IV. ENVIRONMENTAL DATA

Sampling and Chemical Analysis

Air sampling for chromium compounds has been performed by a variety of methods suitable for particulate sampling and poses no significant problems. Samples have been collected using electrostatic precipitators, [5,92] standard and midget impingers, [5,92,126-129] and numerous kinds of filters. [5,92,126,129-133] All such sampling methods are in reality methods for total chromium and are not specific for chromium(VI). On the basis of convenience and sampling efficiency, the use of membrane filters is preferred, and several methods rely on collection by this means. [132] It has been shown, [134] however, that chromium(VI) may be reduced to chromium(III) by reaction with cellulose filters, hence such filters are not recommended if samples must be stored for an appreciable length of time prior to analysis. Abell and Carlberg [66] demonstrated that the use of polyvinyl chloride (PVC) filters eliminates this difficulty and presented data to show that storage of collected samples for periods up to 2 weeks did not result in a measurable amount of reduction of chromium(VI).

It is probable that chromium in other oxidation states will accompany chromium(VI) in the air; hence, analytical methods are required which differentiate between chromium(VI) and the other forms. Most published methods relying on instrumental analysis are in reality total chromium methods, and will differentiate chromium(VI) from chromium(III) only if certain separation steps are included in the procedure. One separation procedure, the method for determining chromium(VI) recommended in the NIOSH criteria document for occupational exposure to chromic acid, [122,135]

relies on the complexation of chromium(VI) with ammonium pyrrolidine dithiocarbamate (APDC), followed by extraction with methylisobutyl ketone (MIBK). Under the conditions described, [135] chromium(VI) is complexed, thus effecting a separation of chromium(VI) from chromium(III).

Numerous methods have been published in which analysis is accomplished by means of atomic absorption spectrophotometry, [132,135-142] neutron activation analysis, [143-145] emission spectrography, [146,147] polarography, [92,130] spark source mass spectrometry, [148] and X-ray fluorescence. [149] It is also feasible, after forming chromium acetylacetonates or trifluoroacetylacetonates, to determine chromium by means of the very sensitive and selective gas chromatographic procedures. [150-153]

Beyerman [154,155] published a comprehensive review of the analytical methods for minute amounts of chromium. He critically compared the many methods with regard to their sensitivities, specificities, accuracies, and precisions. In addition he examined certain processes which are common to many methods such as the digestion of biologic samples in various strong acids. He specifically noted that consistently low results occurred when digestions were performed with perchloric acid due to the formation of chromyl chloride which was emitted as a gas. He further studied many common analytical reagents and showed that some of them were significantly contaminated with chromium, which could lead to erroneous results and high blank values. Errors due to the adsorption by the walls of glassware used were also appreciable, and other errors inherent in common analytical procedures were described. A particularly thorough study of extraction of chromium compounds with organic solvents was made, and various means of

separating chromium(VI) by extraction were described. The analytical methods considered by Beyerman included those based on colorimetric measurements, emission spectrography, flame photometry, X-ray emission spectrography, activation analysis, and 2 electrometric methods—polarography and biamperometry.

Most instrumental procedures are generally not specific for chromium(VI) and are not suitable for such analyses unless, as stated above, prior separations are made. In the NIOSH method recommended in the criteria document for occupational exposure to chromic acid [122] for example, atomic absorption spectrophotometric analysis is performed after extraction of chromium(VI) from the chromium(III).

There are means of performing an analysis in such a manner that only chromium(VI) is determined, and several such methods are based on the fact that chromium(VI) reacts with iodide to form iodine that may thereafter be determined by a variety of standard iodometric procedures. [86,126,128] Such methods are not truly specific for chromium(VI) for they may be subject to interference by other oxidants or reductants. The reagents hematoxylin [86,128] and s-diphenylcarbazide [5,126-128,131,133,156-158] have been used for chromium(VI) analyses, and the latter reagent in particular is widely favored for analysis of chromium(VI) in air. s-Diphenylcarbazide forms a colored complex with chromium(VI), but not with other chromium compounds, and the stability of the color formed contributes to the sensitivity of the method. Several materials, notably iron, copper, nickel, and vanadium, may interfere with the analysis [156], but relatively large amounts are tolerated without significant effect. In addition, certain other compounds such as cyanides, organic matter, and reducing

agents may also interfere. The effect of reducing substances, if present, must be taken into account in any method for determining chromium(VI), since they tend to decrease the actual airborne concentration of chromium(VI). In many sampling situations, however, the presence of significant quantities of such interferences may be ruled out and it is probable that in all but exceptional circumstances the method may be considered specific for chromium(VI) and subject to a minimum of interferences. As noted previously, Abell and Carlberg [66] have demonstrated that reduction of chromium(VI) by the organic matter of the filter does not occur if polyvinyl chloride filters are used, and it is likely, though not proved, that certain other types of filtration media would also be suitable.

Subsequent experience with, and the development of, refinements to the s-diphenylcarbazide method by NIOSH demonstrates the superiority of this method. NIOSH now recommends this as well for chromic acid instead of the method in the chromic acid criteria document [122] because the s-diphenylcarbazide method has shown at least indirectly the ability of many hygienists to obtain excellent results with it. In addition, the s-diphenylcarbazide method is simpler to use than the method in the chromic acid criteria document [122] and requires the purchase and use of less expensive, more commonplace analytical instrumentation.

For many years, test papers have been commercially available which rely on the reaction of chromium(VI) with a paper impregnated with s-diphenylcarbazide reagent. [96] Such papers, at best, give only an approximate indication of the concentration of chromium(VI) if present in a mist and cannot be expected to reliably indicate the presence of dry

particulate matter containing chromium(VI).

There has been great interest in the determination of chromium in biologic materials, both for nutrition studies and in relation to occupational exposure to chromium compounds. [137,138,142,147,151,159-162] Differential analysis for chromium(VI) in biologic samples is not easy, and most analyses reflect the total chromium intake. Many of the analytical difficulties encountered in chromium analyses are particularly troublesome in biologic samples where the extremely low concentrations of the element and the difficulties of ensuring complete oxidation of the chromium may cause substantial analytical errors. It is perhaps for these reasons that biologic monitoring of chromium, as discussed in Chapter III, is of relatively little value in assessing exposure to chromium(VI) in the occupational environment.

Control of Exposure

In many operations in the production and use of chromium(VI), exposures can be eliminated or kept within safe limits by use of closed system operations for reactors, conveyors, and holding or storage containers. [3,91,123] In such systems care must be exercised to ensure tight and reliable seals and joints, access ports, covers, and other such places. Failure of such seals can result in dust or spray emission into the atmosphere of the workroom. [123] When possible, such closed systems should be maintained under negative gage pressure. Even with closed systems, there will be unloading, charging, transferring, discharging, packaging, and transporting operations which afford various opportunities for contact with chromium(VI) and for the emission of dust and mist

containing chromium(VI).

Emission of airborne chromium(VI) can be controlled at the source by suitably designed exhaust ventilation. In employing exhaust ventilation for such control, certain recommended practices, [163] and design and operating fundamentals [164] should be followed. Sources of emission should be as fully enclosed by hoods as possible. The exhaust air should be passed through air cleaners of suitable efficiency to reduce the chromium(VI) concentration to acceptable levels before discharge into the community air.

Atmospheric exposure to and other contact with chromium(VI) can and should be reduced or controlled by isolating the process or emission source from employees. Location of an operation in an isolated area can also limit the number of employees who will be exposed in that operation. Such operations must be amenable to remote or automated control or to only intermittent attention by an operator.

In effect, the worker can be isolated from the process by providing a clean area (clean room) in which the atmosphere is maintained essentially free of chromium(VI) and other significant contaminants. This may be accomplished by supplying air from an uncontaminated area or by filtering ambient air through high-efficiency filters. A clean area may be established as the control room for remote control operations or as an area to which operators may retreat for such periods as their presence may not be required at the process equipment.

Ventilation and isolation of the processes will reduce the probability of excessive contact with chromium(VI). For protection of eyes and skin, however, these measures may not be adequate for some operations.

For those operations where contact of the chemicals with the eyes or skin may occur, whether by the nature of the work or by accidental splashes, sprays or spills, proper protective equipment, work clothing, and good work practices are required to control the exposure (see Chapter VI).

The operations for which it is most difficult to control exposures are those of the maintenance and repair workers. The duties of these employees require that they enter or otherwise come into close contact with equipment or areas which may be grossly contaminated with chromium(VI). Often they must work under emergency conditions. The duration and frequency of their exposures are variable and irregular. Exhaust ventilation, protective clothing, and respiratory protective equipment should be used as practicable and combined with good work practices, carefully supervised, to ensure that exposures are below the recommended workplace environmental standard. Administrative controls may be used in addition, if necessary.

V. DEVELOPMENT OF STANDARD

Basis for Previous Standards

The first standard in the United States specifically applicable to chromium(VI) was published by the American Standards Association Inc (now the American National Standards Institute Inc) in 1943. [165] It specified that "The maximum allowable concentration of chromium as chromate or dichromate dust, or as chromic acid mist, shall be 1 milligram of chromic acid anhydride (CrO3) in 10 cubic meters of air, for exposures not exceeding a total of eight hours daily." The standard was based largely on the 1928 report by Bloomfield and Blum. [22] In 1971, the ANSI Z37 committee [166] reaffirmed the 1943 standard [165] thus updating it, but leaving it unchanged.

In 1973, the American National Standards Institute Inc [167] recommended a standard which included a ceiling of 0.3 mg chromium(VI) oxide for chromic acid anhydride and soluble chromates, and a TWA concentration of 0.1 mg chromium(VI) oxide/cu m for an 8-hour day, 40-hour week. Thus, the TWA of 1 mg/10 cu m was left unchanged. For workweeks longer than 40 hours, it was recommended that the TWA concentration be reduced proportionately. The same TWA was recommended for insoluble chromates but no ceiling was recommended for these compounds. The standard [167] recommended a TWA concentration of 0.1 mg/cu m of lead chromate as chromium(VI) oxide because that was equivalent in terms of lead content to the current [168] ANSI lead standard of 0.2 mg/cu m. In the 1973 standard, the American National Standards Institute Inc cited reports by Bloomfield and Blum, [22] Mancuso, [41] Mancuso and Hueper, [90] Bourne and Yee, [3]

129

the US Public Health Service, [5] Kleinfeld and Rosso, [59] Dankman, [169] Bidstrup, [100] Bidstrup and Case, [102] Vigliani and Zurlo, [85] the Threshold Limit Committee of the American Conference of Governmental Industrial Hygienists, [170] a private communication from Mancuso to ANSI, [167] Hartogensis and Zielhuis, [171] Baetjer, [87] Machle and Gregorius, [33] Alwens and Jonas, [30] and Pfeil. [26]

In 1948, the Threshold Limits Committee of the American Conference of Governmental Industrial Hygienists [172] adopted a Threshold Limit Value for chromic acid and chromates of 0.1 mg chromic acid anhydride/cu m, which remained unchanged until 1973. [173] The reports by Bloomfield and Blum, [22] Mancuso, [41] the US Public Health Service, [5] Kleinfeld and Rosso, [59] Vigliani and Zurlo, [85] Baetjer, [87] Mancuso and Hueper, [90] Bidstrup, [100] Buckell and Harvey, [101] Machle and Gregorius, [33] and Hueper and Payne [108] were considered when documentation for the TLV was published in 1971. [170] The TLV documentation stated "A review of the present status of the suitability of the TLV between TLV subcommittee members and industrial-hygiene representatives of the chromate industry 10 years after improved controls had been in operation revealed that (1) the TLV for chromic acid mist was satisfactory; (2) it contained a safety factor of 3 or 4; and (3) the limit was probably satisfactory for the prevention of lung cancer, as no new cases had appeared during the 10-year period; but (4) that the 10-year period was probably too short to be certain of its validity in this respect." [170] Data in support of these points were not presented and discussed.

In the 1973 edition of the Threshold Limit Values [173] a change was proposed in the chromium TLV's. The TLV for chromic acid and chromates

130

remained 0.1 mg/cu m as chromic acid anhydride. The TLV for "Chromium, sol. chromic, chromous salts as Cr" remained 0.5 mg/cu m, but the category "chromium... metal and insoluble salts", which had been 1.0 mg/cu m, [170] was marked for intended changes in order to be included as a group of substances in industrial use that have proved carcinogenic in man, or have induced cancer in animals under appropriate experimental conditions. The group was labeled "Chromates, certain insoluble forms" with a TLV of 100 μg/cu m. This group of certain insoluble chromates probably included calcium and zinc chromates and sintered chromium(VI) oxide (called chromic chromate) and others. The group was discussed in the 1971 TLV documentation [170] under "Chromic Acid and Chromates" for which the TLV was 0.1 mg/cu m, but in 1973 these materials were apparently removed from that group and placed under "chromium...metal and insoluble salts." It was not mentioned, however whether this intended TLV, 100 μg/cu m, was in terms of chromium, chromium(VI) oxide, or as chromates. Thus, the intended change to 100 μg/cu m may have been an increase, no change, or a decrease in the TLV for these materials. Nonetheless, the intent was apparently to denote "Chromates, certain insoluble forms" as "Human carcinogens."

In 1974 the situation was clarified, [174] in that the TLV for "chromic acid and chromates" was 0.1 mg/cu m as chromium(VI) oxide and that the TLV's of "Chromates, certain insoluble forms, (Pb, Zn, and chromate-chromite ore...)" were 0.1 mg/cu m as chromium and these materials were noted as human carcinogens. It should be noted that the 1974 TLV for these compounds represented an increase in the TLV over the 1972 TLV.

The present (1975) federal standard for chromic acid and chromates is a ceiling concentration of 1 mg/10 cu m, ie, 100 μg/cu m, (29 CFR

131

1910.1000) based on the American National Standard Z37.7-1971. [166]

In 1963 [175] the Threshold Limits Committee recommended a limit of 0.1 mg chromium(VI) oxide/cu m for tertiary butyl chromate, an ester of tertiary butyl alcohol and chromic acid, which was unchanged in the 1974 TLV's. [174] As support for this recommendation, they cited the study by Roubal and Krivucova [176] in the 1971 documentation. [170] Roubal and Krivucova [176] reported that tertiary butyl chromate is readily converted to tertiary butyl alcohol and chromate by water. They reported that a technician experienced nausea and vomiting when exposed to an unknown airborne concentration of tertiary butyl chromate. When they exposed rats to unspecified airborne concentrations of tertiary butyl chromate, the animals experienced rapid breathing, signs of irritation, muscular weakness, twitching neck and diaphragm muscles, and coughing. Microscopic examinations showed focal edema of the lungs and inflammatory alterations in the bronchial pathways. There was also some evidence of liver damage and hyperemia of the kidneys. Where the skin was in contact with tertiary butyl chromate, necrosis occurred.

The present (1975) federal standard for tertiary butyl chromate is a ceiling concentration of 0.1 mg chromium(VI) oxide/cu m (29 CFR 1910.1000) based on the 1968 TLV. [177]

Standards have also been reported for chromium(VI) in other countries and in several states. In 1971, the West German maximum workplace concentration (MAK) [178] for chromate was established at as low a concentration as possible, ideally approaching zero, because, "no concentration can be stated which may be viewed as harmless." This MAK was set because "according to experience" this material is able to cause cancer

132

in humans. In 1975, Sweden [179] set an occupational environmental limit for chromic acid and chromates, as chromium(VI) oxide, of 50 μg/cu m and considered poorly soluble chromates as carcinogens, as capable of causing sensitization, and as absorbable through the skin. Standards have been set in other countries and are summarized in Table XI-8; however, the basis in most cases was the same as that for the TLV for the US described above.

Basis for a Recommended Environmental Standard

Certain effects such as contact dermatitis, [7-11,21,25,61,62,71-77] skin ulcers, [5,16-20,22-25,41,56-60,62] irritation and ulceration of the nasal mucosa, [5,19,22-24,41,56-60,63] and perforation of the nasal septum [5,18,19,22-24,33,41,56-58,60] have been reported and have resulted from contact with many different chromium(VI) materials. Since there is no evident demarcation of categories of such compounds, it is concluded that all chromium(VI) materials can cause these effects. Other effects which have resulted from exposure to chromium(VI), eg, kidney damage, [5,83,84,105] liver damage, [5,68,83] pulmonary congestion and edema, [67] epigastric pain, [59] erosion and discoloration of the teeth, [5,56] and perforated eardrums [19] have been reported on occasions, but again it seems reasonable that sufficient contact with any chromium(VI) material could cause these effects.

In addition to causing these effects, some chromium(VI) compounds have been found to be associated with an increased incidence of lung cancer. [3,5,33,41,88-93,95,180] Because of the many valid reports showing this association and because of experimental studies [107,117-120, LS Levy, written communication, March 1975] demonstrating some chromium(VI) compounds to be carcinogens in animals, it is concluded that the

association is causal, ie, that some chromium(VI) compounds cause lung cancer.

Recommending standards to protect workers from all these effects of chromium(VI) poisoning poses several difficulties because chromium(VI) is likely to be encountered in workplace air in a wide variety of forms and is often mixed with other materials. Sampling and analytical methods have not been developed which adequately distinguish between different compounds of chromium(VI).

Although there are insufficient data available to allow the derivation of an appropriate environmental limit for each chromium(VI) compound, grouping of compounds with similar toxicities is possible. One such group of compounds includes chromium(VI) oxide, sodium bichromate, sodium chromate, potassium bichromate, and potassium chromate. From the data reviewed below, it appears that these chromium(VI) compounds are capable of producing similar toxic effects upon inhalation.

Delpech and Hillairet in 1869 [18] described the effects of potassium chromate and bichromate on workers in the French chromate industry. Workers suffered respiratory ailments from the first day of their employment. One assigned the task of washing "simple chromates", began to suffer from nasal membrane injury, headache, and shortness of breath several days after he started this job. Another worker, involved in calcining and bichromate extraction also had shortness of breath. No environmental data were reported but exposures were probably high because of the then prevailing poor hygiene around reverberatory furnaces.

In the chromate-producing industry in the United States, only a small part of which produced chromic acid anhydride, the principal exposures to

chromium(VI) were evidently to sodium chromate and bichromate because these were and are the principal intermediate and product of the alkaline roasting operation. To a lesser degree, there was also exposure to potassium chromate and bichromate. In 1884 Mackenzie [19] related having been told by a workman that destruction of the nasal septum sometimes took place after 24-48 hours of exposure. This destruction was associated with general congestion of the mucous membrane, nosebleed, coryza, ulceration of the turbinates, nasal pharynx, and lower pharynx, and inflammation of the lower respiratory tract. Intense headache, inflammation and perforation of the tympanic membranes, and subsequent otorrhea also occurred. Exposures in this plant were probably very high, based on remarks about the history of the operation. [6]

In 1948, Machle and Gregorius [33] reported the incidence of nasal septal perforation in a sodium chromate-sodium bichromate-producing plant to be 43.5% in 354 employees. Airborne chromate concentrations were 10-2,800 μg/cu m at the time of the study. The plant had been in operation for at least 17 years; thus, some employees had probably worked in the plant when reverberatory furnaces were used, a notorious source of exposure. This study provided evidence that exposure to sodium bichromate and chromic acid anhydride does not produce lung cancer. During the 17-year period plant D2 had been in operation, no deaths from lung cancer occurred. By contrast, in plant D1, which used alkaline roasting of chromite ore to manufacture sodium chromate, there were 5 deaths from lung cancer in the same period. As discussed in the section on Epidemiologic Studies, exposure to the intermediate in alkaline roasting has been associated with an increased incidence of lung cancer.

135

In the early 1950's, an epidemiologic study [3,41] was carried out in a single chrome plant in Ohio which produced sodium chromate and bichromate but no chromium(VI) oxide. In this study, the overall incidences of nasal septum perforations, chronic chemical rhinitis, and chronic chemical pharyngitis were significantly greater than those of the control group. The chromium(VI) concentration was as great as 0.5 mg/cu m. However, the incidences of these disorders in the groups of workers exposed at less than 85 μg chromium(VI)/cu m were not significantly greater than those of control groups.

In 1953 the US Public Health Service [5] investigated the hazards associated with some of the chromium-producing industry in the United States. As mentioned above, it is likely that throughout the industry most of the exposures to chromium(VI) were to sodium chromate and bichromate. The range of time-weighted exposures was 5-170 μg water-soluble chromium(VI)/cu m based on the s-diphenylcarbazide method of chemical analysis. The mean exposure was 68 μg water-soluble chromium(VI)/cu m. Results of analysis of airborne chromium showed cross-contamination of work areas in that airborne chromite ore and water-soluble chromium(VI) as well as acid-soluble, water-insoluble chromium, were found in nearly all areas of the plants; the acid-soluble, water-insoluble chromium was analyzed by direct colorimetry. Of the 897 workers examined, 57% had perforation of the nasal septum, 11% had a severely red throat, 8% had edema of the uvula and 50% had cutaneous ulcers or scars. The incidence of severely reddened throat and edema of the uvula was greater than twice that of control groups. Data on cutaneous effects in the control group were not given. There was also an increased incidence of lung cancer in these chromate

workers. A more recent study [57,58] has indicated poor work practices (eg, nose-picking) to be the likely causes of nasal ulcers and perforations. It seems evident that ulcers on the skin and hands (and other exposed skin areas) are also from local contact, thus the result of poor work practices. Although Mancuso [41] and the US Public Health Service report [5] did not make observations on this point, it seems likely that the high incidence of nasal and cutaneous ulcers and sequelae in their studies was also largely, conceivably entirely, due to such work habits. However, a contributory role of airborne chromium(VI) in the development of nasal ulcers and septal perforations and the major role in the development of primary nasal irritation must be considered.

Liver enlargement was noted in about 2% of the chromate workers. Those with enlarged livers were at least 15 years older and had worked an average of 4 years longer in the chromate industry than those without enlarged livers. The frequency with which white and red blood cells and casts were found in the urine was usually greater than that in the average industrial population, suggesting kidney damage.

The nonneoplastic signs of exposure to chromium(VI)--nasal mucosal irritation and ulceration and, to a lesser extent, nasal septal perforation--were likely to be closely related to airborne chromium(VI) at the average concentration measured at the time of the study, ie, 68 $\mu g/cu$ m. There was some evidence that liver and kidney damage occurred as a result of long-term exposure to chromium(VI). Results were more conclusive relative to kidney damage in controlled experiments with monkeys, which sustained [105] kidney damage after subcutaneous injections of sodium bichromate. Absorption of large amounts of chromium(VI) has, on a few

137

occasions, [68,83] resulted in hepatic injury; it has also produced severe nephritis. [83,84] Because there have been several instances [5,83,84,105] in which kidney damage has apparently been the result of chromium(VI) absorption, routine urinalysis should be performed where there is occupational exposure to chromium(VI). Hepatic injury [5,68,83] has also been reported [5,68,83] as the result of chromium(VI) absorption; for this reason, it is recommended that in routine medical examinations the responsible physician should consider appropriate liver studies.

From these studies of the effects of exposure to sodium or potassium chromate or bichromate, two [5,41] contain information useful in deriving an exposure-effect relationship. The work of Mancuso [41] indicated only a slight and statistically insignificant increase over controls in the incidences of nasal and pharyngeal disorders in workers exposed at less than 85 μg chromium(VI)/cu m. From the US Public Health Service report, [5] it appears that an average exposure of 68 μg water-soluble chromium(VI)/cu m, comprising chromate and bichromate, was enough to produce irritation of the nasal mucosae and severely reddened throats in some workers.

Based on several studies [22,56,59,63,64] which showed that inflammation and ulceration of nasal mucous membranes can occur at airborne chromium(VI) oxide concentrations in excess of 0.1 mg/cu m in a short period of time, it was recommended in the chromic acid criteria document [122] in 1973 that the then current federal standard (ceiling) of 0.1 mg/cu m (reported as chromium(VI) oxide) (29 CFR 1910.93, recodified in 1975 to 29 CFR 1910.1000) be retained and supplemented by a TWA concentration limit of 0.05 mg/cu m in order to afford the worker additional protection against

138

possible effects of chronic exposure. After reconsideration of evidence presented in the chromic acid criteria document, NIOSH reaffirms, in principle, its recommendations for the workplace environmental standard proposed for chromium(VI) oxide. The TWA workplace environmental limit of 0.05 mg/cu m as chromium(VI) oxide is 26 µg/cu m as chromium(VI). If this recommended environmental limit is extended to sodium chromate and bichromate and potassium chromate and bichromate, it would represent a considerable reduction from 68 µg/cu m chromium(VI) average airborne concentrations which produced [5] a slightly greater incidence of irritation of eye and throat mucous membranes in the chromate-producing industry than in the control groups. Because the exposure-effect relationships for sodium chromate and bichromate and potassium chromate and bichromate appear to be nearly identical with those described in studies of plating and anodizing operations, [22,56,59,63,64] a recommendation that the previously (1973) proposed environmental limit in the chromic acid criteria document [122] be modified and expanded to include these salts in addition to "chromic acid anhydride and aqueous solutions thereof" would be addressing a group of compounds of uniform toxicity.

In the light of the study by Machle and Gregorius [33] which showed an elevated incidence of lung cancer only in that part of the operation involving lime roasting, it seems clear that the lung cancer found in the US Public Health Service study [5] occurred in that part of the population involved in lime roasting. This is supported by some observations of the authors, [5] in that, of those workers with lung cancer whose work history was sufficiently described, most had worked at or near the lime mills or kilns. It is also supported by Laskin et al [118] and written information

139

supplied by Levy in 1975 which indicated that the highest incidence of lung cancer was found in animals treated with calcium chromate. The information from Levy indicated no lung cancers were produced in animals treated with sodium chromate or bichromate.

When the toxicities of chromium(VI) compounds are examined, it becomes apparent that several have demonstrated carcinogenic activity. [3,5,33,41,88-93,95,107,117,118,120,161,180] Nearly all the implications of carcinogenicity have arisen from studies of the worker population of the chromate-bichromate producing industry and from animal studies using the intermediates produced in that industry. Some implications have arisen from the pigment-producing industry [88,89] and from animal studies [116, LS Levy, written communication, March 1975] using pigments and chemically analogous chromium(VI) compounds. Other industries and processes are suspect despite the absence of appropriate studies because they use or produce materials chemically similar to the intermediates in the chromate-bichromate industry or chromium(VI) pigments. [124,181]

The only industry which has been extensively studied [5,33,41,90-93,95,161,180] has been the chromate-bichromate producing industry in the United States. However, even studies of this industry have provided only small amounts of information. Thus, the relationship between airborne concentrations of certain chromium(VI) compounds and the incidence of cancer is uncertain. Machle and Gregorius [33] published the first report of a high incidence of lung cancer among workers in the US chromate industry. In 1,966 man-years of employment in 5 plants, there were 32 deaths from lung cancer. The death rate for chromate workers from cancer of the bronchi and lungs was 29.2 times that of a control population. This

study indicated that a high incidence of lung cancer was associated with exposure only to the alkaline roasting and roast leaching operations which produced intermediates of ill-defined, only slightly soluble chromium(VI) compounds. Plant D1 manufactured sodium bichromate from chromite ore using alkaline oxidation (roasting) and leaching. Airborne concentrations of "chromates" in the kiln and milling areas were 0.8-4.6 mg/cu m. It is reasonable to conclude that in terms of chromium(VI) this range was approximately 0.4-2.3 mg/cu m. In this plant, the SMR from cancer of the lungs and bronchi in the <50-year age group was 2,420 (P<0.01). In the >50-year age group, the SMR was 1,090 (P<0.05). Overall SMR for all ages for death from this cause was 1,499 (P<0.01). The incidence of deaths from other causes was not significantly greater in the chromate industry than in the control population.

Plant E, studied by Machle and Gregorius, [33] was later examined extensively by another team of investigators. [3,41, 90-93,95,161,180] This plant produced sodium chromate and sodium bichromate through alkaline roasting of chromite ore, but no chromium(VI) oxide.

In 1 study, Mancuso and Hueper [90] reported 7 deaths from lung cancer in Plant E (v.s.), the calculated TWA exposures being 10-150 μg chromium(VI)/cu m. It is unclear how the authors derived these TWA concentrations because the range of exposures in the various departments was 30-260 μg chromium/cu m. Because of (1) the time which elapsed between the dates at which the 7 workers began their chromate employment (January 1932-October 1941) and their death dates (December 1938-March 1950) and (2) the time between their periods of employment and the analysis of airborne chromium(VI), it is unlikely that the calculated TWA exposures adequately

reflected the actual exposure to chromium(VI) the men had while working. In addition, airborne chromium(III) and chromium(VI) were present in all areas of this plant making it impossible to associate the high incidence of lung cancer with exposure to a particular chromium compound.

In 1953 the US Public Health Service published a survey [5] describing conditions in other chromate-producing plants. This study of 897 workers revealed 10 workers with bronchogenic carcinoma, a rate of 1,115/100,000 population. By contrast, they reported that, in a general Boston chest X-ray survey, 54 of 259,072 had bronchogenic carcinoma, an incidence of 20.8/100,000 population. These 10 workers had various job classifications in the chrome plants studied. Mean exposures to chromium(VI) in the various job classifications studied were 5-170 μg/cu m. Again, it is unlikely that these exposures were true indications of the exposures experienced by the 10 who developed bronchogenic carcinoma because all had begun their chromate exposure between 1910 and 1942. Nine probably had exposure to the reverberatory furnaces abandoned in the early 1930's. The average number of years of exposure was 22.8 (range: 8-39). As in the above study [90] the large number of variables in this study [5] precludes the derivation of a dose-response relationship.

In 1975, Watanabe and Fukuchi reported preliminary results [182] of a recent survey of a Japanese chromate-producing plant. The survey showed that in 136 workers who had been employed for at least 9 years there were 10 cases of lung cancer. The number of deaths from lung cancer was 21.2 times as high as the expected number of deaths. Table XI-9 provides the data which have been reported; the proper analysis of the results of this study is contingent on the future publication of the necessary details.

142

Publication of additional details of this study has not yet (October 1975) been accomplished.

Because of the uncertain character of the airborne chromium(VI) present in the chromate-producing plants studied, [3,5,33,41, 90-93,95,161,180,182] and the wide ranges in airborne chromium(VI) concentration--reported as 0-600 μg/cu m, [5] 30-280 μg/cu m, [90] 3-21,000 μg/cu m [33]--it is impossible to derive a dose-response relationship and thus it is impossible to derive a safe environmental limit for chromium(VI) carcinogens.

In the plants studied by Gross and Kolsch [88] which produced lead chromate pigments and zinc chromate pigments from chromium(VI), a high incidence of lung cancer was also reported. Unfortunately, no information was provided on airborne concentrations of chromium(VI) materials in these plants.

Langard and Norseth [89] found the incidence of lung cancer in a plant producing both lead chromate and zinc chromate pigments to be 38 times the expected incidence. In a cohort of 24 workers, the 3 who developed lung cancer were exposed for 6, 7.5, and 8 years. In this plant they estimated the exposures of those who developed lung cancer to have been 0.19-0.43 mg chromium(VI)/cu m.

Preliminary results (JF Morgan, written communication, October 1975) of an epidemiologic study of 3 lead chromate manufacturing plants in the US have indicated that there has been an excess of lung cancer deaths, as a percentage of total deaths, among the exposed group of employees. The expected date of completion of this epidemiologic study has been estimated to be the last quarter of 1975.

143

In animal studies, inhalation of calcium chromate was found [118] to produce 1 keratinizing squamous cell carcinoma, 1 laryngeal squamous cell carcinoma, and 1 malignant peritruncal tumor in rats, and a squamous cell carcinoma of the larynx in a hamster. In other animals, laryngeal hyperplasia, laryngeal squamous metaplasia, and a squamous papilloma were found. Intrabronchial implantation of calcium chromate in cholesterol in rats produced [117] squamous cell carcinomas with metastases, adenocarcinomas with mucus production, and atypical squamous metaplasia of the bronchus.

Chromate roast material produced squamous cell carcinomas in rats following intrapleural deposition. [107]

From the above, it can be concluded there is a great likelihood that the solubility or leachability of a chromium(VI) material has some influence on its carcinogenicity. Less-soluble chromium(VI) compounds-- lead chromate and zinc chromate pigments, calcium chromate of ill-defined origin, and chromate roast material--are suspect carcinogens while the highly soluble chromium(VI) materials have not been found to be carcinogenic. There are insufficient data available, however, to accurately identify carcinogenic chromium(VI) materials solely on the basis of solubility. From the above information, it is likely that alkaline earth monochromates, most of which are only slightly water soluble, are carcinogenic despite the lack of experimental or epidemiologic evidence on some of these compounds.

On this basis, a grouping of chromium(VI) compounds is possible, despite the lack of sufficient toxicologic information on each. To the group of compounds for which the toxicity has been shown not to include

144

carcinogenicity, additional compounds may be added, based on known chemical and inferred toxicologic properties. They are the chromates and bichromates of hydrogen, lithium, rubidium, cesium, and ammonium. Protection from these compounds will be afforded by the same environmental limits recommended in the chromic acid criteria document, [122] a TWA of 26 μg chromium(VI)/cu m, a ceiling of 52 μg chromium(VI)/cu m, and appropriate work practices.

Although arithmetical conversion of the workplace environmental limits expressed as chromium(VI) oxide in the chromic acid criteria document [122] to expressions as chromium(VI) generates 26 μg and 52 μg, respectively, these limits suggest more accuracy is possible in deriving safe workplace environmental concentrations than is warranted; therefore, it is recommended that a TWA limit of 25 μg Cr(VI)/cu m and a ceiling limit of 50 μg Cr(VI)/cu m be applied instead.

As was expressed in the chromic acid criteria document, [122] a ceiling on airborne workplace concentrations of noncarcinogenic chromium(VI) is needed to augment protection provided by the recommended TWA limit. This additional protection should prevent adverse effects which have been found [19,22,64] to result from exposures to chromium(VI) for short periods of time.

Lithium, rubidium, and cesium are included because, like sodium and potassium, they are alkali metals. Ammonium salts of chromium(VI) are included because of their high solubility and other similarities to other alkali metal salts. [183] Hydrogen chromates and bichromates are hydrated forms of chromium(VI) oxide.

145

The remainder of the chromates and polychromates constitute a group containing several compounds which are potent carcinogens—the only slightly soluble chromates of lead, zinc, or calcium, and complex mixtures produced as intermediates in the chromate-manufacturing process. Because toxicologic evidence is not available to exonerate any of the many compounds in this group, and because there is strong evidence that several are carcinogens, it is concluded that all of this group should be treated as carcinogens. It is interesting that all of these compounds are only slightly soluble in water, which is consistent with the postulate that water solubility is one of many factors in the carcinogenicity of chromium(VI) compounds. In view of the fact that there are no reliable data on which to base a safe airborne concentration of this group of chromium(VI) compounds, exposure to them should be kept as low as possible.

From the above discussion, it is concluded that different recommendations are appropriate for noncarcinogenic chromium(VI) than those for the chromium(VI) carcinogens. The standard includes different recommendations for the environmental limit, monitoring chromium(VI), medical surveillance, labeling, and respiratory protection. However, there is no sampling and analytical method that will adequately determine the recommendations that should apply to a given workplace. The compliance officer will not be able to determine the correct regulation to use solely on results of environmental monitoring.

For this reason, it is proposed that the recommendations for the carcinogenic chromium(VI) compounds be routinely applied. When it is demonstrated that only the noncarcinogenic compounds are present in a discrete area the recommendations for noncarcinogenic chromium(VI)

146

apply. Thus, within a given plant, different recommendations might apply to specific discrete areas within the plant. The term "discrete areas" implies no cross-contamination from one area to the other. Whether cross-contamination is prevented by separate ventilation systems and barriers, by physical isolation, or by other means, contamination of areas subject to the standard for noncarcinogenic compounds by carcinogenic chromium(VI) compounds should invalidate the arrangement.

Evidence relevant to a demonstration that only noncarcinogenic compounds are handled in a specific area could include identification of the compounds brought in and those transported out as well as chemical substances involved in the operation itself. For example, if chromite ore were roasted with lime and then converted to sodium dichromate or chromium(VI) oxide, a significant likelihood of exposure to calcium chromate, a carcinogenic compound, would exist.

It is possible that sampling and analytical methods may be developed which adequately distinguish, on the basis of samples of airborne chromium(VI). These may also be used as evidence for such a demonstration.

Two analytical methods have been evaluated by NIOSH for the determination of chromium(VI). [66,122] The first [122] uses atomic absorption spectrophotometry for the determination of chromium after chromium(III) is removed from the sample by solvent extraction. This method was recommended in the chromic acid criteria document. [122] The second method [66] uses a simpler, colorimetric procedure, not requiring solvent extraction. NIOSH has found that each of these 2 methods is capable of determining 0.5 μg chromium(VI) with 10-20% precision. Each method can detect smaller amounts of chromium(VI) but without acceptable

147

reliability. Analyses by the method recommended in the chromic acid criteria document, which uses atomic absorption spectrophotometry, have been subsequently found by NIOSH to be much more time consuming than those using the s-diphenylcarbazide colorimetric method; thus, it appears that routine analysis would be simplified by a recommendation that the s-diphenylcarbazide colorimetric method be used for the determination of all chromium(VI) compounds, whether or not carcinogenic.

Therefore, the recommended analytical chemical method is that described in Appendix II and it uses the spectrophotometric determination of a colored complex of chromium(VI) and s-diphenylcarbazide.

Because of the carcinogenicity of some chromium(VI) materials and the lack of evidence suggesting a safe workplace environmental limit, it seems appropriate to recommend that no detectable amounts of these substances be allowed in workplace air with a specified method of sampling and chemical analysis. The recommended analytical method (v.s.) will reliably detect 0.5 μg chromium(VI). The lower detection limit is approximately 0.05 μg chromium(VI) by this method but detection and determination are not reliable at this limit because of (1) variations in the background concentrations of airborne and reagent substances that interfere with the determination of chromium(VI) at this trace level and (2) the inherent unreliability of the calibration curve generated by determinations of known amounts of chromium below, at, and slightly above the detection limit. Because of this unreliability at this limit of detection and the resultant questions about the validity of compliance actions at airborne chromium(VI) concentrations at this limit, it is concluded that a finite workplace environmental limit based on the least reliably detectable and determinable

concentration of chromium(VI) should be recommended. To ensure that this environmental limit is very low, a long sampling time to increase the volume of air sampled is proposed.

In order to collect sufficient airborne particulates in a day to allow the presence or absence of carcinogenic chromium(VI) to thus be reliably detected and determined, it is recommended that the largest sample feasibly collected by currently available sampling pumps and filters for the periods of workers' daily activities be taken. Personal sampling pumps are reliably operated for up to 8 hours if they operate at approximately 1 liter/min. In this time, about 0.5 cu m of air will be filtered.

It is concluded that (a) 0.5 μg chromium(VI) should be collected in order to evaluate whether or not carcinogenic chromium(VI) is present in the workplace air and (b) that 0.5 cu m of air should be filtered over the period of a workday in order to effectively sample the workers' environment. As a result of these recommendations, it can be calculated that the workplace environmental limit for airborne carcinogenic chromium(VI) is 1 μg Cr(VI)/cu m as a TWA for an 8- to 10-hour workday.

Because carcinogenic chromium(VI) and noncarcinogenic chromium(VI) are frequently encountered in the same workplace and because of the long latent period for the development of lung cancer, it seems appropriate to recommend that medical records for employees with either type of exposure be retained for a similar length of time, ie, 30 years.

It is recognized that many workers may handle small amounts of non-carcinogenic chromium(VI) compounds or are working in situations where, regardless of the amount used, there is only negligible contact with these compounds. Under these conditions, it should not be necessary to comply

149

with many of the noncarcinogen provisions of this recommended standard, which has been prepared primarily to protect worker health under more hazardous circumstances. Concern for worker health requires that protective measures be instituted below the enforceable workplace environmental limit to ensure that exposures stay below that limit. For these reasons, "occupational exposure to noncarcinogenic chromium(VI)" has been defined as exposure above half the time-weighted average environmental limit, thereby characterizing those work situations which do not require the expenditure of resources for environmental and medical monitoring and associated recordkeeping. Half the environmental limit has been chosen on the basis of professional judgment rather than on quantitative data that differentiate nonhazardous areas from areas in which a hazard may exist. However, because of nonrespiratory hazards such as those resulting from skin irritation or eye contact, it is recommended that appropriate work practices and protective measures be required regardless of the airborne concentration of chromium(VI).

There are several gaps which have been found in the available information relating exposure to chromium(VI) compounds and effects on humans. One such gap is the lack of appropriate sampling and analytical methods which can elucidate directly, on the basis of samples of airborne chromium(VI), whether carcinogenic chromium(VI) is present or not. Another gap pertains to chromium(VI) materials for which the toxicity is not well known. One such compound is chromyl chloride, a chromium(VI) compound generated from chromium(VI) oxide and chloride. It is a liquid with a vapor pressure of 20 mmHg at room temperature. Gaseous chromyl chloride, which is a vapor-phase chromium(VI) compound, may therefore be liberated by

the appropriate combination of chromium(VI), acid, and chloride in the presence or absence of water. Hill and Worden [184] in 1962 made a preliminary investigation of the preparation and collection of chromyl chloride and experienced insurmountable difficulties in sampling and analyzing airborne chromyl chloride. They speculated that chromyl chloride was produced in a European chrome plant they sampled, wondered whether or not it played a role in the development of lung cancer, and advised readers that "grave industrial exposures" to it have occurred in the US and should be further investigated. WS Ferguson (written communication, February 1975) mentioned that before 1961 the chromic acid operation occasionally used sodium bichromate which contained chloride and that based on his personal observations (further undescribed) chromyl chloride was sometimes present. It seems reasonable, after consideration of these preliminary investigations and observations, that this gaseous chromium(VI) compound and others may be generated in places where chromium(VI) compounds are used. Currently available air sampling and chemical analytical regimens are probably unable to detect gaseous chromium(VI) compounds, eg, chromyl chloride, and in addition, their toxicities are yet unknown.