to changes in exposure, e.g., of cessation of exposure after job shift or during vacation, or similarly, of commencement of exposure for new employees or after long vacation. Care must be taken to distinguish between the results of current and previous exposure, and of accumulated body load (perhaps by magnetic measurements).

It was agreed that each group would provide a set of biological-monitoring reference values for unexposed controls to be collected by the group in Porsgrunn (Norway). Furthermore, the Institute of Occupational Health, Helsinki, would act as reference laboratory for biological monitoring. Two sets of reference samples would be obtained for distribution in a round robin quality control exercise, one based on standardized material, and the other based on actual collected samples.

The details of biological monitoring within the individual studies were as follows:

Denmark

1. Study of 3-month body burden for TIG/SS welders. Urinary chromium after second Monday morning void and on Tuesday and Thursday (or Friday) after last shift.

2. Urinary chromium and nickel in spot sample of Tuesday (same day as air monitoring) and serum chromium and nickel on Wednesday. Eight blood samples taken, the 7th is used for chemical analysis.

Finland

Urinary and blood chromium before and after a work shift in highly exposed MMA/SS welders.

France

Blood and urinary nickel and chromium before and after work shift during one week and the following Monday. Pilot study to correlate air chromium with biological chromium in MMA/SS, and look for cumulative effects.

German Democratic Republic

Hair chromium.

Hungary

Urinary chromium, nickel and Aluminium during one work week before and after shift and on the following Monday. Blood analysis before first Monday shift, after last Friday shift and before second Monday shift.

Norway

Previous Friday, full week daily before and after shift (second void Monday) and the following Monday MMA/SS welders: urinary chromium and nickel. Whole blood, serum, erythrocyte chromium and nickel on Wednesday.

3.3 Review of respiratory effects

The general discussion centered around what effects should be measured and under what circumstances. It was agreed that cigarette smoking played a central role in determining the extent of reduction in pulmonary function and in respiratory illness. There was some indication that the effects of welding were reversible in nonsmokers after cessation of welding, but that the effects of smoking were irreversible. There was some evidence that cross-sectional studies viewed illness through a narrow window, and that drop-out due to respiratory discomfort (and effects) could continuously remove effected populations from the study group (healthy worker effect). This could explain the Danish observation that there was little difference in respiratory function parameters and chronic bronchitis incidence between cohorts of nonsmoking welders with low exposure (e.g., 2.5 years of average, below 5 years as maximum) and cohorts with massive exposure (e.g., 15 years average, ranging up to 35 years), but that both of these groups were significantly different from nonsmoking non-welding fume exposed controls. Furthermore, the effect of smoking on the nonsmoking lightly exposed welder was many times greater that that of going from light to massive welding exposure among nonsmoking welders. This was especially important since at least one study reported that there was no difference in the effect of one intensive week of welding on the average of lung function measurements, and no difference in values with matched controls. In all cases, controls should be matched for age, smoking habits and, if possible, place of residence.

It was agreed to use questionnaire-interview to establish respiratory health status, but that inventories of symptoms were most useful in follow-up studies of intervention (e.g., removal of exposure). Recording spirometry was to be the standard instrumentation. Diffusing capacity should be measured, if possible (a new infra-red CO instrument provides an inexpensive field measurement capability). Total lung capacity was also of interest and could be measured in the field by planimetry of posteroanterior and lateral chest radiographs. The development of reliable values for nonexposed controls on the part of each laboratory was strongly recommended. These values would be collected by the coordinating institutes for use in data pooling. The University of California laboratory will provide standard reference procedures and act as the quality control laboratory. The Danish coordinating laboratory (Rigshospitalet) will act as a secondary reference laboratory to deal with immediate and local problems.

The outline programme for respiratory effect monitoring is as follows:

Denmark

Follow-up on highly exposed and control, never smokers. Magnetic measurements and flow volume curves, diffusing capacity.

Finland

VC, MMEF, DC, DL, CV, CV (difference), FEV1, Alveolar volume.

France

Flow volume curves, VC, CV, FEV 75, 50, 25. Perhaps diffusing capacity. Changes across shift (3 measurements during the day).

German Democratic Republic

Previous observation of no effect of welding on bronchial challenge, but some diffusing capacity impairment (Oscillatory). Flow volume measurements, perhaps in a follow-up.

Hungary

Flow volume measurements. VC, FEV, DC before shift only. Alveolar and residual volume and diffusing capacity in those with respiratory impairment only.

USA

Total lung capacity (chest X-ray planimetry at full inspiration in the field). Cross-sectional studies of residual volume, decline by fall in TLC, spirometry, diffusing capacity, alveolar volume: cross-shift changes in spirometry and diffusing capacity.

3.4 Review of nonrespiratory effects

In the general discussion, it was made clear that non-respiratory effects should not be ignored. Central nervous system effects due to exposure to metals, paints, solvents, etc., might be of considerable importance in terms of the overall health insult. The current group of studies, however, dealt with only a limited catalogue of measurements. It was suggested that musculo-skeletal effects, especially low back pain, could be dealt with by questionnaire, since there were standard forms in use by WHO. Data on days lost and accidents should be collected and pooled to try to establish the relative importance of respiratory vs non-respiratory effects in terms of priority setting. An attempt to generate such data will be made by the coordinating institutes.

The following is a brief outline of the non-respiratory effects studied by the programme participants:

Denmark

1. Sperm (semen) quality, hormone analysis, genetic abnormality (y chromosome disjunction).

2. Fertility impairment.

3. Sperm quality, cytogenics (CA, SCE, UDS). Ames test in urine, IGG, chromosome analysis, sensitivity to infection.

Finland

1. Kidney function (creatinine in urine and blood); headache.

2. Nasal biopsy, cytology, macroscopy of nasal mucosa, saccharine test (mucocillary function), metaplasia (cytology).

France

Chronic aberrations in lymph. Eye, head, neck and kidney dysfunction.

German Democratic Republic

Sickness leave data, musculoskeletal problems, cardiovascular (cystolic time due to Mn exposure). Questionnaire on psychological-neural symptoms due to solvents and Mn exposure, heart rate, step test.

Hungary

Urinary enzymes (B_2-microglobulin, urea) to study early changes in renal function.

Italy

Mortality study. Participation in quality control. Development of a risk index.

Norway

Nasal brush cytology of non-shipyard welders. Cytogenetic study of stable chromosome aberrations.

USA

Urinary mutagens (Ames test post shift), sputum cytology (atypia, antinuclear antibodies), SCE, neural behaviour (sleep, balance, mood).

4. Core protocols

The core protocols were developed in four subgroups and unanimously adopted in plenum. It was agreed that responsibility for amendment and control of the protocols (Annexes 3-6) would be dealt with by each reference laboratory, as follows:

1. Occupational monitoring: the Danish Welding Institute.

2. Biological monitoring: Institute of Occupational Health, Helsinki.

3. Pulmonary function methodology: University of California, with the help of the coordinating institutes and Rigshospitalet, Copenhagen.

4. General quality management for non-respiratory effects: Rigshospitalet, Copenhagen. Individual techniques: SCE/CA (Porsgrunn); brush cytology (Oslo); sperm quality (fertility clinic, Rigshospitalet, Copenhagen).

5. Further programme activities

It was decided that the current set of core protocols could be useful for other studies involving similar exposures, e.g., Chrome and nickel plating, ferrochrome and ferrosilicon industries. Efforts were being made to recruit such studies to act either as additional positive or negative controls.

The timetable is such that a final report of the current set of mortality and morbidity studies could be prepared at the end of 1989. An intermediate status report would be useful, however, and is planned for the Spring of 1988. It was felt that the next activities should be:

1. Publication of the quality control exercise of chemical analysis of welding fumes.

2. Initiation of the quality control study for biological monitoring.

3. Preparation of a status report including the results of this consultancy in Autumn 1987.

A meeting of the principle investigators responsible for the core protocols and reference laboratory activities should be planned for November 1987. An attempt will also be made to identify and communicate with principle investigators studying health effects of welding but not currently participating in the WHO/EURO multi-national study.

6. Recommendations

The following recommendations were agreed upon by the consultancy.

1. Based on the results of the completed and ongoing studies, pursuit of the main study was found to be justified and feasible; it was therefore

recommended to proceed with the remaining activities as planned under the WHO/EURO programme.

2. The studies performed in Finland, the German Democratic Republic, Norway and the USA were viewed as pilot studies; it was recommended that their results be used as a basis for development of the minimum core protocols.

3. It was recommended that the Core Protocols developed during the meeting be followed in detail, and that the questions concerning procedures, etc., especially on the part of new programmes, be referred to the appropriate reference laboratories.

4. It was recommended that the Coordinating Institute (Rigshospitalets Arbejdsmedicinsk Klinik, Copenhagen University Hospital, Denmark) act as a local reference clearing laboratory for both respiratory and non-respiratory effects, drawing on the experience of the individual reference laboratories previously identified.

5. It was recommended that each core protocol establish a quality control procedure; such procedures were essential to the success of any pooling exercise.

6. It was suggested that, for each study, the most highly exposed individuals, or groups of individuals, be chosen for study as this would maximize the likelihood of finding effects of exposure, if any.

7. It was recommended that standard forms for reporting of data and for establishing control values be followed so as to optimize the results of the data pooling.

8. It was recommended that the exposure monitoring protocol be harmonized with that being developed under the mortality study programme under IARC, and that the intermediate and final reporting of the mortality and morbidity programmes be closely coordinated to permit a joint evaluation of the health effects of welding and of welders' exposure to chromium and nickel.

IARC - WHO/EURO Consultation on Development of Epidemiological Studies on Health Effects of Welding Fumes in Stainless Steel Welders

ICP/CEH 540/Rev 2
4491i
18 March 1987

International Agency for Research on Cancer, Lyon, 17-18 November 1986

SUMMARY REPORT

1. Introduction

The Consultation, jointly organized by WHO/EURO and IARC, was attended by 22 participants from 11 European countries and the United States, and representatives of IARC and WHO/EURO.

Following the Copenhagen meeting of February 1985, a number of research projects which would investigate health effects of welders under the core protocol were identified. It was also agreed that pooling of mortality data should be conducted by IARC, Lyon, while coordination of morbidity studies, occupational and biological monitoring, etc., should be undertaken on behalf of WHO/EURO by the Joint Coordinating Institutes in Copenhagen (Occupational Health Clinic of the National Hospital and the Welding Institute). In order to share experience among principle investigators, it was agreed to convene a joint meeting of project participants at IARC, Lyon. The prime aim of this meeting was to review the progress and assess future needs of the mortality studies, and at the same time to establish firm interactions between the groups performing occupational monitoring and dose estimation, and the epidemiological projects.

2. Discussion

An initial plenary session, chaired by Professor Kilburn, was devoted to a brief orientation and review of the current status of the three project areas: 1. Historical mortality (cancer incidence and mortality) (Simonato and Fletcher); 2. Prospective morbidity (clinical) (Gyntelberg) and 3. Environmental and biological monitoring and experimental studies (Stern).

It was remarked that studies of negative health impact of welding were complicated by the heterogeneity of exposures, and by evidence of improved protection at work, so that exposures of 20-30 years ago, relevant to historical studies, were not necessarily to be found today. Furthermore, there was beginning to emerge some evidence that the effects of welding among nonsmokers were reversible (50% of functional impairment recovering after 2 years without welding exposure) while the effects of welding and smoking among smoking welders were not reversible (no recovery of impairment after exposure to welding stopped). The effects of welding fume were to be examined on a. upper airways; b. bronchial tree; c. lungs; and d. central nervous system. Exposure analysis was to be studied via occupational and biological monitoring. Health effects could be either acute or chronic, but in all cases should be studied by means of a simple standard protocol for clinical examination: these cross-sectional studies could only have meaning if performed prospectively. (CNS studies were perhaps of great importance because of the ubiquitous presence of potential sources of toxic effect (e.g., oxidants, Cr, Ni, Mn, Al), provided that neural, psychological or computer-driven tests were validated.)

Following the plenary session, three subgroups met to review current status concerning the historical mortality, prospective morbidity and environmental and biological monitoring. The final session on Tuesday morning was devoted to review progress, a discussion of future activities, and conclusions. After closure, a brief meeting of Group 2 with representatives of Group 1 was convened to establish a time, place and programme for a joint meeting with the intention of revision of the details of the morbidity, and biological and exposure monitoring protocols to achieve maximum compatibility.

3. Conclusions

The following conclusions were reached.

a. Mortality studies (historical)

Ongoing or completed studies were described in the summary report of Group 1 (Annex 1, Part 2). These studies which involve stainless steel and mild steel cohorts, will have a total of 14 000 welders in both categories, with an expected number of lung cancer deaths of 43 for those with stainless steel exposures and 60 with mild steel welding exposures. In each category, one half of the cases come from a single study. It is expected that the mortality studies will be substantially finished my mid-1989.

b. Occupational hygiene and biological monitoring studies

A number of projects specifically deal with problems of estimating historical exposures, and interpreting biological monitoring results in terms of delivered dose and exposure regimen, as follows:

Norway

A group of 25 stainless steel welders are followed from midweek to midweek. Hygienic monitoring: TWA with filter cassette placed outside the shield (5 days, full shift, cellulose acetate for total fume, PVC for chromium specification). Biological monitoring: blood analysis (Cr, Ni in whole blood, plasma, red blood cells) before and after shift; urine analysis (Cr, Ni first two daily samples, and last after shift); chemical, electron microscopic and solubility analysis of welding fume; sputum cytology; detailed questionnaire for exposure and job classification; and an interview and preparation meeting to ensure adherence to the protocol.

Finland

Analysis of lung retention of welding fumes in shipyard welders, and clinical studies of stainless steel welders (lung function, biopsy, respiratory symptoms, biological monitoring (1 week urinary chromium, plus effects of weekend and summer vacation). Laboratory studies of the kinetics, following a standard exposure to welding fumes, of Ni and Cr in urine and blood in 7 asthmatic welders, unexposed to welding fumes for several years, and with low basal Ni and Cr levels.

Observation of a rapid compartment (a maximum in urinary concentration after 1.0 h following a 30-minute exposure at 30 mg/m^3, 10% of the dose eliminated after 24%, an additional 10% in plasma).

These two studies indicate a correlation between exposure and urinary Cr only for high exposures, and emphasize the need for careful planning of biological monitoring protocols under working conditions to avoid random and uninterpretable results.

Denmark

Questionnaire-based study of 14 000 welders, 3 500 of which have ever worked on stainless steel. Development of a database consisting of 1 800 field measurements of TWA values (cassette behind welding shield) at numerous work places since 1975. This provides an information matrix with parameter dependence of exposure (process, filler material, dimensions, surface treatment, working conditions, ventilation, plant type, measurement type, etc.).

This study provides a unique basis on which to verify the correlation between questionnaire-based exposure index and actual TWA levels. It is planned to use the database to generate TWA levels based on questionnaires from other ongoing studies (French, Norwegian, German) and compare these values with those actually measured for the individuals in question.

Denmark

Project for screening of workplace carcinogens. Case control study of 100 welders/100 controls. Measurement of air pollution, biological monitoring (Cr, Ni in blood and urine) and cytology (CA, SCE, UDS, mutagens in urine, semen quality).

Denmark

Development of a process-dependent TLV value to replace chemical analysis by gravitational measurements alone, based on historical measurements of fume chemistry for specific processes.

Denmark

Quality control project for welding fume analysis among 11 participating laboratories. First round completed with results indicating several problems in some laboratories including contamination of Ni and Cr, and systematic errors in analysis of Fe and Mn. Second round underway. Development of a magnetopneumograph: observation that only 5-15% of welders accumulate significant quantities of welding fumes, regardless of exposure. Indicates wide individual variation in deposition and clearance. Suggests that high background levels of Cr and Ni in blood and urine might be due to a slow compartment in those individuals with large thorax burdens of welding fume, and that for these cases, the levels are independent of recent exposures, and remain high after exposure ceases.

Italy

Study of origin of uncertainties in fume analysis due to matrix effects. Development of a qualitative risk index, with estimates of uncertainty.

c. Morbidity studies

Four morbidity studies (FRA, GDR, HUN, USA) were described in detail, and two studies in Denmark identified. In general, these were complex clinical studies with an emphasis on the effects of stainless steel welding, as follows:

Hungary

30 shipyard welders, 200 assembly welders, xx aluminum welders to be examined and followed up in the period 1986-1996. Occupational monitoring for Cr, Ni, total fume, NO_x, Mn and Cr in urine, Cr in blood. Clinical studies of lung function, x-ray, etc.

German Democratic Republic

450 mild steel welders, 150 stainless steel welders, 450 controls. Estimate of effective exposure index through total fume, Mn in hair, or welding fraction per day (arc time). Observation of possible effects of early drop-out, and an age effect on pulmonary function which is identical to the exposure effect indicating very weak clinical effects of welding, in a preliminary analysis.

France

1 000 stainless steel welders, 1 000 mild steel welders, 1 000 controls. Environmental and biological monitoring (end of shift Cr and Ni in urine and blood); questionnaire for exposure and medical history; environmental monitoring, lung function measurements, x-ray; cytogenic monitoring of a 10% sample.

USA

Cross shift changes in pulmonary function for 200 highly exposed (worst case-closed space, no ventilation), 200 lightly exposed stainless steel welders, and 200 controls. Weekend, pre- and post-shift biological monitoring; possibility of both stationary and personal sampling.

Denmark

Studies of cytotoxic and biological monitoring, and semen quality and fertility.

Following presentation of the above projects, a discussion developed between the subgroups for biological and hygienic monitoring, and the clinical prospective studies focusing on several issues, as follows:

(i) The kinetics of Cr and Ni after inhalation of welding fumes is so complex as to require careful planning for biological monitoring protocol in any proposed prospective study. The need for the Norwegian and Finnish groups to guide the French, Hungarian and GDR studies was emphasized and an agreement reached on a rapid transfer of information, especially with respect to sources of contamination, sample preparation, and sampling schemes.

(ii) Differences in hygienic monitoring protocols, e.g., placement of filter cassette behind the mask, on the collar, or on the hand-held shield, may make intercomparison of exposure data difficult unless a specific attempt at harmonization and cross calibration is made. The question of the importance of measuring peak values (as suggested at the Copenhagen meeting) vs the usual TWA over a work shift must be resolved.

(iii) The Danish database is to be made available so as to permit any investigator to reconstruct expected breathing zone levels from questionnaires with adequate technical data concerning actual welding conditions. In a pilot programme, completed exposure questionnaires from the Norwegian study are to be given to Denmark, whereupon the expected breathing zone level will be calculated for each case. These results will be compared with the measured TWA values for each exposure, in a first verification of the ability to predict exposures from welding conditions. Eventually, the Danish database will be available so that individual investigators can perform their own calculation of the job-exposure matrix. A second activity is an attempt to determine if there are significant differences in the TWA exposures nationally, i.e., to establish if specific local welding practices lead to non-comparability of exposures.

4. Reconstruction of exposures for historical studies

A specific problem arises in historical mortality studies because of the need for classifying welders (lifetime) exposures. Although some countries have found it possible to establish working conditions and exposure levels on the basis of employee questionnaires, it was felt that since this could not be done for lung cancer cases, all historical studies should rely on the same employer-based questionnaire for exposure category assignment.

An enterprise-based questionnaire is under preparation, with the intent of permitting an expert group to establish exposure category either for individual workers, or for job categories or shop assignments (see enclosure). The details with which exposure must or should be established must be determined by consensus of the historical study group. In principle, one would like to be able to have a finely graded scale based on the questionnaire, although the ultimate use might be to establish only two subgroups (never stainless steel welding, and ever stainless steel welding), three exposure levels (<1 mg/m^3, 1-10 mg/m^3, >10 mg/m^3), and perhaps two frequency categories ($<20\%$ full time, $>20\%$ full time). The details should be worked out in advance, but the questionnaire should not limit the ultimate exposure classification to any great extent.

5. Conclusions

The following conclusions were reached.

1. There was unanimity with respect to the immediate need for a job-exposure matrix to serve the historical studies. This was to be prepared by SVC/IARC and be distributed for comments.

2. There was a need for a meeting of the morbidity (prospective) study groups and experts in biological and occupational monitoring, to establish final protocols for planned studies. A meeting is planned to be held in WHO/EURO, Copenhagen, on 9-10 February 1987. At this time, all protocols, methodologies and study aims will be finalized, and a timetable established for completion of the studies.

3. Current progress within the historical study group is such that a meeting in mid-end of 1988 would be realistic. At this time, one could essentially review both the effects of welding and the differences in the apparent effects of stainless vs mild steel welding.

ANNEX 1 - PART 2

16/XII/86

TF/az

SUMMARY REPORT:

COLLABORATIVE EUROPEAN STUDY OF WELDERS' MORTALITY AND CANCER INCIDENCE

Meeting of study collaborators in conjunction with WHO(EURO)

Biological Effects of Welding Fumes and Gases Working Group

17-18 November 1986, Lyon, France

<u>Present:</u> K. Anderson
N. Becker
N. Charnay
T. Fletcher
S. Langard
F. Merlo
J.-J. Moulin
M.L. Newhouse
J. Peto
L. Simonato
B. Sjogren
K. Stagis-Hansen
R. Winkelmann

The discussions of the historical cohort studies greatly benefitted from discussions with the other scientists present, conducting studies on respiratory morbidity, biological monitoring and environmetnal assessment. The hygienists in particular were helpful on the question of historical exposure assessment.

It was decided to:

1. go ahead with the pooling of the data for an agreed analysis of the pooled data to be carried out.

2. To establish a checklist of welding conditions that can form the basis of a questionnaire for each company, to allow allocation of jobs/individuals to different exposure categories for the analysis.

Below are summarized:

- the nature of each cohort,
- the issues discussed in the meeting,
- the agreed timetable.

Cohorts in the study

Investigators from nine countries are willing to contribute their data to the pooled analysis. In one case (Norway) delays in the data availability mean that they will most probably not be able to participate in the 2 year programme of data pooling. In addition, data from the U.S. may be available some time in 1988, but it may be too late for the time schedule as agreed. For these reasons these two countries have been excluded from the Tables summarising the data: Table 1 summarises the cohort sources and size and Table 2 the expected numbers of lung cancer deaths and the availability of smoking data for cohort members. The expected values are derived from the true expected deaths up to the end of follow-up shown or, for 3 studies, they are estimated assuming a similar age structure as the equivalent national cohort in the European MMMF study.

Denmark - Dr K. Staqis Hansen, Odense

90 factories known to be carrying out welding have been included in the study. Occupational histories have been assembled using company records and questionnaires to foremen and/or work colleagues, the workers pension register which lists employees since 1964 and questionnaires sent to individuals or telephone interviews of the next of kin. The questionnaires attempt to

estimate lifetime employment and smoking behaviour. Job categorisation relies primarily on the questionnaire for the living and colleagues/foremen for the deceased. Response rates have been in excess of 80% to the questionnaires/-interviews. Linkage is being made to the cancer registry, death registry and patients registry (for hospital admissions). The cohort definition is at least one year of employment 1964-1984. Follow-up is complete to 1984 and the numbers are as follows:

	Number	Dead
Mild steel welder	2040	134
Stainless steel welder	3228	134
Stainless steel grinder	588	61
Controls (other production)	3711	404
No information	787	98
Total	10354	831

England - Dr J. Peto, Dr K. Anderson, Dr M. Newhouse

18 factories have been enrolled in the cohort and it is hoped to increase the number to 25. The criterion of inclusion is at least 5 years employment with job title "welder" in employment or wages department records, up to 1970. This provides a minimum of 15 years follow-up but for a substantial minority, the follow-up is a maximum of 20-25 years since first employment in these factories. Numbers are estimated as 600 stainless steel, and 600 mainly mild steel (although some of these may have mixed exposures). Follow-up should be complete to about 9 months prior to data submission. A questionnaire circulated to current employees is being considered, to evaluate current smoking prevalence and the pattern of lifetime employment reported by welders.

Finland - Dr S. Tola

Dr Tola could not attend the meeting but he provided a paper describing the results of a follow-up for cancer incidence of the Finnish welders cohort up to December 1981. It is hoped that the follow-up of this population may be extended. The population comprises workers from 4 machines shops and 5 shipyards as follows:

	Welders	Platers, machinists and pipefitters
Shipyards	1308	6467
Machine shops	381	4537

The welders are all mild steel and the results of the analysis show 14 observed versus 10.4 expected lung cancer cases among the machine shop welders and 27 observed versus 23.5 expected for the shipyard welders. In addition an excess incidence of prostate cancer (14/6.8) was noted as present in both groups of welders. The welding exposure has been MMA with a change-over to MIG during the 1970s in the machine shop population; asbestos was used in the shipyards during 1955-1970. A smoking questionnaire was distributed to a stratified sample of the living (81% of 749 replied) and relatives of deceased (77% replies from 212), which revealed no substantial differences either between subcohorts or between the study population and the general population.

France - Dr J.-J. Moulin

Four factories are currently in the study although it is hoped to be able to included further factories. The cohort is defined as those employed at the end of 1975 or beginning of 1976 (this varies slightly between factories), and these have been followed up for mortality until 1985. From other production workers in the same factory, 2-3 controls per case, matched on sex and year of birth have been selected. Smoking data is available from the medical department records. The cause of death can only be established by contacting the physician of the deceased individual, which although this may not always give exactly the same diagnosis as was entered on the death certificate, is considered sufficiently accurate for a disease such as lung cancer. The numbers are as follows:

	Number in cohort	Expected deaths	Expected lung cancer deaths
Stainless steel	440	20	1.6
Mild steel	600	27	2.2
Controls	2560	116	9.1

Germany (Federal Republic of) - Dr N. Becker

The cohort comprises 1221 stainless steel welders and 1624 production worker controls employed before 1970 in 25 factories. The follow-up until 1982 has already been published (Becker et al, Scand. J. Work Environ. Health (1985) 11, 75-82) and there were 6 observed lung cancers, 6.3 expected among the welders. The type of welding and nickel content of parent material and smoking status has been characterised at an individual level. The factories include producers of power plant and nuclear power plant equipment and pressure vessels for the chemical industry. Welders must pass 2 yearly examinations to retain the stainless steel welder's qualification. It should be possible to extend the follow-up but this would necessitate contacting relatives and doctors as the previous method of linkage has now been restricted by a change in the law. IARC may be able to help by writing to the relevant ministry supporting the value of this kind of research.

Italy - Dr F. Merlo

Two companies are included in this cohort, one manufacturing tanks and the other including shipyard welders. The population is being followed up to 1986. The data is being collected and it is estimated that the final population will comprise 500-700 stainless steel and 2-300 mild steel welders. Smoking data is being collected from currently employed welders. Hygiene measurements are available since about 1979 along with Cr in air and Cr in urine.

Sweden - Dr B. Sjogren

Factories excluding those with significant asbestos exposure were selected and welders with at least 5 years' employment were recruited into the cohort. The selection was carried out by foremen or long-service welders, and two cohorts were established. One of 234 stainless steel and one of 208 mild steel welders. The results of a follow-up until 1977 of the stainless steel welders (from eight companies) was published in 1980 (Sjogren et al. Scand J. Work Environ. Health (1980), 6, 197-200). The follow-up is now complete until 1984 and there are 5/2.0 lung cancers in the stainless group and 1/3.0 in the mild steel group. Smoking data has not been collected for the cohort.

Norway - Dr S. Langard

The original intention to include 4 shipyards in Eastern Norway in this cohort has not been achievable because lack of ship orders has led to partial or complete shut down of these yards. They may be included in the future if funds can be found to support the data extraction. The personnel and wages records have to be kept for 40-50 years. However it is hoped to be able to establish shortly a cohort from 2 yards on the West coast, both employing between 1000 and 2000 workers and both of which were quite small until one expanded in the 1950s the other in the 1960s. It is estimated that it will take 2 years to extract the data and then not long to process the data and thus late 1988, early 1989 would be a feasible time to be able to make the data available for pooled analysis. There should be about 1500 welders including 5-600 stainless steel welders with at last 5 years experience on which the analysis should be concentrated.

POINTS RAISED IN THE DISCUSSION

Aim of study

The primary aim of the study is to quantify the level of risk associated with welding in the absence of confounding by asbestos or smoking, and to evaluate how this differs between mild steel and stainless steel welding. A related question is to identify high exposure/high risk subgroups in either of these exposure groups.

A second aim would be to investigate other causes of death for which there have been some suggestive findings in studies of welders already: non-malignant respiratory disease, nasal and larynx, kidney and bladder cancers. In addition, other causes of death will be investigated such as leukaemia because of the link to some electrician's jobs with exposure to electric fields.

Date of end of follow-up

Most of the cohorts can be followed-up to 1985. This implies increasing the follow-up of those that have been published. The only problem may be in Germany where follow-up is now more difficult than previously. Thus the numbers of expected deaths may be larger than the total estimated in Table 2.

Power of the study to detect excess risk

The total estimated numbers of expected lung cancer cases are 40 and 60 for mild steel and stainless steel respectively. The overall power to detect a two-fold excess risk (significant at 5% level - one sided test) is better than 99.9% for both subcohorts, and to detect a risk of 1.5, the power is 90% and 95% for stainless and mild steel respectively. It was agreed desirable to try and include any other studies that may be available but in addition to the Norwegian (SS) and USA (MS) cohorts no other suitable cohort studies were currently known.

Exposure assessment

It was felt quite viable to be able to separate mild steel and stainless steel welders sufficiently to make a comparison between them. What was doubted was whether individuals could be assigned to categories implying different cumulative doses to either total fume or chromium. This related to two problems, that of assessing known exposure and the relevance of the exposure known in one plant to the biologically relevant total lifetime exposure to welding fume. This second point is discussed in the next section. In the Danish, Finnish, Italian and Swedish cohorts, the technological history of the study factories has been characterized. In addition in the Danish and German cohorts, each individual's type of welding work has been characterised for the lifetime and single factory employment, respectively. In the English and French cohorts systematic collection of the historical exposure patterns by factory is to be carried out shortly. It was agreed desirable to establish

1) a checklist of key parameters (type of welding, size of workspace, etc which could be used by each investigator to collect a standard useful set of background data on the welding technological history of each factory. This information may be obtained by using data already collected, establishing a new interview or a bit of both depending on local

circumstances. An interim version is appended to this report.

2) a list of workplace factors which would allow identification of a high fume exposure subgroup to be used to identify a priori high risk subcohorts. After further discussion it was agreed to attempt to establish a Job Exposure Matrix, drawing on hygienists' expertise, and making some use of an extensive data base developed by Dr Beck-hansen. This would be a means of converting the information derived from each company into an exposure index: for example high/med/low or <1, 1-10, >10 mg/m^3.

Sources of data on employment

The Danish cohort has data on total lifetime employment as a welder, though with the potential problem of non-comparability because the living reported their own history and the deceased person's history is mainly estimated by work colleagues. With few exceptions the rest of the cohorts have only the employment category in the index factory, employment in which placed them in the cohort. Because of the uncertainly as to whether employment in one type of welding job would be necessarily representative of previous and subsequent employment it was suggested to firstly see what kind of stability in type of welding exposure was found in the Danish cohort, and to secondly consider a questionnaire survey of current employees to ask them about previous employment (as well perhaps as smoking). The problems of comparability of sources of employment history data would render invalid a pooled analysis by duration of employment of all the cohorts together.

Non-welding exposures

Although the cohorts contain few shipyard welders where exposure to asbestos was considered to be sometimes very high, it is still not clear if the levels of exposure to asbestos from gloves, blankets etc, may be sufficient to be a significant confounding factor, so the checklist of questions should address these exposures for subsequent evaluation by a hygienist.

Data on smoking in the cohort itself is being collected for 3 cohorts and for a subset (usually current employees) for 3 more cohorts. While some doubt was expressed as to whether these data may be valid enough to be able to investigate the risk of welding in smokers and non-smokers separately, some analysis along these lines will be attempted.

More detailed investigation

The desirability of collecting more data on a subset of the cohort: the cases, cases and controls within the cohort, the most highly exposed, or cases in the cohort and population controls was suggested, but no agreement on a coordinated approach was reached . The extra information would comprise in particular, more detailed occupational history during employment in the plant and before, and smoking data.

The protocol

The protocol for supplying data to IARC was considered and some modifications were suggested: to allow the simultaneous inclusion of more than one description of a welding process as some workers spent part of the week on one and part on the other; to change the qualitative proportion of time to a quantitative figure; to allow the inclusion of some intensity of exposure estimate (although subsequent discussion on exposure assessment made it clearer that this was better handled at a plant level); add plasma cutting to job titles. This and other modifications will be included by IARC and circulated for comment before the end of the year.

TIMETABLE OF WORK

Exposure assessment

The checklist will be finalised by IARC hygienists (M. Gerin/A. Tossavainen) in consultation with other hygienists and then circulated to the study collaborators for comment by the end of this year. The same group will investigate the possibility of a formal job exposure matrix relating exposure intensity to the checklist parameters.

Deadlines for data supply, analysis and publication

June 1987 was agreed as a target date for the supply of most cohorts' data, with or without final vital status/cancer registration.

The final complete cohort data will be supplied to IARC by the end of 1987.

IARC will carry out data quality checks after receipt of each tape and the analysis in early 1988. The types of checks anticipated were discussed at the meeting as was the kinds of analysis. The detail of the analysis depends on what kind of exposure categorisations can be developed over the coming months, and will be agreed in writing in advance of being carried out. It is anticipated that all collaborators will meet in early to mid 1988 to consider the preliminary results and final analysis and again at the end of the year to agree the final results, conclusion and joint publication.

Table 1. Summary of data for each national cohort (figures in parentheses are estimates)

Country	— Size of cohort Stainless	Mild	Reference	Type of cohort
Denmark	3228	2040	3711	Welders plus other workers from 90 factories employed >=1 year who had not left before 1964
England	(600)	(600)	-	Welders in 18 (perhaps up to 25) factories employed >=5 years before 1970
Finland	-	1689	11004	Welders in 4 machine shops and 5 shipyards employed > 1 year. Controls were platers machinists and pipefitters.
France	440	600	2560	Welders in 4 factories employed at beginning of 1976. About 3 age matched controls per welder from same factories
Germany	1221	-	1624	Welders in 25 factories employed before 1970
Italy	(600)	(250)	-	Welders in 2 factories
Sweden	234	208	-	Welders in 8 factories identified by colleagues as employed >=5 years
Total	6323	5387	18899	

Note: Norway is excluded from this table as delays now mean that the cohort will not be ready in time

Table 2. Follow up, expected lung cancer deaths (estimates in brackets) and smoking data

Country	End of follow-up	Expected cases SS	MS	Smoking data collected
Denmark*	1984	(20)	(13)	Entire cohort by questionnaire
England	1985	(7)	(7)	Perhaps for currents
Finland*	1981	-	33.9	Sample of cohort by questionnaire
France	1985	1.6	2.2	Entire cohort from medical records
Germany*	1982	6.3	-	Entire cohort by questionnaire
Italy	1985	(3)	(1)	Currents
Sweden*	1984	2.0	3.0	No
Total		40	60	

*It is hoped to extend these dates of end of follow-up to 1985 and then revise upwards slightly the expected deaths

16/XII/86

TF/az

COLLABORATIVE EUROPEAN STUDY OF WELDERS MORTALITY

AND CANCER INCIDENCE

Draft protocol for supply of data

This protocol gives a form for standard organisation and presentation of the data for submission to IARC on computer tape for the joint analysis of the data.

Investigators in each country will need for the purpose of establishing vital status, individual identification data for individuals such as name, address, date of birth, sex, social security number or national registration number. Of these only sex and date of birth are necessary for the analysis and thus to ensure confidentiality, unique identity numbers should be assigned to each individual in the cohort by the investigator. These consist of the codes for country (1 digit) then cohort (2 digits) then a running number (0001 to 9999) to specify each individual.

To avoid problems of bias the cohort assembled for follow-up and analysis should completely represent all people ever employed in the job categories being investigated. If for any reason this is not met (for example only those employed at least one year) these restrictions must be clearly described and the completeness of the cohort within these criteria evaluated by the local investigator.

Accompanying the data, investigators will be asked to complete a questionnaire on the population, and the method of follow-up: description of the study population, sources of the data, dates of starting and stopping activity of the employer, dates within which follow-up is complete, method of establishing vital status and cause of death, the periods covered by each ICD revision used.

While most of the information described below is essential for the analysis of the cohort, it has to be recognised that some information may be missing for some individuals and provision is made for coding such "missing data". Individuals should not be excluded from the cohort because of such missing data. Some information may be desirable but not available; for example smoking histories may be available for no members of a cohort, and in this case the data fields for such data should be left blank.

The occupational history (by which is meant the occupational history in the company records) should be as complete as possible, listing all job periods with as specific a job code as possible. The simple categories of welder and non-welder may be expanded if more detailed codes can be specified for particular cohorts; in this case a detailed description of the job titles in each job category should be supplied to IARC. Where possible, individuals should be assigned exposure categories according to the degree of stainless steel exposure and welding technology used.

The data to be supplied on record types 1-4 represent the extent of data that should be available for a reasonable proportion of all the eligible cohorts.

The data is stored and managed in "SIR" Scientific Information Retrieval, a database management system where the data are stored hierarchically in a structure as follows, with records containing data at each level:

- For each individual there is one record type 1 giving personal data such as date of birth, and one record type 2 with vital status
- For each individual there is at least one record type 3 describing the occupational history (in the company records). For each period of unbroken employment in one occupational category, there should be one record. Each change of occupational, or work area category means another record.
- For each individual there may be one or more records type 4 describing cancer registrations. With no record if there are no registrations.

The data on these 4 types of records for each individual are to be submitted to IARC on computer tape using the format described on the following pages.

Type 1 Individual identification, with date of birth, employment status, dates of first and last employment and smoking habits if available.

Type 2 (multiple record) occupational history, with for each job period, dates of start, stop and coded occupational/exposure categories

Type 3 Vital status, with vital status, date of death or loss to follow-up and cause of death

Type 4 (multiple record, optional) cancer registration, with date of registration, site and histology.

The data should be supplied on a computer tape:

The records should be of fixed length (equivalent to the longest record length used) with the records (1 then 2 then 3 then 4) for each individual grouped together. The tape should be unlabelled of density 800, 1600 or 6250 bpi, in EBCDIC or ASCII code, blocked by any reasonable factor (up to a maximum block size of 32760). Please mark the tape with a label specifying the character code, density, record size and blocking factor.

Record Type 1 (one per individual): <u>Identification</u>

Information	Column	Code
1. Record type	1	~~2~~ 1
2. Individual identification number	2-9	
a) Country	2-3	code supplied by IARC
b) Workplace	4-5	code supplied by IARC
c) Sequential identification Number	5-9	Defined by local investigator
3. Date of birth	10-16	
Day DD	10-11	99 = unknown
Month MM	12-13	99 = unknown
Year YYY	14-16	999 = unknown
4. Sex	17	1 = male 2 = female 9 = unknown
5. Date of first employment	18-24	
Day DD	18-19	99 = unknown
Month MM	20-21	99 = unknown
Year YYY	22-24	999 = unknown
6. Date of leaving employment	25-31	Blank if still employed
Day DD	25-26	99 = unknown
Month MM	27-28	99 = unknown
Year YYY	29-31	999 = unknown
7. Employment status at data collection	32	1 = if currently employed in company at time of data collection 2 = left 9 = unknown

8. Smoking status	33	Blank if unavailable for whole cohort, else: 1 = smoker (cigarettes) 2 = exsmoker 3 = never smoker 4 = piper/cigar smoker 9 = unknown
9. Race (optional)	34	Blank if unvailable for whole cohort, else: 1 = indigenous 2-8 = optional code for specific ethnic groups defined by local investigator 9 = unknown

Record type 2 (Multiple) <u>Occupational History</u>

Information	Column	Code
1. Record type	1	32
2. Individual Identification number	2-9	
3. Date of start	10-16	
Day DD	10-11	9 = unknown
Month MM	12-13	99 = unknown
Year YYY	14-16	999 = unknown
4. Date of stop	17-23	
Day DD	17-18	99 = unknown
Month MM	19-20	99 = unknown
Year YYY	21-23	999 = unknown
5. Job title	24-25	
General category	24	1 = welder 2 = plasma burner 3-8 = other job may be defined (eg caulker, rivetter) 9 = unknown
More detailed job code	25	0 if not used Else, local codes for more specific job coding to be defined by local investigator, eg department code 9 = unknown
6. Welders exposure category	23-27	
a) Type of metal welded	23	1 = stainless steel 2 = mild steel 3 = non ferrous only 9 = unknown

b)	Welding technology used	24	1 = mixed 2 = MMA 3 = MIG 4 = MAG 5 = TIG 6 = Gas welder/cutter 7 = Burner/Gouger 8 = Other 9 = unknown
c)	Proportion of working time exposed. This is the proportion of time being eg an MMA welder compared to being burner/ cutter or other, non-welding tasks; this is <u>not</u> the arcing time.	25-27	Give percentage 999 = unknown

7. Repeat as for 6 in columns 28-32 if there is a second concurrent exposure.

Record Type 3 (one per individual): <u>Vital status</u>

Information	Column	Code
1. Record type	1	23
2. Individual identification number	2-9	
3. Vital status	10	1 = alive 2 = dead 3 = lost to follow-up 4 = emigrated
4. Date of death, loss to follow-up or emigration	11-17	Blank if status = 1 (alive)
Day DD	11-12	99 = unknown
Month MM	13-14	99 = unknown
Year YYY	15-17	999 = unknown
5. Cause of death	18-21	Blank if status NE 2, if status eq 2 and death certificate missing = 9999. (For violent causes use "External cause")
6. Revision of ICD	22	Blank if status NE 2

Record Type 4 (Multiple, optional). Cancer Registration

Information	Column	Code
1. Record Type	1	4
2. Individual identification Number	2-9	
3. Date of Registration	10-16	
Day DD	10-11	99 = unknown
Month MM	12-13	99 = unknown
Year YYY	14-16	999 = unknown
4. Cancer site	17-20	9999 = unknown
5. ICD Revision number	21	
6. Histology	22-25	ICD-O codes 9999 = unknown
7. Diagnostic Evidence	26	1 = histological confirmation 2 = cytology 3 = autopsy without histology 4 = exploratory surgery without histology 5 = X-ray only 6 = clinical only 7 = death certificate only 9 = unknown

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INSTRUCTIONS FOR HYGIENISTS IN THE IARC COLLABORATIVE WELDING FUMES EPIDEMIOLOGICAL STUDY

The hygienists in the study have the task of eliciting from the companies historical information on their welding activities (Part 1) and of summarizing the information so that it can best be used for an overall exposure assessment (Part 2).

Where individual exposure (type of welding, SS or MS etc.) can be defined this data will be incorporated in the data base. However for many if not most factories in the study such individual exposure will have to be inferred from an appraisal of the history of each factory, combined with the dates of employment taken from company records for each cohort member. In broad terms the analysis of the cohort is intended to make use of subgroups of the population defined by their probable exposure at a qualitative level (e.g. ever/never stainless, MMG vs MMA etc.) and a semiquantitative level. The quantitative approach would involve the a priori assignment of exposure configurations (parent metal/welding technology/degree of confinement/-ventilation) to categories of total fume exposure (<1 mg/m^3, 1-10, >10 mg/m^3) and chromium fume exposure (<1 ug/m^3, 1-10, > 10 ug/m^3).

To enable the hygienists in the study to assign exposures to subgroups in a factory, in a systematic way across factory (many of which may have only one or two characteristic exposure situations) and across country it will be necessary to have a historical summary for each factory and a summary table as explained below.

1. COMPANY INFORMATION

The following is a list of items of information that should be gathered from each company. It is not a questionnaire to be sent and filled in by company officials but rather the backbone of an interview or series of interviews between a hygienist (or equivalent) sufficiently knowledgeable in welding and company personnel knowledgeable on the historical development and technical details of welding in their firm (e.g. foremen, long service welders, personnel officers, separately or in group).

There are three main groups of questions, relating to the company in general, its workforce and its welders. Each item has to be evaluated historically; any significant change should be noted with the relevant dates. The main interest lies not in recent data, the most easily accessible, but in past data that could go back to the 1940's for some companies.

1.1 General information on the company

- Company: name, address
- Description of activities:
  - history of company
  - branch of activity (e.g. construction, manufacturing, transportation)
  - manufactured products (main, secondary, quantities, tonnage)
  - processes used (all processes, not only welding)
  - materials used (metals, alloys, raw materials, other products, quantities, tonnage)

1.2 Description of the workforce

. Non-welders:

- types of workers, numbers, turnover

. Welders:

- types of welders by process and numbers (e.g. oxyacetylene welders, cutters, arc welders of various kinds, gougers), turnover
- types of welders by metal most frequently welded, and numbers
  * mild steel
  * stainless steel
  * other metal (detail)

. Lay-out of workplace:

- relative location of departments, shops, processes

1.3 Description of welders and welding activities

For each welding process (e.g. MMA, MIG, TIG ...), same as in 1.2:

- dates
- description of tasks/ % time spent in tasks other than welding
- base metals welded, proportion of SS, of MS
- types of electrodes or rods (number) and average consumption per welder per day
- outdoors vs indoors
- if indoors:small confined space (e.g. pressure tank, small compartment) vs regular shop, % time
- presence of local ventilation (at source), other type of ventilation
- personal protection effectively worn (respiratory)
- passive exposure to asbestos (through gloves, aprons...)
- process exposure to asbestos (use in the company)

- bystander or active exposure to sand blasting, solvents, paints, primers, grinding
- other welding processes at close proximity

1.4 Access to industrial hygiene surveys

- done by company hygienists or contractors
- done by government agencies and available at the company

2. PRESENTATION OF INFORMATION

Information relating to welders should be summarized in a tabular form describing the historical evolution in the use of various processes (see sample table attached). Each line should represent a homogenous exposure situation (HES) (see below) and its historical development expressed as the estimated percentage of study welders or of study welders' time when some welders share more than one HES in that situation. An HES should group together workers believed to be exposed on the average to approximately similar levels of the same substances. This would result essentially from the use of the same welding processes, on the same metals in a similar environment: indoors, outdoors, confined, respiratory protection and ventilation. Depending on the evolution and size of the company there could be one or several HES's. The proportion of welders or workers should add up to 100 in any given period of time.

COMPANY SUMMARY TABLE

HES number	TASK	PROCESS						METAL			CONDITIONS			% of welders			
	TASK	MMA	MIG	TIG	MAG	OXY	?	MS	SS	?	IND	CONF	NO LOC VENT	1940	1950	1960	1970
1																	
2																	
3																	
4																	
5																	

OTHER EXPOSURES (Indicate yes/no, HES number and years)

- asbestos
  - . casual (gloves, aprons...)
  - . process
- grinding dusts
- solvents
- paints, primers
- sand blasting

Employer (enterprise) based exposure questionnaire.

The questionnaire can either be prepared for each employee, or for a job-classification and shop assignment, covering all employees in the time period of interest. If based on an individual, it should follow employment, giving dates of entering and leaving each assignment. For an enterprise, it should give a historical development of the overall pattern of job and shop assignments of welders.

1) Industrial activity.
In order for the expert group to establish a general picture of exposures it is necessary to classify each enterprise as follows: Industry branch(construction, transport, assembly repair etc), types and amounts of products, raw materials and quantities, welding and non-welding processes, shop inventory where welders work.

2) Workforce.
Size of welding and non-welding workforce. Number of welders for each process and application, turnover.

3) Welding activities.
For each welding process (including automatic welding) or for each welder if an individual is followed: separately for stainless and for mild steel welding; task description or job assignment, dates for starting and stopping, proportion of all welding, hours per week welding, rods, materials used (dimensions, types, trade names etc.), welding parameters (current, voltage), productivity (arcing time, kg weld metal per man(year)) provision for ventilation (natural, shop, point extraction, forced ventilation), provision for personal protective equipment, bystander exposures (other activities), specifically asbestos, sandblasting, grinding, solvents, paint, primers, other welders and their processes, shop layout.

4) Asbestos.
The historical use of asbestos must be specifically determined.

5) Specific exposure questions.
Do welders work (or has the individual worked) in small, confined, small confined spaces. If so, how long and how often? Hard surfacing; flame, plasma spraying; gouging? Outdoor welding? Have hygienic monitoring measurements been made? If so, where, when, details of levels, shop background, variation in exposures with time.

The questionnaire can either be designed as a guideline for an informal interview with shop foremen or shop stewards, or can be formally designed for coding and data entry with a list of specific questions (see core protocol for such a formal list). One could also devise separate questionnaires for shipyards because of the specific shop inventory found.

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In reply please refer to : WH/92/2
Prière de rappeler la référence :

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IARC, Lyon, 17-18 November 1986

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ВСЕМИРНАЯ ОРГАНИЗАЦИЯ ЗДРАВООХРАНЕНИЯ
ЕВРОПЕЙСКОЕ РЕГИОНАЛЬНОЕ БЮРО

ANNEX 2

Consultation on Health Hazards and Biological Effects of Welding Fumes and Gases

Copenhagen, 9-10 February 1987

ICP/CEH 540/5/Rev 2
4425i
16 February 1987
ENGLISH ONLY

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ANNEX 3

MINIMUM CORE PROTOCOL - OCCUPATIONAL EXPOSURE MONITORING

1. Breathing zone sampling

   a. sampling behind the face shield*
   b. filter located in the shield at the same side as the work hand

2. Sampling procedure

   a. 6-8 hours (1 or successive samples according to protocol), afternoon shift to correlate with post shift urinary Cr/Ni
   b. airflow 1.25 m/s in the filter inlet
   c. cellulose acetate 0.8 my (total fume) or/and PVC (Cr VI) 4 my filters

3. Exposure data

   a. total fume concentration
   b. total Cr (Cr VI, water solub.) CR VI total
   c. total Ni
   d. procedures for laboratory controls to be followed

4. Sampling record

   a. welding process or processes (% time in each process)
   b. base materials
   c. filler materials
   d. surface coatings
   e. welding parameters, Amp, Volt, AC/DC, position
   f. location (work situation): open, semi-, confined
   g. ventilation
   h. welding time (if possible, arcing time)
   i. other activities
   j. for TIG-welding, both personal sampling and BG-sampling necessary

* study: correction factor for sampling outside/inside shield

ANNEX 4

MINIMUM CORE PROTOCOL - BIOLOGICAL MONITORING

1. Extent and sample size

a. For acute effect studies

U-Cr, Ni - before shift and after shift on two consecutive days. The "before shift" urine sample should be from the second void in the morning.

Wanted, but not as a minimum requirement, is U-Cr, Ni on a Monday morning with B-Cr, Ni; S-Cr, Ni and Er-Cr taken at the same time as the urine sample.

Sample collection should be performed on the same day/days as the exposure monitoring.

b. For semi-acute and chronic effect studies

U-Cr, Ni on a Monday morning (second void in the morning) and previous Friday after shift.

B-Cr, Ni; S-Cr, Ni and Er-Cr on the same Monday morning and Friday as the urine samples are collected.

For follow-up studies, this sample collection should be done four times a year, including before and after long vacation with sample collection before and after shift on the last day before vacation and before and after shift on the first day of work after vacation.

2. Exposure recording

A questionnaire should be used to collect the needed information of previous and actual exposures.

3. Collection procedure

Urine sample: polyethylene or polypropylene bottle specially washed, at least 50 ml bottle.

The morning urine should be collected before work and in private clothing to avoid Cr and Ni contamination from work clothing.

The after-shift urine sample should be collected after work clothing has been taken off and the welder has taken a shower.

Blood sample: venous blood samples of 10 ml should be drawn into venflow or with a type of needle that has been controlled for chromium and nickel release. The first 10 ml should not be used for Cr and Ni determination.

The blood should be collected in polyethylene or polypropylene tubes. Blank controls of collection tubes should be done as a routine.

Haematocrite must be taken both in whole blood and erythrocyte suspension.

Urinary density and creatinine should be determined. Collect blanks for urine as well as for blood.

4. Analysis procedure

Analysis of chromium and nickel in urine and blood as recommended in WHO/EURO Interim Document 15, Health Aspects of Chemical Safety, Part 1, Annex 3 (p. 131-194). Recommended quality control is included in Annex 3. Internal and external quality control should be done as a routine.

5. Control persons

Unexposed control persons should be used when performing biological monitoring on SS welders. These should be matched as to sex, age, smoking habits and also living area, if possible.

U-Cr, Ni and B-Cr, Ni, S-Cr, Ni and Er-Cr should be measured at least one day in the morning or afternoon as for the welders. Urine and blood samples should also be collected on a Friday afternoon and the following Monday morning.

A questionnaire on previous exposures and actual exposures should be used for the controls.

The number of controls will depend on the number of welders studied, e.g., 100 welders - 10 control persons; 20 welders - 5 control persons.

NOTE: It is strongly suggested to consult the reference laboratory to verify procedures for collection and analysis before proceeding with a monitoring programme.

ANNEX 5

MINIMUM CORE PROTOCOL - RESPIRATORY FUNCTION MONITORING

The questionnaire should include:

1. Cigarette smoking (WHO/EURO Interim Document 15, p. 179, questions 1-6)

2. Bronchitis questions (WHO/EURO Interim Document 15, MRC, p. 177)

3. Dyspnea questions (WHO/EURO Interim Document 15, as on p. 177)

4. a. Have you ever had attacks of wheezing accompanied by shortness of breath or chest frightness?

   b. Is your breathing normal between such attacks?

5. Nasal and upper airway symptoms especially dryness, obstruction

Although an inventory of symptoms occuring during welding is possible the difficulties in interpretation do not allow a recommended form. Inventories are useful in clinical follow-up and in evaluating the same person after changes in work process or hygiene measures.

To assess the chronic respiratory effects of exposure to welding fumes and gases expiratory forced vital capacity should be measured with a device capable of recording 7 liters which preserves the full curve duration to permit measurement of FEV, and flows FEF 25-75 and FEF 75-88. Welders should be measured standing or sitting upright with a nose clip. Smokers should refrain from smoking for a period of at least one hour prior to measurement. Spirometers should be calibrated frequently for volume and time. It is desirable to measure diffusing capacity for carbon monoxide, single breath to obtain also alveolar volume. A new infrared CO meter from Japan is more satisfactory than previous devices. Measurement of total lung capacity is suggested. For field studies, planimetry of posteroanterior and lateral chest radiographs produces a total lung capacity which is accurate so long as radiographs were obtained in full inspiration. Original measurements should be retained on each individual together with height, age, weight and ethnicity. In this way, comparisons to various predicted or control on measurements can be made and comparisons made over time. ?Provide standard national (or local) values for control.

ANNEX 6

MINIMUM CORE PROTOCOL - NON-RESPIRATORY EFFECTS

Chromosomal aberrations and SCE:

In design: adjust for age, smoking habits, sex.

Adjustment can only be done by matching because sampling and analysis must be carried out at the same time.

Blood sampling technique

Venous blood sampling should be carried out in heparinized vacuutainers. Extra heparin may be necessary due to storage over night. The blood must be kept sterile. At time of sampling, ask about medicine, X-ray, infection and alcohol intake.

Cell culture technique:

Consult reference laboratory.

Same technique during the whole study in detail: controls and welders are always analysed in the same batches.

Chromosomal aberration culture time: 48-53 hours

Important: selecting the time with most cells in first division in culture.

SCE culture time: 61-72 hours.

Important: selecting the time with most second cell divisions.

Scoring: Studies must be coded and scored blindly. One observer should be preferred, if not, control system must be used.

Important that matched pairs are scored by one and by the same observer.

The number of cells scored should be at least 100 (chromosome aberration) and for SCE 30.

If more than one culture is scored, take equal number of cells from each culture!

Classification: Consult reference laboratory.

Statistical method: Wilcoxon's ranking test and Fischer-Irvin's exact test.

Sperm analysis

Use WHO method (1980), Singapore: Press Concern, 1980.

Important problem: adjust time from sampling until analysis.

Ames test

Sampling

Fixed time in relation to exposure. Minimum sampling size: 50 ml. Clean sampling, but not sterile.

Analysis

Same procedure during the whole study. Matched pairs should be analysed simultaneously. Always two control analyses.

Scoring

Positive test definition:

1. more than twice the background level in one plate; or
2. more than 1.5 times the background level in two or more plates.

Remember adjustment for:

- volume;
- density;
- creatinine in urine sample used.

Sampling procedure for detection of nasal mucosal changes by exfoliative cytology

1. Mucous covering the nasal mucosa may be removed by carefully rinsing the mucosa with physiological saline (0.9%) on a cotton swab under examination.

2. Anaesthesize the mucosa for some minutes using a 1.5% tetracain - 0.1% adrenalin solution (spray or carefully use gaze or a cotton swab).

3. Brush gently with a small cylindrical interdental brush (1.2-1.5 cm length) mounted on a handle.

4. Wipe the brush immediately off on a slide and fix within seconds with a cytological fixative solution (commercial spray).

5. Stain the specimen according to the Papanicolaou method before examination.

Remarks

1. This sampling procedure is not painful. Without anaesthesia, the individuals will feel only a brief discomfort in the nose. When the access is sufficient, anaesthesia may be omitted. However, the anaesthesia decongests the nasal mucosa, thereby improving the access to the nasal cavity structures, and is therefore recommended.

2. Airborne toxins and carcinogens are preferentially deposited on the anterior part of the middle nasal turbinate. Pathological changes are therefore more often found in this region and it is thus the most important one when cytological samples are taken.

3. It is very important that drying of the smears is avoided since air-drying seriously changes the morphology of the cells and thus impairs the diagnosis.

4. The slides should be examined by a trained cytologist.

5. Cytological smears are found to be more representative than biopsis in detecting nasal mucosal changes.

6. The Norwegian Radium Hospital (with 100 000 smears screened annually) serve as a reference laboratory.