V. DEVELOPMENT OF STANDARD

Basis for Previous Standards

Bowditch et al [163] reported in 1940 that Massachusetts was suggesting a 3 ppm (2.5 mg/cu m) MAC for hydrogen fluoride as a guide for occupational exposure.

In 1945, Cook [164] compiled a list of standards and recommendations for MAC's for industrial atmospheric contaminants. Three ppm (reported by Cook as equivalent to 2.0 mg/cu m, but actually equivalent to about 2.5 mg/cu m) was the value suggested for HF by California, Connecticut, New York, Oregon, Utah, and the US Public Health Service, while Massachusetts proposed 1.5 ppm (1.2 mg/cu m). There was no discussion of the MAC value in Massachusetts of 1.5 ppm (1.2 mg/cu m) which differed from the 3 ppm (2.5 mg/cu m) reported by Bowditch. [163] Cook reported a generally accepted MAC value of 3 ppm (2.5 mg/cu m).

The efforts of a committee within the American Conference of Governmental Industrial Hygienists (ACGIH) to develop a MAC which could be adopted by all the states was reviewed by Bloomfield [165] in 1947. The committee had received replies from 24 states and 3 cities. Three respondents did not list a MAC value for HF while 24 reported an established MAC value of 3 ppm (2.5 mg/cu m) for "fluorine (hydrogen fluoride)."

At its 1947 meeting, the ACGIH [166] accepted a MAC of 3 ppm (2.5 mg/cu m) for HF. It was not specified if this MAC was intended as a ceiling value or as a TWA. At its meeting in April 1948, the ACGIH [167] adopted a TLV of 3 ppm (2.5 mg/cu m).

Data presented in the 1962 Documentation of the Threshold Limit Values for Substances in Workroom Air [168] supported a 3 ppm or approximately 2 mg/cu m (sic) threshold limit for HF. However, the data referred to in the Documentation were primarily concerned with human exposure to fluoride and animal exposure to HF. One unpublished industrial medical study on workers exposed to 50% gaseous and 50% particulate fluorides was cited [168] which indicated that workers excreting urinary F values of 1.5-2.5 mg/day, corresponding to 1-4 ppm F in the working environment, would not be expected to experience any changes "of health significance." Elkins [36], however, stated that workers in the etching process had nosebleeds as did welders exposed to 0.4-0.7 mg F/cu m who were excreting 2-6 mg F/liter of urine but he did not cite any supportive environmental data. Other workers exposed to 0.1-0.35 mg F/cu m and excreting, on the average, 4.5 mg F/liter of urine reportedly experienced sinus trouble. [36] The ACGIH [168] suggested that the urinary excretion values reported by Elkins [36] seemed "inconsistently" high relative to airborne HF levels, and dietary F was suggested as a possible factor.

The 1966 Documentation [169] reiterated that the 3 ppm threshold limit for hydrogen fluoride was "securely based for protection against long-term chronic effects." References previously cited in the 1962 Documentation [168] formed the basis for the selection of 3 ppm. In order to take into account Elkins' [36] findings, this TLV was designated a ceiling limit in the 1966 Documentation. However, this ceiling limit was never proposed in any subsequent Threshold Limit Values booklet, including the 1971 Documentation, [170] published by the ACGIH.

The 1971 Documentation [170] again recommended a TLV of 3 ppm (2.5 mg/cu m). Additional studies by Largent [26] related to animal experiments; Kleinfeld [34] reported a fatal HF poisoning, without any exposure data; Heyroth's data [171] related to the highest concentration of hydrogen fluoride that could be tolerated by man for one minute. However, a second Largent study [172] reported by the Documentation reported that "some redness of the skin of the face was induced by exposure to the concentration of 3.39 ppm [2.8 mg/cu m] and by higher concentrations...." The Documentation presumed that prolonged inhalation of HF at high concentrations would lead to fluorosis.

The United States of America Standards Institute [173] (now referred to as ANSI) listed an 8-hour TWA concentration of 3 ppm (2.5 mg/cu m) as an acceptable standard (Z37.28-1966) for hydrogen fluoride. This TWA, according to ANSI, was supported by observations of animals exposed to HF by Stokinger [55] and Machle and co-workers [35,54] as well as supported in a review by Heyroth. [174] The United States of America Standards Institute [173] stated that an acceptable ceiling concentration had not been documented, but suggested that exposure be kept below 10 ppm.

Pennsylvania [175] adopted 3 ppm (2.5 mg/cu m) as both a TWA and a 15-minute short-term limit for HF. The short-term limit represented the maximum airborne concentration of a contaminant to which a worker might be exposed for 15 minutes, based on the assumption that there were sufficient recovery periods between episodes for recuperation. In <u>Short Term Limits for Exposure to Airborne Contaminants, A Documentation</u>, [176] Machle et al, [54] the 1966 Documentation, [169] and the Manufacturing Chemists' Association [2] were cited as supporting this short-term limit.

The following MAC values for HF have been set by foreign countries: Hungary and Poland, 0.5 mg/cu m [177]; East Germany and Czechoslovakia, 1 mg/cu m [177]; Yugoslavia, 1.7 mg/cu m [177]; Italy, [178] and Finland, [179] 2 mg/cu m. Bulgaria [179] listed a 1-mg/cu m permissible level. West Germany [180] and Britain [181] adopted a value of 2.5 mg/cu m. Hungary [177] also proposed a 1-mg/cu m peak, and Czechoslovakia [177] suggested a peak MAC of 2 mg/cu m.

In the Soviet Union, a mandatory maximum permissible concentration of 0.5 mg HF/cu m in the workroom air was established in 1959 by the Main State Health Inspector of the USSR. [182] The USSR allowed the permissible concentration to be exceeded if workers were in an industrial area for a brief, unspecified period.

In Japan in 1971, the Subcommittee on Permissible Concentrations of Hazardous Substances [183] recommended a permissible concentration for HF of 3 ppm (2.5 mg/cu m). This permissible concentration was an average concentration below which workers should not be adversely affected. In their documentation, [178] the Subcommittee reported that Japanese studies were insufficient, so the permissible concentration value of 3 ppm (2.5 mg/cu m), generally in use in Western European countries and the US, was chosen.

The present federal air contaminant limit (29 CFR 1910.1000) for hydrogen fluoride is an 8-hour TWA of 3 ppm (2.5 mg/cu m) based on the American National Standard Z37.28-1969 and published in the Federal Register 39:23543, June 27, 1974.

Basis for the Recommended Environmental Limit

The recommended occupational environmental limit for HF is expressed on a weight of HF/volume of air basis (mg/cu m). In evaluating the data presented, the ppm values in the cited literature have been converted to mg/cu m by assuming a molecular weight of 20 amu for HF. The basis of the limit is prevention of: (a) irritation of the skin, eyes, and respiratory tract; and (b) deleterious effects of skeletal fluorosis (increased bone density or osteosclerosis due to retention of fluoride).

The data collected by Largent [26] from human experimental studies are most relevant in establishing an environmental limit to prevent irritant effects. No noticeable adverse effects were found in one subject exposed for 15 days (6 hours/day, 5 days/week) to HF at concentrations which averaged 1.2 mg/cu m. Slight irritation of the exposed skin, eyes, and nose occurred in all five human subjects exposed for periods of up to 50 days at concentrations averaging between 2.1 and 3.9 mg/cu m, with ranges of concentrations between 1.5 and 6.5 mg/cu m. Slight desquamation of the superficial epithelium of the face was observed in one subject after several successive days of exposure to HF at 2.8 mg/cu m. No symptoms or signs of lower respiratory tract irritation occurred at any exposure levels. Comprehensive medical examinations before the exposures and at the end of each of the experiments did not detect adverse effects of any kind except for minor irritations which quickly subsided.

Hydrofluoric acid at concentrations of 25 mg/cu m could be tolerated by two human subjects for several minutes; only mild irritation of the eyes, nasal passages, and middle respiratory tract occurred. [35] Subjects did not cough during a 3-minute exposure. At 50 mg HF/cu m, these irritating effects were marked, and at 100 mg HF/cu m, the highest concentration of HF that was tolerated for more than one minute, there was immediate smarting of the exposed skin and marked eye and respiratory tract irritation.

Animal studies by Ronzani [52] showed that inhalation produced no adverse effects in rabbits, guinea pigs, and doves at an exposure level of 2.5 mg HF/cu m for 31 days. Stokinger [55] found only minor pulmonary changes in one out of five dogs exposed at 7 mg HF/cu m for 6 hours/day, 6 days/week, for 5 weeks. Renal and hepatic degenerative changes were reported by Machle and Kitzmiller [54] in rabbits, guinea pigs, and monkeys exposed at 15 mg HF/cu m for 6-8 hours daily, except weekends, until 309 hours had accumulated.

In man, kidney damage was only reported in severe, acute overexposures. [29,31] In a series of human HF inhalation experiments by Largent [26] with average exposure levels ranging from 1.2-3.89 mg HF/cu m for periods of up to 50 days, the lack of adverse effects on the kidneys was indicated by "normal" urinalyses.

The only epidemiologic study [49] reported which was designed to identify a chronic respiratory effect in workers exposed for many years to HF did not show any abnormal pulmonary function which was reasonably attributable to HF exposure. The averages of the observed values for FVC, FEV 1, and FEV 1/FVC from 305 chemical workers, including 11 HF workers (values for the HF workers were not separated) were within about 3% of the predicted values, with no significant difference between the chemical workers and a control group. The ratio of RV:TLVol was within normal limits for both groups. Determinations of HF in the air averaged about

1.03 ppm (0.85 mg/cu m), ranging from 0.07 to 10 ppm (0.06-8.2 mg/cu m).

The US Public Health Service [49] evaluated the effects of chemical irritants on exposed workers in a chemical plant where HF was one of the primary chemicals produced. Twenty-eight samples of airborne HF were taken with sampling periods ranging from 10 to 30 minutes. Results ranged from 0.07 to 10.0 ppm (0.06-8.2 mg/cu m), with a mean of 1.03 ppm (0.85 mg/cu m). Pulmonary function tests were performed on 305 chemical workers including 11 workers exposed to HF, and a control group of 88 workers in a box plant. The observed FVC, FEV 1, and FEV 1/FVC values for the total group were within about 3% of the predicted normal values with no significant difference between the chemical workers and the control group. The residual volume expressed as a percentage of total lung volume was 30.8% in the chemical workers, as contrasted with 26.8% for the box-plant workers, with both values within normal limits (35% being the upper limit of normal). The authors pointed out that this difference could be explained by the higher average age of the chemical workers, since RV:TLVol usually increases with advancing years.

Rye [45] reported that there was not a higher incidence of respiratory complaints in an unspecified number of phosphoric acid production workers when compared to a control group. According to the author, airborne concentrations of HF and silicon tetrafluoride were kept below 2.5 mg HF/cu m. One determination of airborne HF averaged 2.0 mg/cu m during an 8-hour period.

Correlation between airborne concentrations of HF and skeletal fluorosis has not been systematically investigated. Cases of osteosclerosis have been reported in workers exposed to HF, [37-41, HR

Henderson, written communication, September 1974] but no airborne concentrations were given. In at least two of the studies, [37,39] exposures apparently occurred to both gaseous and particulate fluorides. Considering the lack of any meaningful data for evaluating threshold airborne HF levels producing skeletal fluorosis, one has to refer to inorganic fluoride studies. Comparison of absorption and excretion of inhaled inorganic fluorides and HF [43] showed the same changes in the rate of urinary F excretion during and after exposure, indicating that the metabolism of absorbed F is the same whether the F is inhaled as inorganic fluoride or as HF. Based on this similarity of absorption, excretion, and, by inference, retention of F in osseous tissue, findings from inorganic fluoride studies can be applied in establishing an environmental limit for the prevention of osteosclerosis from HF exposure.

A study on inorganic fluorides relevant to the development of a workplace environmental standard is the one by Derryberry et al. [48] They provided comprehensive environmental and urinary F excretion data on each worker included in the survey and correlated it with radiologic findings. Environmental workplace fluoride levels were evaluated from approximately 750 air samples over a period of many years. An average daily fluoride exposure for each job was established, and from these data a weighted workplace airborne exposure was calculated for the period of employment of each worker. The range of individual average weighted exposures was 0.50-8.32 mg F/cu m, with 1.78-7.73 mg F/cu m being associated with minimal increased or questionable bone density (Table III-4). The difference in averages between the increased bone density group (average exposure 3.38 mg F/cu m) and the group with normal bone density (average exposure 2.62 mg

F/cu m) is significant by both t test ($t = -2.75$, $p = 0.0045$) and rank test ($Z = 2.2$, $p = 0.014$). The increased or questionable bone density was not associated with any musculoskeletal disability.

While the work of Derryberry et al [48] is helpful in developing a workplace environmental standard, it has inherent weaknesses which limit the extent to which the findings of the authors can be directly applied to the determination of a workplace environmental limit. The smallness of the test population placed limitations on the statistical significance of the findings. In the study, 17 out of 74 workers exposed to F at various concentrations were diagnosed as having bone density changes of minimal or questionable degree. The authors stated that these diagnoses were made by a radiologist who had prior knowledge that the tested individuals had potential fluoride exposures and who did not feel that the radiographs showed sufficient increase in bone density to be recognized as such in routine radiologic practice.

The Derryberry et al [48] study is of value, however, because it is comprehensive and it indicates that a threshold for minimal increases in bone density exists. From all aspects of the study, this threshold is best represented by an average exposure below 3.38 mg F/cu m.

In summary, studies by the US Public Health Service [49] and by Rye, [45] although limited in extent, suggest that no chronic pulmonary effects would be expected at exposure levels of 2.5 mg HF/cu m. The human experimental study by Largent [26] showed that only temporary, slight irritation of the skin, eyes, and nose resulted from exposure to HF at average concentrations of 2.12-3.89 mg/cu m. No signs or symptoms of lower respiratory tract irritation were reported at these average concentrations.

The study by Derryberry et al [48] indicates that exposures to HF somewhat below 3.38 mg F/cu m should prevent deleterious increases in bone density.

It is concluded that the recommended workplace environmental limit for HF of 2.5 mg/cu m as a TWA will provide protection of workers from the effects of HF over a working lifetime. In addition, in order to preclude acute irritation from HF, it is concluded that exposure of workers should not exceed 5 mg/cu m. Therefore, a ceiling limit of 5 mg HF/cu m based upon a 15-minute sampling period is proposed.

It is recognized that many workers handle small amounts of HF or are working in situations where, regardless of the amount used, there is only negligible contact with the substance. Under these conditions, it should not be necessary to comply with many of the provisions of the 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 limit to ensure that exposures stay below that limit. For these reasons, "occupational exposure to HF" has been defined as exposure at or above half the workplace environmental limit, thereby delineating those work situations which do not require the expenditure of health 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 delineate nonhazardous areas from areas in which a hazard may exist. However, because of nonrespiratory hazards such as those leading to skin burns or irritation or eye contact, it is recommended that appropriate work practices and protective measures to limit such contact be required regardless of the air concentration.

It is recognized that slight irritation to the skin, eyes, and nose may occur at exposure levels below the recommended environmental limit. This possibility emphasizes the need for further study relating to the acute and chronic effects of HF on the skin, eyes, and respiratory system. In addition, several animal studies reported kidney damage [54,55,58] after exposures to HF at concentrations as low as 15 mg/cu m. [54] These studies reveal a need for additional information regarding human exposures, and the possible acute or chronic effects of HF on the renal system.

Basis for Biologic Monitoring

Since the deposition of the F ion in the osseous system requires transport via the circulatory system (excluding topical application to the teeth), F is found in some physiologic fluids, eg, in blood and urine. This fact, combined with the fact that the urinary F concentration can be related to the onset of osteofluorosis, [HR Henderson, written communication, September 1974, 48,50] provides the basis for the recommendation that biologic monitoring of workers exposed to HF be performed as an acceptable means of identifying workers at risk. In the case of fluoride exposure (HF and associated gaseous and particulate inorganic fluorides), determination of airborne HF is not an entirely satisfactory alternative procedure as it is not feasible to estimate the quantity of F ingested by each worker. One may generalize that good personal hygiene will minimize the problem of F ingestion, but the quantity ingested is small, a few mg/day, as shown by the data supporting the recommended workplace environmental limit. Occupational exposure to HF and F is not the only source of F intake, food and fluoride in water are also influencing factors. Furthermore, unless the air sampling program included all employees at all times of exposure, it would be necessary to assume that exposure conditions at the time of sampling would be representative of exposure conditions when no sampling was conducted, which may not be the case. Biologic monitoring allows for the determination of total F excretion and therefore provides an indication of total fluoride intake. This serves as a means of spotting breakdowns in engineering controls and work practices. NIOSH therefore concludes that biologic monitoring shall be a part of the total worker protection program.

(a) Postshift Urinary F Biologic Standard

Several studies [26,43,45] demonstrated a rapid rise in urinary F excretion, within 2 hours of exposure to HF, which remained at high levels for 2-4 hours after cessation of exposure. Thus, end-of-shift urine samples, as recommended by NIOSH, will reflect exposure conditions occurring during the working day. Although this fact is not relevant to the correlation of postshift urinary F excretion with osteofluorosis, it does provide a means of monitoring employee work practices and engineering control measures.

Unfortunately, insufficient HF data are available to correlate osteofluorosis with postshift urinary F excretion. As with the establishing of the environmental limit, one has to rely on inorganic fluoride data. Collings et al [43] demonstrated that inhalation of HF and inorganic fluorides gave similar results both in regard to the rapidity with which urinary F excretion increased, and in relation to the extent of the increase in amounts of fluoride excreted in the urine. The study by Derryberry et al [48] provided long-term individual worker postshift urinary F excretion data which can be related to reported cases of increased bone density. In this study, average postshift urinary F levels of workers were determined from an average of 38 urine specimens for each worker. The data from this study demonstrated that, as the average urinary F excretion level increased, the percentage of cases of minimal or questionable increase in bone density gradually became greater until excretion in the range of 8-8.9 mg F/liter was reached; at this point, 60% of the group excreting F in that range showed minimal or questionable bone density increases (Table III-5).

Kaltreider et al [50] found osteofluorosis in 76 of 79 aluminum potroom workers. Urinary spot samples collected during working days showed an average F excretion of 8.7 mg F/liter for pot tenders, 9.8 mg F/liter for tapper-carbon changers, and 9.6 mg F/liter for cranemen. In a later study [50] at a different aluminum plant, no cases of increased bone density in a group of 231 potroom workers were found. Averages of postshift urinary F concentrations taken on the last day of the workweek over a 5-year period and corrected to a specific gravity of 1.024 ranged from 3.0 to 10.4 mg F/liter.

Largent et al [38] reported three workers with "slight" skeletal fluorosis who had been exposed to HF. The average postshift urinary F concentrations of these workers over a 3-year period were 10.09, 10.62, and 12.29 mg F/liter, respectively.

Four workers engaged in the production of HF [49] who had no osteofluorosis discernable by radiologic examinations had average urinary postshift F excretions of 4.31, 6.85, 17.5, and 26.6 mg/liter over a 5-day period. One of the two workers with high urinary F levels was exposed to a "gas out" during the week of urine collection and the other worker was exposed to a "reboiler leak." Although the determinations of F concentrations in these urine samples, taken only for a 1-week period, are of little value in establishing a postshift urinary F biologic standard, they nevertheless demonstrate that end-of-shift urine samples reflect exposure conditions. One of the four workers (HR Henderson, written communication, September 1974) showed "first-degree" osteofluorosis on follow-up examinations 2 years later. His average postshift urinary F level over a period of 7 years was 11.5 mg/liter.

The data provided, although limited, indicate that a postshift urinary F level, averaged over an extended period of time, of less than 8 mg/liter, as recommended by NIOSH, will not lead to osteofluorosis, although a minimal or questionable increase in bone density might develop after many years of occupational exposure. It is concluded that a postshift urinary biologic standard of 7.0 mg F/liter corrected to a specific gravity of 1.024 will provide an acceptable margin of safety.

(b) Preshift Urinary F Biologic Standard

Upon cessation of F exposure, the initial rapid rise of urinary F concentration is followed by a return to stable and relatively low levels of urinary F excretion within about 24 hours. [43,45] Urinary F concentrations approached preexposure values within 1-6 days. [43-45] These studies reveal that (1) the time required for the preshift sample to stabilize is quantitatively related to the urinary F concentration in the postshift sample, and (2) urinary F analyses conducted before exposure (preshift), as recommended by NIOSH, and after a nonexposure period of 1 day or more will provide a stable baseline value indicative of a worker's residual F retention (body burden).

The precise relationship of the concentration of fluoride in the preshift urine sample to the onset of osteofluorosis has not been sufficiently demonstrated, but a limited number of industrial exposure studies [49,50, HR Henderson, written communication, September 1974] as well as one nonindustrial exposure study [184] enable some inferences to be drawn regarding the relationship of osteofluorosis to the preshift urine sample.

Preshift urinary F excretions were analyzed [49] in 25 chemical workers exposed to HF or particulate fluorides in concentrations ranging from 0.077 to 10.0 ppm (HF) and 0.1-0.49 mg/cu m (particulate F). Preshift urine specimens, which were collected after the workers had been away from the plant on their days off, had F concentrations that ranged from 0.33 to 4.48 mg F/liter. Corresponding levels for a control group of 10 office workers not exposed to HF or particulate fluorides were 0.5-1.88 mg F/liter.

Additional data on environmental and urinary F levels of the same plant population were made available by the company (HR Henderson, written communication, September 1974). Periodic urinary F determinations on 13 HF workers over a 10-year period indicated that the average preshift levels for the workmen ranged from 2.0 to 5.7 mg/liter. One of four workers with high postshift urinary F concentrations whose X-rays did not indicate osteosclerosis when he was examined 2 years earlier demonstrated minimal osteosclerosis upon a follow-up examination. His average preshift urinary

F level was 5.3 mg/liter, ranging from 2.6 to 16.3 mg F/liter.

No osteofluorosis was found in a group of 147 potroom workers excreting 1.4 mg F/liter of urine (calculated as a preshift average) ranging from 0 to 11.9 F/liter. [50] Urine samples were collected after the workers were off work for 48 hours. The results were corrected to a specific gravity of 1,024.

Stevenson and Watson [184] reviewed medical records of patients residing primarily in Texas and Oklahoma where drinking water supplies contained up to 8 ppm fluoride. A diagnosis of fluoride osteosclerosis was made in 23 patients living in communities whose drinking water supplies contained 4-8 ppm fluoride. It was concluded that fluoride osteosclerosis did not develop in patients who drank water with a F concentration of less than 4 ppm.

The preceding data [49,50, HR Henderson written communication, September 1974] suggest that preshift urinary values up to 5.3 mg F/liter were not associated with osteofluorosis. While the findings of the nonindustrial exposure study [184] cannot be strictly applied to the determination of a preshift level, the results of the study indicate that a preshift level below 5.3 is desirable. It is concluded that a preshift level of 4 mg/liter will provide adequate worker protection. The validity of the value, as a preshift level, should be tested and adjusted in the future as more information is gained.

(c) Urine Specific Gravity

Urinary fluoride levels should be corrected to a uniform specific gravity of 1.024 to compensate as adequately as possible for various dilutions of urine samples and for the impracticality of collecting 24-hour specimens. Elkins et al [185] concluded that, although the true mean value for specific gravity is probably 1.022, the value most widely used for specific gravity correction in the US is 1.024, and it should continue as a reference to enable data comparisons among different investigators.

Basis for Radiologic Examination

The early signs of increased bone density from F absorption are most apparent in the lumbar spine and pelvis. [39] Since changes in the osseous system may be the only evidence of increased absorption and retention of fluorides, periodic X-ray examination of the pelvis may be valuable in cases where urinary F levels have been found to be high. It should be noted that the first changes produced by fluoride absorption and retention are difficult to recognize without prior knowledge that the individual had a fluoride exposure. Radiologic examination of the pelvis can result in irradiation of the gonads and embryos. [186] This may lead to deviation from normal mutation rates and may produce developmental abnormalities in the human embryo. Because of the difficulty of ensuring adequate protection for female gonads and for embryos, it is recommended that radiologic examination of the female pelvis not be conducted. Since male gonads can be protected adequately during pelvic X-ray examination, preplacement male pelvic examinations should be considered to obtain baseline radiologic information.