

**criteria for a recommended standard....**

**OCCUPATIONAL EXPOSURE  
TO  
HYDROGEN CYANIDE  
and  
CYANIDE SALTS  
(NaCN, KCN, and Ca(CN)<sub>2</sub>)**



**U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE**  
Public Health Service  
Center for Disease Control  
National Institute for Occupational Safety and Health  
**OCTOBER 1976**

**DHEW (NIOSH) Publication No. 77-108**

## CONTENTS

|  |             |
|--|-------------|
|  | <u>Page</u> |
| PREFACE  | v           |
| REVIEW COMMITTEES  | viii        |
| I. RECOMMENDATIONS FOR CYANIDE STANDARDS                               | 1           |
| Section 1 - Environmental (Workplace Air)                              | 2           |
| Section 2 - Medical  | 3           |
| Section 3 - Labeling (Posting)   | 5           |
| Section 4 - Personal Protective Equipment and Clothing                 | 10          |
| Section 5 - Informing Employees of Hazards of<br>HCN and Cyanide Salts | 17          |
| Section 6 - Work Practices and Control Procedures                      | 18          |
| Section 7 - Sanitation Facilities                                      | 31          |
| Section 8 - Monitoring and Recordkeeping Requirements                  | 31          |
| II. INTRODUCTION   | 35          |
| III. BIOLOGIC EFFECTS OF EXPOSURE                                      | 37          |
| Substances Presenting Exposure   | 37          |
| Occurrence and Use   | 37          |
| Extent of Exposure   | 41          |
| Historical Reports   | 41          |
| Metabolism and Theoretical Considerations                              | 45          |
| Effects on Humans  | 49          |
| Epidemiologic Studies  | 66          |
| Animal Toxicity  | 70          |
| Correlation of Exposure and Effect                                     | 86          |
| Carcinogenicity, Mutagenicity, and Teratogenicity                      | 94          |
| IV. ENVIRONMENTAL DATA   | 96          |
| Sampling and Analytical Methods  | 96          |
| Continuous Monitoring of HCN in Air                                    | 103         |
| Control of Exposure  | 104         |
| V. DEVELOPMENT OF STANDARD   | 106         |
| Basis for Previous Standards   | 106         |
| Basis for the Recommended Environmental Standards                      | 107         |
| VI. WORK PRACTICES   | 115         |

## CONTENTS

|       |  |     |
|-------|--|-----|
| VII.  | RESEARCH NEEDS   | 124 |
| VIII. | REFERENCES   | 126 |
| IX.   | APPENDIX I - Methods for Sampling<br>Cyanides in Air and Calibration | 147 |
| X.    | APPENDIX II - Method for Analysis of<br>Cyanide Samples              | 151 |
| XI.   | APPENDIX III - Hydrogen Cyanide Monitors                             | 157 |
| XII.  | APPENDIX IV - Material Safety Data Sheet                             | 160 |
| XIII. | APPENDIX V - First-Aid and Treatment Kits                            | 170 |
| XIV.  | TABLES AND FIGURE  | 174 |

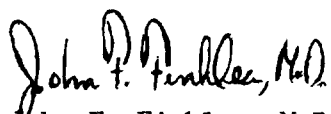
## PREFACE

The Occupational Safety and Health Act of 1970 emphasizes the need for standards to protect the health and safety of workers exposed to an ever-increasing number of potential hazards at their workplace. The National Institute for Occupational Safety and Health has projected a formal system of research, with priorities determined on the basis of specified indices, to provide relevant data from which valid criteria for effective standards can be derived. Recommended standards for occupational exposure, which are the result of this work, are based on the health effects of exposure. The Secretary of Labor will weigh these recommendations along with other considerations such as feasibility and means of implementation in developing regulatory standards.

It is intended to present successive reports as research and epidemiologic studies are completed and as sampling and analytical methods are developed. Criteria and standards will be reviewed periodically to ensure continuing protection of the worker.

I am pleased to acknowledge the contributions to this report on hydrogen cyanide and the cyanide salts by members of NIOSH staff and the valuable constructive comments by the Review Consultants, by the ad hoc committee of the the American Medical Association, by Robert B. O'Connor, M.D., NIOSH consultant in occupational medicine, and by Edwin C. Hyatt on respiratory protection. The NIOSH recommendations for standards are not necessarily a consensus of all the consultants and the professional society

that reviewed this criteria document on hydrogen cyanide and cyanide salts.  
Lists of the NIOSH Review Committee members and of the Review Consultants  
appear on the following pages.

A handwritten signature in black ink, reading "John F. Finklea, M.D." The signature is written in a cursive style with a large, stylized "J" and "F".

John F. Finklea, M.D.  
Director, National Institute for  
Occupational Safety and Health

The Division of Criteria Documentation and Standards Development, National Institute for Occupational Safety and Health, had primary responsibility for development of the criteria and recommended standards for hydrogen cyanide and the cyanide salts. The Division Review staff for this cyanide document consisted of J. Henry Wills, Ph.D., (chairman), Frank L. Mitchell, D.O., and Bert J. Vos, Ph.D., M.D., (consultant).

The University of Michigan developed the basic information for consideration by NIOSH staff and consultants under contract No. HSM-99-73-31. Alfred N. Milbert, Ph.D., had NIOSH program responsibility and served as criteria manager.

REVIEW COMMITTEE  
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

John F. Bester, Ph.D.  
Office of Extramural Coordination  
and Special Projects

Bobby J. Gunter, Ph.D.  
Division of Prevention  
Region VIII

Robert N. Ligo, M.D.  
Division of Surveillance, Hazard Evaluations,  
and Field Studies

Lester D. Scheel, Ph.D.  
Division of Laboratories and Criteria Development

Department of Labor Liaison:

David Lee  
Office of Standards



NIOSH REVIEW CONSULTANTS ON HYDROGEN CYANIDE

Carl D. Bohl, D.Sc.  
Monsanto Company  
St. Louis, Missouri 63166

Robert M. Clyne, M.D.  
Corporate Medical Director  
American Cyanamid Company  
Wayne, New Jersey 07470

James F. Morgan  
Haskell Laboratory  
E. I. DuPont de Nemours & Company  
Wilmington, Delaware 19898

James H. Sterner, M.D.  
Professor, Environmental Occupational Health  
The University of Texas  
Health Science Center at Houston  
School of Public Health  
Houston, Texas 77025

Grant S. Winn, Ph.D.  
Chief, Air Quality Section  
Utah State Division of Health  
Salt Lake City, Utah 84113

NIOSH REVIEW CONSULTANTS ON CYANIDE SALTS

William J. Andresen, Director  
Occupational Environmental Services  
American Cyanamid Co.  
Wayne, New Jersey 07470

James Dahlgren, M.D.  
American Board of Internal Medicine  
Los Angeles, California 90019

Ted A. Loomis, M.D., Ph.D.  
Professor of Pharmacology and State Toxicologist  
School of Medicine  
University of Washington  
Seattle, Washington 98105

James F. Morgan  
Industrial Hygienist  
Havertown, Pennsylvania 19083

Leonard D. Pagnotto  
Division of Occupational Hygiene  
Massachusetts Department of Labor and Industry  
Boston, Massachusetts 02116

Edward P. Radford, M.D.  
Professor of Environmental Medicine  
School of Hygiene and Public Health  
Johns Hopkins University  
Baltimore, Maryland 21205

## I. RECOMMENDATIONS FOR CYANIDE STANDARDS

The National Institute for Occupational Safety and Health recommends that employee exposure to hydrogen cyanide (HCN) and the cyanide salts in the workplace be controlled by adherence to the following sections. The standards are designed to protect the health of workers for up to a 10-hour workday, and a 40-hour workweek over a working lifetime. Compliance with the standard should therefore prevent adverse effects of HCN and cyanide salts on the health of workers. The standards are measurable by techniques that are valid, reproducible, and available to industry and government agencies. Sufficient technology exists to permit compliance with the recommended standards. The standards will be subject to review and revision as necessary.

These criteria and recommended standards apply to occupational exposure of workers to HCN and cyanide salts. Synonyms for HCN are hydrocyanic acid, prussic acid, and formonitrile. For the purpose of this document, cyanide salts are defined as sodium cyanide (NaCN), potassium cyanide (KCN), or calcium cyanide (Ca(CN)<sub>2</sub>). The word, cyanide, or the symbol, "CN", is used to designate salts as well as hydrogen cyanide.

The "action level" for hydrogen cyanide or a cyanide salt is defined as one-half the corresponding recommended ceiling environmental exposure limit. "Occupational exposure" to these compounds is defined as exposure to airborne concentrations greater than the corresponding action levels.

The criteria and recommended standards apply to any area in which HCN, any of the cyanide salts or materials containing any of them, alone or in combination with other substances, is used, produced, packaged,

processed, mixed, blended, handled, stored in large quantities, or applied. Exposure to cyanide at concentrations less than or equal to the respective action levels will not require adherence to the recommended standards except for sections 2-7, and 8(c). If "exposure" to other chemicals also occurs, for example to a combination of cyanide and methyl alcohol, provisions of any applicable standards for such other chemicals shall be followed also.

#### Section 1 - Environmental (Workplace Air)

##### (a) Concentration

Employee exposure to HCN shall be controlled so as not to exceed 5 milligrams per cubic meter of air expressed as CN (4.7 ppm), determined as a ceiling concentration based on a 10-minute sampling period.

Employee exposure to cyanide salts shall be controlled so as not to exceed 5 milligrams per cubic meter of air expressed as CN, determined as a ceiling value based upon a 10-minute sampling period.

Whenever the air is analyzed for cyanide salts, a concurrent analysis shall be made for HCN. Neither of the respective ceiling values may be exceeded nor may the combined values exceed 5 mg/cu m measured as CN during a 10-minute sampling period.

##### (b) Sampling and Analysis

Procedures for sampling, calibration of equipment, and analysis of air samples for HCN and cyanide salts shall be as provided in Appendices I and II, or by any method shown to be equivalent in precision, accuracy and sensitivity to those specified. A sampling period of about 10 minutes is

necessary to provide an amount of cyanide readily amenable to analysis by the cyanide selective electrode.

## Section 2 - Medical

Medical surveillance shall be made available as specified below for all workers occupationally exposed to HCN or cyanide salts.

(a) Preplacement and annual medical examinations shall include:

(1) An initial or interim work and medical history with special attention to skin disorders and those non-specific symptoms, such as headache, nausea, vomiting, dizziness or weakness, that may be associated with chronic exposure.

(2) A physical examination giving particular attention to skin, thyroid, and the cardiovascular and upper respiratory systems.

(3) An evaluation of the advisability of the worker's use of negative- or positive-pressure respirators.

(b) Initial medical examinations shall be made available to presently employed workers within six months of the promulgation of a standard.

(c) The responsible physician and the employer shall be aware of the material contained in Appendix V and shall ensure that employees trained in these first-aid measures are on duty whenever there is occupational exposure to HCN or a cyanide salt.

(d) Two physician's treatment kits shall be immediately available to trained medical personnel at each plant where there is a potential for the release of, accidental or otherwise, or for contact with, hydrogen cyanide or cyanide salts. One kit should be portable in order that it may be carried by medical personnel while accompanying a patient to the

hospital. The other kit should be kept under lock and key to assure that it is intact and available when and if needed. The key should be readily available at all times to the work supervisor on duty and the storage place should be of such construction as to allow accessibility in the event of loss of the key.

(e) First-aid kits shall be immediately available at workplaces where there is a potential for the release, accidental or otherwise, of hydrogen cyanide or a potential for exposure to cyanide salts. This kit shall contain as a minimum two (2) boxes of ampules (2 dozen), each containing 0.3 ml of amyl nitrite. Ampules shall be replaced biannually or sooner if needed to ensure their potency. The amyl nitrite ampules should be protected from high temperatures. In all cases, the contents of the medical and first-aid kits shall be replaced before the manufacturer's assigned expiration dates. Suggested contents for these kits are listed in Appendix V.

(f) Medical records shall be maintained for all workers occupationally exposed to HCN or cyanide salts. Pertinent medical records shall be maintained for 5 years following the last exposure to HCN or cyanide salts. These medical records shall be made available to the designated medical representatives of the Secretary of Health, Education, and Welfare, of the Secretary of Labor, of the employer, and of the employee or former employee.

Section 3 - Labeling (Posting)

(a) All shipping and storage containers of HCN shall bear the following labeling in addition to, or in combination with, labels required by other statutes, regulations, and ordinances:

HYDROCYANIC ACID, LIQUID

DANGER: EXTREMELY HAZARDOUS LIQUID AND GAS

EXTREMELY FLAMMABLE

MAY BE FATAL IF SWALLOWED, INHALED,

OR ABSORBED THROUGH THE SKIN.

USE ONLY IN CLOSED SYSTEM.

In case of contact, immediately flush skin or eyes with plenty of water for at least 15 minutes; get medical attention. Remove contaminated clothing and wash before reuse.

POISON  
First Aid

Carry patient to fresh air.  
Have the patient lie down.  
Remove contaminated clothing but keep patient warm.  
Start artificial respiration if breathing stops.  
Administer antidote (amyl nitrite ampule).  
Call a physician.

Temporary Antidote

If cyanide gas is inhaled: Break an amyl nitrite ampule in a cloth and hold lightly under nose for 15 seconds. Repeat at about 15-second intervals.

If cyanide is swallowed: Break an amyl nitrite ampule in a cloth and hold lightly under nose for 15 seconds. Repeat inhalation of amyl nitrite 5 times at about 15 second intervals. If patient is conscious or when consciousness returns, give emetic (1 tablespoonful of salt to each glass of warm water) and repeat until vomit fluid is clear. Do not give an emetic to an unconscious or barely conscious person.

(b) The following warning sign shall be affixed in a readily visible location at or near entrances to areas containing HCN and where there is reasonable potential for emergencies:

DANGER!

CYANIDE HAZARD AREA

UNAUTHORIZED PERSONS KEEP OUT

DO NOT WORK ALONE IN THIS AREA

IN EMERGENCY: (Here include, as applicable,

- (1) location of gas masks and other emergency equipment,
- (2) instructions for sounding emergency alarm,
- (3) location of first-aid equipment and supplies, and
- (4) instructions for summoning medical aid.)

The sign shall be printed both in English and in the predominant language of non-English-reading workers. All workers shall receive training and information on the hazards and safe work practices in handling HCN and cyanide salts, and on first-aid procedures in poisoning by these compounds.

(c) When HCN gas is used as a fumigant, warning signs shall be prominently displayed about the area and at all entries to the area as follows:

DANGER!

HYDROGEN CYANIDE

EXTREMELY POISONOUS GAS

UNAUTHORIZED PERSONS

KEEP AWAY



Where state or local laws, ordinances, or regulations specify the wording and use of warning signs for use by fumigators, such required wording and posting may be used in conjunction with the wording given in this subsection.

(d) All containers of solid cyanide salts shall bear the following labeling in addition to or in combination with labels required by other statutes, regulations and ordinances. The proper chemical name for the specific cyanide compound being labeled shall appear in large, bold face type at the top of the label.

(Insert name of compound)  
Inorganic Cyanide  
DANGER! MAY BE FATAL IF SWALLOWED OR INHALED  
CONTACT WITH ACID LIBERATES POISONOUS GAS  
CAUSES EYE BURNS AND MAY IRRITATE SKIN.

Do not breathe gas or dust.  
Do not get in eyes.  
Avoid contact with skin.  
Wash thoroughly after handling.  
Keep container closed and away from acids. Store in a dry place.  
In case of contact, immediately flush skin or eyes with plenty of water for at least 15 minutes; for eyes call a physician.  
Sweep up spillage. Do not flush to sewer which may contain acid.

POISON  
First Aid

Always have on hand a Cyanide First-Aid Kit.  
Carry patient to fresh air, have him lie down.  
Remove contaminated clothing but keep patient warm.  
Start artificial respiration if breathing stops.  
Administer antidote (amyl nitrite ampule).  
Call a physician.

Temporary Antidote

If aerosolized salt has been inhaled or if solid or dissolved salt has caused poisoning after contact with the skin: Break an amyl nitrite ampule in a cloth and hold lightly under nose for 15 seconds. Repeat 5 times at about 15-second intervals. Repeat as necessary using a fresh amyl nitrite ampule every three minutes. Use artificial respiration if breathing stops.

If cyanide salt in any form is swallowed: proceed as above. If the victim is conscious and capable of some activity, give an emetic (1 tablespoonful of table salt in a glass of warm water) in repeated doses until the vomit fluid is clear. Never give anything by mouth to an unconscious person.

(e) Containers of  $\text{Ca}(\text{CN})_2$  shall be labeled in the same manner as other solid cyanide salts, except that an additional warning is necessary because this material will react with water to release hydrogen cyanide. The statement of the hazard shall read as follows for  $\text{Ca}(\text{CN})_2$ :

DANGER! MAY BE FATAL IF SWALLOWED OR INHALED  
CONTACT WITH WATER OR ACID LIBERATES POISONOUS GAS  
CAUSES EYE BURNS AND MAY IRRITATE SKIN

(f) All containers of solutions of cyanide salts shall bear the following labeling in addition to, or in combination with, labels required by other statutes, regulations, or ordinances. The proper chemical name of the specific inorganic cyanide compound followed by the word "solution" shall appear in large, bold face type at the top of the label.

(insert name of compound) SOLUTION  
(Inorganic Cyanide Solution)  
DANGER! MAY BE FATAL IF SWALLOWED OR ABSORBED THROUGH SKIN  
CAUSES BURNS  
CONTACT WITH ACID LIBERATES POISONOUS GAS

Do not breathe gas.  
Do not get in eyes, on skin, on clothing.  
Wash thoroughly after handling.  
Keep container closed and away from acids.  
In case of contact, immediately flush skin or eyes with plenty of water for at least 15 minutes and call a physician.  
Treat spillage with strong calcium hypochlorite solution and flush to sewer.

POISON  
First Aid

Always have on hand a Cyanide First-Aid Kit.  
Carry patient to fresh air, have him lie down.

Remove contaminated clothing but keep patient warm.  
Start treatment immediately.  
Call a physician.

#### Temporary Antidote

If gas is inhaled: Break an amyl nitrite ampule in a cloth and hold lightly under nose for 15 seconds. Repeat 5 times at about 15-second intervals. Repeat as necessary, using a fresh amyl nitrite ampule every three minutes. Use artificial respiration if breathing stops.

If swallowed: Break an amyl nitrite ampule in a cloth and hold lightly under nose for 15 seconds. If patient is conscious, or when consciousness returns, give emetic (1 tablespoonful of salt in a glass of warm water) and repeat until vomit fluid is clear. Repeat inhalation of amyl nitrite ampule every three minutes. Use artificial respiration if breathing stops.

Never give anything by mouth to an unconscious person.

(g) In areas where cyanide salts, as either solids or solutions, are stored, used or handled, the following sign shall be posted in readily visible locations, particularly at entrances to the area:

CAUTION  
INORGANIC CYANIDE  
Contact with Acid Will Release Poisonous Gas  
ONLY AUTHORIZED PERSONS PERMITTED

IN EMERGENCY: (Here give the location of emergency equipment, instructions for sounding emergency alarm, and instructions for summoning medical aid.)

(h) During the loading or unloading of a cyanide salt solution into or from a tank car, tank truck, or other bulk transport container, the following warning signs shall be prominently displayed before and behind the transport vehicle or container and at other points of possible entry to the area:

WARNING  
CYANIDE SOLUTION  
Transfer of poisonous solutions in progress  
UNAUTHORIZED PERSONS KEEP OUT

#### Section 4 - Personal Protective Equipment and Clothing

Engineering controls and safe work practices shall be used to maintain exposures to HCN and cyanide salts below the prescribed limits. Administrative controls may also be used to reduce exposure. However, because the inhalation of cyanides or their absorption through the skin may be immediately dangerous to life, the added protection of personal protective equipment and clothing must be provided for work procedures and for emergency situations as discussed below. Such equipment and clothing must be provided to the workers engaged in work with cyanide. Emergency equipment shall be located at well marked and identified stations within the cyanide work areas. This equipment must allow each and every worker to escape the area in case of a cyanide emergency.

##### (a) Respiratory Protection

Engineering controls shall be used whenever feasible to maintain airborne cyanide concentrations at or below the environmental limits recommended in Section 1 above. Compliance with the permissible exposure limits by the use of respirators is only allowed when airborne cyanide concentrations are in excess of the workplace environmental limits while required engineering controls are being installed or tested, when nonroutine maintenance or repair is being accomplished, or during emergencies. Appropriate respirators as described in Table I-1 for HCN and Table I-2 for cyanide salts shall be used only when permitted by the above restrictions. Respirators shall be selected and used in accordance with the following requirements:

(1) For the purpose of determining the type of respirator to be used, the employer shall measure, when possible, the airborne

concentration of HCN or cyanide salt in the workplace initially and thereafter whenever process, worksite, climate, or control changes occur which are likely to increase the airborne concentration of these cyanides. The employer shall ensure that no worker is being exposed to cyanide in excess of the standards either because of improper respirator selection, fit, use, or maintenance.

(2) A respiratory protective program meeting the requirements of 29 CFR 1910.134, which incorporates the American National Standard Institute's Practices for Respiratory Protection Z88.2-1969, shall be established and enforced by the employer.

(3) The employer shall provide respirators in accordance with Tables I-1 and I-2 and shall ensure that the employee uses the respirator provided.

(4) Respiratory protective devices shall be those approved under the provisions of 30 CFR 11, published in the Federal Register, March 25, 1972, as amended.

(5) Respirators specified for use in higher concentrations of HCN may be used in atmospheres of lower concentrations. Likewise, respirators specified for use in higher concentrations of cyanide salts are permitted in atmospheres of lower concentrations.

(6) The employer shall ensure that the respirators are adequately cleaned, maintained, and stored when not in use, and that employees are instructed in the use of respirators assigned to them and in testing for facepiece leakage before each use.

(7) Cartridges or canisters shall be discarded and replaced with fresh canisters after each use. Unused canisters shall be discarded and replaced when seals are broken, after three years if seals are unbroken, or on the manufacturer's recommendation, whichever is first. Cartridges and canisters shall not be used for periods of time in excess of those indicated in Tables I-1 and I-2.

(8) Emergency and escape-type respirators shall be made immediately available at the work stations for each worker when there is potential for exposure to concentrations of the various cyanides above the ceiling values. For purpose of selection of respiratory protective equipment, entry into areas containing unknown and/or suspected dangerous atmospheric concentrations of HCN or cyanide salts shall be treated as an emergency.

TABLE I-1  
REQUIREMENTS FOR RESPIRATOR USAGE - HYDROGEN CYANIDE

| Maximum Use Concentration<br>(ppm of HCN)        | Respirator Type<br>for HCN Gas   |
|--|--|
| Less than or equal to 90 ppm                     | <p>(1) Type C supplied-air respirator, demand or continuous-flow type (negative or positive pressure), with half or full facepiece.</p> <p>(2) Full facepiece gas mask, chin-style canister specific for HCN. The maximum service life of canisters is one hour.</p>   |
| Less than or equal to 200 ppm                    | Full facepiece gas mask, front- or back-mounted type canister specific for hydrogen cyanide. The maximum service life of canisters is one hour.  |
| Greater than 200 ppm                             | <p>(1) Self-contained breathing apparatus in pressure-demand mode (positive pressure) with full facepiece worn under gas-tight suit providing whole body protection.</p> <p>(2) Combination supplied-air respirator, pressure-demand type (positive pressure), with auxiliary self-contained air supply and full facepiece; all worn under gas tight suit providing whole body protection.</p> |
| Emergency<br>(no concentration limit)            | <p>(1) Positive pressure self-contained breathing apparatus worn under a gas-tight suit providing whole body protection.</p> <p>(2) Combination supplied-air respirator, pressure-demand type, with auxiliary self-contained air supply; all worn under gas-tight suit providing whole body protection.</p>  |
| Evacuation or Escape<br>(no concentration limit) | <p>(1) Self-contained breathing apparatus in demand or pressure-demand mode (negative or positive pressure).</p> <p>(2) Gas mask, full facepiece or mouthpiece type, with canister specific for HCN.</p>   |

NOTE:

During the use of any respirator with half mask, full facepiece or hood, protective clothing should be worn if there is a chance that liquid HCN may contact any part of the body.

TABLE I-2  
 REQUIREMENTS FOR RESPIRATOR USAGE - CYANIDE SALTS

| Maximum Use Concentration<br>(mg/cu m expressed as CN) | Respirator type<br>for Cyanide Salts  |
|--|---|
| Less than or equal to<br>25 mg/cu m                    | <p>(1) Filter type respirators, approved for toxic dust, with half-mask (not applicable for <math>\text{Ca}(\text{CN})_2</math>).</p> <p>(2) Chemical cartridge respirators with replaceable cartridge for toxic dusts and acid gases; with half-mask. Maximum service life 4 hours.</p>  |
| Less than or equal to<br>50 mg/cu m                    | <p>(1) Full-face gas mask, chest or back mounted type, with industrial size canister for toxic dust and hydrocyanic acid gas. Maximum service life 2 hours.</p> <p>(2) Type C supplied air-respirator, continuous-flow or pressure-demand type (positive pressure) with full facepiece.</p> <p>(3) Type A supplied-air respirator, (hose mask with blower) with full facepiece.</p> |
| Greater than 50 mg/cu m                                | <p>(1) Self-contained breathing apparatus with positive pressure in full facepiece.</p> <p>(2) Combination supplied-air respirator pressure-demand type with auxiliary self-contained air supply.</p>   |
| Emergency (no concentration limit)                     | <p>(1) Self-contained breathing apparatus with positive pressure in facepiece.</p> <p>(2) Combination supplied-air respirator, pressure-demand type, with auxiliary self-contained air supply.</p>  |
| Evacuation or Escape (no concentration limit)          | <p>(1) Self-contained breathing apparatus in demand or pressure-demand mode (negative or positive pressure).</p> <p>(2) Full-face gas mask, front or back mount type with industrial size canister for toxic dust and hydrocyanic acid gas.</p>   |



(b) Protective Clothing

Because HCN and cyanide salts, dry or in solution, may be absorbed readily through the skin or any break in the skin, the provision and use of protective clothing are necessary for the protection of workers in most operations where HCN and cyanide salts are used in pure or diluted condition.

(1) When entering a HCN gas-filled area in emergency situations, when the airborne concentration of HCN is unknown, or when the known airborne concentration is greater than 200 ppm, employees shall wear gas-tight suits in addition to the required respiratory protection. The gas-tight suits shall provide full body protection.

(2) Employees engaged in maintenance, repair, or other work on equipment, or in circumstances whereby they may be exposed to HCN liquid or gas, shall wear protective garments or suits made of material impervious to HCN and providing full body protection.

(3) Employees shall wear rubber gloves when engaged in any activity which may involve the handling of, or possible contact with, HCN.

(4) Employees shall wear footwear impervious to HCN when working in areas or engaged in activities where spillage of liquid cyanide is likely. Such footwear or overshoes should be worn by workers handling cylinders of HCN or cans of absorbed HCN.

(5) Eye protection shall be provided by the wearing of a full facepiece respiratory protective device whenever there exists a hazard of contact of the eyes or conjunctivae with HCN in liquid form. Any circumstances having the potential for injury of the eye by exposure to HCN

liquid or gas almost certainly will also present a potential for hazard by inhalation which requires the wearing of respiratory protection. In case of doubt, the respiratory protective device should be worn. Eye and face protective equipment and its use shall conform to 29 CFR 1910.133. Selection, use, and maintenance of eye protective equipment shall be in accordance with provisions of the American National Standard Institute's Practice for Occupational and Educational Eye and Face Protection, ANSI Z87.1-1968.

(6) Employees working in tanks or other confined spaces shall wear approved harness and lifelines. All standard safety precautions for work in such spaces shall be observed with special vigilance because of the great toxicity of HCN. In all such cases, at least one other employee shall be in attendance and in contact (preferably in sight contact) and in a safe area or at a distance where he will not be affected by emergencies involving the first employee. The second employee (buddy) should be alert and equipped to summon help and render aid if needed.

(7) Employees shall wear gloves when handling dry cyanide salts and when using or handling equipment whose surfaces may be contaminated with these salts in such manner that contact of the chemical with the employee's hands is possible or likely.

(8) Employees shall wear gloves made of rubber or other impervious material when engaged in any operation wherein contact of the hands with solutions of cyanide salts is possible or likely.

(9) Employees shall wear protective sleeves, aprons, and/or full body protective clothing as needed to protect their skin from contact with cyanide salts, dry or in solution. When handling solutions,

the outer garment shall be of rubber or other material impervious to the solutions involved in the exposures. The garments shall fit snugly about the wrist, arm, neck, waist, and/or ankle (as appropriate to the particular garment) and shall have closures which will exclude dust, powder, mist, and/or splashes of cyanide salts in either dry or liquid formulations.

(10) In areas where spills or splashes of solutions of cyanide salts are likely to occur, the employees shall wear shoes, boots, or overshoes made of rubber or other material impervious to these solutions.

(11) Chemical safety goggles shall be worn by employees engaged in any operation wherein there is danger or likelihood that dusts or solutions of cyanide salts will come into contact with the eye.

Full-length face shields with forehead protection shall be worn by employees engaged in any operation wherein there is danger or likelihood that dusts, molten salts, or solutions of cyanide salts may contact the face.

(12) The employer shall be responsible for maintaining all devices and clothing to be used for personal protection in a clean and effective condition.

#### Section 5 - Informing Employees of Hazards of HCN and Cyanide Salts

At the beginning of employment or assignment for work at operations or in areas which may involve potential exposure to HCN and/or to cyanide salts (dry solids, solutions, melts, aerosols), employees shall be informed of the hazards of such employment and the possible injuries. They shall be

instructed in the proper procedures for the safe handling and use of these compounds, in the operation and use of protective systems and devices, and in appropriate emergency and first-aid procedures.

Instructions shall include, as a minimum, all information in the pertinent Materials Safety Data Sheet(s) (Appendix IV). This information shall be posted in the work area and kept on file, readily accessible to the worker at all places of employment where exposure may occur. The worker shall be informed of the location and availability of this information.

Information as required shall be recorded on US Department of Labor Form OSHA-20 "Material Safety Data Sheet", or on a similar form approved by the Occupational Safety and Health Administration, US Department of Labor. In addition, workers shall be advised of the availability of pertinent sources of information on the toxicity and safe use of HCN and cyanide salts.

## Section 6 - Work Practices and Control Procedures

### (a) Hydrogen Cyanide

(1) HCN liquid and gas must be handled in closed systems or containers insofar as is practical. The equipment, containers, and work procedures shall be designed to prevent the escape of HCN into the surroundings and to prevent or minimize hazards of fire, explosion, and of worker exposure to HCN.

(2) Buildings in which HCN is to be stored, handled, or used must be designed to prevent fire and explosion hazards and to minimize the release of the highly toxic liquid or gas. Equipment and vessels

containing or using HCN should be isolated in rooms or buildings designed for, and devoted to, these purposes.

Building construction shall be fire- and explosion-resistant and shall meet the requirements of the National Fire Protection Association codes and of the local codes, regulations, and ordinances. Explosion vents and fire doors shall be provided in accordance with codes and good practice.

Each room or building shall have no less than two means of exit, with doors opening outward and provided with "panic bar" release latches. Exits shall be provided so that no location within the room or building is more than 75 feet from an exit and personnel can be evacuated in less than 1 minute.

(3) All regular work areas where HCN is handled or used must be adequately ventilated so that, under normal or reasonably anticipated operating conditions, the airborne concentrations of HCN will not exceed the standard recommended in Section 1. Local exhaust ventilation shall be used at points or areas of regular or anticipated release of HCN gas.

Equipment for very high rates of ventilation of an area may be provided for the rapid reduction of contamination of air by HCN when emergency situations arise.

The HCN-contaminated air from an exhaust ventilation system must either be passed through a suitable collector to remove the HCN or be discharged at a location or in a manner such that persons or animals will not be endangered by the toxic gas.

Ventilation equipment must meet the applicable codes for

explosionproof and fireproof installation of such equipment.

(4) Workers entering any space or area known to have, or suspected of having, a dangerous concentration of HCN in the air shall wear a self-contained breathing apparatus, pressure-demand type (positive pressure), with full facepiece and a gas-tight suit giving full body protection (see Section 4). Workers entering such areas must not remove the protective suits until they have showered because residual HCN may be on their surfaces. (Breathing apparatus using compressed oxygen shall not be used when entering tanks or similar confined spaces which may contain HCN.)

Any area or space in which HCN contamination is likely and the concentration of HCN in the air is unknown shall be considered dangerous until the concentration is determined and found to be safe (see Chapter IV.) Persons entering such an area or space to make tests or measurements of the concentrations shall use the buddy system and shall wear self-contained breathing apparatus and protective clothing.

(5) Workers engaged in operations, maintenance, or repair work wherein release of HCN liquid or gas and contact with the liquid or gas is possible or likely shall be provided with, be fully trained in the use of, and wear approved respiratory protective devices and gas-tight suits (see Section 4).

Rubber gloves must be worn while performing activities which may involve contact with HCN.

(6) No employee shall work alone in any area or space in which HCN exposure, contamination, or an emergency potentially dangerous to the employee's safety and health either exists or is likely to occur. A

second worker shall be in attendance and shall be equipped, as minimal protection, with impervious footwear and gloves, and an easily donned respirator. This second worker shall maintain contact with the first employee from a safe location and shall be ready to summon aid and to render assistance, if needed. In the event of leaks or spills of HCN liquid or gas, only authorized, trained personnel with proper protection may remain in the area. All other personnel shall leave or be removed from the area immediately and shall be observed for any signs or symptoms of cyanide poisoning and need for treatment. Leaks and spills should be made safely alkaline and/or cleaned up as quickly as possible.

(7) HCN shall be treated at all times as a flammable and explosive substance with the exercise of all usual precautions in handling such materials and in the elimination of ignition sources.

(8) All applicable laws, regulations, and ordinances, the supplier's recommendations, and the provisions of Chapter VI shall be observed in regards to the following:

(A) Unloading, emptying, returning, shipping, and/or disposing of cylinders of HCN.

(B) Handling, storing, opening, and using of absorbed liquid HCN.

(C) Loading and unloading tank cars and motor truck tanks for transport of HCN.

(D) Safeguarding of loading, unloading, and other transfers of HCN liquid.

(E) Inspecting and approving storage facilities.

(F) Preparing, cleaning, and maintaining tanks and vessels to contain HCN.

(G) Disposing of HCN waste.

(9) Each plant having HCN exposures shall develop emergency procedures for its specific circumstances and the emergencies which may arise therefrom. The employees shall be fully informed of the emergency procedures and of their responsibilities under the plan. Each employee shall receive careful instruction and detailed training in the actions and procedures required of him in an emergency, and necessary actions should be prominently posted in all potential hazard areas.

(10) In the event of excessive or continued airborne concentrations of HCN above the standard, immediate action must be taken to determine and to eliminate or to control the source or cause of the elevated HCN concentrations.

In work areas where the concentration of HCN exceeds 20 ppm or where there is a potential through leaks to produce HCN concentrations approximating the lethal concentration in a matter of minutes, an alarm shall be sounded and the following emergency procedures shall be instituted:

(A) All nonemergency personnel shall be evacuated from the area immediately.

(B) Only emergency personnel properly trained and equipped to deal with the emergency shall either remain or reenter the area.

(C) The area shall be roped off and warning signs posted to exclude all others from the area until tests show that the



atmospheric concentration of HCN is below the recommended standard.

Every plant to which the above may be applicable shall prepare workable HCN emergency procedures, augmenting overall plant emergency procedures. Each plant's HCN emergency procedures must be tailor-made for the requirements of that specific plant.

(11) In developing HCN emergency procedures, the following should be kept in mind:

(A) The plan must be concise. If it is complicated, it will not serve its purpose.

(B) Any plan adopted in any particular plant should be well known to all in that plant.

(C) Each individual in the plant should know what he personally must do immediately in the event of an HCN emergency.

(D) Any worker whose clothing has absorbed HCN liquid or gas should remove this clothing immediately. Workers wearing respiratory protective devices should not remove them until their clothing has been removed or thoroughly rinsed off.

(E) The buddy system should be used in all emergency work in an HCN-contaminated area.

(12) In using HCN for fumigation, the space shall be sealed by appropriate means to prevent gas leakage into surrounding spaces and areas. Warning signs shall be posted in accordance with Section 3, subsection (c) above. Alert guards shall be in attendance while fumigation is in progress and until the space being fumigated is opened up and thoroughly ventilated. Access routes shall be locked to prevent entry by unauthorized personnel. All laws, regulations, ordinances, and codes,

where applicable, shall be followed.

(b) Cyanide Salts

(1) All necessary precautions must be taken to prevent cyanide salts from coming into contact with liquid or airborne acids. In addition, precautions must be exercised to prevent  $\text{Ca}(\text{CN})_2$  from coming into contact with water or humid atmospheres.

Cyanide salts must be protected also from contact with large concentrations of carbon dioxide. Carbon dioxide fire extinguishers must not be used where cyanide salts are present.

In any circumstance in which there is probable contact of cyanide salts with liquid or airborne acids such as  $\text{CrO}_3$ ,  $\text{SO}_2$ ,  $\text{CO}_2$ ,  $\text{HCl}$  etc, or of  $\text{Ca}(\text{CN})_2$  with a high concentration of water vapor or with liquid water, the standards and requirements applicable to exposures to  $\text{HCN}$  shall also apply.

(2) Cyanide salts as solids or solutions must be stored in sealed or tightly closed containers. The containers must be protected from moisture or other sources of erosion or damage which destroy the integrity of the container or closure. No hooks should be used in handling cyanide containers.

Cyanides should be stored in an area where there is no likelihood of contact with acids, acid vapors, including large concentrations of carbon dioxide, nitrate-nitrite mixtures, or peroxides.

Storage areas must be adequately ventilated to ensure that cyanide concentrations do not exceed the recommended workplace environmental limits in Section 1.

All containers of cyanide salts must be labeled in accordance

with the recommendations in Section 3.

Areas in which cyanides are stored must be posted in accordance with the recommendations in Section 3.

(3) When containers of cyanide salts are removed or unloaded from trucks, boxcars, or poorly ventilated spaces, these should be thoroughly ventilated, purged, and tested before a worker enters.

When cyanide salts are placed in other containers for transport or temporary storage, such containers must be properly covered and labeled.

(4) Mechanical exhaust ventilation by local exhaust shall be provided for all operations producing, or likely to produce, dust or mists of cyanide salts in excess of the limit recommended in Section 1, or to vaporize HCN in excess of the recommended limit for that vapor.

Examples of such operations are:

(A) Transferring or moving powdered or granular forms of cyanide salts;

(B) Using solutions of cyanide salts in electroplating;

(C) Using baths of molten cyanide salts or mixtures of salts containing cyanides for case hardening.

(D) Crushing or abrading cast forms of cyanide salts.

(5) Employees engaged in the transfer or use of cyanide salts or solutions thereof shall wear gloves and other personal protective clothing or equipment as recommended in Section 4 to prevent contact of the

cyanide salt as either solids or solutions with the skin of the employees.

Clothing which has become wet with any solution containing compounds of cyanide should be removed at once. If the skin has been wet, the worker should wash the skin area with a copious flow of water, and he should be observed for any signs or symptoms of cyanide poisoning. First aid and/or medical treatment should be started immediately on appearance of any such signs or symptoms. (See for example Appendix V) Gloves and other protective clothing should be changed daily, more often if significant contamination occurs. Protective clothing and equipment which has been contaminated with inorganic cyanide solids or solutions should be placed in a closed container provided for this purpose and should be cleaned or laundered thoroughly before reuse.

(6) Employees should exercise caution to prevent or minimize splashes of cyanide containing solution or liquids. When engaged in operations likely to result in exposure to splashes of such fluids, employees must wear protective goggles and/or a full-length face shield. Cyanide salts or solutions thereof being added to open containers of fluid should be added slowly and carefully to minimize the chance of spillage or splashing. When powdered or granular cyanide salts are being added or when there is evolution of mist from the bath, the employees shall be encouraged to wear at least a filter type respiratory protective device as a measure of protection in addition to that provided by ventilation.

(7) Care must be exercised to avoid spills of cyanide salts or cyanide-containing solutions. Spills of cyanide salts should be immediately and carefully cleaned up by shoveling the material into a proper container. Care must be exercised to minimize any dispersal of

cyanide dust into the air. The worker should wear a filter-type respirator as added protection when engaged in such work. Any remaining residue of solid should be flushed away with water containing some alkaline material ( $\text{Na}_2\text{CO}_3$ ,  $\text{NaOH}$ ,  $\text{KOH}$ , etc), or taken up by a wet cleaner after application of an alkaline fluid. Spills of cyanide solutions should be immediately flushed away with a copious flow of alkalinized water.

(8) Cyanide salts should not be flushed into any drain which may contain or subsequently receive acid waste. The cyanide spill should be flushed into a drain in a cyanide waste disposal system. Cyanide process waste solutions and flushings from spills should be passed through a cyanide waste disposal system. Such systems destroy the cyanide in alkaline solution by chlorination or treatment with other oxidizing agents.

(9) Nonreturnable containers and other containers or equipment contaminated with cyanides before being discarded should be washed thoroughly with alkalinized water to remove cyanide residues.

(10) When cyanide salts are used in fused salt baths, mechanical local exhaust ventilation should be provided to control any cyanide emissions.

Care in operation of the bath and in housekeeping must be exercised so that the area around the bath does not become covered with cyanide-containing powder or dust. Employees working at baths of fused cyanide salts should wear face shields and appropriate protective clothing to protect them from burns and skin contact with cyanides in the event of splashes. A shovel or similar tool should be used to add cyanide salts to a fused salt bath. The cyanide salt should not be added directly by hand.

(11) Inspection, cleaning, or repairing of tanks or other

equipment used with solutions of cyanide salts should be performed only by properly trained workmen under careful supervision.

(A) The tank should be drained of all cyanide solution as completely as possible, then filled with alkalized water and allowed to stand for 15 minutes, preferably with agitation. This procedure should be repeated; then a preliminary inspection may be made. Any encrustation should be removed by mechanical means and/or by means of a stream of water from a hose.

(B) If the tank is to be entered, the atmosphere in the tank should be tested for the presence of hydrogen cyanide and cyanide salts, to be certain it does not contain a dangerous airborne concentration of these or other materials.

(C) The tank should be purged with fresh air to ensure an adequate oxygen supply and air should be supplied to the tank while the worker is in the tank.

(D) Equipment other than tanks should be washed and vented similarly, as applicable.

(12) In the event of finding airborne concentrations of cyanide salts in excess of the limit, immediate action must be taken to eliminate the cause of the elevated airborne cyanide concentration. In case of any emergency situation (spills, leaks, or other unusual emissions of cyanide which result or potentially may result in dangerous airborne concentrations), all personnel shall be evacuated from the area. The personnel required to return to the area to institute corrective measures shall wear approved respiratory protective gear while entering and working

in the area until the situation is corrected.

(13) Any area in which there is the potential of an emergency involving HCN or a cyanide salt shall be posted in accordance with the provisions of Section 3, and emergency equipment stations shall be established. These stations shall be sufficient in number and so located as to be readily and immediately accessible to the workers in the area. The stations shall be provided with first-aid supplies and instructions for first-aid treatment of any persons suffering excessive exposure to cyanide. Approved type respiratory protective devices, as indicated in Section 4, shall be available at designated emergency stations. These devices shall be sufficient in number for the workers in the area and readily accessible.

(14) Workers entering any space or area known to have or suspected of having a dangerous concentration of HCN or a cyanide salt in the air shall wear a self-contained breathing apparatus (see Section 4) and full body protective clothing.

Any area or space in which cyanide contamination of the air is likely and the airborne cyanide concentration is unknown shall be considered dangerous until the concentration is determined and found to be safe (see Chapter IV). Persons entering such an area or space to make measurements of the concentrations, shall wear self-contained breathing apparatus and gas-tight suits.

(15) In the event of cyanide salts or solutions thereof coming into contact with the eyes, the eyes should be flushed for 15 minutes with a copious, gentle flow of water. Medical attention should be obtained immediately.

(16) No employee shall work alone in any area or space in

which exposure to cyanide salts or an emergency potentially dangerous to the employee's safety and life either exists or is likely to occur. A second worker shall be in attendance and in contact in a safe location and ready to summon aid and to render assistance, if needed.

(17) Eating, smoking, and the chewing of tobacco or gum shall be forbidden in areas where cyanide salts are handled. Carrying food, gum, and tobacco shall also be prohibited. Employees shall be required to wash carefully after working with cyanide salts and before eating, smoking or chewing.

(18) Each plant having potential exposure to cyanide salts shall develop emergency procedures for their specific circumstances and the emergencies which may arise therefrom. The employees shall be fully informed of the emergency procedures and of their responsibilities under the plan. Supervisors or other qualified persons shall give each employee careful instruction and detailed training in the actions and procedures required of the employee in an emergency. Instructions for sounding emergency alarms, reporting the emergency, and initiating the emergency procedures adopted by the plant shall be prominently posted in all potentially hazardous areas.

Designated employees shall be trained in the proper first aid and the use of the cyanide first-aid kits which shall be provided in nearby areas. A sufficient number of such employees shall be trained so that at least two employees at work in each shift are so trained. All workers shall be supplied with protective and safety equipment and fully trained in its use. Only specially trained employees shall be authorized to work in



areas in which a hazard of exposure to cyanide salts is present.

#### Section 7 - Sanitation Facilities

(a) Eyewash facilities and emergency showers shall be provided in areas where contact with HCN liquid or with cyanide salts as either solids or solutions is likely.

(b) Work clothing which has been contaminated by absorption of, or contact with, cyanide shall be thoroughly laundered before it is worn again.

(c) Clothing-change and locker-room facilities shall be provided in a nonexposure area. Workers should be encouraged to shower after work and to change work clothing frequently. Showers and basin washing facilities shall be located in the locker-room area.

(d) Food storage, preparation, and eating shall be prohibited in areas where HCN or cyanide salts are used. Smoking and the carrying of tobacco and other smoking materials shall also be prohibited in these areas. Clean and sanitary lunchroom facilities, if provided, must be in non-exposure areas.

(e) General plant housekeeping should be of a high order, assuring that escape routes and cyanide control equipment are kept clear. Plant sanitation shall meet the requirements of 29 CFR 1910.141.

#### Section 8 - Monitoring and Recordkeeping Requirements

Workers will not be considered to have occupational exposure to HCN or cyanide salts if environmental concentrations, as determined on the basis of an industrial hygiene survey conducted within 6 months of the

promulgation of standards, do not exceed half the recommended ceiling values. Surveys shall be repeated at least once every 3 years and within 30 days after any process change likely to result in increases of airborne concentrations of HCN or cyanide salts. Records of these surveys, including the basis for concluding that airborne concentrations of HCN and cyanide salts are at or below the occupational exposure levels, shall be maintained until a new survey is conducted. If the survey indicates that airborne concentrations of HCN or cyanide salts may exceed the respective occupational exposure levels, then the following requirements apply:

(a) Personal Monitoring

(1) A program of personal monitoring shall be instituted to identify and measure, or permit calculation of, the exposure of all employees who are occupationally exposed to HCN and/or cyanide salts. Interim monitoring of employee exposure to airborne concentrations of cyanide compounds shall be conducted at least every 6 months. If monitoring of an employee's breathing zone reveals that this employee is exposed to concentrations of cyanide in excess of the recommended ceiling value, the exposure of that employee shall be measured at least once every 30 days, control measures shall be initiated, and the employee shall be notified of his or her exposure and of the control measures being implemented to correct the situation. Such monitoring shall continue until two consecutive samplings, at least a week apart, indicate that employee exposure no longer exceeds the ceiling values in Section 1(a). Semiannual monitoring may then be resumed.

(2) In all personal monitoring, samples of airborne HCN and cyanide salts that, when analyzed, will provide an accurate

representation of the concentration of HCN and/or cyanide salts in the air which the worker breathes shall be collected. Procedures for sampling, calibration of equipment, and analysis of HCN and/or cyanide salts in samples shall be as provided in Section 1(b).

(3) For each determination, a sufficiently large number of samples shall be taken to characterize each employee's exposure during each workshift. Variations in work and production schedules shall be considered in deciding when samples are to be collected. The number of representative determinations for an operation or process shall be based on the variations in location and job functions of employees in relation to that operation or process.

(b) Area Monitoring

In workplaces where there is the potential for release of HCN in sufficient quantities to be lethal in a short time, airborne HCN concentrations shall be monitored continuously. Monitoring procedures to be followed should be in keeping with the guidelines in Appendix III.

(c) Recordkeeping Procedures

Records shall be maintained and shall include sampling and analytical methods, types of respiratory protective devices used, and ceiling concentrations found. Each employee shall have access to data on his or her own environmental exposures and records of such data shall be included in his or her medical records. Pertinent records of required medical examinations, including records of occupational accidents and environmental exposures within the workplace, shall be maintained for 5 years after the worker's last occupational exposure to cyanide and shall be

available to the designated medical representatives of the Secretary of Labor, of the Secretary of Health, Education, and Welfare, of the employer, and of the employee or former employee.

## II. INTRODUCTION

This report presents the criteria and the recommended standards based thereon which were prepared to meet the need for preventing occupational diseases arising from exposure to hydrogen cyanide (HCN) and to cyanide salts. The criteria document fulfills the responsibility of the Secretary of Health, Education, and Welfare, under Section 20(a)(3) of the Occupational Safety and Health Act of 1970 to "...develop criteria dealing with toxic materials and harmful physical agents and substances which will describe...exposure levels at which no employee will suffer impaired health or functional capacities or diminished life expectancy as a result of his work experience."

The National Institute for Occupational Safety and Health (NIOSH), after a review of data and consultation with others, formalized a system for the development of criteria upon which standards can be established to protect the health of workers from exposure to hazardous chemical and physical agents. It should be pointed out that any recommended criteria for a standard should enable management and labor to develop better engineering controls resulting in more healthful work practices and should not be used as a final goal.

These criteria for a standard for HCN are part of a continuing series of criteria developed by NIOSH. The proposed standards apply to the processing, manufacture, and use of HCN and cyanide salts or their release as intermediates, byproducts, or impurities as applicable under the Occupational Safety and Health Act of 1970.

The standards were not designed for the population-at-large, and any

extrapolation beyond general occupational exposure is not warranted. They are intended to (1) protect against injury from HCN, and cyanide salts , (2) be measured by techniques that are valid, reproducible, and available to industry and official agencies, and (3) be attainable with existing technology.

For the purpose of this document, cyanide salts are defined as sodium cyanide, potassium cyanide, or calcium cyanide. Other cyanide salts are not included in this standard. The word cyanide is used to designate all the above mentioned salts and hydrogen cyanide as well. Lithium cyanide, gold cyanide, and silver cyanide, as well as all compounds which can hydrolyze or decompose to release the cyanide ion (CN), should be considered as potential contributors of CN ions to the atmosphere of the workplace although they are not specifically covered in this document.

There exists a paucity of information on the chronic toxicity of the cyanides in concentrations of up to 20 ppm. Further epidemiological research on populations likely to be occupationally exposed to HCN and cyanide salts is necessary. Animal toxicity experiments are needed to elucidate the relation and severity of vascular and neural lesions associated with chronic exposure at these levels, as well as to evaluate any possibility of carcinogenicity, mutagenicity, or teratogenicity.

### III. BIOLOGIC EFFECTS OF EXPOSURE

#### Substances Presenting Exposure

The physical and chemical properties of hydrogen cyanide (HCN) are given in Table XIV-1. The boiling point of liquid HCN is sufficiently close to room temperature that it may be found in the workplace both as a liquid and as a gas.

The compounds herein denoted as cyanide salts are (1) inorganic, (2) appreciably dissociated or ionized in aqueous solution to produce cyanide ion or HCN, and (3) commercially important. The chemical and physical properties of various other cyanide containing compounds are listed in Table XIV-2. Those of major importance are described below.

#### Occurrence and Use

HCN is a colorless gas [1] or a colorless or bluish-white liquid [1,2] with a faint, characteristic odor of bitter almonds [2,3,4] perceptible to some people. [3,4] Kirk and Stenhouse [5] reported that 88% of 244 persons tested could smell hydrogen cyanide but that in a fourth of these, the determination was made only with difficulty.

The glucoside amygdalin which occurs in nature in some plants, notably almonds, [3] readily yields HCN upon hydrolysis. Recently, attention has been brought to the presence of HCN in automobile emissions. [6,7]

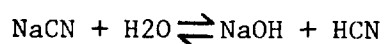
HCN is manufactured in the United States from coke-oven gas by reaction with sodium carbonate, from cyanide salts by reaction with acid, by the decomposition of formamide, from the reaction of ammonia, air, and

natural gas, or, most commonly, from the reaction of methane and ammonia under specific controlled conditions. [8]

The great bulk of the HCN synthesized is used directly in the same process system. [8] In 1973, the estimated consumption of HCN in the United States was approximately 310,000 short tons. [9] HCN is used primarily in the production of chemical intermediates for the manufacture of synthetic fibers, [8,10] plastics, [8] cyanide salts [8,10] and nitrites; in the fumigation of ships, [11,12,13,14,15] railroad cars, [14] buildings, [10,13,14,15,16,17,18] orchards, [10,19] tobacco, [20] and various foods [14]; it may be produced in electroplating, [21,22,23] metallurgy, [24,25,26] and photographic development. [27]

HCN is commonly sold as a technical grade liquid which assays between 96 and 99.5% HCN, as 5% and 10% solutions, as a 2% USP grade solution, or as a gas. [8] All grades usually contain a stabilizer (usually 0.05% phosphoric acid) to prevent explosive decomposition. When not pure or stabilized, it may polymerize spontaneously with explosive violence. [8] It is commonly sold or shipped in tanks, 75-lb cylinders, drums, or 5-lb bottles. [8]

Sodium cyanide, NaCN, is a white crystalline solid at normal temperature. [28] Currently, NaCN is manufactured chiefly from coke-oven gas, [8] by the reaction of HCN and NaOH, [29] or by the reaction of sodium carbonate, carbon, and ammonia. [28] Aqueous solutions of NaCN are slightly hydrolyzed ( $K_h = 2.5 \times 10^{-5}$ ) at ordinary temperatures to produce HCN according to the reversible reaction shown below. [28]





In the presence of any source of hydrogen ions in quantity, eg, strong mineral acid, the production of HCN from cyanide salts becomes both rapid and large. Above 50 degrees C, an irreversible decomposition to formate and ammonia, as shown below, becomes important. [28]



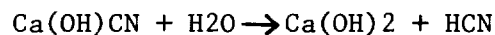
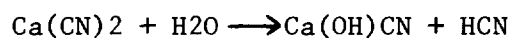
In the presence of NaCl, the hydrolysis of NaCN to HCN is increased at temperatures below 80 C, but decomposition to ammonia and formate is retarded. [28]

Sodium cyanide is marketed as a powder, granule, flake or block in pillow-shaped pieces weighing about 1 oz, and as a 30% aqueous solution. [28] Solid sodium cyanide is packed in steel or fiber drums, and the aqueous solution is shipped in tanks by truck or rail. [28,30] Potassium cyanide, KCN, is a white crystalline, deliquescent, solid. KCN is produced by methods similar to those for NaCN. [28,29]

The chemical reactivity of KCN is similar to that of NaCN. [28] Hydrolysis to HCN, as was the case with NaCN, is slight ( $K_h = 2.54 \times 10^{-5}$ ). [28] Potassium cyanide is sold in forms similar to those of NaCN but because KCN is more expensive, its world production for 1963 was only 5,000 tons. [28]

Calcium cyanide,  $\text{Ca}(\text{CN})_2$ , is also called "black cyanide" and is the only commercially important alkaline earth cyanide. [31] The hydrolysis of  $\text{Ca}(\text{CN})_2$ , which takes place in two steps, as shown below, is complete. [31] The resulting calcium hydroxide has dissociation constants of  $3.74 \times 10^{-3}$  and  $4.0 \times 10^{-2}$  but is much less soluble in water at 0 degrees C than sodium hydroxide [1,32] so that its aqueous solutions are

not as alkaline. For example, the pH of an aqueous solution of  $\text{Ca(OH)}_2$  saturated at 25 degrees (about 0.0203 M) is 12.4, while the pH of a 0.0125 M (0.05%) solution of NaOH is approximately 12. [33,34]



The basic cyanide is similar in general appearance and properties to  $\text{Ca(CN)}_2$ . [31] HCN is released from  $\text{Ca(CN)}_2$  by water or even water vapor present in relatively humid air. Calcium cyanide does not melt but forms calcium cyanamide ( $\text{CaCN}_2$ ) on heating above 350 degrees C. [31]

Calcium cyanide, which is manufactured [31] in large tonnages, is made by heating crude calcium cyanamide, which contains elemental carbon, in an electric furnace above 1000 C in the presence of sodium chloride. [31] Rapid cooling apparently prevents the reversion to calcium cyanamide. [31] It is manufactured primarily in Canada, South Africa, and East Germany and sold as flakes or blocks. There is also some production elsewhere in Europe and Japan. [31]

Sodium cyanide is used in the extraction of gold and silver, [35,36, 37, 38] heat treating of metals, electroplating, hardening of metals, coppering, zincing, bronzing, manufacture of mirrors, soldering, manufacture of or as a pesticide, photography, fumigation, [39,40] and the preparation of derivative chemicals. [8] Potassium cyanide is used in the extraction of gold and silver, [35,36,37,38,41] in electroplating, gilding of precious metals, soldering, hardening of metals, coppering, zincing, bronzing, manufacture of mirrors, preparation of derivative chemicals, photography, fumigation, [39,40] and in laboratory testing. Calcium

cyanide is used as a fumigant, [39,42,43,44] stabilizer for cement, in the preparation of derivative chemicals, in the manufacture of steel, in gold extraction, and in case hardening. [31]

#### Extent of Exposure

Some occupations which entail possible exposure to dangerous concentrations of HCN and/or a cyanide salt are listed in Table XIV-3. The number of workers with potential exposure to HCN has been estimated by NIOSH to be approximately 1,000. The number of workers with potential exposure to NaCN has been estimated by NIOSH to be 20,000. The number potentially exposed to KCN, and  $\text{Ca}(\text{CN})_2$  has not been estimated by NIOSH.

#### Historical Reports

The first experimental generation of HCN was reported by Scheele [45] in 1782-3. He reported that aqueous solutions of HCN had a peculiar, not unpleasant, smell and a slightly sweet taste. Scheele described many chemical properties of HCN and found that mixtures of air and HCN burned readily.

In 1884, De Tatham [46] reported a case of temporary hemianopsia after exposure to HCN. The woman affected had used a dilute HCN solution to clean some gold lace. The author [46] presumed that her only exposure was to HCN vapor. However, the possibility cannot be excluded that the intimate contact of the HCN solution with her skin resulted in skin absorption.

The first uses of the gas as a fumigant were in 1886 to control scale on citrus trees in California, [19] in 1898 to kill vermin in railway

cars, [11] in 1901 to kill bed bugs in prisons, [11] and, after 1910, for the fumigation of the holds of ships. [11]

Stock and Monier-Williams [11] observed several cases of occupational exposure to HCN used in fumigation in 1923. In one report, sailors were engaged in dropping cyanide eggs into vats of acid laid out in various locations on board ships and were overcome by HCN gas, presumably from other parts of the ship; five died. A second case was that of a would-be thief who entered the Krupp works in Essen, Germany, while it was being fumigated. Two other cases were due to pipe or duct connections to space adjoining that being fumigated. In other cases, workers entered spaces and were quickly overcome by "pocketed" HCN fumes in places that had been presumed to be safe.

In 1919, Fuhner [12] reported the death of a mate of a Swedish vessel, whose cabin had been fumigated with HCN. He returned to the ship the same day accompanied by a woman who remained in the cabin from 11:30 pm to 4:30 am. She said she was overcome, could scarcely stand upon reaching the open air, and had to sit down and rest before proceeding home. The mate was found dead at 7:30 the next morning, his body still warm. The author suggested that the bedding in the cabin had absorbed a good deal of gas and that the concentration of HCN in the air was too low to cause death in 5 hours, but sufficient to do so in 8.

Bernstein and Avital [20] reported an accidental mass poisoning in 1960 in Israel following fumigation of a tobacco warehouse with HCN. The warehouse was sealed for 3 days for effective fumigation. Windows were then opened and remained so for 48 hours, at which time they were closed so that a second fumigation with a 6.6% solution of an unspecified oil-soluble

fumigant could be performed. The building remained closed until the next morning. By 8:00 am that day, 46 of the 53 people who had entered the warehouse that morning had been affected. The symptoms of those poisoned included headache, dizziness, gastrointestinal upset, dyspnea, and heart palpitations.

The day after the incident, a test of the air in the warehouse was made using benzidine and copper acetate test papers. HCN was not found in the general room air but was detected in the vicinity of the tobacco bales in undetermined concentrations.

The problem of commercial fumigation of buildings as well as ships was discussed in a 1935 report by Cousineau and Legg [16] detailing their experiences in Montreal and Detroit, respectively. They noted that 1 death was reported as a result of every 2,000 fumigations in Detroit. They further noted that the addition to HCN of lacrymatory gases, such as CNCl and chloropicrin, was beneficial in the protection of public health. There apparently was controversy among others as to whether or not such additives were beneficial. [16]

There were several early cases of poisoning resulting from the inhalation of inorganic cyanide aerosol or contact with cyanide solutions. [47,48,49,50,51] In 1878, Souwers [50] reported the nonfatal poisoning of a photographer who had been working with both solid KCN and KCN solutions and complained of soreness of the scalp, heaviness of the head, sleeplessness, pain in the lumbar region, delirium, ringing in the ears, swelling of the upper eyelids, loss of appetite, nausea, constipation, and chills and cold sweats upon awakening from cat-naps. In addition, he complained of shortness of breath. Souwers removed him from KCN exposure and treated his symptoms. The patient made a full recovery in 3 days.

Skin absorption of inorganic cyanide was implicated in cyanide poisoning as early as 1905, when McKelway [51] reported a case of a woman hairdresser who moistened her fingers and rubbed them with solid KCN in an effort to remove a stain from a silver-based dye. She experienced vertigo and difficulty in breathing within 5-10 minutes and subsequently collapsed into an unconscious state. She was revived, treated with 2 oz whiskey, strychnine, atropine, and morphine, and recovered despite the therapy administered.

In 1913, Rambousek [49] noted that skin contact with cyanide solutions had been sufficient to cause symptoms of cyanide poisoning among electroplaters, especially among those with deep ulcerations and fissures from working with caustic soda. No further elaboration of systemic symptoms was offered.

Similarly, the International Labour Office [48] reported several cases of dermatitis which occurred prior to 1912 in the United States as a result of direct contact of the skin with cyanide solutions. In 1923, seven men were poisoned while emptying casks of KCN. [48] One died.

Industrial cases reported by the International Labour Office [47] in 1930 included a sudden death from inhalation of HCN escaping from a leaking pipe in a sodium cyanide factory, several severe cases of intoxication in a factory adjacent to a metal-treating plant, and several cases associated with factory or home fumigation operations. It is likely that many of these illnesses were the result of exposure separately or concomitantly to HCN.

The ingestion of KCN solutions has been a suicidal method since the nineteenth century. [51,52] Accidental ingestions in the workplace have

been rarely reported, but the International Labour Office [48] did report a case which occurred in 1920 in Germany where a female jewel worker died after drinking from a bottle which was previously washed with a solution of KCN.

### Metabolism and Theoretical Considerations

It appears that HCN and cyanide salts have a common mechanism of action, ie, inhibition of cytochrome oxidase via reaction of its ferric iron with the cyanide ion in vivo.

Once absorbed into the body, cyanide can form complexes with heavy metal ions. [29,53,54] Formation of these complexes can rapidly cause disturbances in enzyme systems in which heavy metal ions, alone or as part of organic molecules, act as cofactors. [29,53,54]

Albaum et al [55] published in 1946 an in vitro study of the competition of methemoglobin and cytochrome oxidase for cyanide. Cytochrome c absorbs radiation at 550 nanometers (nm). In the presence of cytochrome oxidase, the optical density at 550 nm decreases at a rate directly proportional to the activity of cytochrome oxidase. This rate of change was determined in the presence of cyanide, demonstrating the ability of cyanide to inhibit cytochrome oxidase activity. Additions of methemoglobin, in which the iron had been oxidized electronically to the ferric state, to a solution containing cytochrome c, cytochrome oxidase, and cyanide were found to increase the activity of cytochrome oxidase, thus reversing the inhibitory effect of cyanide. The authors also found that the addition of cyanmethemoglobin to a solution of cytochrome c and cytochrome oxidase had no immediate effect on enzyme activity, but after a

few minutes the enzyme became increasingly inhibited. Thus, the authors demonstrated in vitro the abilities of cytochrome oxidase and methemoglobin to compete in a reversible fashion for the cyanide ion.

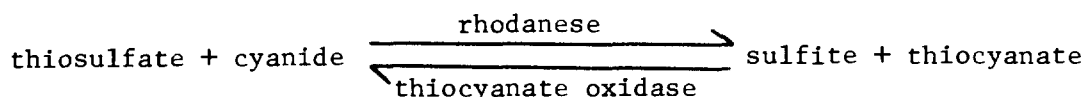
In a 1958 survey, Dixon and Webb [56] found that the concentration of cyanide necessary for inhibition of cytochrome oxidase was 2-6 orders of magnitude less than those required for inhibition of other enzymes. The interference of CN with many different enzyme systems other than those involved in respiration may thus contribute to its toxicity.

Schubert and Brill [57] in 1968 measured the inhibition and recovery of liver cytochrome oxidase in mice, rats, and gerbils after the intraperitoneal administration of KCN. Inhibition of the enzyme was found to reach a maximum 5 to 10 minutes after the cyanide injection. Depending on the dose, the enzyme activity returned to normal 5 to 20 minutes after maximal inhibition in mice but required up to 1 hour or more in the rat and gerbil. Interestingly, they found that the abilities of mice and rats to tolerate divided doses of cyanide depended on the total dose as well as on the time-dependent degree of enzyme inhibition. For example, they found that mice invariably survived a single sublethal dose of 6 mg/kg of KCN but not two doses of 3 mg/kg given 6 minutes apart or three doses of 2 mg/kg given at 6 minute intervals. They further showed that sodium thiosulfate and nitrite were able to reactivate liver cytochrome oxidase within minutes when administered to cyanide-treated rats and mice.

This mechanism of action was reported [58] in 1971 to be sufficiently well understood to be traceable from the initial lesion through the pathophysiologic responses to the clinical picture. The chain



of events is shown in Table XIV-4. Further, unless death intervenes, most of the HCN absorbed or formed in the tissues by biotransformation of cyanogenic substances is converted to the much less toxic thiocyanate which is then excreted, mainly in the urine. [58,59,60] The reaction for this conversion, which takes place in the presence of rhodanese, a sulfur transferase enzyme, is shown below. The reaction is reversible in the presence of thiocyanate oxidase, [61] so that if excretion of thiocyanate is not prompt there may be some regeneration of cyanide.



The reaction has been verified in animals. [62] Inhibition of rhodanese, and thereby inhibition of the ability to convert cyanide to thiocyanate, or an inability to excrete thiocyanate [25] is perhaps responsible for the occasionally observed chronic toxicity of cyanide. [17,63,64] Thiocyanate itself has toxic effects, especially inhibition of uptake of inorganic iodide into the thyroid gland for incorporation into thyroxine. [65] Thus, failure to excrete thiocyanate or chronic exposure to elevated concentrations of this ion in the blood may have a deleterious action on the ability and inclination of an employee to perform his work. Other minor pathways for detoxication and excretion include direct excretion as HCN in breath or cyanide ion in secretions, oxidation to formic acid, metal coordination, and condensation with cystine to 2-iminothiazolidine-4-carboxylic acid and excretion. [66,67] The metabolism of cyanide as

summarized by Williams [66,67] is shown in Figure XIV-1. The detoxication rate for HCN injected intravenously in man has been estimated to be about 0.017 mg/kg/min. [68]

Cyanide is present in normal healthy human organs at concentrations ranging up to 0.5 mg/kg. [67] In 1954, Feldstein and Klendshoj [69] found concentrations of zero to 10.7  $\mu\text{g}/100\text{ ml}$  (mean 4.8  $\mu\text{g}/100\text{ ml}$ ) in 10 blood plasma samples. These authors [69] also measured cyanide plasma levels in several cases of mild industrial exposure to cyanide fumes which did not terminate fatally. Their data suggested that the plasma levels returned to the normal range [67] within 4 to 8 hours from the time of exposure. [69] Their data also indicate that the half-life for the conversion of cyanide to thiocyanate from a non-lethal dose in man is between 20 minutes and 1 hour. Thus, as a rough approximation, one-half hour after exposure the plasma level of cyanide was 35  $\mu\text{g}/100\text{ml}$  and after an additional half-hour, it was 18  $\mu\text{g}/100\text{ml}$ . Normal concentrations of cyanide in tissues and fluids have been attributed to metabolism of foods [52,70,71] and cigarette smoking. [52,67,72,73,74,75,76] In 1973, Pettigrew and Fell [77] however, could not detect a significant difference between the amount of cyanide in the whole blood of smokers and non-smokers, but, as expected, the plasma thiocyanate levels of the smokers were significantly elevated. They suggested that the ratio of cyanide to thiocyanate in body fluids was about 1 to 1000 (1 to 50 in blood plasma [78]) and stated that a more reliable index of cyanide exposure may be measurement of plasma thiocyanate rather than determination of whole blood cyanide.

In 1950, Hardy et al [24] observed a group of 25 workers exposed to HCN who consistently excreted small amounts of thiocyanate, with average

spot urinary thiocyanate concentrations of 6-13 mg/liter. Three workers had no thiocyanate in their urine and three had concentrations of 21, 22, and 29 mg/liter. Those with the high concentrations may have been cigarette smokers. In a study of 10 spot urinary samples from 5 people not employed in industry, the thiocyanate concentration was 0-23 mg/liter; the highest was that from a man who smoked two packages of cigarettes a day.

Radojicic [79] in a 1973 study to be discussed below, found that smokers always eliminated more thiocyanate in the urine than nonsmokers. His values (n=10) were  $4.40 \pm 1.400$  for smokers and  $0.17 \pm 0.136$  mg/liter for nonsmokers. Maehly and Swensson [76] also found that non-smokers exposed to moderate cyanide concentrations in the air, as well as individuals exposed to high cyanide levels, show higher than average concentrations of cyanide and thiocyanate in their urine.

#### Effects on Humans

Illness and death due to exposure to cyanide have resulted from exposure to gaseous or liquid HCN itself, exposure to the cyanide salts, and exposure to HCN generated by the misuse of cyanide salts. In the last situation, the cyanide salt is converted to airborne HCN by treatment with acids, acid salts [8,29,30] or by water. [29,30] It has been noted [5,29,30] that cyanide salts have the odor of HCN. The rate of HCN release is much greater when acids contact cyanides than when they are treated with water. Considerable amounts of HCN are evolved when moisture acts on a dry alkaline cyanide, particularly  $\text{Ca}(\text{CN})_2$ . [42] The rate of such evolution from aqueous solution increases upon heating. [63,80]

Chronic HCN poisoning, at least in the serious or incapacitating form, is rare. Isolated reports [17,24,26,81] have described signs and symptoms of patients suspected of having chronic HCN poisoning. In 1899, Merzbach [81] reported a case of a printing shop worker exposed to cyanide aerosols generated when he placed copper plates in a cyanide bath and allowed an electric current to pass through the solution. His exposure probably also included skin contact with silver cyanide-potassium cyanide solutions. After 1 year of exposure, he experienced severe gastrointestinal symptoms and a generalized disturbance of the nervous system, including behavioral and mental disorders. He continued working for 12 years before he was completely disabled and died 2 years after cessation of exposure. A determination of the degree of his exposure is not possible from the data provided.

Hardy et al [24] in 1950 described two men who may have had chronic cyanide poisoning. Both men complained of headache and weakness or fatigability and were observed to have slight lid lag, enlarged thyroids, and excessive perspiration. One of the two also experienced dizziness and mental confusion, slurring of speech, coughing, sneezing, and occasional abdominal cramps, nausea, vomiting, and coarse tremor of the extremities followed by their temporary paralysis. Both men were exposed to cyanide aerosols generated by case hardening. Some exposure to HCN may have occurred.

Wuthrich [25] in 1954 described a 39-year-old German blacksmith who was exposed to cyanide in case hardening on a sporadic basis for 2 years and then more frequently for the next 4 years. The worker noticed some initial irritation, followed by a general worsening of health. He experienced loss of appetite, nervousness, vertigo, headaches, nausea, and

vomiting. During 2-3 week vacations, the symptoms disappeared but reappeared within a month after returning to work. His thyroid gland was slightly enlarged. After exposure to cyanide had ceased for about 14 days, the man was given a placebo of NaCl, iv, for three days during which time he reported an improvement in his condition. On the 4th day, 1.4 g of sodium thiocyanate was substituted for NaCl in the daily injections. The thiocyanate concentration in the blood serum increased rapidly following these injections and did not decay to normal between injections. From the day of the first NaSCN injection, the man began to complain of nausea, lack of appetite and nervousness. After three NaSCN injections, he reported nausea and vomiting and spontaneously stated that he felt the same symptoms as at his workplace.

If there are 5200 ml of blood in the average man, then a dose of NaSCN of 1.4g would give an immediate concentration in the blood of 27 mg %. The effect of these injections was a daily, stepwise increase in the concentration of thiocyanate in the plasma until the injections ceased. At this time, the serum thiocyanate concentration was approximately 20 mg %. The half-time of decay of the thiocyanate concentration in the serum was approximately 2 days. Urinary thiocyanate was also monitored, reaching a maximum of about 550 mg % 1 day after the maximum concentration of thiocyanate in the serum had been attained. The half-time of decay of the concentration of urinary thiocyanate also was approximately 2 days. When the daily NaSCN injections were replaced with ones of NaCl, the patient's symptoms disappeared completely after 2-3 days.

In 1932, Smith [26] reported three cases; first, a case hardener who experienced weakness, nausea, dizziness, and semiconsciousness following an

acute exposure to visible aerosols of potassium cyanide. The second was a gold plater of 20 years' tenure in a plant with poor ventilation. When plating and making up the cyanide solutions, he habitually heated them to the boiling point--an activity that may have evolved HCN gas. (The author pointed out that potassium or sodium cyanide solutions give off HCN when heated above 176 degrees F.) The health of the plater prior to 1931 was described as "good." He was first bothered by a rash on his arms, hands, and face, and occasional spells of nausea and vomiting. Prior to his vacation, he made up a large batch of KCN. On the 1st night after leaving, he experienced severe abdominal pains and convulsions. This attack lasted a week with persistent vomiting. After 10 days, he returned to work. His symptoms recurred on the 1st day back, and he was hospitalized. Incapacitated by weakness, headache, dizziness, muscular cramps, and recurring attacks of abdominal pain, he gave up work. Smith stressed that absorption of cyanide from the solution may have been a factor in this case. Each of the last two illnesses was caused apparently by a large, acute exposure to cyanide superimposed on a low-level, chronic exposure. Unfortunately no exposure data were made available.

The third case [26] concerned a 45-year-old case hardener who had worked for 15 years in a poorly ventilated shop plunging steel objects into a pot of molten potassium cyanide. He had spells of weakness and dizziness to the extent that he would fall down. He lost weight and became weakened. Three months later, he had to give up his job. Three years later he was entirely disabled, with paralysis and wasting of the muscles of his arms and legs. No exposure data were given, but the chronic effects may have been the result of acute and chronic exposure to inorganic cyanide and HCN.

In 1966, Jaroschka and Kropp [17] reported an illness following exposure for 2 years to KCN and HCN. The worker supervised operation of the galvanizing baths and made up cyanide solutions as a part of his principal job. He observed that his cigarettes had an unpleasant, metallic, sweet taste when he smoked in the cyanide area. He complained of weakness, debilitation, headache, dizziness, weight loss, coughing, and lack of appetite. He was depressed and suicidal. Upon examination, he was found to have toxic hepatitis and a moderate kidney insufficiency, but no thyroid enlargement. His condition improved after he began work without exposure to cyanide and was later found to have a normal liver and only a slight kidney insufficiency. Exposure data were not presented.

Chaumont [82] in 1960 described a case in which a foreman in a galvanizing shop who had been working near large ventilated cyanide and chromic acid tanks for 3 years and near small unventilated brass-plating tanks for 3 months experienced nausea, vertigo, tenesmus, and cold perspiration sporadically for about 49 days. He was then hospitalized for 11 days. Upon his return to work he was granted a transfer to another work site but was denied (French) compensation benefits because the "essential factors of sudden occurrence and violence" were missing. Chaumont [82] went on to describe the various symptoms which have been reported for chronic cyanide exposure and stated that it is clinically undeniable that cyanides can cause this type of occupational intoxication.

Colle [83] in a 1972 review paper also described the various symptoms reported for cyanide intoxication. He grouped them into systemic, digestive, pulmonary, cardiovascular, and nervous disturbances, as well as

hematic disorders and cutaneous and mucous lesions. He concluded that the symptomatology and pathoanatomic findings establish chronic cyanide poisoning as a true clinical entity. Colle also based his conclusion on the fact that this syndrome of chronic intoxication does not develop insidiously but that it improves or regresses when work is stopped for at least 2-4 weeks and that it recurs in 5-6 days when the individual returns to his old work. He pointed out that the experienced cyanide workers are aware that the subacute symptoms are transitory and that the breathing of fresh air or the stopping of work for awhile causes their disappearance.

Sato et al in 1955 [84] had occasion to open several 100-liter chambers containing 10 ppm of HCN. It was noted that persons who were working in the laboratory about 3 meters from the chambers at the time of opening complained of headache several hours later. The authors recommended that on the basis of headache development, human exposure should be kept down to about 2 ppm.

In 1947, Wexler et al [85] gave to 16 normal soldiers iv injections of NaCN sufficient to stimulate respiration and observed their electrocardiograms. The dose was 0.11-0.2 mg NaCN/kg, varying with the amount that was needed to elicit respiratory stimulation. The electrocardiograms of 15 of the 16 men revealed a sinus pause without evidence of auricular activity persisting for 0.88-4.2 seconds. This sinus pause immediately preceded or accompanied the respiratory stimulation. Immediately after the pause, there were marked sinus irregularity and a decreased heart rate which persisted for periods ranging from a few seconds to 2 minutes. Heart rates then accelerated to above preinjection rates. Heart rate and rhythm were generally restored within three minutes. The 16th subject failed to



show a sinus pause and exhibited only a slight acceleration in heart rate. One of the subjects experienced what the authors described as a momentary dim-out during the test. It should be noted that the doses of 0.11 to 0.20 mg/kg of NaCN are equivalent to approximately 0.06 to 0.11 mg/kg of HCN.

Wexler et al [85] also observed the execution of four men by HCN inhalation. These men exhibited striking electrocardiographic aberrations and had a marked decrease in heart rate which reached its nadir between the 1st and 3rd minutes. This slowing was accompanied by sinus irregularity and eventually by complete disappearance of P waves. A secondary increase in rate, but not to the rate prior to administration of HCN, was observed during the 3rd and 4th minutes along with the irregular reappearance of P waves, some of which were not conducted. All subjects showed A-V dissociation with a secondary decrease in rate during the 5th minute. During the 6th and 7th minutes, the heart rates again showed a slight increase and a return to normal sinus rhythm. Thereafter, the heart rates slowed progressively. Normal A-V conduction in one man and incomplete A-V block in another were maintained throughout the period of observation (approximately 13 minutes). A third subject developed Wenckebach's phenomenon, (2:1 block), and, finally, complete heart block. The fourth subject's heart had normal A-V conduction until the 14th minute, when it developed ventricular tachycardia and ventricular fibrillation. It must be remembered that the concentrations of HCN to which these men were exposed were huge, so that the details of the changes in their ECG recordings may not be entirely typical of those to be expected in occupational exposures. Wexler's observations do seem to demonstrate that cyanide has no specific action on the heart but rather exerts on the myocardium actions that are typical of hypoxia and anoxia.

There have been several reports of exposure to HCN which included both the airborne concentration of HCN and the human physiological response. However, in many cases no additional information relating to worker exposure was provided. These reports are summarized in Table XIV-5. In many cases it is difficult to attribute a specific concentration range directly to a group of investigators since many of the citations involve reference to the work of others with no additional supporting information. Therefore, the validities of concentrations presented only by secondary references may be questioned. In large part they appear to be based on the unreferenced work of Lehmann and Hess. However, the application of Lehmann's data to man has been questioned by McNamara [68] because Lehmann's work was apparently done entirely with rabbits, which McNamara considers to be more sensitive to a given dose (product of concentration and time) of HCN than man. He concluded that man has a susceptibility to HCN more like those of the comparatively resistant goat and monkey and on this assumption (and one that the LCt50 for man is four times that for the mouse) has estimated that 3,404 mg/cu m will cause 50% mortality in humans exposed to it for one minute. McNamara estimated that a concentration of HCN of 607 mg/cu m would kill 50% of men after a 10-minute exposure.

The various fatal doses of HCN seen in Table XIV-5 vary according to the species and method used for projection of data obtained with experimental animals to predictions of human responses. The wide variability in susceptibility between animal species and between individuals may be responsible for the discrepancies. Although the rapidly fatal dose has not been firmly established, it appears that concentrations above 90 ppm are incompatible with life and that concentrations from 5 to

45 ppm produce diverse symptoms (Table XIV-5). However, it is difficult to identify a threshold concentration for the appearance of these symptoms. A few of the studies included in Table XIV-5 provide additional information on workplace exposures and are described below.

In 1926, Parmenter [27] reported a mild cyanide poisoning of a photographic darkroom worker, who on three separate occasions had attacks of numbness, weakness, vertigo, nausea, rapid pulse, and a flushing of the face after working for only 1 hour. These attacks came each time at the end of the week and were followed the next day by headache and vague gastric distress with a rapid return to normal. During the course of his job, he routinely poured iron(II) sulfate solution from a washed plate into a sink, followed by an equal amount of a 30% KCN solution. It is likely that if the first solution had not drained, it would have reacted with the second, producing HCN. Even without supposing reaction with the ferrous sulfate, some HCN would be evolved from the KCN solution in the trap unless the latter was flushed away by a large volume of water. The author felt that the HCN produced could have accumulated in the unventilated room. No airborne concentrations of HCN were determined prior to the installation of ventilation equipment. After ventilation equipment was installed, the airborne concentration of HCN was 75 ppm at 6 in. above the sink under the hood and in the exhaust air. General room air contained 25-50 ppm HCN. It is likely that prior to the installation of the ventilation equipment, the worker was periodically exposed to concentrations of HCN greater than 50 ppm.

In a 1931 experiment [86] in which a 12-kg dog and a 70-kg man were exposed simultaneously in a chamber containing 500-625 ppm HCN, the dog

became unsteady in 50 sec, unconscious in 75 sec, convulsive in 90 sec, and developed respiratory arrest in 93 sec. At 91 sec, the man had developed no symptoms and left the chamber. Three and one-half minutes later, he had a momentary feeling of nausea; 8.5 minutes after leaving the chamber, he experienced difficulty in concentrating on conversation. The dog was presumed dead but recovered within about 12 hours without residual effects from the poisoning. Apparently there is considerable difference between the susceptibilities of man and the dog to acute poisoning by the cyanide ion. McNamara [68] has reported uncovering a statement in the literature to the effect that the exposed man suffered nausea and definite mental symptoms a few minutes after his exit from the chamber but that at least some of these symptoms persisted for about a year.

The signs and symptoms resulting from exposure to cyanide salts fall into two distinct classifications. The first class of inorganic cyanide symptoms is characterized by systemic effects which are the same symptoms as those described for HCN. [27,85] The second set of sequelae, distinct from those observed in response to HCN exposure, are upper respiratory irritation and dermatitis produced by inhalation and skin contact with cyanide salts. The salient details of some cases of human exposures involving each of these classifications are given below.

In 1970, Thomas and Brooks [87] reported a case in which a bag of KCN powder burst in the face of a 19-year-old photographic employee. He suffered from stomach cramps followed by abdominal pain and pallor, and then collapsed. He was revived with amyl nitrite inhalation followed by gastric lavage and injections of sodium nitrite and sodium thiosulfate. He later experienced tingling and numbness in his hands and abdominal cramps. He recovered in 48 hours following continued treatment.

Sandberg [88] reported in 1967 a case of a goldsmith's apprentice who experienced headache, general malaise, paresis of his left arm and left leg, grey skin, a dilated left pupil, left-sided hemianopsia, and an altered EEG showing diffuse frontal theta activity. During the previous 4 years, the man had cleaned goldenware with a 1.5% aqueous KCN solution but had just returned from a 13-month leave of absence 5 months prior to this episode. In use, the solution was heated to boiling whereupon 50 ml of hydrogen peroxide were added. The gold articles were cleaned in a manner causing splashing on the skin and the production of a visible aerosol. There may have been some exposure to HCN. No protective clothing was worn and ventilation was poor in the room in which the work was performed. The man's blood contained 10-12  $\mu\text{g}/100\text{ ml}$  of CN and his urine contained 2  $\mu\text{g}/100\text{ ml}$  of CN. He was treated with hydroxycobalamin. All symptoms subsided within 3-4 months and the cyanide concentration in his blood fell to 2-3  $\mu\text{g CN}/100\text{ ml}$ .

Courville [89] in 1963 reported a case of a 22-year-old man found unconscious under a fumigation tent spread over an orange tree which had just been sprayed with a cyanide solution. He was probably exposed to  $\text{Ca}(\text{CN})_2$  and HCN. Post-mortem examination revealed microscopic changes in the brain. Cortical nerve cells showed either mild swelling or pyknosis, total loss of tigroid material, and shrinkage of nuclei. Occasional neuronophagia was also seen. Sections from the hippocampus showed areas of focal necrosis. Sections from the cerebellar cortex showed early softening of the molecular layer with loss of structural detail and loss of tigroid staining of the Purkinje cells.

Johnstone [42] in 1948 reported an incident in which three men were dusting grapevines with  $\text{Ca}(\text{CN})_2$  powder thrown 24 feet on each side of the truck at a height of 6 feet. The calcium cyanide decomposes upon coming into contact with water vapor, liberating HCN. The men usually worked at night when it was not windy and were instructed to work upwind from the section already dusted. At midnight, one man was found dead and the other two unconscious. The two were given first aid and were hospitalized. They developed pneumonia but recovered without disability.

Barsky [90] in 1937 reported a study of nasal lesions in 17 people in a plating department. One of these was a departmental foreman. In addition, two other employees, a forelady and an electrician, spent a good deal of time in the plating area. Plant conditions and operating procedures were very poor and housekeeping was nearly nonexistent. The facility contained five bronze-plating tanks, four nickel-plating tanks, one large acid copper-plating tank and four soft copper-plating tanks, tumbling barrels, storage crocks containing copper, bronze, and nickel solutions, crocks of potash and soda solutions, acids, etc. A 10 x 15 foot corner section of the plating department, which served as the acid room, had been partitioned off by 3/4 inch boards. All plating tanks had 300-gallon capacity except for the larger acid copper tank. The aqueous solution in the copper tanks contained 8 oz  $\text{Cu}(\text{CN})_2$  and 8 oz NaCN per gallon. The aqueous solution in the bronze tank contained 6 oz  $\text{Cu}(\text{CN})_2$ , 6 oz NaCN, and 1/2 oz  $\text{Zn}(\text{CN})_2$  per gallon. No chrome plating was done at this plant. The only forced ventilation was local exhaust over the acid tank. General ventilation was provided only by opened windows, which were routinely closed in cold weather.

Of the 17 employees, 9 had been engaged in this particular work for 1-8 weeks. The other eight, as well as the electrician and the forelady, had had one to several years of experience. All 19 persons had nasal lesions of varying severity, characterized by congestion of the nasal mucosa and superficial sloughs of varying size on the anterior portion of the septal wall and middle and inferior turbinates. Ulcerations of considerable size and depth were present at these sites. Two of the employees developed perforations during the course of observation and treatment. In all cases, pharyngeal congestion was pronounced. Particular note was made of the departmental foreman's case, which progressed from alternate running and dryness of the nose, nasal bleeding, obstruction, headache, and sore teeth to weight loss, increased body temperature, and a crusty nasal lesion which spread eventually to the right eyelid. Finally, he developed pneumonia of the left lower lobe and signs of meningeal irritation. He died 5 days later. Autopsy findings were ulcerated nasal septum and middle and inferior turbinates, carbunculosi of the tip of the nose, cavernous sinus thrombosis, basilar meningitis, septic pleurisy, septic pneumonia, and septic infarct of the right lung.

A study of plant records revealed another plater who developed typical signs and symptoms in 1 month. The man had been treated for 7 weeks, was removed from exposure, and recovered. An investigation of the plant was made and these 19 illnesses were attributed to aerosols emitted by the improperly operated plating tanks. After engineering controls and housekeeping procedures had been instituted, there were no recurrences of these illnesses. No airborne concentrations of contaminants were reported.

Elkins [91] in 1963 reported that in a plant where there was considerable brass plating the ambient air contained a mist. The mist was reported to have contained NaCN in a concentration not greatly exceeding 5 ppm, expressed as HCN. Severe irritation was a widespread complaint and there were some incidents of ulceration of the nasal septum. The author noted that other alkalies of undetermined concentration in the air may have contributed to the irritating action of the mist.

Cohen et al [92] studied nasal and skin irritation in two groups of electroplaters in 1974. One group only was exposed to chromic acid and the other one had been exposed to cyanide in the course of copper and zinc plating. Airborne cyanide concentrations were determined in seven locations by collection into 10 ml 0.1 M NaOH in a midjet impinger and analysis by specific ion electrode. Air levels ranged from not detectable to 0.09 mg/cu m of CN with an average of 0.006 mg/cu m of CN. No cutaneous or nasal injury was found in the 15 workers in the cyanide-exposed group with the exception of one with a perforated septum who gave a history suggestive of previous exposure to chromates. The cyanides were not described but they were likely a mixture of NaCN, KCN, and some alkaline complex of CuCN in the copper plating tanks, and alkaline NaCN in the zinc bath. [93]

In 1905, McKelway [51] reported a case of a 38-year-old female hairdresser, who used a hickory-nut-sized piece of KCN to remove stains from a silver-containing dye from her fingers. She moistened her fingers and hands and rubbed them vigorously with the lump of KCN for 5-10 minutes, thus removing the stain. Before washing her hands, she experienced vertigo, then screamed and fainted. Her husband revived her in fresh air. Later that evening she vomited, and a physician was called. He found her



in a state of shock and that her lips, fingers, and hands were deeply cyanosed. She was treated for shock and recovered in 3 days.

In 1908, Nolan [94] reported a case of dermatitis in a worker engaged in scrubbing zinc shavings in the KCN "clean up" in the cyaniding process of gold reduction. In this process, the auriferous ore is crushed into a fine aggregate through which a 0.5% KCN solution is passed. This solution then passes into boxes filled with zinc shavings onto which the gold is precipitated from the auro-potassic cyanide in solution. The man's hands and arms were in close contact with this solution. He experienced an itching sensation immediately upon immersion of his hands. Scarlet specks soon appeared on the skin in contact areas and grew larger with time. They coalesced to form a large scarlet area with darker scarlet papules where the original lesions had been. They itched and burned for about 2 hours and the redness began to disappear after 12 hours. Slight giddiness and headache were the only systemic symptoms noted.

Collins and Martland [95] in 1908 reported that cyanide was absorbed through the skin of a 38-year-old hotel worker who polished silver for 2 years by placing it by hand in a KCN solution and then drying it. His hands and arms became brownish-red, his fingernails were black, and he had distressing itching, diarrhea, headache, pain and stiffness in the back and neck, weakness in the arms and legs, and retention of urine. He eventually developed clinical manifestations resembling those of acute anterior poliomyelitis. He remained incapacitated during 6 months of treatment and then gradually responded to electrical treatment to the point where he could walk with braces and crutches. Whether this paralysis should be attributed to cyanide is not clear.

The International Labour Office [48] in 1930 summarized a report first presented by Bridge in 1923 of a fatal case of skin contact with an unspecified inorganic cyanide. The skin of the victim had been removed in patches as if it had been burned.

Smith [26] in 1932 reported a case of a gold plater who had worked at his trade for 20 years, 10 in a small shop plating rings and pins in small pans containing KCN solution, which he made up. When plating, he heated the solution to boiling, which probably resulted in splattering and caused HCN evolution. He had a rash on his hands, arms, and face which he attributed to the cyanide solution. He also had abdominal pain, convulsions, weight loss, weakness, dizziness, muscular cramps, and vomiting. Some of these signs and symptoms could be attributed to skin absorption and some to inhalation of HCN and aerosolized cyanide salts.

In 1955, Tovo [96] described a fish poacher who died from absorption of KCN through the skin. The poacher added KCN to a river upstream and others netted the trout downstream. He was found 3 hours later curled up on the side of the road and without his boots and stockings, which were found on the river bank. He died later that day without recovering consciousness. Necropsy revealed brownish-red blotches from knee to instep that smelled of bitter almonds, as did the blood. The body had a violet hypostatic coloration. The mother of the man pointed out that the legs of his trousers had been rolled up above his knees and were dry but that those of his long cotton underwear were wet at the bottom. Chemical examination showed the presence of cyanide in the blood, urine, and several of the vital organs, but concentrations were not reported. Tovo suggested that

the man had placed his stock of KCN temporarily in his boots to wade into the water and that, either by accident or by misjudging the depth of the water, he stepped into water deep enough to flow over the tops of his boots. Although he escaped from the river as quickly as possible and removed his boots and stockings, he did not have the caution to remove his long underwear soaked with a solution of KCN. Consequently the poison was able to continue to penetrate through the man's skin, more readily because of its corrosive activity, and eventually to cause his death.

In 1926, Raestrup [97] described an accident in which a man was killed when the fused KCN that he was carrying spilled into a puddle of water. The boiling water-cyanide solution splashed in his face. He lost consciousness and died 3 hours later. A similar case was reported by Muller-Hess [98] in which a worker was struck in the head and shoulders with a splash of 80% NaCN and died in less than 1 hour. Several other similar cases reported by various authors were summarized by Tovo [96] but most of these did not involve occupational poisonings.

Specific antidotes for cyanide intoxication have been shown to be effective in 49 cases. [87,99-106] Forty-nine of these involved the use of nitrites to form methemoglobin. Of these, 20 received artificial respiration or oxygen, 41 received amyl nitrite inhalations, 40 received  $\text{NaNO}_2$  injections, and 39 received sodium thiosulfate. Specific procedures used upon humans have been reviewed by Chen et al [101], Wolfsie and Shaffer, [107] and Wolfsie [100], who all agree that such treatments are effective because they produce methemoglobin and become more effective if sodium thiosulfate is provided to assist in the detoxication of cyanide to thiocyanate. A recent review on the use of oxygen in the treatment of poisoning by cyanide is also available. [108]

### Epidemiologic Studies

In 1970, Saia et al [22] reported examining 62 workers; 21 worked near cyanide vats in the galvanizing department, 19 were either wire handlers or zinc platers in the same department and a 22-member control group washed wire in caustic soda. A questionnaire was also given to the 62. Venous blood was analyzed for cyanmethemoglobin. The incidences of insomnia, agitated sleep, tremor, eczematous dermatitis, and nosebleed among the workers exposed to cyanide were more than twice those of the control group. The incidence of vertigo was nearly twice. It is significant that comparatively high incidences of frequent and prolonged headache, vertigo, rapid pulse, buzzing in the ears, eye irritation, frequent cold sweat, sluggish digestion, abdominal pain, weakness in the legs, and dyspnea were found in the control group of men who washed wire with caustic soda at elevated temperatures and had no cyanide exposure. Further, it should be noted that the high incidence of dermatitis was likely caused by poor work practices. Five of the 21 cyanide workers' blood had changes in hemoglobin indicative of cyanide absorption. In one of these five men, the condition persisted for weeks after he quit working. No workplace environmental data were given. [22]

In 1955, Carmelo [109] observed about 600 HCN fumigators and noted a sense of suffocation, tachycardia with palpitation, vertigo, buzzing in the ears, headache, epigastric burning, vomiting, general weakness, tremor, sensory obtusion, dyspnea, precordial pain, and loss of consciousness in workers who, in the opinion of the authors, received small acute intoxications from HCN.

Carmelo [109] examined in detail 17 fumigators using HCN, 13 of whom had suffered acute episodes with loss of consciousness. He recorded ages, qualifications, places of origin, duration of service in fumigation work, frequency of accidental inhalations, medical histories and subjective complaints at the time of examination, as well as objective results of various general examinations and diagnostic tests. These men had worked for from 1 to 27 years; the four without histories of acute episodes of intoxication by HCN had worked for 7, 8, 25, and 27 years. A high incidence of nervous disorders, including equilibrium disturbances, vertigo, nystagmus, and Moebius sign, were found. Nine of the 13 experienced precordial pain after exposure to HCN; eleven of the 13 had electrocardiographic alterations. Eleven of the 13 had radiographic evidence of hypertrophic gastritis. None of the four unexposed men had evidence of disease of the stomach or duodenum. The author reported that three of the exposed and two of the unexposed men had erythrocyte counts above 5,000,000 but below 6,100,000/cu mm and that seven of the exposed and none of the unexposed men had a percentage of lymphocytes above 40 but below 49%. He attributed the latter change to stress resulting from repeated exposure to small doses of HCN. He concluded that his results demonstrated that not all the effects of repeated acute or subacute exposures to HCN are entirely reversible.

In 1972, Dinca et al [23] published a study of leukocytic oxidative enzyme changes in 31 men and 12 women in Romania engaged in galvanizing metal who were chronically exposed to low airborne concentrations of HCN. Their ages were 18-49 (mean 36); their years on the job were 0.25-16 (mean 5.4); their average exposure for the past 5 years to HCN at a concentration of 0.26 mg/cu m (0.23 ppm). No exposure to cyanide salts was mentioned and

no details of cutaneous exposure or general health were given. Samples of blood were analyzed for serum catalase. Blood smears were also stained with various dyes to enhance particular granules of the neutrophilic leukocytes. The authors compared the number and intensity of "cytochrome oxidasic", "peroxidasic", and "succinodehydrogenasic" granules with similar findings in a control group. No details of the size or nature of the control group were presented. Based upon the percentage of subjects whose rating was "0", "+", "++" or "+++", the authors concluded that there was a significant decrease in the cytochrome oxidase activity of the leukocytes of workers exposed to HCN at 0.23 ppm. Further, they felt that the peroxidase and succinodehydrogenase activities of the exposed group were considerably reduced, while serum catalase was lowered less markedly. It should be noted, however, that the staining techniques used by the authors were quite crude and were not confirmed by quantitative analysis of the activities of any of the enzymes. Therefore, these data must be regarded as questionable until substantiation of the conclusions of Dinca et al is obtained. Therefore, a "?" has been inserted after the response noted in the last entry in Table XIV-5.

In 1973, Radojicic [79] reported a study of 43 workers in the electroplating division of an electronics firm in Nis, Yugoslavia. Among them, 28 worked in the electroplating shop and 15 in the annealing department. A control group of 20 non-exposed workers was used for comparison. The cyanide concentration was measured at four work places in the electroplating shop and ranged from 7 to 11 mg/cu m.

At three sites in the annealing shop the cyanide ranged from 6- mg/cu m. It was found that the majority of the exposed workers complained

of fatigue, headache, asthenia, tremor of the hands and feet, and pain and nausea. The urinary thiocyanate concentrations of both of the exposed groups were higher at the end of the work shift than before work. Workers who had been on the job longer usually eliminated more thiocyanate than those with fewer years of exposure. In both groups, the exposed workers who smoked eliminated more thiocyanate (both before and after work) than smoking controls. Likewise, the nonsmokers in both departments who had cyanide exposure eliminated more thiocyanate than nonsmoking controls. These values were reported to be significantly different. The smokers eliminated more thiocyanate than the nonsmokers in each case. It appears that the workers in the group with higher exposure (electroplating) also eliminated more thiocyanate than the workers with less exposure (annealing), regardless of smoking habit.

Most recently, El Ghawabi et al [110] studied the effect of chronic cyanide exposure in the electroplating sections of three Egyptian factories. A total of 36 male employees were interviewed, medical histories were taken and medical examinations, which included radioisotope assay of iodine uptake and hematological evaluation, were performed. The ages of the employees ranged from thirty years into at least the fifties and their durations of exposure up to at least 15 years. The results were compared with those from a control group of 20 normal male non-smokers, as the exposed employees all disliked the smell of cigarettes. The breathing zone cyanide concentrations at the three plants averaged 8.1, 6.4, and 10.4 ppm, respectively. Two employees were encountered who exhibited psychotic episodes. None of the exposed employees exhibited clinical signs of hypo- or hyperthyroidism. However, 20 had mild to moderate thyroid enlargements.

Sixteen of these enlarged glands were soft and smooth while the remaining four were firm and slightly nodular. The radioactive iodine uptakes of the thyroid glands of the exposed workers 4 and 24 hours after administration of  $^{131}\text{I}$  were significantly higher than those of the controls. (38.7 versus 22.4%,  $P=0.001$ ; and 49.3 versus 39.9%,  $P=0.001$ , respectively). At 72 hours, the  $\text{PB}^{131}\text{I}$  was within normal limits and no significant difference was found between the two groups. As thiocyanate blocks the uptake of iodine by the thyroid [111] and as there was no cyanide exposure for two days preceding the study, the authors expected this rapid accumulation of iodine by the thyroids of the exposed group. Another possibility put forward by the authors was that the competition between thiocyanate and iodide had resulted in a hypertrophied thyroid and thus to a sufficient concentration of organic iodine through an expanded volume of tissue, which would not be saturated with iodine, however. The authors also found slightly increased hemoglobin and lymphocyte percentages in the blood, as well as cyanmethemoglobin, in the exposed group. The urinary thiocyanate levels were found to increase at the beginning of a work week and to remain almost stationary during the latter half. These stationary values were said to be related to the airborne cyanide concentrations but no correlation coefficient was reported.

#### Animal Toxicity

In 1900, Heymans and Masoin [112] found that the lethal dose of KCN (calculated as HCN) was 2-3 mg/kg for the rabbit. When this dose was divided into 12 equal parts and administered during an hour at 5 minute



intervals, it still proved fatal. Using this method they were able to show that the detoxication potential of the rabbit for KCN was about 0.5 mg/kg per hour (as HCN) for at least 10 hours and that the dose-time of survival relationship was hyperbolic. The authors concluded that at low concentrations, normal metabolism was able to detoxify the cyanide but that upon prolonged exposure this metabolic potential became exhausted and with high exposure levels this metabolic mechanism became saturated.

Lehmann [113] reported in 1903 that inhalation of 30-40 mg/cu m of HCN (27-36 ppm) did not affect cats after exposures of 4-5 hours. However, cats exposed to airborne HCN concentrations of 50 mg/cu m (45 ppm HCN) for 1.5 hours exhibited respiratory distress, increased salivary flow, vomiting, dilatation of pupils, and convulsions. Most cats died after 2.5-5 hours of exposure to HCN at 50-60 mg/cu m (45-54 ppm).

In 1906, Kobert [52] reported that the dog was the species most sensitive to HCN, but that it was less sensitive to the cyanogenic glycoside, amygdalin, than the rabbit. He also explained the complex effects of HCN on man and higher animals by differentiating four basic effects: those on the nervous system, on metabolism, on blood, and on the heart. Effects on the nervous system were primarily motor disturbances, including paralysis, but could also include some of the symptoms of peripheral nervous disorders, more commonly associated with exposure to cyanogen gas at that time. Experiments with "surviving hearts" showed that they are paralyzed by small doses of HCN, but that the nervous system could be paralyzed with even less. Blood was shown to be affected by "losing its ability to split up H<sub>2</sub>O<sub>2</sub>" (presumably an inactivation of catalase) and by the formation of what Kobert discovered and called cyanmethemoglobin.

In 1915, Creel et al [114] exposed groups of 1-6 rats to various concentrations of HCN generated from potassium cyanide and sulfuric acid. Rats generally died within 15 minutes when exposed to HCN concentrations above 500 ppm HCN.

In 1917, Grubbs [115] exposed guinea pigs, rats, mice, cats, sparrows, and pigeons to various concentrations of HCN in an airtight room of 500 cu ft in order to find an animal that could be used as an index of safety on fumigated ships. Airborne concentrations calculated from the data were about 130-540 mg/cu m. The effects which were observed are included in Table XIV-6. Sparrows and small birds were said to be the most susceptible to HCN and guinea pigs the least susceptible.

Walton and Witherspoon [116] investigated the degree to which HCN penetrates the skin in 1926. In one series of experiments, they shaved the abdomens of eight guinea pigs and 24 hours later fastened them, belly down, to a board with a large hole in it. A circular area of 1 in in diameter was exposed to the vapor from a preparation of HCN that contained 97% HCN and 3% water. First signs, appearing in a few minutes, were rapid respiration followed by general twitching of muscles, convulsions, and finally death. In a second series of experiments, the authors [116] exposed the abdomens of nine dogs shaved or depilated 24 hours earlier and of two additional unshaven dogs to various concentrations of airborne HCN. The dogs were lightly morphinized before being placed in a chamber in which their bodies, except for the head and a portion of the neck, were exposed to airborne HCN. These experiments were designed to minimize HCN entry by any route other than absorption through the skin. This experiment showed that HCN penetrated the intact skin of the dogs. For example, a fatal

result was obtained with exposure to 15,200 ppm of HCN after 47 minutes whereas no symptoms were observed with exposure to 5,000 ppm HCN for 180 minutes.

Fairley et al [117] in 1934 exposed 1.23 sq in of the closely clipped bellies of five guinea pigs (approximately 2% of the surface area of their bodies) to HCN at a theoretical concentration in the range of 312,500-455,000 ppm. Coma, convulsions, or death resulted in four of the guinea pigs in 45-65 minutes; the fifth was removed from exposure when it collapsed at 15 minutes. It appeared to have recovered 45 minutes later.

In 1931, Flury and Zernik [118] recorded the results of extensive exposures of mice, rats, guinea pigs, rabbits, cats, dogs, pigeons, and a monkey to airborne HCN concentrations of 50-1450 mg/cu m (45-1305 ppm). The salient results presented in this paper are summarized in Table XIV-6. These authors also noted that differences in individual animal responses were pronounced at HCN concentrations of 40-70 mg/cu m (36-63 ppm). Reactions proceeded more slowly at these levels and vomiting, convulsions, unconsciousness, and difficult breathing were the chief signs. They noted further that concentrations under 35 mg/cu m (31.5 ppm) were generally completely and lastingly safe except for certain individual animals which were especially sensitive. They further noted that, at concentrations of 100-140 mg/cu m of HCN (90-126 ppm), monkeys were slightly, but not significantly, less sensitive than cats and dogs.

Prior to 1933, methylene blue was recommended as a treatment for HCN poisoning. In 1933, Trautman [119] demonstrated that injections of methylene blue were of no value in the treatment of overexposure to HCN gas. He placed the animals in large glass jars, added small amounts of liquid HCN

and noted the results. Rabbits were exposed to HCN at approximately 450 ppm, while white rats and guinea pigs were exposed to HCN at approximately 900 ppm. (The exposure concentration for the rats was variously stated as 450 or 900 ppm.) Animals were exposed until they breathed a lethal or near lethal amount of gas, the times of exposure were noted, and then the animals were removed and given injections of a 1% solution of methylene blue. Fifty-four guinea pigs were exposed to HCN and 29 were injected ip with a 1 cc/100 g dose of methylene blue solution. Seventeen (59%) recovered and 12 (41%) died. Of the 25 control guinea pigs, 15 (60%) recovered and 10 (40%) died. Of the 35 rabbits exposed to HCN, 18 were injected iv with 1 cc/kg of methylene blue and 17 received no treatment. Three (17%) of the 18 treated animals died as did 2 (12%) of the 17 untreated animals. Results were again similar when 98 white rats were exposed to HCN. Twelve (38%) of the 32 receiving 1 cc/kg of methylene blue ip died, as did 11 (32%) of the 34 given 0.5 cc/kg of 1% methylene blue solution ip and 10 (31%) of the 32 controls.

Gettler and Baine [120] in 1938 gave doses of 16.0 and 10.1 mg of HCN, respectively, to two dogs by inhalation. The former died in 12-15 minutes and the latter in 8-10 minutes. They also injected 20, 50, and 100 mg of KCN (expressed as HCN) into the stomachs of three other dogs, and they died in 155, 21, and 8 minutes, respectively. It was determined by analysis of stomach contents that the three dogs had absorbed 14.4, 12.0, and 16.6 mg of KCN (expressed as HCN), respectively. The authors calculated the lethal oral absorbed dose for dogs to be 1.06-1.40 mg/kg of HCN.

In 1939, Etteldorf [121] exposed dogs in a dynamic system to various airborne concentrations of HCN, which were determined by sampling and analysis. The author noted that convulsions were always preceded by definite prodromal signs, namely salivation, lacrimation, defecation, urination, and increasing restlessness. Three dogs exposed to 0.05 mg HCN per liter of air developed convulsions, while three others pretreated with sodium thiosulfate and sodium nitrite did not develop convulsions until the HCN concentrations were 0.175, 0.29, and 0.30 mg/liter.

In 1946, Jandorf and Bodansky [122] reported testing the therapeutic and prophylactic effects of methemoglobinemia in HCN poisoning by exposing dogs to HCN. The concentration of HCN in the chamber was sampled with a sodium carbonate solution and analyzed by silver nitrate titration. Amyl nitrite was administered 30-45 seconds after removing the animals from the chamber by exposing their noses to 0.3 ml of the liquid in a muzzle. Manual artificial respiration was used to facilitate the inhalation of the amyl nitrite and was continued until respiration resumed or death occurred. Eighteen dogs were exposed in pairs to HCN at 170-1400 mg/cu m for 1-10 minutes. Nine dogs were given artificial respiration and treated with amyl nitrite. The other nine served as controls and received only artificial respiration. Five of nine (56%) treated dogs were revived, while only three of nine (33%) untreated dogs were revived. The authors felt that this difference was not significant.

In a second phase of the study, [122] dogs were exposed to HCN at 530-2200 mg/cu m after treatment with oral doses or injections of p-aminopropiophenone to induce methemoglobinemia. Dogs protected with 4-10% methemoglobin were able to withstand 2-8 times more HCN than the unprotected dogs.

unprotected dogs.

Gordh and Norberg [123] published a study of oxygen treatment of HCN poisoning in 1947. They exposed 2-3 kg rabbits to HCN at 284-1290 mg/cu m (256-1,161 ppm) for 37-47 minutes. Exposure was continued until the animals became apneic, their heart beats became irregular and weak, and distinct cyanosis was apparent. Administration of oxygen through a plaster of Paris mask, modelled to fit the rabbit's muzzle, by hand pressure applied to a rubber bag connected to the mask succeeded in reviving 18 of the 36 rabbits. The authors stated that the hearts of the other 18 rabbits had become too weak when oxygen administration was started to be able to perform the necessary movement of oxygenated blood to the important organs.

In 1951, Moss et al [124] exposed 16 rats to HCN at 24-465 ppm for up to 22 minutes. The rats exposed at 25-50 ppm survived, except for one exposed at 50 ppm. This rat was violently agitated after 1 minute 49 seconds, paralyzed after 2 minutes 30 seconds, unconscious after 3 minutes, and dead after 8 minutes.

In experiments reported in 1952 by Haymaker et al, [125] six dogs were exposed at concentrations of 620, 590, 700, 700, 165, and 690 mg/cu m, for periods of 2.0, 2.0, 1.75, 1.75, 10.0, and 2.0 minutes, respectively. The first three dogs died in 20 hours or less and the others were killed 24, 26, and 28 hours after exposure. Four of the six dogs had convulsive seizures. The dog exposed at 620 mg/cu m had marked proliferation of histiocytes in the leptomeninges and in the perivascular spaces of the molecular layer of the cerebellum. Only shadows of the Purkinje cells remained. Some of these dogs suffered necrosis of gray matter. Definite alterations of structure were not seen in dogs that died within 21 minutes

after being exposed to HCN; they were found in dogs that died 2.5 or more hours after exposure. At these comparatively early times, there was subpial edema of the cerebrum and the cerebellum. Dogs that survived for as long as 16 hours had cellular damage, particularly in the cerebral cortex. The frontal and parietal lobes were more likely to be affected than the temporal or occipital. Cortical damage was concentrated frequently in the trough of a sulcus in the form of massive coagulation necrosis.

Valade [126] in 1952 exposed four dogs to HCN at 50 mg/cu m for 12 30-minute periods, conducted at 8-day intervals. Of these dogs, two survived, one died after 38 days, and one died of an intercurrent disease. In a second experiment, four dogs were subjected to 19 30-minute inhalation periods at 2-day intervals and at the same HCN concentration. One died after 73 days, the other after 77 days. Another group of five dogs went through seven 30-minute inhalations at 2-day intervals, but this experiment was interrupted when pulmonary inflammation occurred, causing the death of three dogs. Still another group of four dogs were subjected to fourteen 30-minute inhalation periods at 2-day intervals; one of these died after 34 days. The first signs were dyspnea, nausea, exaggerated intestinal peristalsis, and diarrhea. Later, the dogs developed tremors followed by loss of equilibrium and convulsions. These observations tend to support the hypothesis of a cumulative effect from exposure to HCN.

Valade [126] autopsied the dogs immediately after they died or were killed and observed similar central nervous system lesions in each of them. Vascular changes were vasodilatation and hemorrhages which were most pronounced in the central gray nuclei, brain stem, bulb, and medulla

cervicalis. Cellular lesions manifested themselves by glial reactions throughout the central nervous system and by cytologic changes in the Purkinje cells of the cerebellum and in the bulbar gray nuclei. These histopathologic examinations led the author to conclude that the lesions resulted from anoxia caused by inhibition of cytochrome oxidase or from a selective effect of the poison. To support the contention that the latter cause was the more significant, the author noted that the dogs were very quickly affected by respiratory disorders before the onset of other signs. He thought there was reason to believe that the suddenness with which these disorders appeared was linked to a particular sensitivity of these animals' bulbar cells to cyanide, rather than to an inhibition of cytochrome oxidase.

Sato et al in 1955 [84] placed groups of 10 mice in a series of 100 liter air tight chambers containing HCN gas in various concentrations, which were verified during the experiments by occasional analysis. The amount of HCN was kept constant throughout the experiments. At 20 ppm, about 20% of the mice died after 4.5 hours. Some mice also died after 4 hours at 15 ppm. Mobility became hindered and respiration rough when exposed at 10 ppm for 2 hours. At 5 ppm, there was a marked decrease in food intake compared to that of controls. The authors concluded that chronic HCN intoxication at low concentrations would eventually exhaust the detoxication ability of the mice and eventually cause adverse effects.

In 1955, Howard and Hanzal [127] reported a feeding study with HCN-fumigated food. Thirty male and 30 female weanling albino rats were divided into 3 groups of 10 males and 10 females each. Two of the groups were given dog meal containing 300 ppm and 100 ppm of HCN, respectively. A



third, similar group was fed unfumigated food as a control. At the end of a 2-year feeding period, no gross signs of cyanide toxicity were observed. Autopsies revealed the same general abnormalities and signs of senility in control and experimental rats. Microscopic examination of heart, lungs, liver, spleen, stomach, small and large intestines, kidneys, adrenal, thyroid, testes or uterus and ovary, and the cerebrum and cerebellum revealed no evidence of pathology due to HCN feeding. All findings were compatible with those usually seen in aging animals, and the same general changes were found in both the control and the experimental animals. Thiocyanate concentrations in plasmas, RBC's, and kidneys, but not in the livers, of rats given food containing 300 or 100 ppm HCN were about twice as high as those in controls.

In 1959, Levine and Stypulkowski [128] reported lesions in several areas of the brains of rats which survived exposure for 20-45 minutes at an unknown concentration of airborne HCN. The concentration of the airborne cyanide aerosol, which the authors presumed to be HCN, was not determined but was sufficient to debilitate the rats in 10 minutes. Earlier, Flury and Zernik [118] found that persisting prostration occurred in 9.5 minutes at 127 ppm and, thus, it may be estimated that the rats in this experiment had exposures to HCN at approximately 127 ppm. Below this concentration (127 ppm), exposure to HCN for 2 hours did not produce brain lesions. Above this concentration at which persisting prostration occurred, brain lesions were produced readily in 20-30 minutes. These lesions involved a multiplicity of sites in the brain although they were not universal in distribution. For example, the cord, most of the stem, cerebellum, diencephalon, and portions of the cerebrum were spared. A predominance of

isolated lesions appeared in the callosum and striatum. Later that same year, Levine and Weinstein, [129] using the same technique described above, reported that high concentrations of HCN generally caused the death of rats without causing brain damage. Low concentrations did not produce either, but moderate concentrations (perhaps 100-150 ppm) caused brain lesions while consciousness was maintained for an hour or so, followed by sudden unconsciousness and death. Unfortunately, in neither of these studies was the airborne concentration reported.

Necrotic lesions and demyelination were also observed in the rat brain by Ibrahim et al [130] in 1963 with chronic subcutaneous injections of NaCN. The initial dose was 8 mg/kg with increments of 0.5 to 1.0 mg up to a maximum of 6 mg per animal per day. This schedule was maintained 5 days per week for 3 weeks. The brains of injected animals were examined by cytological and histochemical methods and compared with those of controls.

In 1963, Smith et al [131] noticed cellular changes and neuronal degeneration in the cortex, hippocampus, and cerebellum of three adult Wistar albino rats receiving 0.5 mg of KCN subcutaneously once weekly for 22 weeks. They reported some pallid myelin but found it difficult to estimate whether or not there was demyelination. The animals appeared to be without other ill-effects from these small doses. The authors suggested that these lesions were due to excessive utilization of hydroxocobalamin to form cyanocobalamin. Whether these effects on nervous tissue are due to a specific action of the cyanide ion or of the thiocyanate ion, or to general histotoxic anoxia, is not clear.

Moss et al [124] in 1951 subjected from one to three rats to mixtures of CO and HCN. Atmospheres containing either HCN or CO alone were

generally lethal to rats at concentrations of 50 or 5000 ppm, respectively. A mixture of 10-20 ppm of HCN and 2000 ppm of CO was lethal to some. Mixtures of 30 ppm of HCN and 1000 ppm of CO and of 5 ppm of HCN and 2000 ppm of CO were not lethal.

Hirner [132] in 1969 subjected male rats weighing about 250 g to subcutaneous injections of 0.2% KCN. The daily dose, which averaged between 3 and 5 mg/rat, was divided into parts, which were injected within the span of 1 hour. Five rats received single daily doses and were killed 2 or 3 days later. Six rats received 4 to 12 daily doses, two received 14, and four received 20. All the multiply dosed rats were killed at the end of 9 weeks from the first daily dose. These rats were perfused through the left ventricle with a sodium cacodylate-glutaraldehyde solution; appropriate samples of nervous tissue were ultrasectioned and examined electronmicroscopically as well as by conventional optical microscopy. The principal lesion found in this study was necrosis in the caudal part of the corpus callosum, with spongy alteration at the margin of the necrotic area. Phagocytes invaded the necrotic area 2 days after the last dose of KCN; astrocytic gliosis followed. In the area of spongy change, there was vacuolization of axons and swelling of the astrocytes and oligodendroglia. Demyelination was visible in the later stages of the study. Hirner considered that the effects on glial cells were primary effects of cyanide, but that disintegration of myelin and axonal degeneration were secondary effects, the axon remaining intact when swelling of the glia had occurred. He stated the belief that the oligodendroglia are particularly susceptible to injury by cyanide.

In 1972, Higgins et al [133] exposed 6 groups of 10 rats each to HCN

for 5 minutes at 283,357,368,497,583, and 690 ppm, respectively. Deaths occurred within 20 minutes for 0,1,2,2,8, and 10 rats, respectively. In another experiment 6 groups of 15 mice each were exposed to HCN for 5 minutes at 200, 283, 357,368,414, and 427 ppm, respectively. Deaths occurred within 20 minutes for 0,4,12,10,12, and 15 mice, respectively. The LC50 was 503 ppm for rats and 323 ppm for mice. In later experiments, the authors found that the presence of CO at 2,100 ppm for rats and 1,500 ppm for mice changed the LC50's for HCN to 467 ppm and 289 ppm, respectively, so that there seems to be some slight additive action between CO and CN.

Studies of the systemic toxicity of cyanide salts usually involved the injection, infusion, or oral administration of cyanide solutions into experimental animals. The studies designed to elicit dose-response relationships are summarized by animal, compound given, route of entry, dose, and response in Table XIV-7. These studies have been extremely useful in describing the metabolism and toxicities of cyanide salts.

Three recent reports by Ballantyne et al [134,135,136] addressed themselves to the question of whether or not there is a difference between the acute toxicities of KCN and HCN. They administered intramuscular injections to male and female rabbits. In essence, they found only a slight difference in the observed LD50's in that the LD50 for HCN (as CN) in female rabbits was about 69.5% of that for KCN (as CN) in female rabbits, whereas for male rabbits the corresponding figure was 117.9%. [134] The times to death with HCN for male and female rabbits were 44.1% and 90.6% of those with KCN, respectively. The authors [134,135,136] also analyzed for cyanide in skeletal muscle, kidney, liver, spinal cord, brain,

whole blood, and serum from rabbits killed with HCN or KCN at a dosage of 8 mg CN/kg before and after perfusion with saline. Results showed that observed increases in various tissues generally were due to the cyanide in the blood. However, brain and spinal cord samples from both the HCN- and KCN-injected rabbits remained elevated after saline perfusion and were thus shown to be cyanide depots.

There have been only two animal studies reported of inorganic cyanide aerosol inhalation. [128,137] Both sought to generate HCN by passing air at various flow rates into a 5% aqueous solution of KCN. In both cases the apparatus undoubtedly created a mixture of HCN generated from the hydrolysis of the KCN and of a fine aerosol of KCN. Unfortunately, neither report sought to quantify the dose of either HCN or KCN.

In the first study, Levine and Stypulkowski [128] in 1959 controlled both the depth and duration of intoxication and classified their findings by the observed reactions in exposed rats. Their Stage 1 response was characterized by restlessness, increasing activity, and violent attempts to leave the chamber. Stage 2 involved a decrease in voluntary muscular activity followed by collapse to the floor of the exposure chamber and convulsive movements of the extremities and tail with respiration varying from very deep, slow, and regular to irregular respiration with short periods of apnea. Stage 3 was evidenced by a more complete loss of motor activity with only slight twitching of extremities and respiratory frequencies varying between 40 and 80 per minute. In Stage 4, there was no movement at all other than respiration, which diminished in both amplitude

and frequency until death.

In the second study, Levi and Amaducci [137] in 1968 brought their animals through the first two stages, after which they were allowed to partially recover, and were then killed by decapitation. The meninges appeared congested. Some rats had hemorrhagic pulmonary infarctions. In some animals trypan blue was injected iv to test the integrity of the blood-brain barrier. Subsequent examination of the brains did not show any abnormal passage of the trypan blue into the nervous tissue. Brain slices of other rats were used to study the active transport of amino acids. Initial and steady state accumulation of amino acids and rates of amino acid exit were identical in brain slices from control and treated animals when a glucose-containing incubation medium was used. Tissue respiration rates were also measured in vitro and found to be identical in both control and treated animals.

In 1935, Perry [138] found that prolonged inhalation of cyanide arrested body growth in young rats and retarded the growth of Jensen sarcoma implants. However, she concluded that the effective dose was too close to the lethal dose to be practical. No conclusions can be drawn from this study as to any possible carcinogenicity of cyanide or thiocyanate.

In 1973, Hrizu et al [139] found slightly increased 21-day survival rates in mice inoculated with Ehrlich ascites tumor cells and given two or three injections of 0.2 ml of a 22% potassium thiocyanate solution. However in non-inoculated mice, the thiocyanate injections decreased the survival rate below that of controls (60 versus 74%). Assuming the average weight of the mice to be 15 g, these doses were approximately 3 g/kg of KSCN. They [139] also reported cytostatic effects on cultures of rabbit

spleen and human KB cells with KSCN in concentrations of 110 to 2200  $\mu\text{g/ml}$  of buffered solution. These constitute high doses or high concentrations and any extrapolation to the human experience in the working environment appears meaningless.

In 1946, Nowinski and Pandra [140] injected unincubated chick eggs with 0.3-0.7 ml of sodium thiocyanate solutions of varying concentrations (0.1, 0.5, 1.0 M). Upon incubation for 42-47 hours, the embryos developed anomalies in the rates of development of different organs. For example, in comparison with the rest of the body, the heart was found to show a slower growth rate than other organs. NaSCN was found to have its greatest effect on the brain; however, no definite changes other than inhibitory effects on mesodermal and endodermal development were evident. For an egg with a weight of 50 g, 0.7 ml of 1.0 M solution of NaSCN would correspond to approximately 1,000 ppm on a w/w basis. The possibility of conversion of thiocyanate to cyanide and cellular inhibition by enzymatic blockade should be noted. [65] In light of the high concentration of thiocyanate used and the closed system of the egg, extrapolation of the results of this study to exposure of humans to cyanide does not appear to be warranted.

In 1969, Ortolani [141] exposed unfertilized ascidian eggs to 0.8% NaSCN in sea water (approximately 8,000 ppm) for 12 hours. They were then washed, fertilized, and allowed to develop in sea water. The larvae were found to have abnormalities in the development of the nervous system, sense organs, palps, tails and in the overall size of the organism. Similar results were obtained with treatment of fertilized eggs (2-8 blastomeres) for two hours. Ascidian larvae have the same fundamental structure as vertebrates; however, since their eggs were directly exposed at 8,000 ppm,

the significance of this study to the occupational environment is not clear.

#### Correlation of Exposure and Effect

HCN is primarily a rapid acting acute poison which can be dangerous to life for humans at concentrations of 90 ppm (about 100 mg/cu m) or more. [118,142,143] However, it is apparent from the data in Table XIV-5, which lists the observed human responses as a function of airborne HCN concentration and time, that this acute human toxicity is truly a function of dose, ie, a function of concentration and time of exposure, rather than just a function of concentration, since exposures at concentrations of between 90 to 135 ppm may be fatal if continued for 30-60 minutes; while exposure above 300 ppm may be fatal within a few minutes. This fact is reinforced by the animal responses to given concentrations of HCN for given periods of time. These data, which confirm that animal responses are also a function of dose, are listed in Table XIV-6 by species. However, as discussed above, these values of 90, 135, and 300 ppm appear to come from research performed by Lehmann and by Hess and known to us only through quotations by other authors (see Table XIV-5). Lehmann's values were apparently derived from studies with rabbits, [68] whereas those of Hess seem to come from exposures of human subjects to low concentrations of HCN vapor. [118]

Inorganic cyanides are also rapid-acting acute poisons to humans. [51,120,144] They also appear to exhibit a dose-response relationship. The primary routes of entry of significance in the workplace are inhalation [26,27,63,81, 88,90,95,145] and absorption through the skin. [26,88,95,



96,145,146] Ingestion as a route of entry for occupational exposure could be significant but is probably secondary. Further, NaCN, KCN, and  $\text{Ca}(\text{CN})_2$  will liberate HCN gas upon hydrolysis [28,31] or in the presence of acids. [39,40,115]

HCN may also be fatal to humans when absorbed through the intact or damaged skin. [39,118,147,148] Drinker [147] described three men who entered a 2% HCN atmosphere wearing working gas masks and no additional protective clothing. Presumably inhalation was not a factor. They were overcome in 8 - 10 minutes but escaped before they collapsed. The men were incapacitated for 2 or 3 days but apparently recovered completely. This could easily have resulted in three fatalities in view of animal responses to cutaneous exposures to HCN at concentrations near or below 20,000 ppm. [116, 117] The incapacitation of these men suggests that, although the dose required is higher, the same general symptoms occur following exposure to adequate concentrations of HCN via either inhalation or percutaneous absorption.

Although acute poisoning is the chief hazard from HCN, there have been reports of isolated cases of chronic poisoning. [17,24-26,81] In one of these reports, it was pointed out that there was normally an increased urinary thiocyanate level in case hardeners and that, if a person did not excrete thiocyanate well, he could be susceptible to chronic poisoning. Credence is given to this argument by noting that the symptoms observed in this [24] and other cases [17,25,26,81,99] are similar to those noted when thiocyanate is administered. [25] Many of the symptoms reported for chronic poisoning have also been reported after short term exposure. [27,118] These include weakness, vertigo, nausea, rapid pulse, headache,

flushing of the face, and gastric distress. Therefore, the chronic effects appear to result from summation of repeated small exposures, discounted by the extent of detoxication of cyanide within the period elapsed between the exposures. The truth of this supposition has not been demonstrated unequivocally, however.

Regardless of whether it is defined as acute or chronic, exposure to HCN in concentrations of 20 ppm or more has produced adverse effects in humans in a matter of hours. [20,118,142,143] At lower levels of human exposure the effects are not as dramatic, do not occur as rapidly after exposure, and are not as well documented.

Hess (see Flury and Zernik [118]) reported 18-36 ppm to be effective after several hours of exposure. This statement has been interpreted to mean minimal symptoms after several hours of exposure. [29,149] Meanwhile, Lehmann (see Flury and Zernik [118]) reported that humans survived 6 hours without symptoms at these same concentrations.

Hardy et al [24] did observe increased urinary excretion of thiocyanate in a group of case hardeners who were exposed to HCN and possibly to cyanide salts. Breathing zone concentrations of HCN among those workers in controlled operations were measured and found to be 4-6 ppm HCN or less, but neither the HCN levels among those in uncontrolled operations nor any of the inorganic cyanide exposures were quantified. No symptoms were noted in those exposed to 4-6 ppm; however these men may have been included in a group of 25 workers with increased thiocyanate excretions.

Lazareff, in review papers [142,143], described some headache and vertigo in a group of workers exposed to HCN concentrations between 5 and 18 ppm while no ill-effects were noted on exposure at 0.1-0.9 ppm. Details

were not given, however. Similarly, Grabois [150] did not note any symptoms in a group of workers exposed to HCN at concentrations of less than 1 to 17 ppm; however, medical history questionnaires were not given.

Dinca et al [23] reported slight decreases in the activity of cytochrome oxidase, peroxidase, and succinyldehydrogenase in the leukocytes of a group of 12 men and 31 women working in the Romanian galvanizing trade. The group had worked at this trade for an average of 5.4 years. The average concentration for the 5 years preceding the study was 0.26 mg/cu m of HCN (about 0.23 ppm), or just below the Soviet limit of 0.3 mg/cu m of HCN. The tests used to determine enzyme activities involved selective staining of the neutrophilic granules. Such a test is an estimation at best. In addition, it is difficult to detect a significant difference of response in control versus exposed subjects from the data presented. Further, leukocytes are not the normal choice for sampling to determine the activity of oxidative enzymes, particularly cytochrome oxidase. No information was given regarding cutaneous exposure or exposure to any other form of cyanide. Since the staining techniques used were unsupported by quantitative biochemical studies, one can not put much weight on the authors' conclusions. Therefore, one doubts that workers would be adversely affected by prolonged exposure at 0.26 mg/cu m (0.23 ppm).

It appears that there are no documented pathological conditions or major adverse effects from human exposure to airborne HCN at concentrations below a value somewhere between 5 and 18 ppm. However, chronic exposure at levels of 5.4 to 12.7 ppm was reported by Radojicic [79] to give rise to subjective complaints and disturbances in the normal well being of 43

cyanide workers. These complaints included headache, weakness, nausea, and what was described as effort dyspnea. These symptoms were also reported in 40 cyanide workers by Saia et al [22], although the airborne cyanide concentrations were not determined. Similarly, El Ghawabi et al [110] found these same complaints in 36 cyanide workers at airborne cyanide concentrations of 4.2 to 12.4 ppm.

Colle [83] advanced the belief that these symptoms of headache, dyspnea, epigastric burning, vertigo, tinnitus, nausea, vomiting, tremor, and precordial pain represent a true clinical entity and that they are sufficiently documented and characteristic of chronic cyanide exposure to be grouped into a true syndrome. He suggested that these symptoms are due to subacute exposure and are transitory in that rest and the breathing of fresh air cause their reversal, but that these subacute exposures, when repeated regularly over a long period, lead to vascular and cellular lesions which eventually result in this classic syndrome.

Chaumont [82] also stated that there is no clinical evidence to deny that cyanides can cause this type of occupational intoxication. He apparently found the debate on whether this intoxication is truly chronic or whether it involves repeated subacute symptoms to be semantic in nature and opted for the admission that chronic intoxication caused by HCN and the cyanide salts is a true occupational disease.

Heymans and Masoin [112] showed in 1900 that fractions of a lethal dose were cumulative if administered in adequately shortened intervals, and noncumulative when given at widely spaced intervals. The authors suggested that these small fractional doses caused a general weakening of the organism. The authors went on to attribute this general weakening of the

organism's cyanide detoxicating potential to the removal of sulphur by each successive dose, thus reducing the organism's natural defenses and increasing its sensitivity to the poison. Thus one might describe chronic cyanide poisoning as a slow deterioration of resistance, and, therefore, an intensified sensitivity, due to inadequate time between exposures for replacement of damaged tissues, enzyme systems and metabolic stores, the elimination of detoxication products, and the regeneration of homeostatic mechanisms.

Unfortunately, there are only a few studies involving humans which quantified the inhaled or administered dose of cyanide salts. [23,27,85,91,92] Wexler et al [85] gave iv injections of NaCN to 16 soldiers. They noted altered electrocardiograms with doses of 0.06, 0.08, and 0.11 mg/kg of CN. One case of a momentary dim-out was encountered at 0.11 mg/kg. If these soldiers weighed approximately 70 kg, then these doses would correspond to the injection of approximately 4.2, 5.6, and 7.7 mg of CN, respectively. Further approximations extending these injected amounts to air concentrations, given an assumed absorption efficiency, are fraught with peril. However, estimates of the air concentrations of HCN which would produce 50% mortality in humans exposed for different lengths of time have been made assuming an iv LD50 of 1.1 mg/kg and a pulmonary absorption of 70%. [68] Landahl and Herrmann [151] found that the percentage of HCN retained in the human lung with a normal breathing pattern approximated 60% at air concentrations of 0.5 to 18 ppm when breathing through the mouth. Higher absorption might be expected when breathing through the nose. The report by Parmenter [27] mentioned earlier detailed some after-the-fact measurements of HCN taken in such a manner as

to have included any other cyanide aerosol present. Similarly, Dinca et al [23] reported HCN air concentration in a galvanizing shop but did not mention cyanide salts.

However, the reports which give both airborne HCN levels and the human response are essential in evaluating the hazard potential associated with HCN released during the use of cyanide salts in the workplace. There have been several such reports, which are summarized in Table XIV-5.

The only human dose-response information for the cyanide salts is represented by estimations of a lethal dose [29,44,152,153] and the study by Wexler et al. [85]

Sollmann [152] estimated the lethal dose of KCN in man to be 0.2-0.3 g, although it has been reported [153] that ingestion of an estimated 3-5 g was survived without specific treatment. Fassett [29] estimated the lethal dose of NaCN to be 1-2 mg/kg.

Two cases of upper respiratory irritation have been reported. [90,91] The study by Barsky [90], described previously, failed to measure any air cyanide concentrations. However, the incidence of the lesions in a plant with poor housekeeping was given. Conditions were such that one fatality resulted as a consequence of secondary infection.

Elkins [91] noted nasal irritation in an electroplating room where brass plating was being done. He stated that irritation was a common complaint and in some cases ulceration of the nasal passages resulted. The concentration, expressed as HCN, did not greatly exceed 5 ppm. He did not state whether this concentration was found in the area just above the plating tanks or the general workroom air.

Recently, Cohen et al [92] reported a study in which 15 people exposed to CN at an average concentration of 0.006 mg/cu m showed no ill effects whatsoever.

Skin contact with concentrated cyanide solutions has been responsible for deaths [48,96] and permanent disability. [95] Contact with inorganic cyanide solutions as dilute as 0.5% KCN have caused headache and dizziness. [94]

Although no further systemic toxicity studies in humans have measured the inorganic cyanide exposure levels, the work of Ballantyne et al [134, 135,136] has clearly demonstrated in animals that the systemic toxicities of HCN and KCN are roughly equivalent on the basis of the cyanide contents of the two materials (mean toxicity of CN administered im to rabbits as HCN was 106.7% of that administered as KCN). This study is reinforced by the numerous previously described cases of inorganic cyanide exposure which gave the same symptoms as HCN poisoning. Treatment as outlined in Appendix V has been shown to be equally effective for cases of acute poisoning resulting from HCN and cyanide salts.

Cyanide solutions or cyanide aerosols generated in humid atmospheres have also been reported to cause irritation to the skin [26,48,94,96,145,154] and to the upper respiratory tract [90,91] and to cause allergic contact dermatitis. [155] Human skin has been irritated by solutions as dilute as 0.5% KCN (0.2% CN). [94] The typical lesion is manifested in eczematoid dermatitis or skin discoloration or a rash of a nonuniform nature which may itch or burn. [26,48,94-96, 146] Long periods of close contact with solutions of the cyanide salts have been sufficient to cause caustic burns. [48,96] These cases were generally fatal. [48,96]

The cases reported as allergic contact dermatitis by Somov and Khaimovsky [155] in the USSR involved 37 workers in galvanic gilding shops. The condition involved the hands and was caused by prolonged contact with solutions of a gold cyanide. Applications of 1% solution of gold cyanide gave positive results in 28 of 35 patients so tested. Plant conditions were improved and barrier creams were employed. The conditions of 31 of the 37 workers improved and they resumed work. The other six were given work where they would not come in contact with gold cyanide.

#### Carcinogenicity, Mutagenicity, and Teratogenicity

Data on other possible effects of hydrogen cyanide, sodium cyanide, potassium cyanide, and calcium cyanide, such as carcinogenicity, mutagenicity, and teratogenicity, have not been reported and there is no analogy on which to postulate such effects on long-term, low-level exposure. It seems probable that cyanide as a general cell poison and histotoxic agent would depress the activity of all cells, both normal and transformed. Indeed, Perry [138] found a low therapeutic index for cyanide in the treatment of rat sarcomas.

Thiocyanate, the main metabolic product of cyanide detoxification, has been shown to cause abnormalities in the development of chick [140] and ascidian [141] eggs at high concentrations. However, these studies do not allow extrapolation to the human experience of industrial exposure to cyanide. Hrizu et al [139] found that thiocyanate exhibited a cytostatic effect on human KB cells in vitro and an increased survival rate in mice inoculated with Ehrlich ascites tumor cells. However, the amounts used



preclude any meaningful extrapolation to the in vivo response of humans. Thus, NIOSH has no evidence that chronic exposures to HCN and cyanide salts should be considered as possible causes of carcinogenicity, mutagenicity, or teratogenicity.

#### IV. ENVIRONMENTAL DATA

##### Sampling and Analytical Methods

Cyanide compounds may be dispersed in workroom air as gaseous HCN or as an aerosol consisting of small particles of the salt being used. Many air sampling methods do not differentiate between gaseous and particulate cyanides, inasmuch as collection takes place in alkaline solutions which efficiently absorb most cyanide compounds. Thereafter, the analytical method selected determines cyanide radical content, and it is impossible to say what fraction of the total was attributable to any particular compound. In order to differentiate between HCN gas and other cyanide compounds, it is necessary to first remove particulates by passing the air through an efficient filter, then absorb HCN from the stream by passage through an alkaline absorbing solution. The filtered cyanides can subsequently be leached from the filter by treatment with alkaline solution, and the same analytical technique applied to both portions of the sample.

The presence of small quantities of cyanide in water was of concern long before relatively recent ecologic considerations led to an awareness that many other substances were toxic at trace concentrations. As a result, there exists substantial literature dealing with the qualitative and quantitative detection of cyanides in air and water, with at least one method (the titrimetric estimation of cyanide with silver nitrate published by Liebig [156] in 1851) still in use today, more than a century after its origination. [6,7] Almost all the methods proposed for the analysis of water or other materials have been, or can be, applied to the analysis of cyanides in air, for most air methods ultimately involve the determination of cyanide ion in solution.

The frequent use of cyanide compounds for suicidal or homicidal purposes has also led to the development of numerous means for analyzing body tissues or fluids for cyanide content, and concern with chronic exposure to low levels of hydrogen cyanide resulting from occupational exposure or cigarette smoking has similarly led to the development of sensitive methods for determining cyanide or thiocyanate levels in blood, saliva, or breath.

It is not possible to completely review all published methods for determining amounts of hydrogen cyanide and cyanide salts, because there are several hundred literature references. Only a fraction of these analytical methods have been applied to air analysis. A good summary of such methods can be obtained from several comprehensive reviews and compendia. [157-164] The review of Bark and Higson [159] is particularly thorough and is recommended as a survey of methods in use before 1963.

Most analytical methods for cyanide ion depend upon the formation of a colored compound or, in some cases, the attenuation of a color formed by other compounds. Many of the color reactions require the presence of the cupric ion, which forms cupric cyanide with hydrocyanic acid. This salt is easily reduced to the cuprous state and is used to oxidize a number of organic compounds to colored substances which may be detected visually or by spectrophotometric measurement. Some of the more commonly used organic compounds are benzidine [160,165], phenolphthalein [163, 166-169], and o-tolidine. [161] Another widely used color reaction [170,171] is based on the oxidation of hemoglobin to methemoglobin, which reacts with cyanide to form cyanmethemoglobin. This compound has a characteristic red color and a characteristic absorption spectrum. Several methods rely on the

displacement of an acidic anion by cyanide, with the consequent production of a strong acid which thereafter affects some acid-base indicator. Examples are the so-called Congo red-silver nitrate test, [160] in which a silver cyanide complex is formed along with nitric acid which thereafter causes the indicator Congo red to turn blue. A similar reaction occurs with mercuric chloride [160, 163,172], with release of hydrochloric acid, causing the indicator methyl orange to become red. [165] Cyanides can also be made to form complex thiocyanates [160] or ferricyanides with the production of such familiar colors as prussian blue. [160,163,173]

One of the most widely used colorimetric methods is the so-called pyridine-pyrazolone method, an example of the Konig synthesis for pyridine dyes, first published by Aldridge [174] in 1944 (using pyridine and benzidine) and subsequently modified by various authors. [78,175-181] In this method, cyanides are converted to cyanogen bromide or cyanogen chloride, which then reacts with pyridine to form a glutaconic aldehyde. Next, a primary aromatic amine reacts with the aldehyde to yield a colored Schiff's base. In the original procedure of Aldridge, the aromatic amine used was benzidine, but the more frequently used modification of Epstein [179] involves the reaction of cyanogen chloride with pyridine and 1-phenyl-3-methyl-5-pyrazolone, in the presence of bis-(1-phenyl-3-methyl-5-pyrazolone).

Other colorimetric methods which have been described include those based on demasking palladium chelates, [159,182] on the formation of a complex with tris-(1,10-phenanthroline)-iron(II) triiodide, [183] or on reaction with picric acid [160,165,184] and numerous other substances. A fluorometric procedure was also suggested, [185] using the reagent quinone monoxime benzene sulfonate ester.

The basic titrimetric method first published by Liebig [156] has been modified many times, so that even today it is one of the standard methods widely used for water analysis. [186,187] The most common modification consists of adding the silver-sensitive indicator, para-dimethylamino-benzylidene rhodanine, which turns from a yellow to a salmon color with a small excess of silver ion.

Numerous other techniques have been used to determine cyanide, including electrometric techniques such as polarography [188-190], voltammetry [191], amperometry [192,193], coulometry [194] potentiometry [195] and others. [196,197] The most recently introduced and probably most useful in its application to air analysis, is the electrometric technique relying on specific ion electrodes, or ion selective electrodes which respond only to cyanide ion concentrations. [198-205]

Cohen et al [92] used the specific ion electrode to measure total cyanide, as collected in 10 ml of 0.1N NaOH, and reported results as low as 0.006 mg/cu m in various areas of a plating shop.

Several gas chromatographic procedures have also been described, [161, 206-208] though such procedures have not in general been favored for air analysis to date.

A novel approach to determining cyanide levels has been described by Danenik and Bolcz [209] involving indirect atomic absorption spectrometric analysis. In the first of two methods, the complex dicyano-bis-(1,10-phenanthroline)-iron(II) is formed and then extracted into chloroform. The chloroform is evaporated and the residue is taken up in ethanol. The ethanol solution is aspirated directly into the flame, and iron equivalent

to a known amount of cyanide is then determined. The second method is based on precipitating silver cyanide, then determining the excess silver ion in the supernatant by atomic absorption spectrometry.

In place of titrimetric techniques, several investigators have described methods in which turbidity resulting from the formation of silver cyanide, or the reduction in turbidity due to the formation of a cyanide complex with silver iodide, are measured. [210,211]

The methods which have been used for air analysis are generally modifications of the methods just described. Most frequently, papers or other absorbants have been impregnated with various combinations of chemicals so that a color change results from exposure to air containing hydrogen cyanide. [160,161,163,166, 172,173,212-214] Such testing must be considered qualitative or semiquantitative at best, although some procedures call for considerable care to be exercised and yield results that may be adequate for evaluation of concentrations in air under some circumstances.

All such procedures must be considered unsuited to the estimation of particulate cyanide compounds unless steps are taken to ensure that all particles collected on the filter are dissolved and can react with the color-forming or otherwise acting reagent.

In 1944, Lester [171] described a quantitative method in which methemoglobin was used as the color-forming agent and subsequently published a paper [215] describing a portable analyzer which enabled the determinations to be made in the field. Phenolphthalein reagent was first described by Robbie and Leinfelder [167] in 1945 and thereafter was used as the basis for a field sampling instrument described by White. [169] A similar device was also devised by Gisclard et al. [168]

Church and Campbell [216] used the ferric thiocyanate method, and described an improvement in the colorimetric estimation of cyanides by this means. The Aldridge method [174] was first applied to air sampling by Saltzman [175], who recommended certain improvements in the procedure and, in addition, described a method of preparing standard gas concentrations of hydrogen cyanide. Saltzman collected the gas in 5% sodium hydroxide in a midget impinger.

A quantitative cyanide method in which samples were collected in 0.1 N sodium hydroxide with the subsequent formation of ferric thiocyanate was used by Zhdanov [217] as an approved method in the USSR. In later Russian publications, [218,219] the formation of glutaric aldehyde dianilide was described as an improvement on previous methods. A Romanian method for cyanide [220] in air and biologic samples made use of the pyridine-benzidine reaction. A similar method by Hungarian authors [176] elected to use the pyridine-pyrazolone method. Truhaut et al [221] also used the pyridine-benzidine method and applied it to air and biological analyses. The American Industrial Hygiene Association [222] recommended collection of hydrogen cyanide in sodium hydroxide, followed by analysis using the pyridine-pyrazolone method. Hanson et al [161] described several methods, including the use of pyridine-p-toluidine after collection in 1 M sodium hydroxide solution, a gas chromatograph method, and the use of indicator tubes and test papers. As stated earlier, many methods rely upon collection in sodium hydroxide solution, and although frequently described as HCN methods, they are in reality total cyanide methods.

Tada [223] is one of the few authors to recommend the use of the benzidine-pyridine reaction specifically for air sampling, as well as a method using picric acid.

Forensic analyses generally used for cyanides are described in books by Thienes and Haley [157], Stolman [224], Curry (Guatelli), [160] and Sunderman and Sunderman (Free and Free) [225], while specific methods for biologic sample analyses include the use of methemoglobin as a reagent [170], a specific ion electrode method [198], and a blood method using microdiffusion [77], first used by Conway. [226] A respired air method based on the pyridine-pyrazolone reagent [227], as well as more general methods applicable to biologic samples using this same reagent are also used. [220,228] The rationale used in making a forensic diagnosis of cyanide poisoning have also received some attention. [21,229]

Many of the methods listed have also been used for water and waste water analyses, and currently the methods most favored appear to be colorimetric, using some version of the pyridine-pyrazolone method, or modifications of the titrimetric determination with silver nitrate. [177,178,186,187] Specific ion electrodes [198], and picric acid [184] have also been used. Recently, an opto-acoustic infrared absorption technique as well as the titrimetric method utilizing silver nitrate have been used in the analysis of HCN in automobile exhaust. [6,7]

Virtually every method used for cyanide analyses is subject to some interferences, usually due to the presence of certain metals which may form complexes, other anions, particularly sulfide, and a host of oxidizing and reducing agents. It is, therefore, frequently necessary to isolate the cyanide by some means, most frequently by a distillation from strongly acid



solution, where all but the most tightly bound metal complexes are dissociated to release hydrogen cyanide which is then absorbed in alkaline solution.

The recommended sampling and analytical method for the cyanides covered by this document is essentially that of the standard NIOSH method for cyanide in air as published in the NIOSH Manual of Analytical Methods. [203] HCN is collected in an impinger containing 0.1 M NaOH and the sample is analyzed directly, using an ion specific (cyanide) electrode. When alkali metal cyanides or alkaline earth metal cyanides are also to be analyzed, they are collected on a pre-filter prior to the impinger. They are then leached off the filter with base and analyzed by the cyanide electrode. These methods are detailed in Appendices I and II.

#### Continuous Monitoring of HCN in Air

Whenever pure HCN is manufactured, used, or stored in reaction vessels, cylinders, and other containers, accidental leakage or spillage may occur, giving rise to potentially lethal concentrations of the gas. Because of the lethality of the gas, combined with its poor warning qualities, it is essential to monitor the airborne HCN in areas where leakage might occur to prevent loss of life. Air sampling by any of the methods previously described, with considerable time lapse between sampling and reporting of results, is inadequate and cannot be relied upon to prevent disaster. Most of the sampling and analytical methods described could be the basis for a monitoring device for HCN, but in practice relatively few devices are commercially available.

One currently (1976) available monitoring device [230] uses amperometry, the sensing device being two electrodes in an electrolyte flowing through a porous glass cell. The instrument relies on diffusion into the cell, where contact with the measuring electrode generates a current proportional to the concentration of gas present. The instrument which covers the 0-50 ppm range, with a half-scale reading of 10 ppm, is lightweight, rugged, stable, low in cost, and permits 2 weeks of continuous operation. An alarm circuit is also available for this instrument.

### Control of Exposure

Operational equipment, procedures, and work practices should be designed to prevent the dispersal of dusts or mists of cyanide salts or the escape of HCN gas into the atmosphere of the working environment. The airborne concentration must be kept within the limits of the recommended standards. When the necessary control is not ensured by operational conditions and work practices, mechanical ventilation is required.

Ventilation should be provided in all areas where release of any inorganic cyanide dust or mist or of hydrogen cyanide gas into the atmosphere is known or possible. The ventilation system must ensure that the cyanide is removed or is diluted to concentrations below the standards recommended in Chapter I. General ventilation may be adequate in some circumstances; however, control by ventilation can be achieved best by use of local exhaust ventilation at the source of emission. [63,90] In employing exhaust ventilation for such control, the design principles given in Industrial Ventilation - Manual of Recommended Practices [231] and Fundamentals Governing the Design and Operation of Local Exhaust Systems

[232] should be followed. High ventilation rate systems for the rapid dilution or removal of HCN gas and aerosols may be useful in some areas.

Control of the hazard of potential release of hydrogen cyanide from cyanide salts requires constant care and attention to good work practices. The cyanide salts should be kept well apart from, and protected from contact with, acids, moisture, or elevated concentrations of carbon dioxide. [30,233] Even weak acids contacting cyanide salts will result in the rapid evolution of hydrogen cyanide. Moisture alone releases hydrogen cyanide slowly from sodium or potassium cyanide and rapidly from calcium cyanide. Normal atmospheric concentrations of carbon dioxide in the presence of moisture generate a sufficient concentration of hydrogen ions that the rate of evolution of hydrogen cyanide from cyanide salts may become dangerous in closed or poorly ventilated spaces. High concentrations of carbon dioxide from fire extinguishers, process gases, and combustion gas can seriously accelerate the release of HCN from the cyanide salts. Special care must be exercised to protect calcium cyanide from moisture and carbon dioxide because of its particularly rapid rate of reaction with these environmental factors.

## V. DEVELOPMENT OF STANDARD

### Basis for Previous Standards

In 1948, the American Conference of Governmental Industrial Hygienists [234] adopted a Threshold Limit Value (TLV) for HCN as a time-weighted average (TWA) of 10 ppm (approximately 11 mg/cu m as HCN). This TLV of 10 ppm was considered by the ACGIH to contain a two-fold margin of safety against mild symptoms and a seven or eight-fold margin against lethal effects according to the 1971 Documentation of the Threshold Limit Values. [235]

In this documentation [235], the ACGIH cited Henderson and Haggard [149] as reporting that 20-40 ppm of HCN caused slight symptoms. Henderson and Haggard, however, credited these values to numerous review authors and to Flury and Zernik. [118] It turns out that all these reviews derived their data from the 1931 publication of Flury and Zernik. In turn, Flury and Zernik credited the values to the works of Lehmann and Hess (please see discussion in Chapter III).

The ACGIH [235] further cited the HCN air levels of Grabois [150] as being of the order of 10 ppm. Actually, Grabois reported concentrations ranging from less than 1 to 17 ppm and reported only two areas in one of the five plants sampled which had levels over 8.6 ppm. These high levels were 17.0 and 13.9 ppm. The median HCN levels for each operational area sampled at the five apricot kernel processing plants were as follows: comminuting, 5.0 ppm; cooking, 2.5 ppm; debittering bath, 3.3 ppm; and general workroom air, 1.0 ppm. Perhaps a better statement would be that no ill effects were found at levels up to 5 ppm.

The present federal standard for HCN is also 10 ppm HCN, or 11 mg HCN/cu m, as a time weighted average (29 CFR 1910.1000, which has been published in 39 FR 23541, June 27, 1974, as amended) and is based upon the 1962 ACGIH Threshold Limit Value. Thirteen other countries and six states in the United States have set standards for HCN. These standards are presented in Table XIV-8.

The American Conference of Governmental Industrial Hygienists [236] based their selection of an alkali cyanide TLV as a TWA of 5 mg/cu m (as CN) on the work of Elkins [91], in which air concentrations above 5 ppm (as HCN) were stated to cause nasal irritation and ulceration of the septum.

The present Federal standard for alkali cyanides is 5 mg/cu m (as CN) as a time-weighted average (29 CFR 1910.1000, which has been published in 39 FR 23541, June 27, 1974, as amended) and is based upon the 1968 ACGIH threshold limit value. Nine other countries and five states in the United States have set standards for inorganic cyanide. These standards are presented in Table XIV-9.

#### Basis for Recommended Environmental Standard

Cyanide is well known as an acute, fast acting poison which can be described as insidious in that its toxic action at high concentrations is so rapid that its odor has no value as a warning. [2] At lower concentrations the sense of smell may provide forewarning. For HCN, the primary routes of entry from occupational exposure are inhalation and absorption through the skin. [29,39,107,118,147,233,237] Absorption by either route is apparently rapid. [147]

Direct exposure to cyanide salts in the workplace has occurred via inhalation of the aerosol [26,63,81,88,91,95,145] and absorption through the skin. [26,50,88,95,96,147] In addition, inhalation [3,29,238,239] and skin absorption [29,63,238,239] have been mentioned by others as the primary routes of entry for cyanide salts. Despite the fact that ingestion has been the classic route of entry for the cyanide used for attempts of homicide, [19,101,240] suicide, [19,51,101-106,240,241,242,243,244] and in accidental poisoning [51,96,102] in the general population, ingestion can be considered to be of secondary importance as a route of entry for occupational exposure.

Although Wolfsie and Shaffer [107] have stated that gaseous HCN is normally, in itself, not irritating to cutaneous or respiratory tissue, Hamilton and Hardy [145] noted that low level exposures to HCN vapors produce a blotchy eruption on the face; Williams [39] stated that in fumigation a concentration of 6-10 g/cu m produces a sensation of warmth over the entire body, followed by a reddening of the skin.

Skin contact with solutions of cyanide salts can cause itching, discoloration, or corrosion [26,94-96,154,155], which is most likely due to the alkalinity of the solution. [28,96,154] The irritant response is characterized by a discoloration or rash of a non-uniform nature which may itch or burn. [26,48,94-96,146] Such lesions have been caused by cyanide solutions as dilute as 0.5% KCN. [94] Skin contact with aqueous cyanide solutions for long periods have caused caustic burns. [48,96] These cases were generally fatal. [48,96]

Besides systemic toxicity and skin irritation, cyanide salt aerosols cause upper respiratory irritation. This has been investigated as a

response to inorganic cyanide inhalation in three separate studies. [90,91,92] The study by Barsky [90] did not include air concentrations but described the nature and incidence of the response in a copper-plating plant with poor housekeeping. Elkins [91] stated that nasal irritation and ulceration of the septum were found in an electroplating room where the concentration of cyanide, expressed as HCN, did not greatly exceed 5 ppm, (about 5 mg CN/cu m). Cohen et al [92] found no ill effects in a group of 15 electroplaters exposed to breathing zone concentrations of 0.006 mg/cu m of CN.

It appears to be generally accepted that HCN and cyanide salts act by the same mechanism, namely, the release of the cyanide ion, which inhibits cytochrome oxidase and results in histotoxic anoxia. [107] Thus, it may be presumed by analogy that if 90 ppm of HCN is fatal, 96 mg/cu m of CN, derived from cyanide salts, may be also. Extending this analogy to threshold levels, presumably 11 mg/cu m of CN would be equivalent to the current Federal standard of 10 ppm of HCN and restriction of exposures to 11 mg/cu m of CN would protect against acute toxicity from cyanide salts. However, taking into account the irritant effects observed from exposure to cyanide salts, [90,91] the current Federal standard of 5 mg/cu m of CN as an 8-hour time-weighted average appears to be too high in that it allows substantial excesses above that concentration for short periods of time. Therefore, NIOSH recommends that the current value of 5 mg/cu m of CN be retained, but that its basis be changed from an 8-hour time-weighted average to a 10-minute ceiling. This action should provide the employee with adequate protection from the systemic effects of cyanide and prevent the erosional effects produced by the alkalinity associated with the cyanide salts.

A review of the cases involving exposure to cyanide reveals that they fall into three general categories. First are those cases in which there was an acute or subacute exposure followed immediately by an acute illness. [11,13,20,26, 27,42,48,51,87,88,94,101,240] Secondly, there are those cases involving a chronic, or prolonged, low-level exposure followed by a chronic or slowly developing malaise. [17,25-27, 63,81,90,91,95,99,146] In at least two of these cases, [26,27] it is uncertain whether the coexisting long-term low-level exposure or the infrequent acute or subacute exposures were responsible for the signs and symptoms noted.

The third category is represented by those cases involving an acute exposure and a delayed chronic response occurring or worsening after the cessation of exposure. [26,109] The first of these two papers [26] concerns workers who had received a mixture of acute and chronic exposures, with effects which worsened after cessation of the exposures. The second study [109] involved 13 fumigators who also received a mixture of acute and chronic exposures, with at least one severe nonlethal acute exposure. These men exhibited a high incidence of delayed signs of effect by CN some time after their acute episodes, but less marked than those induced by the acute exposure. The author [109] suggested that damage due to cyanide may not be entirely reversible. It appears that the case for a chronic effect from an acute exposure is very weak and a better classification would be simply acute and chronic cases. All the chronic cases may be attributed to either the anoxia resulting from the inhibition of cytochrome oxidase by cyanide or a reaction by sensitive individuals to the thiocyanate produced



in detoxication of cyanide, or by those unable to excrete thiocyanate at a sufficient rate.

Hardy et al [24] did observe increased urinary excretion of thiocyanate in a group of case hardeners who were exposed to HCN and possibly to cyanide salts. Breathing zone concentrations of HCN in those workers in controlled operations were measured and found to be 4-6 ppm of HCN or less, but neither the HCN concentrations in uncontrolled operations nor any of the exposures to cyanide salts were quantified. No symptoms were noted in those exposed to 4-6 ppm. However, these men may have been included among the 25 workers with increased thiocyanate excretions. An increase in urinary excretion of thiocyanate upon exposure to cyanide has been reported by several authors. [24,60,76,79] Hardy [24] also described two cases of severe chronic cyanide poisoning which included the appearance of enlarged thyroids and attributed these to the rare inability of these individuals to excrete thiocyanate.

Two other papers [25,110] also noted thyroid enlargements, however. El Ghawabi et al [110] noted that in 36 employees exposed to cyanides at concentrations of 4.2 to 12.4 ppm, 20 workers (56%) had slight or moderate thyroid enlargements, 4 of these were firm and slightly nodular while the remaining 16 were soft and smooth. It is generally accepted that thiocyanate competes with iodide for uptake by the thyroid gland. In his recent review on the biochemistry of thiocyanate, Wood [65] has concluded that the blood level necessary for this effect is far less than the concentration which is toxic. Maehly and Swensson [76] have suggested that smoking may produce a larger effect on urinary cyanide and the thiocyanate levels than occupational exposure to HCN at concentrations between 2 and 8

ppm. They also stated that it was difficult to give reliable limits for normal levels of cyanide and thiocyanate in the urine. However, in order to assess the hazards of occupational exposure, they considered it safe to state that nonsmokers who have greater than 400  $\mu\text{g}/100\text{ ml}$  of free thiocyanate in the urine, or smokers with urinary concentrations exceeding 1 mg/100 ml, should be given repeated tests. An evaluation of working conditions was proposed if the concentrations should remain elevated upon repeated determinations. The concentration of thiocyanate in body fluids at which goiterogenic effects begin is not known and would probably vary with the individual and his dietary iodide intake.

Changes in the chemical and cellular composition of the blood of employees exposed to cyanide have been reported also. [23,82,83,110,118] Most notably, El Ghawabi et al [110] found significantly higher hemoglobin concentrations and lymphocyte counts in 36 cyanide workers exposed to concentrations ranging from 4.2 to 12.4 ppm for an average duration of 7.5 years (as a broad approximation) than in 20 controls.

Although increases in urinary thiocyanate excretion, lymphocytes, and thyroid size do occur, these deviations, at least when small, have not been related to any lesion or pathological symptom or sign. Rather, they may represent the body's adaptation in maintaining homeostasis to the stress of exposure to cyanide.

El Ghawabi et al [110] were able to construct a graph of urinary thiocyanate versus the concentration of cyanide in the air. The equation for the regression line was  $M=0.65\ C$ , where M is the amount in mg of thiocyanate excreted in the urine during 24 hours and C is the concentration of cyanide in the air in ppm. Using this equation and the

value of 1400 ml for total daily urine output, the 400  $\mu\text{g}/100$  ml concentration of thiocyanate in the urine suggested as the upper limit of normal for non-smokers by Maehly and Swensson [76] corresponds to an occupational exposure level of 8.6 ppm of cyanides (presumably expressed as HCN).

As discussed in Chapter III, there are no substantial studies in the scientific literature demonstrating major lesions which result from long-term occupational exposure to HCN at 10 ppm. The epidemiologic study by El Ghawabi et al [110] showing an increase in the subjective symptoms of headache, weakness, changes in taste and smell, irritation of the throat, vomiting, effort dyspnea, lachrymation, abdominal colic, precordial pain, and nervous instability among cyanide workers exposed for an average of 7.5 years (as a broad approximation) at concentrations ranging from 4.2 to 12.4 ppm, as well as the papers by Colle, [83] Radojicic, [79] Saia et al, [22] Sato et al, [84] Heymans and Masoin, [112] and Chaumont, [82] leads NIOSH to recommend that employee exposure to HCN be controlled so as not to exceed 5 mg/cu m of air expressed as CN (4.7 ppm), determined as a ceiling concentration based on a 10-minute sampling period.

Many of the previously enumerated symptoms are not unique to cyanide intoxication and can be caused by a wide range of other chemical and physical stressors. However, this cyanide syndrome, or set of subjective symptoms, appears to be sufficiently well documented as characteristic of exposure to low concentrations of cyanide to warrant its being considered an indicator of impairment of worker health and well-being.

It is recognized that many workers are exposed to cyanides in concentrations considerably below the recommended occupational limits.

Under these conditions, it should not be necessary to comply with many of the provisions of the recommended standards. However, concern for worker health and well-being requires that protective measures be instituted below the enforceable limits to ensure that exposures do not exceed the standard. For this reason, occupational exposures to HCN and cyanide salts have been defined as exposure above one-half their recommended ceiling values, thereby delineating those work situations which do not require the installation of unnecessary controls and the expenditure of health resources for environmental and medical monitoring and associated recordkeeping. These occupational exposure values have 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 resulting from skin or eye contact or from ingestion, it is recommended that appropriate work practices and protective measures be required regardless of concentrations of HCN or other cyanide compounds in the air.

## VI. WORK PRACTICES

Good work practices are of major importance for the prevention and control of exposures in the use of HCN and of cyanide salts. The effectiveness of other control measures is enhanced by, or even dependent on, adherence to good work practices. [30,245] Because the danger arises from the cyanide radical common to both HCN and the cyanide salts, the recommended work practices must apply to all forms, melts, and solutions of these cyanides, unless exceptions or special requirements are specifically mentioned.

Because of the special importance of work practices in the safe handling of cyanide compounds, the employer must take the necessary steps to ensure that each employee:

(1) receives adequate instruction and training in safe work procedures, in the proper use of all operational equipment and protective devices, and in all emergency procedures;

(2) is periodically given additional periods of training and instruction to maintain a high level of awareness and competence in safe work practices;

(3) engages in periodic drills or tests pertinent to emergency situations relating to cyanide compounds, fires, and explosions;

(4) receives periodic drills or quizzes regarding location, purpose, and use of emergency equipment and supplies;

(5) is provided with necessary tools, equipment, and personal protective clothing or devices;

(6) is given the supervision necessary to assure that all safety requirements and practices are followed;

(7) is instructed to shower before removing any respirator or gas-tight suit if prior contact with HCN liquid has occurred or is suspected;

(8) reports to the proper authority all equipment failures and signs and symptoms of illness.

Only properly trained and authorized persons should be permitted in areas where HCN is manufactured, transferred, stored, used, or generated, or in areas where there is a likelihood of exposure to cyanide salts as solids or solutions. Workmen and supervisors should be alert to exclude any unauthorized persons. Such areas should be clearly identified by appropriate posted warnings.

All employees should be thoroughly trained in first aid and other emergency procedures. Any person showing evidence of HCN intoxication should be removed immediately from exposure and given first aid while medical aid is summoned. [2]

The specific procedures used in humans overexposed to HCN and the excellent results obtained have been reviewed by Chen et al, [101] Wolfsie and Shaffer, [107] and Wolfsie. [100]

Approved-type, self-contained breathing apparatus with a full facepiece should be worn by any employee entering or working in an area of known or suspected life threatening concentrations of HCN. [2,239,246]

Gas-tight suits should be worn by persons entering or working in any area of known or suspected life threatening concentrations of HCN. Such suits must be impervious to HCN. [2,3,247,248]

Gas masks with canisters should never be relied upon for protection when entering areas or spaces where the airborne concentration of HCN is unknown.

Clothing contaminated by HCN should be removed as soon as possible and laundered before it is worn again. [2,249]

A worker whose clothing has absorbed HCN liquid or gas should not remove his respiratory protective device immediately on leaving the exposure area or while removing his contaminated clothing. Absorbed HCN which may be released from the contaminated garment may be sufficient to be hazardous to the individual. [249]

Employees working with any cyanide salts (cast forms, pellets, and/or powder) should wear work garments covering the arms, legs and body fully to the neck to minimize the degree of contact of cyanide dusts with the skin surfaces. The body garment must be kept buttoned or otherwise kept closed during periods of potential exposure. Gloves should be worn to protect the hands from contact with gaseous, liquid, dust, or solid forms of cyanide compounds while handling cyanides or tools or equipment whose surfaces may be contaminated with cyanide. [30]

Employees working with solutions of cyanide salts should wear personal protective garments and equipment appropriate to prevent contact of the solution with their skin and/or eyes. Gloves of rubber or other material impervious to the cyanide solutions should be worn while working with the solutions or with any tools or surfaces wetted with cyanide solutions. Aprons or other body garments of material impervious to cyanide solutions should be worn while making, mixing or transferring such solutions. Full body protective clothing should be worn in circumstances where splashes or spills are likely or when other factors make such protection necessary to prevent contact of the cyanide solutions with the skin. [30,250]

Gloves, protective clothing, and regular work clothing should be changed at least daily. All such items should be thoroughly washed between uses. When the interior surfaces of any such garments become contaminated with cyanide solids or solutions during the workday, they should be changed for clean garments.

If work clothing becomes wet with cyanide solution, it must be removed immediately and the worker must shower and thoroughly wash the affected area of the body. Wetted or splashed clothing must be washed and dried before it is worn again. [30]

Boots, shoes or overshoes made of material impervious to cyanide solutions should be worn by employees working with such solutions or in areas where spills of such solutions are likely. [30] The trouser leg should be worn outside the top of the footwear to prevent any entrapment of solution in the footwear.

Chemical safety goggles should be worn in all circumstances where there is danger of mists or splashes of cyanide solution coming into contact with the eyes. Full-length plastic faceshields with forehead protection should be worn for protection of the face. If cyanide solution or solid does get into the eye of an employee, he should immediately flush the eye with a copious flow of water for at least 15 minutes and obtain medical attention as soon as possible. Eye-flush fountains or other means for obtaining a copious and gentle flow of water suitable for flushing the eyes must be provided and readily accessible in all areas where cyanide solutions are used. [30,251]



All protective and process equipment must be inspected frequently and maintained in good and safe operating condition. Storage tanks should be thoroughly cleaned, inspected, and conditioned before use. In the unloading of HCN liquid from tank cars or tanks of motor trucks, instructions of the supplier should be carefully followed. All connections and lines should be inspected and secure before the flow of HCN is turned on. Warning signs should be posted fore and aft of the tank car or truck and in a perimeter around the area. Storage tanks should be vented and have provision for destruction or safe dissipation of the vented gas. Cylinders of HCN should be stored in cool areas and away from combustible material, open flames, or other possible sources of ignition. Only responsible, authorized persons should have access to the storage area.

All areas where any cyanide salts are stored should be adequately ventilated to maintain the airborne cyanide concentration below the recommended standards. In many instances, natural ventilation may be adequate, but mechanical ventilation must be used where necessary. [30,63,90] For storage, cyanide salts in solid or solution forms should be in sealed or tightly covered containers in an area remote from any acids or acid vapors. The containers should be protected from moisture. No hooks should be used in handling containers of cyanide salts.

No employee should work alone in an area or space of possible hazard from HCN. [2,239,246] Another employee should be in attendance and contact (preferably sight contact) in a safe area or at a distance so as not to be affected by an emergency situation at the site of the first employee. The second employee ("buddy") should be alert and equipped to summon help and render aid, if needed.

The employee should carefully and precisely follow all operational procedures specified for the handling of HCN in containers, transfer operations, or other equipment. Suppliers' and manufacturers' instructions should be carefully followed. [2]

When HCN is used for fumigation purposes, the space should be sealed to prevent the gas from leaking into surrounding spaces or areas. Warning signs should be posted and guards placed to keep unauthorized persons at a safe distance. All laws, regulations, ordinances, and codes applicable should be followed. Only licensed fumigators should do such work. [246]

Open containers of any solid cyanide salts or of solutions of cyanide salts should be limited to those necessary for operational requirements and procedures. Such open containers must be used only in adequately ventilated spaces so that the recommended standards for the airborne concentration of cyanide are not exceeded. Good practice dictates that, in so far as practical, covers be provided for such containers and used whenever possible.

Solutions of cyanides should be maintained as basic as practical to prevent any evolution of hydrogen cyanide. When weakly basic or neutral solutions are used, ventilation must be provided sufficient to prevent accumulation of the HCN evolved from exceeding the recommended standard for HCN in the work room air. When the addition of an acid to a cyanide solution may be necessary, the process should be fully enclosed and ventilated. Respiratory protection should be provided for all workers potentially exposed to any release of hydrogen cyanide.

Fused salt baths containing cyanide salts should be provided with local exhaust ventilation. Care should be exercised in the operation of

such baths to avoid spills and splashes. Addition of salts should be made carefully, using a shovel or special tool. The area about the bath should be regularly cleaned to prevent accumulation and encrustation of cyanide salts on adjacent areas. Workers at fused salt baths should wear safety goggles with side shields.

Local exhaust ventilation must be used for all operations emitting dusts or mists of cyanide salts. [80,232]

Tanks and other equipment which must be entered for inspection, maintenance or repair, should be drained as completely as possible and then filled with water and agitated. After 15 minutes, they should be drained again and refilled for another 15 minutes, then drained again. The tanks should then be inspected for residue and encrustation of cyanides. These should be broken loose mechanically or by the force of a water stream and flushed away. The tank should then be purged with fresh air, followed by testing for the absence of cyanide in the air before anyone enters. Entering workmen should wear protective clothing. Approved type respiratory protective devices should be available for use, if needed. [30]

HCN liquid should not be transferred from one cylinder to another or from an applicator back into a cylinder.

Waste solutions of HCN should be destroyed by either (1) alkaline chlorination or (2) alkaline reaction with ferrous sulfate. [2]

Cyanide waste solutions and cyanide-contaminated rinse or wash waters should be treated to destroy the cyanide before being discarded. Treatment of cyanide waste is achieved by oxidation of the cyanide in alkaline solution by addition of chlorine or other oxidizing agents. [30,252]

Transfer lines should be thoroughly drained and flushed after each use for transfer of HCN.

In the event of spills of HCN liquid, the area should be cleared of all persons except emergency personnel properly trained and equipped to deal with the emergency. The area should be roped off and warning signs posted to exclude all other employees until tests show that the atmospheric concentrations of HCN are below the recommended standard. [2]

Spills of cyanide solids or solutions should be cleaned up immediately. Spills of NaCN or KCN solids may be shoveled carefully into containers, with care being taken that cyanide dust is not dispersed into the air. The residue after shoveling, or small spills, may be removed by dry vacuuming or flushing with a liberal quantity of water.

Spills of  $\text{Ca}(\text{CN})_2$  solids should be cleaned up by shoveling the bulk of the spill carefully into dry containers, followed by dry vacuuming of the spill area to remove any residual cyanide solids. Water should not be used in the cleanup of  $\text{Ca}(\text{CN})_2$  spills unless it has been alkalized.

Respiratory protection (see Chapter I, Section 6) should be worn by workers while cleaning up spills of cyanide salts. Caution: Filter-type respirators alone do not provide adequate protection in the case of  $\text{Ca}(\text{CN})_2$  spills. Spills of cyanide solution should be washed away with water and with the same precautions stated in the preceding paragraph.

Water from the flushing or cleaning of cyanide spills or cyanide contaminated equipment should be treated as cyanide waste solution. These solutions should not be washed or emptied into a drain system which may contain or receive acid wastes.

When in the judgment of a professional industrial hygienist, the airborne cyanide concentration is likely to be excessive, continuous monitoring should be performed. Areas of potential exposure to HCN gas should be routinely monitored to ensure that concentrations of the gas in the air remain within the recommended standards. Automatic and recording monitoring systems will be desirable in certain areas. [2,247,249]

Each plant must establish an emergency plan and program. The workers and the emergency teams should be thoroughly informed and trained in their responsibilities and actions in emergencies. Emergency stations equipped with first-aid supplies and equipment, a suitable number of approved-type respiratory protective devices, protective garments, and other special equipment as needed should be established and maintained readily accessible to areas wherein cyanide emergencies may be anticipated or may occur. [30,239] A program should be established for the frequent and regular inspection and maintenance of all protective and safety equipment.

Employees should observe good personal hygiene, including showering and changing clothes at the end of a workshift. They should wash well before eating. Eating and smoking should be permitted only in uncontaminated areas designated for these purposes. Food, candy, tobacco, or other items intended for ingestion or oral contact should not be taken (or carried in garment pockets) into an area of cyanide exposure or use because of the potential for contamination. Any such items taken into a cyanide area should be regarded as contaminated and should be discarded.

## VII. RESEARCH NEEDS

Long-term epidemiologic studies of worker populations exposed at or below the recommended environmental limits are needed. Such studies should consider not only the subjective complaints of workers but should also address changes in blood chemistry, thyroid function, and the urinary excretion of thiocyanate. As a minimum, these studies should include breathing zone air measurements, medical histories, smoking habits and histories of previous exposure.

The permeability of gloves, chemical suits, and other protective clothing to hydrogen cyanide should be determined. Methods for automatic, continuous monitoring should be designed and/or tested for sensitivity, accuracy, and specificity by comparison with a reliable standard method. Since one of the primary functions of automatic continuous monitoring is serving as a warning device, alarm systems should be incorporated and tested for reliability.

Animal studies should be conducted to document and verify the dose-response relationship between chronic exposure to low-concentrations of HCN and neural lesions. These studies should also address the issues of carcinogenicity, mutagenicity, and teratogenicity as they pertain to HCN and its metabolites. Information should also be collected to evaluate the possibility of neural lesions as a consequence of human chronic cyanide exposure.

An improved analytical method for urinary thiocyanate should be tested and validated for assessing occupational exposure to cyanide and the normal ranges of cyanide and thiocyanate determined for differing habits of

intake of food, drink, and other xenobiotic substances and for various body fluids.

A compilation of cyanide salt exposure concentrations and the incidence of nasal and mucosal lesions is lacking. Other needed research is in the area of cyanide antidotes. There are indications that dicobalt ethylenediaminetetraacetate and hydroxocobalamin may prove to be useful.

## VIII. REFERENCES

1. Weast RC (ed): Handbook of Chemistry and Physics, ed 56. Cleveland, Chemical Rubber Co, 1975, pp B-149, B-70, B-81, B-92, B-97, B-105, B-110, B-113, B-126, B-138, B-141, B-158
2. Chemical Safety Data Sheet SD-67, Properties and Essential Information for Safe Handling and Use of Hydrocyanic Acid. Washington, DC, Manufacturing Chemists' Association Inc, 1961, pp 5-22
3. Hardy HL, Boylen GW Jr: Cyanogen, hydrocyanic acid, cyanides, in International Labour Office: Encyclopedia of Occupational Safety and Health. Geneva, ILO, 1972, vol 1, pp 352-54
4. Jennings BH: Hydrogen Cyanide - HCN, in Hazardous Vapors and Dusts in Industry. Chicago, Ventilating and Air Conditioning Contractors Association of Chicago, 1957, pp 4-109 to 4-110
5. Kirk RL, Stenhouse NS: Ability to smell solutions of potassium cyanide. Nature 171:698-99, 1953
6. Voorhoeve RJH, Patel CKN, Trimble LE, Kerl RJ: Hydrogen cyanide production during reduction of nitric oxide over platinum catalysts. Science 190:149-51, 1975
7. Dunlevey FM, Lee CH: Hydrogen cyanide formation over automotive catalytic converters. Science 192:809-10, 1976
8. Faith WL, Keyes DB, Clark RL: Hydrogen Cyanide-HCN, in Industrial Chemicals, ed 3. New York, John Wiley and Sons Inc, 1965, pp 450-57
9. Hydrogen Cyanide. Chemical Economics Handbook, Stanford Research Institute, Menlo Park, California, Nov 1975, p 664.5020A-I
10. Shreve RN: Chemical Process Industries, ed 3. New York, McGraw-Hill Book Co, 1967, pp 220-21, 476-83, 696-99
11. Stock PG, Monier-Williams GW: Preliminary report on the use of hydrogen cyanide for fumigation purposes--Reports on Public Health and Medical Subjects No 19. London, Ministry of Health, 1923
12. Fuhner H: [The poisoning by cyanic acid and its treatment.] Dtsch Med Wochenschr 45:847-50, 1919 (Ger)
13. Gettler AO, St George AV: Cyanide poisoning. Am J Clin Pathol 4: 459-37, 1934



14. Scott HG, Littig KS: Insecticidal Equipment for the Control of Insects of Public Health Importance, Publication 774. Training Guide--Insect Control Series. US Dept of Health, Education, Welfare, Public Health Service, Center for Disease Control, Atlanta, 1959, pp 26-27
15. Frear DEH (ed): Pesticide Handbook--Entoma, ed 24. State College, Pennsylvania, College Science Publishers, 1972, pp 63,81,86,114,254, 255
16. Cousineau A, Legg FG: Hydrocyanic acid gas and other toxic gases in commercial fumigation. Am J Public Health 25:277-94, 1935
17. Jaroschka R, Kropp R: [Chronic cyanide poisoning.] Int Arch Gewerbepathol Gewerbehyg 22:202-07, 1966 (Ger)
18. Williams CL: An unusual case of cyanide poisoning during fumigation. Public Health Rep 53:2094-95, 1938
19. Polson CJ, Tattersall RN: Clinical Toxicology. London, Pittman Medical and Scientific Publishing Co Ltd, 1971, chap 9, pp 128-59
20. Bernstein P, Avital YM: [HCN poisoning in a tobacco warehouse.] Harefuah 62:165-67, 1962 (Heb)
21. Sunshine I, Finkle B: The necessity for tissue studies in fatal cyanide poisonings. Int Arch Gewerbepathol Gewerbehyg 20:558-61, 1964
22. Saia B, DeRosa E, Galzigna L: [Remarks on the chronic poisoning from cyanide.] Med Lav 61:580-86, 1970 (Ita)
23. Dinca C, Pod L, Galetariu I: [Considerations on leukocytic oxidative enzyme changes in subjects exposed to the prolonged action of cyanhydric acid in industry.] Med Int 24:1385-92, 1972 (Rum)
24. Hardy HL, Jeffries WM, Wasserman MM, Waddell WR: Thiocyanate effect following industrial cyanide exposure--report of two cases. N Engl J Med 242:968-972, 1950
25. Wuthrich F: [Chronic cyanide poisoning as industrial intoxicant.] Schweiz Med Wochenschr 84:105-07, 1954 (Ger)
26. Smith AR: Cyanide poisoning. NY Dept Labor Ind Bull 11:169-70, 1932
27. Parmenter DC: Observations on mild cyanide poisoning--report of a case. J Ind Health 8:280-82, 1926

28. Mooney RB, Quin JP: Alkali metal cyanides, in Kirk RE, Othmer DF: Encyclopedia of Chemical Technology, ed 2. New York, Interscience Publishers, 1965, vol 6, pp 585-601
29. Fassett DW: Cyanides and nitriles, in Patty FA (ed): Industrial Hygiene and Toxicology, ed 2 rev; Toxicology (Fassett DW, Irish DD, eds). New York, Interscience Publishers, 1963, vol II, chap 44
30. Chemical Safety Data Sheet SD-30, Properties and Essential Information for Safe Handling and Use of Sodium Cyanide. Washington, DC, Manufacturing Chemists Association Inc, 1967
31. Booth RB: Alkaline earth metal cyanides, in Kirk RE, Othmer DF: Encyclopedia of Chemical Technology, ed 2. New York, Interscience Publishers, 1965, vol 6, pp 601-04
32. Clifford AF: Inorganic Chemistry of Qualitative Analysis. Englewood Cliffs, N.J., Prentice-Hall, 1961, pp 446-47
33. The Merck Index, PG Stecher, ed, 8th edition. Rahway, N.J., Merck and Co, 1968, pp 191, 193, 853, 855, 957, 960
34. Dean JA (ed): Lange's Handbook of Chemistry, ed 11. New York, McGraw-Hill Book Co, 1973, pp 5-7, 5-9, 5-11, 5-71, 5-73
35. Fahrenwald AW: The Cyanide Process--Its Control and Operation. New York, John Wiley & Sons, 1918, 256 pp
36. Dorr JVN, Bosqui FL: Cyanidation and Concentration of Gold and Silver Ores, ed 2. New York, McGraw-Hill Book Co, 1950, 511 pp
37. Hamilton EM: Manual of Cyanidation. New York, McGraw-Hill Book Co, 1920, 277 pp
38. James A: Cyanide Practice, ed 2. London, E & FN Spon Ltd, 1902, 104 pp
39. Williams CL: Fumigants. Public Health Rep 46:1013-31, 1931
40. Creel RH: Fumigation by cyanide gas. Mil Surg 39:282-87, 1916
41. MacFarren HW: Text Book of Cyanide Practice. New York, McGraw-Hill Book Co, 1912, pp 43-50
42. Johnstone RT: Occupational Medicine and Industrial Hygiene. St Louis, CV Mosby Co, 1948, pp 130-35
43. Williams CL: The use of hydrocyanic acid for fumigation purposes. Can Public Health J 23:567-70, 1932

44. Gleason MN, Gosselin RE, Hodge HC, Smith RP: Clinical Toxicology of Commercial Products, ed 3. Baltimore, Williams & Wilkins Co, 1969, pp 26-31, 33-42, 44-45, 52-53
45. Scheele CW: Experiments concerning the colouring in prussian blue, in The Collected Papers of Carl Wilhelm Scheele. London, G Bell and Sons Ltd, 1931, pp 238-55
46. De Tatham H: Temporary amaurosis from exposure to the vapour of dilute hydrocyanic acid. Br Med J, 1:409, 1884
47. International Labour Office: Occupation and Health--Encyclopedia of Hygiene, Pathology, and Social Welfare. Geneva, Noirclerc et Fenetrier SA, 1930, vol I, pp 993-98
48. International Labour Office: Cyanogen and its compounds, in Occupation and Health: Encyclopedia of Hygiene, Pathology and Social Welfare. Geneva, Noirclerc et Fenetrier SA, 1930, vol I, pp 553-60
49. Rambousek J: Industrial Poisoning from Fumes, Gases and Poisons of Manufacturing Processes. TM Legge (trans-ed). London, Edward Arnold, 1913, pp 93-95, 195-97, 280, 341, 348-49
50. Souwers GF: A case of peculiar poisoning by cyanide of potassium. Philadelphia Med Times 8:345-46, 1878
51. McKelway JI: Three cases of poisoning by potassium cyanide. Am J Med Sci 129:684-88, 1905
52. Kobert R: [Cyangas, prussic acid, and cyanide], in Lehrbuch der Intoxikationen, ed 2. Stuttgart, Ferdinand Enke, 1906, vol 2 , pp 835-63 (Ger)
53. Binkley, F: On the nature of serine dehydrase and cysteine desulfurase. J Biol Chem 150:261-62, 1943
54. Altschul AM, Abrams R, Hogness TR: Cytochrome c peroxidase. J Biol Chem 136:777-94, 1940
55. Albaum HG, Tepperman J, Bodansky O: A spectrophotometric study of the competition of methemoglobin and cytochrome oxidase for cyanide in vitro. J Biol Chem 163:641-47, 1964
56. Dixon M, Webb EC: Enzymes. New York, Academic Press Inc, 1958, pp 373-76
57. Schubert J, Brill WA: Antagonism of experimental cyanide toxicity in relation to the in vivo activity of cytochrome oxidase. J Pharmacol Exp Ther 162:352-59, 1968

58. Rieders F: Noxious gases and vapors--I.: carbon monoxide, cyanides, methemoglobin, and sulfhemoglobin, in J Dipalma (ed): Drill's Pharmacology in Medicine, ed 4. New York, McGraw-Hill Book Co, 1971, pp 1189-94, 1203
59. Lang K: [Rhoadanyl formation in the animal body.] Biochem Z 259:24356, 1933 (Ger)
60. Sorbo B: Enzymatic conversion of cyanide to thiocyanate, in Uvnas B (ed): Metabolic Factors Controlling Duration of Drug Action. Proceedings of the First International Pharmacological Meeting. New York, The Macmillan Co, 1962, pp 121-36
61. Goldstein F, Reiders F: Conversion of thiocyanate to cyanide by an erythrocytic enzyme. Am J Physiol 173:287-290, 1953
62. Himwich WA, Saunders JP: Enzymatic conversion of cyanide to thiocyanate. Am J Physiol 153:348-54, 1948
63. Young MA: Health hazards of electroplating. J Occup Med 7:348-52, 1965
64. Thienes CH, Holly TJ: Cyanides, in Clinical Toxicology. Philadelphia, Lea & Febiger, 1964, pp 282-86
65. Wood JL, Biochemistry; in Chemistry and Biochemistry of Thiocyanic Acid and its Derivatives, Newman AA, ed, Academic Press, New York, 1975, pp 156-221
66. Williams RT: The metabolism of nitriles, in Detoxication Mechanisms. London, Chapman and Hall Ltd, 1959, chap 12, pp 390-409
67. Ansell M, Lewis FAS: A review of cyanide concentrations found in human organs--a survey of literature concerning cyanide metabolism, 'normal', non-fatal, and fatal body cyanide levels. J Forensic Med 17:148-55, 1970
68. McNamara BP: Estimates of the toxicity of hydrocyanid acid vapors in man. Edgewood Arsenal Technical Report EB-TR-76023, Dept of the Army, August, 1976
69. Feldstein M, Klendshoj NC: The determination of cyanide in biologic fluids by microdiffusion analysis. J Lab Clin Med 44:166-70, 1954
70. Ermans AM, Delange F, Van Der Velden M, Kinthaert J: Possible role of cyanide and thiocyanate in the etiology of endemic cretinism. Adv Exp Med Biol 30:455-86, 1972
71. Chronic cyanide neurotoxicity. Lancet (edit) 2:942-43, 1969

72. Rylander R: Toxicity of cigarette smoke components--free lung cell response in acute exposures. *Am Rev Respir Dis* 108:1279-82, 1973
73. Djuric D, Raicevic P, Konstantinovic I: Excretion of thiocyanates in urine of smokers. *Arch Environ Health* 5:12-15, 1962
74. Wilson J, Matthews DM: Metabolic inter-relationships between cyanide, thiocyanate and vitamin B12 in smokers and non-smokers. *Clin Sci* 31:1-7, 1966
75. Heaton JM: Chronic cyanide poisoning and optic neuritis. *Trans Ophthalmol Soc UK* 82:263-69, 1962
76. Maehly AC, Swensson A: Cyanide and thiocyanate levels in blood and urine of workers with low-grade exposure to cyanide. *Int Arch Arbeitsmed* 27:195-209, 1970
77. Pettigrew AR, Fell GS: Microdiffusion method for estimation of cyanide in whole blood and its application to the study of conversion of cyanide to thiocyanate. *Clin Chem* 19:466-71, 1973
78. Pettigrew AR, Fell GS: Simplified colorimetric determination of thiocyanate in biological fluids and its application to investigation of toxic amblyopias. *Clin Chem* 18:996-1000, 1972
79. Radojicic B: [Determining thiocyanate in urine of workers exposed to cyanides] *Arh Hig Rada* 24:227-232, 1973 (Yugoslavian)
80. Moskowitz S: Health hazards in the plating room and their control. *Plating* 38:1141-52, 1951
81. Merzbach, G: [On a case of chronic industrial hydrocyanic acid intoxication.] *Beilage Hyg Rundschau* 9:45-56, 1899, (Ger)
82. Chaumont AJ: [Chronic intoxication caused by cyanides and by hydrocyanic acid.] *Soc de Medecine et D' Hygiene Du Travail*, 660-662, 1960, (Fre)
83. Colle R: [Chronic hydrogen cyanide poisoning.] *Maroc Med* 50:750-57, 1972, (Fre)
84. Sato T, Fukuyama T, Yamada M: The allowable concentration of hydrogen cyanide in air. *Bull Inst Public Health (Tokyo)* 4:3-5, 1955
85. Wexler J, Whittenberger JL, Dumke PR: The effect of cyanide on the electrocardiogram of man. *Am Heart J* 34:163-73, 1947
86. Barcroft J: The toxicity of atmospheres containing hydrocyanic acid gas. *J Hyg* 31:1-34, 1931

87. Thomas TA, Brooks JW: Accidental cyanide poisoning. *Anaesthesia* 25:110-14, 1970
88. Sandberg CG: A case of chronic poisoning with potassium cyanide? *Acta Med Scand* 181(fasc 2):233-36, 1967
89. Courville CB: Forensic neuropathology--X. Common chemical, metallic, and metalloid poisons. *J Forensic Sci* 8:481-502, 1963
90. Barsky MH: Ulcerations of the nasal membranes and perforation of the septum in a copperplating factory--unusual and sudden incidence. *NY State J Med* 37:1031-34, 1937
91. Elkins HB: *The Chemistry of Industrial Toxicology*, ed 2. New York, John Wiley & Sons Inc, 1959, pp 94-95
92. Cohen SR, Davis DM, Kramkowski RS: Clinical manifestations of chromic acid toxicity--nasal lesions in electroplate workers. *Cutis* 13:558-68, 1974
93. Lowenheim FA: Electroplating, in Kirk RE, Othmer DF: *Encyclopedia of Chemical Technology*, ed 2. New York, Interscience Publishers, 1965, vol 8, pp 36-74
94. Nolan JW: Potassium cyanide poisoning. *JAMA* 50:365, 1908
95. Collins J, Martland HS: Disease of the primary motor neurones causing the clinical picture of acute anterior poliomyelitis: the result of poisoning by cyanide of potassium--a clinical and experimental contribution to the toxic effects of cyanide of potassium upon the peripheral motor neurones. *J Nerv Ment Dis* 35:417-26, 1908
96. Tovo S: [Poisoning due to KCN absorbed through skin.] *Minerva Med* 75:158-61, 1955 (Ita)
97. Raestrup: [On cutaneous damage caused by potassium cyanide.] *Zeutralbl Gewerbehyg* 3:103-06, 1926 (Ger)
98. Muller-Hess B: [Intoxication caused by absorption of hydrocyanic acid through the skin.] *Muerch Med Wocheschr* 89:492, 1942 (Ger)
99. Chen KK, Rose CL: Nitrite and thiosulfate therapy in cyanide poisoning. *JAMA* 149:113-19, 1952
100. Wolfsie JH: Treatment of cyanide poisoning in industry. *Arch Ind Hyg Occup Med* 4:417-25, 1951
101. Chen, KK, Rose CL, Clowes GHA: The modern treatment of cyanide poisoning. *Indiana State Med Assoc J* 37:344-50, 1944

102. Ingegno AP, Franco S: Cyanide poisoning--successful treatment of two cases with intra-venous sodium nitrite and sodium thiosulfate. Ind Med 6:573-76, 1937
103. Lee-Jones M, Bennett MA, Sherwell JM: Cyanide self-poisoning. Br Med J 4:780-1, 1970
104. De Busk RF, Seidl LG: Attempted suicide by cyanide--a report of two cases. Calif Med 110:394-96, 1969
105. Hirsch FG: Cyanide poisoning. Arch Environ Health 8:622-24, 1964
106. Mascarenhas BR, Geller AC, Goodman AI: Cyanide poisoning--medical emergency. NY State J Med 69:1782-84, 1969
107. Wolfsie JH, Shaffer CB: Hydrogen Cyanide--hazards, toxicology, prevention and management of poisoning. J Occup Med 1:281-88, 1959
108. Smith RP, Gosselin RE: Current concepts about the treatment of selected poisonings--nitrite, cyanide, sulfide, barium, and quinidine. Ann Rev Pharmacol Toxicol 16:189-199, 1976
109. Carmelo, S: [New contributions to the study of subacute-chronic hydrocyanic acid intoxication in man.] Rass Med Ind 24:254-71, 1955 (Ita)
110. El Ghawabi SH, Gaafar MA, El-Saharti AA, Ahmed SH, Malash KK, Fanes R: Chronic cyanide exposure: a clinical, radioisotope, and laboratory study. Br J Ind Med 32:215-19, 1975
111. Wollman SH: Nature of the inhibition by thiocyanate of the iodide concentrating mechanism of the thyroid gland. Amer J Physiol 186:453-459, 1956
112. Heymans JF, Masoin P: [The diachronic toxicity of some cyanogen compounds.] Arch Int Pharmacodyn Ther 7:297-306, 1900 (Fre)
113. Lehmann, KB: [About the toxicity of gaseous HCN and hydrogen phosphide with a demonstration.] Klin Wochensh 40:918-19, 1903 (Ger)
114. Creel RH, Faget FM, Wrightson WD: Hydrocyanic acid gas--its practical use as a routine fumigant. Public Health Rep 30:3537-50, 1915
115. Grubbs SB: Detection of hydrocyanic acid gas--use of small animals for this purpose. Weekly Public Health Rep 32:565-70, 1917
116. Walton DC, Witherspoon MG: Skin absorption of certain gases. J Pharmacol Exp Ther 26:315-24, 1926

117. Fairley A, Linton EC, Wild FE: The absorption of hydrocyanic acid vapour through the skin--hydrocyanic acid, prussic acid, with notes on other matters relating to acute cyanide poisoning. J Hyg 34:283-94, 1934
118. Flury F, Zernik F: [HCN (hydrocyanic acid, prussic acid).] in Noxious Gases--Vapors, Mist, Smoke and Dust Particles. Berlin, Verlag von Julius Springer, 1931, pp 400-15 (Ger)
119. Trautman JA: Methylene blue in the treatment of HCN gas poisoning. Public Health Rep 48:1443-47, 1933
120. Gettler AO, Baine JO: The toxicology of cyanide. Am J Med Sci 195:182-98, 1938
121. Etteldorf JN: The treatment of gaseous hydrocyanic acid poisoning by sodium thiosulfate and sodium nitrite combination. J Pharmacol Exp Ther 66:125-31, 1939
122. Jandorf BJ, Bodansky O: Therapeutic and prophylactic effect of methemoglobinemia in inhalation poisoning by hydrogen cyanide and cyanogen chloride. J Ind Hyg Toxicol 28:125-32, 1946
123. Gordh T, Norberg B: Studies on oxygen treatment in connection with experimental hydrocyanic poisoning. Acta Physiol Scand 13:26-34, 1947
124. Moss RH, Jackson CF, Seiberlich J: Toxicity of carbon monoxide and hydrogen cyanide gas mixtures--a preliminary report. Arch Ind Hyg Occup Med 4:53-64, 1951
125. Haymaker W, Ginzler AM, Ferguson RL: Residual neuropathological effects of cyanide poisoning--a study of the central nervous system of 23 dogs exposed to cyanide compounds. Mil Surg 111:231-46, 1952
126. Valade P: [Injuries to the central nervous system in chronic experimental poisoning by hydrocyanic acid gas.] Bull Acad Natl Med Paris 136:280-85, 1952 (Fre)
127. Howard JW, Hanzal RF: Chronic toxicity for rats of food treated with HCN. Agric Food Chem 3:325-29, 1955
128. Levine S, Stypulkowski W: Experimental cyanide encephalopathy. Arch Pathol 67:306-23, 1959
129. Levine S, Weinstein B: Neurotoxicity of hydrogen cyanide. J Am Pharm Assoc 48:224-26, 1959
130. Ibrahim MZM, Briscoe PB Jr, Bayliss OB, Adams CWM: The relationship between enzyme activity and neuroglia in the prodromal and



- demyelinating stages of cyanide encephalopathy in the rat. *J Neurol Neurosurg and Psychiatry* 26:479-486, 1963
131. Smith ADM, Duckett S, Waters AH: Neuropathological changes in chronic cyanide intoxication. *Nature* 200:179-181, 1963
  132. Hirner A: [Electron microscopic findings concerning the pathogenesis of callosal lesions after experimental cyanide intoxication.] *Acta Neuropathol (Berl)* 13:350-68, 1969
  133. Higgins EA, Fiorca V, Thomas AA, Davis HV: Acute toxicity of brief exposures to HF, HCl, NO<sub>2</sub>, and HCN with and without CO. *Fire Technol* 8:120-30, 1972
  134. Ballantyne B, Bright J, Swanston DW, Williams P: Toxicity of cyanides given by intramuscular injection. *Br J Pharmacol* 41:423P-24P, 1971
  135. Ballantyne B, Bright J, Swanston DW, Williams P: Toxicity and distribution of free cyanides given intramuscularly. *Med Sci Law* 12:209-19, 1972
  136. Ballantyne B, Bright J, Williams P: Levels of cyanide in whole blood and serum following lethal intramuscular injections to experimental mammals. *Med Sci Law* 10:225-29, 1970
  137. Levi G, Amaducci L: Effect of acute cyanide intoxication on the active transport of amino acids in brain slices. *J Neurochem* 15:459-69, 1968
  138. Perry IH: The effect of prolonged cyanide treatment on body and tumor growth in rats. *Am J Cancer* 25:592-98, 1935
  139. Hrizu D, Gaspar A, Teodorescu M, Mogos I: [Cytostatic effects of potassium sulfocyanate in vivo and in vitro.] *Arch Roum Pathol Exp Microbiol* 32:155-158, 1973, (Fre)
  140. Nowinski WW, Pandra J: Influence of sodium thiocyanate on the development of the chick embryo. *Nature* 157:414. 1946
  141. Ortolani G: The action of sodium thiocyanate (NaSCN) on the embryonic development of the ascidians. *Acta Embryol Exp* 27-34, 1969
  142. Lazareff NV (ed): [Toxic Substances in Industry. Inorganic and Elementary Compounds. A Manual for Chemists, Engineers, and Physicians], ed 6. Leningrad, Khimiya, 1971, pp 228-240, (Rus)
  143. Lazareff NV: [Harmful substances in industry-part II - inorganic and organometallic compounds.] State Technical Publishings, Warsaw, 1956, p 224-235 (Rus)

144. Finck PA: Postmortem distribution studies of cyanide--report of three cases. Med Ann DC 38:357-58, 1969
145. Hamilton A, Hardy HL: Industrial Toxicology, ed 2. New York, Paul B Hoeber Inc, 1949, pp 248-62
146. Davis HJ: Industrial dermatitis--481 cases. Ind Med 12:381-83, 1943
147. Drinker P: Hydrocyanic acid gas poisoning by absorption through the skin. J Ind Hyg 14:1-2, 1932
148. Potter AL: The successful treatment of two recent cases of cyanide poisoning. Br J Ind Med 7:125-30, 1950
149. Henderson Y, Haggard H: Noxious Gases and the Principles of Respiration Influencing Their Action, ed 2. >35 in ACS Monograph Series. New York, Reinhold Publishing Corp, 1943, pp 172-76
150. Grabois, B: Exposure to hydrogen cyanide in the processing of apricot kernels. NY State Dept Labor Month Rev, Div Ind Hyg 33:33-36, 1954
151. Landahl HD, Herrmann RG: Retention of vapors and gases in the human nose and lung. Arch Ind Hyg Occ Med 1:36-45, 1950
152. Sollmann T: A Manual of Pharmacology, ed 8. Philadelphia, WB Saunders Co, 1957, pp 982-90
153. Liebowitz D, Schwartz H: Cyanide poisoning--report of a case with recovery. Am J Clin Pathol 18:965-70, 1948
154. Dermatitis in the manufacture and use of alkalis, in Skin Hazards in American Industry, Part II, Public Health Bulletin 229. US Public Health Service, 1936, pp 69-75
155. Somov BA, Khaimovsky GD: [Allergic dermatitis caused by aurum compounds in watch industry.] Vestn Dermatol Venerol 38:33-36, 1964 (Rus)
156. Liebig J: [Method for determination of the hydrocyanic acid content of medicinal hydrocyanic acid, bitter-almond and cherry laurel water.] Ann Chem 77:102-07, 1851 (Ger)
157. Thienes CH, Haley TJ: Clinical Toxicology. Philadelphia, Lea and Febiger, 1964, pp 376-80
158. Rapid method for the determination of inorganic substances in the air, in Levine BS (trans): USSR Literature on Air Pollution and Related Occupational Diseases--A Survey. Springfield, Va, US Dept

of Commerce, National Technical Information Service, 1964, vol 10, pp 70-75 (NTIS TT-64-11761)

159. Bark LS, Higson HG: A review of the methods available for the detection and determination of small amounts of cyanide. *Analyst* 88:751-60, 1963
160. Guatelli MA: The toxicology of cyanides, in Curry AS (ed): *Methods of Forensic Science*. New York, Interscience Publishers, 1964, vol 3, pp 233-65
161. Hanson NW, Reilly DA, Stagg HE (eds): *The Determination of Toxic Substances in Air*. Cambridge, England, W Heffer and Sons Ltd, 1965, pp 23-28, 138-46
162. Ruch W (ed): *Chemical Detection of Gaseous Pollutants*. Ann Arbor, Mich, Science Publications, 1966, pp 103-11
163. Jacobs MB: *The Analytical Toxicology of Industrial Inorganic Poisons*. New York, Interscience Publishers, 1967, pp 721-41
164. Maehly AC: Volatile toxic compounds, in Stolman A (ed): *Progress in Chemical Toxicology*. New York, Academic Press, 1967, vol 3, pp 88-91
165. Jacobs MB: *War Gases--Their Identification and Decontamination*. New York, Interscience Publishers Inc, 1942, pp 36-37, 119-21
166. Katz SH, Longfellow ES: Tests for hydrocyanic acid gas in air. *J Ind Hyg* 5:97-104, 1923
167. Robbie WA, Leinfelder PJ: A rapid and simple method for measuring small amounts of cyanide gas in air. *J Ind Hyg* 27:136-39, 1945
168. Gisclard JB, Rook JH, Andresen WV, Bradley WR: A simple device for air analysis. *Am Ind Hyg Assoc Q* 14:23-25, 1953
169. White NG: Hydrogen Cyanide as an industrial hazard--methods of detection and control. *Am Ind Hyg Assoc Q* 9:81-84, 1948
170. Baumeister R, Schievelbein H: [Simple method for determining small quantities of cyanide in cigarette smoke and biological material.] *Z Anal Chem* 255:362-63, 1971 (Ger)
171. Lester D: The quantitative determination of cyanide in air. *J Ind Hyg* 26:61-63, 1944

172. Hori T, Yasue G, Kobayashi Y: [A rapid method for microdetermination of hydrogen cyanide in air by means of detector tubes.] Bunseki Kagaku (Japan Analyst) 17:613-15, 1968 (Jap)
173. Gettler AO, Goldbaum L: Detection and estimation of microquantities of cyanide. Anal Chem 19:270-71, 1947
174. Aldridge WN: A new method for the estimation of micro quantities of cyanide and thiocyanate. Analyst 69:262-65, 1944
175. Saltzman BE: Preparation and analysis of calibrated low concentrations of sixteen toxic gases. Anal Chem 33:1100-12, 1961
176. Orsos S: [Determination of the atmospheric cyanide content by the pyrazolone-pyridine method.] Egeszsegtudomány 16:388-91, 1972 (Hung)
177. Goulden PD, Afghan BK, Brooksbank P: Determination of nanogram quantities of simple and complex cyanides in water. Anal Chem 44:1845-49, 1972
178. Ludzack FJ, Moore WA, Ruchhoft CC: Determination of cyanides in water and waste samples. Anal Chem 26:1784-92, 1954
179. Epstein J: Estimation of microquantities of cyanide. Anal Chem 19: 272-74, 1947
180. Boxer GE, Rickards JC: Chemical determination of vitamin B12--II. The quantitative isolation and colorimetric determination of millimicrogram quantities of cyanide. Arch Biochem 30:372-81, 1951
181. Baker MO, Foster RA, Post BG, Hiatt TA: Determination of micro quantities of cyanide in presence of a large excess of sulfide. Anal Chem 27:448-49, 1955
182. Hanker JS, Gelberg A, Witten B: Fluorometric and colorimetric estimation of cyanide and sulfide by demasking reactions of palladium chelates. Anal Chem 30:93-95, 1958
183. Lambert JL, Manzo DJ: Spectrophotometric determination of cyanide ion with tris - (1,10-phenanthroline) - iron(II)-triiodide ion association reagent. Anal Chem 40:1354-55, 1968
184. Fisher FB, Brown JS: Colorimetric determination of cyanide in stack gas and waste water. Anal Chem 24:1440-44, 1952
185. Guilbault GG, Kramer DN: A specific fluorometric method for the detection of cyanide. Anal Chem 37:918, 1965
186. American Society for Testing and Materials: Standard methods of test for cyanides in water, in Annual Book of ASTM Standards, part

- 23: Water; atmospheric analysis. Philadelphia, ASTM, 1973, pp 498-507
187. American Public Health Association, American Water Works Association, Water Pollution Control Federation: Cyanide, in Standard Methods for the Examination of Water and Wastewater, ed 13. Washington, DC, American Public Health Association, 1971, pp 397-406
188. Miller GW, Long LE, George GM, Sikes WL: Submicromicrogram determination of cyanide by a polarographic method. Anal Chem 36:980-83, 1964
189. Jura WH: Shielded dropping mercury electrode for polarographic analysis of flowing solutions--determination of cyanide ion. Anal Chem 26:1121-23, 1954
190. Jenkins SH, Hey AE, Cooper JS: The determination of cyanide in low concentration. Air Wat Pollut Int J 10:495-519, 1966
191. Shinozuka F, Stock JT: Voltammetry and amperometric titrimetry of cyanide at the rotating platinum microelectrode. Anal Chem 34:926-30, 1962
192. McCloskey JA: Direct amperometry of cyanide at extreme dilution. Anal Chem 33:1842-43, 1961
193. Laitinen HA, Jennings WP, Parks TD: Amperometric titration of cyanide with silver nitrate, using the rotating platinum electrode. Ind Eng Chem Anal Ed 18:574-75, 1946
194. Przybylowicz EP, Rogers LB: Coulometric titrations with mercury (I and II)-- determination of cyanide. Anal Chem 30:65-69, 1958
195. Strange JP: Potentiometric recorder for hydrogen sulfide and hydrogen cyanide. Anal Chem 29:1878-81, 1957
196. Baker BB, Morrison JD: Determination of microgram quantities of fluoride and cyanide by measurement of current from spontaneous electrolysis. Anal Chem 27:1306-07, 1955
197. Breuer W: [New methods of continuous trace gas analysis.] Presented at the 4th Interkama Meeting, Dusseldorf, Germany, Bayer-Leverkusen, 1968, 23 pp (Ger)
198. Collombel C, Durand JP, Bureau J, Cotte J: [Determination of the cyanide ion level in the atmosphere, drinking water, industrial effluents and biological mediums by means of a specific electrode.] J Eur Toxicol 3:291-99, 1970 (Fre)
199. Frant MS, Ross JW Jr, Riseman JH: Electrode indicator technique for measuring low levels of cyanide. Anal Chem 44:2227-30, 1972

200. Fleet B, von Storp H: The determination of low levels of cyanide ion using a silver responsive ion selective electrode. Anal Lett 4:425-35, 1971
201. Durst RA (ed): Ion-Selective Electrodes. National Bureau of Standards Special Publication 314. US Dept of Commerce, National Bureau of Standards, 1969, pp 84-86, 364-67, 430, 501-02,
202. Penland JL, Fischer G: [Cyanide determination using ion-selective electrodes subsequent to distillation.] Metalloberflaeche 26:391-94, 1972 (Ger)
203. Cyanide in air, in NIOSH Manual of Analytic Methods. Cincinnati, US Dept of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Physical and Chemical Analysis Branch, Division of Laboratories and Criteria Development, 1974
204. Gyorgy B, Andre L, Stehli L, Pungor E: Direct potentiometric determination of cyanide in biological systems. Anal Chim Acta 46:318-21, 1969
205. Toth K, Pungor E: Determination of cyanides with ion-selective membrane electrodes. Anal Chim Acta 51:221-30, 1970
206. Schneider CR, Freund H: Determination of low level hydrocyanic acid in solution using gas-liquid chromatography. Anal Chem 34:69-74, 1962
207. Isbell RE: Determination of hydrogen cyanide and cyanogen by gas chromatography. Anal Chem (Corresp) 35:255-56, 1963
208. Claeys RR, Freund H: Gas chromatographic separation of HCN on porapak Q-- analysis of trace aqueous solutions. Environ Sci Technol 2:458-60, 1968
209. Danchik RS, Boltz DF: Indirect atomic absorption spectrometric methods for the determination of cyanide. Anal Chim Acta 49:567-69, 1970
210. Brown F, Graham J: Microturbidimetry for the detection of hydrogen cyanide. Anal Chem 24:1032, 1952
211. Bartholomew ET, Raby EC: Photronic photoelectric turbidimeter for determining hydrocyanic acid in solutions. Ind Eng Chem, Anal Ed 7: 68-69, 1935
212. Hill R, Holt JH, Miller B: Rapid test paper methods for hydrogen cyanide in the atmosphere. Ann Occup Hyg 14:289-94, 1971

213. Hydrogen Cyanide Vapour, booklet No 2 in Methods for the Detection of Toxic Substances in Air. London, HM Factory Inspectorate, Dept Employment, 1973, pp 3-11
214. Witten B, Prostack A: Sensitive detector crayons for phosgene, hydrogen cyanide, cyanogen chloride, and lewisite. Anal Chem 29:885-87, 1957
215. Lester D, Ordnung PF: A sensitive, portable, self-contained phototube colorimeter for the field determination of cyanide in air. J Ind Hyg Toxicol 26:197-200, 1944
216. Church FW, Campbell EE: The elimination of background color in colorimetric determination of cyanides and hydrocyanic acid. Am Ind Hyg Assoc J 11:109-10, 1950
217. Quantitative determination of hydrogen cyanide in the air, in Levine BS (trans): USSR Literature on Air Pollution and Related Occupational Diseases--A Survey. Springfield, Va, US Dept of Commerce, National Technical Information Service, 1963, vol 8, pp 15-18, (NTIS TT-63-11570)
218. Mel'nikova LV, Belyakov AA: Determination of atrazine, cyanuric chloride, hydrogen cyanide and aliphatic amines in air. Hyg Sanit 36:408-11, 1969
219. Belyakov AA, Mel'nikova LV: Determination of cyanogen chloride, hydrogen cyanide, cyanuric chloride and simazin in air. Hyg Sanit 34:207-10, 1969
220. Ionescu C, Nestorescu B: A new method for the determination of cyanhydric acid and cyanides in the air and in biologic products. Rom Med Rev 9:17-20, 1965
221. Truhaut R, Boudene C, Phu-lich N: [Specific microdetermination of hydrocyanic acid in the atmosphere and in biological material.] Ann Biol Clin (Paris) 22:901-07, 1964 (Fre)
222. Hydrocyanic acid and cyanides. American Industrial Hygienists Assoc, Anal Abstr, 1965
223. Tada O: Methods for determinations of toxic substances in air--inorganic compounds. J Sci Labour 44:10-22, 1968
224. Stolman A (ed): Progress in Chemical Toxicology, New York, Academic Press, Vol 3, 1967
225. Free AH, Free HM: Laboratory detection of cyanide poisoning, in Sunderman FW, Sunderman FW Jr: Laboratory Diagnosis of Diseases Caused by Toxic Agents. St Louis, Warren H Green Inc, 1970, chap 27, pp 286-91

- 226. Conway EJ: Volatile weak inorganic acids and phenol cyanide, azide, sulphide, phenols, in Microdiffusion Analysis and Volumetric Error. London, Crosby Lockwood & Sons Ltd, 1962, chap xxx, pp 241-42
- 227. Boxer GE, Rickards JC: Determination of traces of HCN in respiratory air. Arch Biochem 39:287-91, 1952
- 228. Tompsett SL: A note on the determination and identification of cyanide in biologic materials. Clin Chem 5:587-91, 1959
- 229. Ballantyne B; The forensic diagnosis of acute cyanide poisoning in Forensic Toxicology, B. Ballantyne, ed, Bristol, J. Wright and Sons Limited, 1974, pp 99-113
- 230. Toxgard Analyzer, Bulletin No. 0710-2. Pittsburgh, Mine Safety Appliance Co
- 231. ACGIH Committee on Industrial Ventilation: Industrial Ventilation - A Manual of Recommended Practices, ed 12. Lansing, Mich, Conference of Governmental Industrial Hygienists, 1972
- 232. Fundamentals Governing the Design and Operation of Local Exhaust Systems, Z9.2. New York, American National Standards Institute Inc, 1971
- 233. Hydrogen Cyanide, AIHA Hygienic Guide Series. Am Ind Hyg Assoc J 31:116-19, 1970
- 234. American Conference of Governmental Industrial Hygienists: Threshold Limit Values adopted at April 1948 Meeting of ACGIH, Boston, Mass
- 235. American Conference of Industrial Hygienists: Documentation of the Threshold Limit Values for Substances in Workroom Air. Cincinnati, ACGIH, 1971, pp 130-31
- 236. American Conference of Governmental Industrial Hygienists: Documentation of the Threshold Limit Values for Substances in Workroom Air. Cincinnati, ACGIH, 1971, p 64
- 237. Mancuso TF: Industrial poisoning--cyanides. Ohio State Med J 51: 1210-11, 1955
- 238. Cyanides and nitriles, Chief Employment Medical Adviser's Notes of Guidance, number 17. EMAS, Department of Employment, Great Britain, 1972
- 239. Johnstone RJ, Miller SE: Noxious Gases in Occupational Diseases and Industrial Medicine. Philadelphia, WB Saunders Co, 1960, pp 119-22, 146-47



240. Kobert R: [Treatment of Poisonings], Chapter 9 in Kompend der prak Toxicol, ed 5, 1912, p 45 (Ger)
241. Griffon H, LeBreton R: [A case of fatal acute intoxication by massive ingestion of pure potassium cyanide.] Ann Med Leg 31:266-69, 1951 (Fre)
242. Halstrom F, Moller KO: The content of cyanide in human organs from cases of poisoning with cyanide take by mouth--with a contribution to the toxicology of cyanides. Acta Pharmacol Toxicol (Kbh) 1:18-28, 1945
243. Robinson A: A case of cyanide poisoning. J R Nav Med Serv 45:93-95, 1959
244. Ernst W: [Is there such a thing as a slowly progressing oral potassium cyanide poisoning?] Dtsch Med Wochenschr 54:1373-74, 1928 (Ger)
245. Thompson TM: Accidental cyanide poisoning--its prevention and treatment. Occup Med 4:419-24, 1947
246. Aero Liquid HCN, Fumigation Manual. Princeton, NJ, American Cyanamid Co, 36 pp
247. Knowles EL, Bain JTB: Medical cover required in large scale production of cyanides and hydrocyanic acid. Chem Ind pp 232-35, February 24, 1968
248. Hydrogen Cyanide. Hygienic Information Guide No 21. Harrisburg, Commonwealth of Pennsylvania Department of Environmental Resources, Occupational Health, 1971
249. Davison V: Cyanide poisoning--kelocyanor - a new treatment. Occup Health 21:306-08, 1969
250. Craig A, Jones RWL: O.H. in the metal finishing industry (2). Occup Health 23:251-61, 1971
251. Fleming AJ: Chemical health hazards, in Fleming AJ, D'Alonzo CA (eds): Modern Occupational Medicine. Philadelphia, Lea & Febiger, 1960, pp 386-88
252. Plating and cyanide wastes--general problems of the metal plating industry. J Water Pollut Control Fed 42:1211-30, 1970
253. Schiede EP, Hughes EE, Taylor JK: A system for producing test atmospheres containing hydrogen cyanide. Final Report NBSIR 73-257, October 1973.

254. Montgomery PD: Hydrogen cyanide, in Kirk RE, Othmer DF: Encyclopedia of Chemical Technology, ed 2, New York, Interscience Publishers, 1965, vol 6, pp 574-585
255. Winter EA, Montesinso MJ, Singley JE: Copper compounds, in Kirk RE, Othmer DF (eds): Encyclopedia of Chemical Technology, ed 2. New York, Interscience Publishers, 1965, vol 6, pp 270-71
256. Bratt J: Mercury compounds, in Kirk RE, Othmer DF (eds): Encyclopedia of Chemical Technology, ed 2. New York, Interscience Publishers, 1967, vol 13, pp 235-38
257. Thompson AP: Zinc compounds, in Kirk RE, Othmer DF, (eds): Encyclopedia of Chemical Technology, ed 2. New York, Interscience Publishers, 1970, vol 22, p 607
258. Gafafer WM (ed): Occupational Diseases--A Guide to Their Recognition, Public Health Service Publication No. 1097, US Dept of Health Education, and Welfare, 1964, pp 7, 77, 160, 161, 249, 336, 348
259. Cyanides, in A Guide to the Diagnosis of Occupational Diseases--A Reference Manual for Physicians. Ottawa, Dept National Health and Welfare, Industrial Health Div and Dept Health for Ontario, Div Industrial Hygiene, 1949, pp 168-69
260. Gonzales TA, Vance M, Helpern M, Umberger CJ: Legal Medicine--Pathology and Toxicology, ed 2. New York, Appleton-Century-Crofts Inc, 1954, pp 801-13
261. Moeschlin S: Poisoning--Diagnosis and Treatment. New York, Grune and Stratton, 1965, pp 255-61
262. Czechoslovak Committee of MAC: Documentation of MAC in Czechoslovakia. The Committee, Praha, 1969, pp 91-92
263. McNerney JM, Schrenk HH: The acute toxicity of cyanogen. Am Ind Hyg Assoc J 21:121-124, 1960
264. Dudley HC, Sweeney TR, Miller JW: Toxicology of acrylonitrile (vinyl cyanide)--II. Studies of effects of daily inhalation. J Ind Hyg Toxicol 24:255-58, 1942
265. Thomas MR, Calaresu FR: Hypothalamic inhibition of chemoreceptor-induced bradycardia in the cat. Am J Physiol 225:201-08, 1973
266. Wheatley MD, Lipton B, Ward AA Jr: Repeated cyanide convulsions without central nervous pathology. J Neuropathol Exp Neurol 6:408-11, 1947

267. Olsen NS, Klein JR: Effect of cyanide on the concentration of lactate and phosphates in brain. *J Biol Chem* 167:739-46, 1947
268. Ward AA Jr, Wheatley MD: Sodium cyanide--sequence of changes of activity induced at various levels of the central nervous system. *J Neuropathol Exp Neurol* 6:292-94, 1947
269. Leimdorfer A: About anoxia of the heart produced by intravenous sodium cyanide injections. *Arch Int Pharmacodyn Ther* 84:181-88, 1950
270. Wheatley MD: Mechanisms of cerebral death with doses of NaCN from which the heart recovers. *J Neuropathol Exp Neurol* 6:295-98, 1947
271. Ferraro A: Experimental toxic encephalomyelopathy--(Diffuse sclerosis following subcutaneous injections of potassium cyanide.) *Psychiatr Q* 7:267-83, 1933
272. Smith RG, Mukerji B, Seabury JH: Thiocyanate formation in cyanide poisoning as affected by methylene blue and sodium nitrite. *J Pharmacol Exp Ther* 68:351-64, 1940
273. Suzuki T, Saito K, Kobayasi Y: Adrenaline secretion of the suprarenal glands in cyanide anoxia. *Tohoku J Exp Med* 54:343-50, 1951
274. Fujimoto M, Nash FD, Kessler RH: Effects of cyanide, Qo, and dinitrophenol on renal sodium reabsorption and oxygen consumption. *Am J Physiol* 206:1327-32, 1964
275. Rose CL, Worth RM, Kikuchi K, Chen KK: Cobalt salts in acute cyanide poisoning. *Proc Soc Exp Biol Med* 120:780-83, 1965
276. Chen KK, Rose CL, Clowes GHA: Comparative values of several antidotes in cyanid poisoning. *Am J Med Sci* 188:767-81, 1934
277. Lappo VG: Experimental standardization of simulataneously present cyanides and mercury in water basins (reservoirs), from *Gig Sanit* 25: 11-17, 1960; in *USSR Literature on Water Supply and Pollution Control*, 1962, vol 2, pp 145-53
278. Dilley JV: Effect of cyanide on liver enzyme activity, in *US Atomic Energy Commision*, BNWL-280, 1966, pp 72-74
279. Hall SM: The effects of injection of potassium cynaide into the sciatic nerve of the adult mouse--in vivo and electron microscopic studies. *J Neurocytol* 1:233-54, 1972
280. Mushett CW, Kelley KL, Boxer GE, Rickards JC: Antidotal efficacy of vitamin B12a (hydroxo-cobalamin) in experimental cyanide poisoning. *Proc Soc Exp Biol Med* 81:234-37, 1952

281. Sheehy M, Way JL: Effect of oxygen on cyanide intoxication-III. Mithridate. J Pharmacol Exp Ther 161:163-68, 1968
282. Ferguson HC: Dilution of dose and acute oral toxicity. Toxicol Appl Pharmacol 4:759-62, 1962
283. Isom G, Way JL: Cyanide intoxication--protection with cobaltous chloride. Toxicol Appl Pharmacol 24:449-56, 1973
284. Hanzlik PJ, Richardson AP: Cyanide antidotes. JAMA 102:1740-45, 1934
285. Bell R Jr, Northup DW: Adaption to histotoxic anoxia. Am J Physiol 163:125-28, 1950
286. Dilley JV: Effect of cyanide on clearance of inhaled particles, in US Atomic Energy Commission, BNWL-280, 1966, pp 70-72
287. Suzuki T: Ultrastructural changes of heart muscle in cyanide poisoning. Tohoku J Exp Med 95:271-79, 1968
288. Rose CL, Harris PN, Chen KK: Effect of cyanide poisoning on the central nervous system of rats and dogs. Proc Soc Exp Biol Med 87:632-36, 1954
289. Albaum HG, Tepperman J, Bodansky O: The in vivo inactivation by cyanide of brain cytochrome oxidase and its effect on glycolysis and on the high energy phosphorus compounds in brain. J Biol Chem 164:45-51, 1946
290. Lessell S: Experimental cyanide optic neuropathy. Arch Ophthalmol 86:194-204, 1971
291. American Conference of Governmental Industrial Hygienists: TLVs--Threshold Limit Values for Chemical Substances in Workroom Air Adopted by ACGIH for 1975. Cincinnati, ACGIH, 1975, pp 15, 21
292. Permissible Levels of Toxic Substances in the Working Environment. Occupational Health and Safety Series. Geneva, International Labour Office, 1970, pp 190, 195, 197, 198, 200, 202, 209, 213, 218, 225, 235, 242, 247, 250, 256, 259, 262, 264, 265, 270, 273, 278, 281, 288, 292, 294, 334, 347, 349

IX. APPENDIX I  
METHODS FOR SAMPLING CYANIDES  
IN AIR AND CALIBRATION

The same sampling and analytical methods are used for atmospheric hydrogen cyanide and the particulate cyanides. They can be collected and analyzed separately or by insertion of a filter can be simultaneously collected and individually analyzed. A sampling period of about 10 minutes is necessary to provide an amount of cyanide readily amenable to analysis by the cyanide selective electrode.

Sampling

All glassware is washed in detergent solution, rinsed in tap water, and then rinsed with distilled or deionized water. Ten ml of an absorbing solution (0.1 M NaOH) is poured into an all-glass midjet impinger using a graduated cylinder to measure the volume. The fritted inlet of the impinger should have a porosity approximately equal to that of Corning EC (170-220 micron maximum pore diameter). A membrane prefilter (0.45  $\mu$ m pore size) should be inserted (by means of an in-line cassette or similar device) before the impinger when sampling for particulate cyanides is to be performed. Sampling for HCN and/or the particulate cyanides is performed for at least 10 minutes at a rate of 2 liters/minute, but the total volume of air sampled should not exceed 200 liters. A personal sampling pump or other satisfactory source of suction may be used for sampling provided it is calibrated as outlined below. Alternate sampling systems may be used, providing the required volume of air is sampled from the breathing zone of the worker.

After sampling, the fritted impinger stem can be removed and cleaned in the following manner. Tap the stem gently against the inside wall of the impinger bottle to recover as much of the sampling solution as possible. Wash the stem with a small amount (1-2 ml) of unused absorbing solution and add the wash to the impinger bottle. Then the impinger bottle is sealed with a hard, non-reactive stopper (preferably Teflon) and an appropriate identifying number attached to it. Do not seal with rubber. The stoppers on the impinger bottle should be tightly sealed to prevent leakage during shipping. If it is preferred to ship the fritted impingers with the stems in, the outlets of the stem should be sealed with Parafilm or other nonrubber covers, and the ground glass joints should be sealed, ie, taped to secure the top tightly. Upon completion of sampling for the particulate cyanides, plastic caps should be replaced on the inlet and outlet tubes of the cassette and an appropriate identifying number attached to it.

Care should be taken to minimize spillage or loss by evaporation at all times. Refrigerate samples if analysis cannot be done within a day. Whenever possible, hand delivery of the samples is recommended. Otherwise, special impinger shipping cases should be used to ship the samples.

A "blank" fritted impinger should be handled as the other samples (fill, seal, and transport) except that no air is sampled through this fritted impinger. Where a prefilter has been used for the collection of particulate cyanides, the filter cassettes are capped and placed in an appropriate cassette shipping container. One filter disc should be handled like the other samples (seal and transport) except that no air is sampled through it, and this is labeled as a blank.

Certain cyanide compounds, especially calcium cyanide, may hydrolyze at sufficiently high relative humidities, resulting in losses of collected sample as HCN gas. In such cases, it may be advisable to minimize losses by keeping the sampling time as short as possible, then storing it in a refrigerator until analysis.

It should be noted that when sampling for HCN without a prefilter, particulates will pass through the midget impinger. Likewise, when sampling for particulate cyanides by means of a midget impinger without a prefilter, HCN gas will also be collected and will constitute a positive interference.

### Calibration

Since the accuracy of an analysis can be no greater than the accuracy of measurement of the volume of air sampled, the accurate calibration of a sampling device is essential to the correct interpretation of an instrument's indication. The frequency of calibration is dependent upon the use, care, and handling to which the pump is subjected. Pumps should be calibrated if they have been subjected to misuse or if they have just been repaired or received from a manufacturer. If the pump receives hard usage, more frequent calibration may be necessary.

Ordinarily, pumps should be calibrated in the laboratory both before they are used in the field and after they have been used to collect a large number of field samples. The accuracy of calibration is dependent on the type of instrument used as a reference. The choice of calibration instrument will depend largely upon where the calibration is to be performed. For laboratory testing, a soapbubble flow meter or wet-test

meter is recommended, although other standard calibrating instruments, such as a spirometer or dry-gas meter, can be used. The actual setup will be connected in sequence to the filter cassette or fritted impinger unit which will be followed by the sampler pump. In this way, the calibration instrument will be at atmospheric pressure. If the personal sampler pump is used, each pump must be calibrated separately. If the buret is used, it should be set up so that the flow is toward the narrow end of the unit.

Care must be exercised in the assembly procedure to ensure that seals at the joints are airtight and that the length of connecting tubing is kept to a minimum. Calibration should be performed under the same conditions of pressure and temperature as those encountered in use. The calibrated pump rotameter should be used to set the flow rate in the field.



## X. APPENDIX II

### METHOD FOR ANALYSIS OF CYANIDE SAMPLES

#### Principle of the Method

Atmospheric samples are taken with midget impingers that contain 10 ml of 0.1M NaOH.

Particulate cyanides are collected on membrane filters and leached with 10 ml of 0.1M NaOH.

Samples are analyzed using the cyanide ion selective electrode.

#### Range and Sensitivity

The ultimate range and sensitivity of the method have not been established at this time. The recommended range of the method is 0.013-13 mg/cu m in air (approximately 0.0117-11.7 ppm of HCN).

#### Interference

Sulfide ion irreversibly poisons the cyanide ion selective electrode and must be removed if found in the sample. Check for the presence of sulfide ion by touching a drop of sample to a piece of lead acetate paper. The presence of sulfide is indicated by discoloration of the paper.

Sulfide is removed by the addition of a small amount (spatula tip) of powdered cadmium carbonate to the sample at pH 11-13. Swirl to disperse the solid, and recheck the liquid by again touching a drop to a piece of lead acetate paper. If sulfide ion has not been removed completely, add more cadmium carbonate. Avoid a large excess of cadmium carbonate and long contact time with the solution.

When a drop of liquid no longer discolors a strip of lead acetate paper, remove the solid by filtering the sample through a small plug of glass wool and proceed with the analysis.

#### Precision and Accuracy

The precision and accuracy of this method have not been completely determined at this time. No collaborative tests have been performed on this method.

#### Apparatus

(a) Sampling and Calibration Equipment

(1) A filter unit (if needed) consisting of the filter media and cassette filter holder.

(2) A midget fritted impinger containing the absorbing solution or reagent.

(3) A pump suitable for delivering desired flow rates. The sampling pump is protected from splashover or water condensation by an absorption tube loosely packed with a plug of glass wool and inserted between the exit arm of the impinger and the pump.

(4) An integrating volume meter such as a dry-gas or wet-test meter.

(5) Thermometer

(6) Manometer

(7) Stopwatch

(b) Analytical Equipment

- (1) Cyanide ion selective electrode
- (2) Single junction reference electrode
- (3) Expanded scale millivolt-pH meter
- (4) Associated laboratory glassware
- (5) Plastic bottles
- (6) Magnetic stirrer and stirring bars

Reagents

The reagents described must be made up using ACS reagent grade or better grade of chemical.

(a) Distilled or deionized water

(b) Potassium cyanide

(c) Sodium hydroxide 0.1 M. Dissolve 2.0 g NaOH in doubly distilled water and dilute to 500 ml.

(d) Potassium cyanide standards

(1) Dissolve 0.65 g KCN in 0.1 M NaOH and dilute to 100 ml with additional 0.1 M NaOH for 0.1 M [cyanide ion] (2600  $\mu\text{g/ml}$ ).

(2) Dilute 10 ml of 0.1 M [cyanide ion] to 100 ml with 0.1 M NaOH for 0.01 M [cyanide ion] (260  $\mu\text{g/ml}$ ).

(3) Dilute 10 ml of 0.01 M [cyanide ion] to 100 ml with 0.1 M NaOH for 0.001 M [cyanide ion] (26  $\mu\text{g/ml}$ ).

(4) Dilute 10 ml of 0.001 M [cyanide ion] to 100 ml with 0.1 M NaOH for 0.0001 M [cyanide ion] (2.6  $\mu\text{g/ml}$ ).

(5) Dilute 10 ml of 0.0001 M [cyanide ion] to 100 ml with

0.1 M NaOH for 0.00001 M [cyanide ion] (0.26  $\mu\text{g/ml}$ ).

- (e) Lead acetate paper
- (f) Cadmium carbonate

### Procedure

- (a) Cleaning of equipment

All glassware is washed in detergent solution, rinsed in tap water, and then rinsed with distilled or deionized water.

- (b) Analysis of Samples

(1) For HCN, transfer the contents of the impinger to a 15-ml volumetric flask. Wash the impinger several times with 1 or 2 ml of 0.1 M NaOH and add to the contents of the flask. Add sufficient 0.1 M NaOH to the flask to make up 15 ml and mix the contents. Test for sulfide and if necessary remove it according to the procedure given above. The loss of solution in these steps (sulfide testing and filtering) should not be made up; sufficient solution should remain for cyanide electrode determination and the sample volume for calculations is therefore 15 ml. This solution is transferred to a 50-ml beaker. For the particulate cyanides, remove the filter from the cassette with tweezers, place in a clean, dry 50 ml beaker, add 15 ml of 0.1 M NaOH, and swirl.

(2) The cyanide ion electrode and the single junction reference electrode are placed in the solution and the resulting millivolt reading recorded. The reading should be taken after the meter has stabilized. Both the samples and standards should be stirred while the readings are being taken.

### Calibration and Standards

Obtain the millivolt readings from each of the cyanide standards. Note that the use of the concentrated standards (0.1 M and 0.01 M) is not recommended since they may badly corrode the electrodes.

Plot the millivolt readings as a function of cyanide ion concentrations of the standards on semilog paper. The cyanide ion concentrations in  $\mu\text{g/ml}$  is plotted on the log axis.

### Calculations

The millivolt readings from the analysis of the sample are converted to  $\mu\text{g/ml}$  of cyanide radical (CN) of solution using the calibration curve.

The  $\mu\text{g}$  content of the sample is multiplied by the sample volume (15 ml) to obtain the total  $\mu\text{g}$  cyanide in the sample.

Convert the volume of air sampled to standard conditions of 25 degrees C and 760 mmHg:

$$VS = V \times P/760 \times 298/(T+273)$$

where:

VS = volume of air in liters at 25 degrees C  
and 760 mmHg

V = volume of air in liters as measured

P = barometric pressure in mmHg

T = temperature of air in degrees C

The concentration of cyanide in the air sampled can be expressed in  $\mu\text{g}$  cyanide/liter or mg cyanide/cu m.

$$\text{mg/cu m} = \mu\text{g/liter}$$

$$\text{mg/cu m} = \text{total } \mu\text{g cyanide/VS}$$

The concentration of cyanide can also be expressed in ppm, defined as  $\mu\text{liters of component/liter of air}$ .

$$\begin{aligned}\text{ppm} &= \mu\text{liters cyanide/VS} \\ &= [R/\text{MW}] [\mu\text{g cyanide/VS}] \\ &= 0.94 \times \mu\text{g cyanide/VS}\end{aligned}$$

where:

$$R = 24.45 \text{ liters/mole at } 25 \text{ C, } 760 \text{ mm Hg.}$$

$$\text{MW} = 26 \text{ (for CN), } 27 \text{ (for HCN).}$$

## XI. APPENDIX III

### HYDROGEN CYANIDE MONITORS

Whenever the possibility exists that high concentrations of hydrogen cyanide may be released or created as a result of leaks, accidents, etc, it is essential that HCN monitoring devices be installed and that these devices give immediate warning of concentrations likely to be hazardous to life. It is difficult to define the limiting circumstances when such devices may be required; if reasonable doubt exists, the decision should be made by a qualified industrial hygienist. Monitoring devices may be based upon several operating principles, and at least one is currently available commercially. In the design or purchase of a HCN monitoring device the following criteria should be considered.

#### Summary of Specifications

- (a) Monitoring device must sound an alarm or otherwise warn employees whenever a concentration of 25 ppm HCN is reached or exceeded.
- (b) The monitoring device must have a response time of 20 seconds or less when exposed to an HCN concentration of 25 ppm.
- (c) Zero drift should be less than 1% of full scale in 24 hours.
- (d) Sampling rate and volume are not critical, and any sampling conditions which will meet the response criteria are adequate.
- (e) The monitoring device must be accurate to within plus or minus 5 ppm when exposed only to HCN gas.

(f) Precision and repeatability must be plus or minus 2% of full scale.

(g) It is desirable that the instrument respond only to HCN, but instruments which respond to other gases not normally present in the atmosphere may be acceptable. In general, it is probable that any gas which causes a reading sufficiently high to set off the alarm will itself be present at a concentration sufficiently high to warrant corrective actions. Whenever there is a possibility that gases or vapors such as hydrogen chloride, chlorine, etc, may be present, it would be desirable to determine the response of the instrument to such gases in advance.

(h) An operating range of 0-100 ppm HCN is optimal, but other ranges may be selected to suit individual needs.

(i) The device should be capable of 7 days of continuous unattended operation.

(j) The device and alarm should be intrinsically safe for use in hazardous locations.

### Discussion

The principal requirements for such monitors in addition to responding to HCN gas are that they be sufficiently rugged to withstand normal extremes of temperature, pressure, vibration, etc, and not be susceptible to plugging or interferences due to contaminants likely to be encountered in most work places. They should be so constructed that it is possible to quickly check the zero setting of the instrument and the response at 25 ppm in a rapid routine manner. It may be permissible to perform such checks by electrical means, but at least once each month



instruments should be checked at or near 25 ppm HCN using a known concentration of HCN-air mixture. For instruments relying on diffusion of the gas to a sensing electrode, it may be necessary to provide a chamber or bag into which the instrument is placed. Those instruments which incorporate an air-moving device can more readily sample gases directly from a cylinder or a plastic bag.

At least once a month, the monitoring device should be calibrated by exposure to known concentrations of HCN. Pressurized cylinders containing concentrations of HCN in nitrogen down to 25 ppm are available commercially. According to work done at the National Bureau of Standards, [253] HCN concentrations in cylinders are unstable during the first 10 days after the tanks are filled. Therefore, it is recommended that when cylinder gases are used to calibrate the monitoring device, the cylinders be allowed to sit for at least 2 weeks before use and that the HCN concentrations be verified by the analytical procedure described in Appendix II. A single calibration point at 25 ppm can be checked to determine if the instrument has maintained its calibration. If the reading differs by more than 5 ppm from the previous calibration, then several other calibration points over the useful range of the instrument should be checked and a new calibration established.

In large plants, where considerable distances between work stations exist, additional monitors may be required to ensure worker safety. Alternatively, a multipoint sampling system bringing sampled air to a single instrument may be satisfactory.

## XII. APPENDIX IV

### MATERIAL SAFETY DATA SHEET

The following items of information which are applicable to a specific product or material containing cyanide shall be provided in the appropriate block of the Material Safety Data Sheet (MSDS).

The product designation is inserted in the block of the upper left corner of the first page to facilitate filing and retrieval. Print in upper case letters as large as possible. It should be printed to read upright with the sheet turned sideways. The product designation is that name or code designation which appears on the label, or by which the product is sold or known by employees. The relative numerical hazard ratings and key statements are those determined by the rules in Chapter V, Part B, of the NIOSH publication, An Identification System for Occupationally Hazardous Materials. The company identification may be printed in the upper right corner if desired.

#### (a) Section I. Product Identification

The manufacturer's name, address, and regular and emergency telephone numbers (including area code) are inserted in the appropriate blocks of Section I. The company listed should be a source of detailed backup information on the hazards of the material(s) covered by the MSDS. The listing of suppliers or wholesale distributors is discouraged. The trade name should be the product designation or common name associated with the material. The synonyms are those commonly used for the product, especially formal chemical nomenclature. Every known chemical designation

or competitor's trade name need not be listed.

(b) Section II. Hazardous Ingredients

The "materials" listed in Section II shall be those substances which are part of the hazardous product covered by the MSDS and individually meet any of the criteria defining a hazardous material. Thus, one component of a multicomponent product might be listed because of its toxicity, another component because of its flammability, while a third component could be included both for its toxicity and its reactivity. Note that a MSDS for a single component product must have the name of the material repeated in this section to avoid giving the impression that there are no hazardous ingredients.

Chemical substances should be listed according to their complete name derived from a recognized system of nomenclature. Where possible, avoid using common names and general class names such as "aromatic amine," "safety solvent," or "aliphatic hydrocarbon" when the specific name is known.

The "%" may be the approximate percentage by weight or volume (indicate basis) which each hazardous ingredient of the mixture bears to the whole mixture. This may be indicated as a range or maximum amount, ie, "10-40% vol" or "10% max wt" to avoid disclosure of trade secrets.

Toxic hazard data shall be stated in terms of concentration, mode of exposure or test, and animal used, eg, "100 ppm LC50-rat," "25 mg/kg LD50-skin-rabbit," "75 ppm LC man," or "permissible exposure from 29 CFR 1910.1000," or, if not available, from other sources of publications such as the American Conference of Governmental Industrial Hygienists or the American National Standards Institute Inc. Flashpoint, shock sensitivity

or similar descriptive data may be used to indicate flammability, reactivity, or similar hazardous properties of the material.

(c) Section III. Physical Data

The data in Section III should be for the total mixture and should include the boiling point and melting point in degrees Fahrenheit (Celsius in parentheses); vapor pressure, in millimeters of mercury; vapor density of gas or vapor (air = 1); solubility in water, in parts/hundred parts of water by weight; specific gravity (water = 1); percent volatiles (indicated if by weight or volume) at 70 degrees Fahrenheit (21.1 degrees Celsius); evaporation rate for liquids or sublimable solids, relative to butyl acetate; and appearance and odor. These data are useful for the control of toxic substances. Boiling point, vapor density, percent volatiles, vapor pressure, and evaporation are useful for designing proper ventilation equipment. This information is also useful for design and deployment of adequate fire and spill containment equipment. The appearance and odor may facilitate identification of substances stored in improperly marked containers, or when spilled.

(d) Section IV. Fire and Explosion Data

This section should contain complete fire and explosion data for the product, including flash point and autoignition temperature in degrees Fahrenheit (Celsius in parentheses); flammable limits, in percent by volume in air; suitable extinguishing media or materials; special firefighting procedures; and unusual fire and explosion hazard information. If the product presents no fire hazard, insert "NO FIRE HAZARD" on the line labeled "Extinguishing Media."

(e) Section V. Health Hazard Information

The "Health Hazard Data" should be a combined estimate of the hazard of the total product. This can be expressed as a TWA concentration, as a permissible exposure, or by some other indication of an acceptable standard. Other data are acceptable, such as lowest LD50, if multiple components are involved.

Under "Routes of Exposure," comments in each category should reflect the potential hazard from absorption by the route in question. Comments should indicate the severity of the effect and the basis for the statement if possible. The basis might be animal studies, analogy with similar products, or human experiences. Comments such as "yes" or "possible" are not helpful.

"Emergency and First Aid Procedures" should be written in lay language and should primarily represent first-aid treatment that could be provided by paramedical personnel or individuals trained in first aid.

Information in the "Notes to Physician" section should include any special medical information which would be of assistance to an attending physician including required or recommended preplacement and periodic medical examinations, diagnostic procedures, and medical management of overexposed workers.

(f) Section VI. Reactivity Data

The comments in Section VI relate to safe storage and handling of hazardous, unstable substances. It is particularly important to highlight instability or incompatibility to common substances or circumstances such as water, direct sunlight, steel or copper piping, acids, alkalies, etc. "Hazardous Decomposition Products" shall include those products released

under fire conditions. It must also include dangerous products produced by aging, such as peroxides in the case of some ethers. Where applicable, shelf life should also be indicated.

(g) Section VII. Spill or Leak Procedures

Detailed procedures for cleanup and disposal should be listed with emphasis on precautions to be taken to protect workers assigned to cleanup detail. Specific neutralizing chemicals or procedures should be described in detail. Disposal methods should be explicit including proper labeling of containers holding residues and ultimate disposal methods such as "sanitary landfill," or "incineration." Warnings such as "comply with local, state, and federal antipollution ordinances" are proper but not sufficient. Specific procedures shall be identified.

(h) Section VIII. Special Protection Information

Section VIII requires specific information. Statements such as "Yes," "No," or "If necessary" are not informative. Ventilation requirements should be specific as to type and preferred methods. Respirators shall be specified as to type and NIOSH or US Bureau of Mines approval class, ie. "Supplied air," "Organic vapor canister," "Suitable for dusts not more toxic than lead," etc. Protective equipment must be specified as to type and materials of construction.

(i) Section IX. Special Precautions

"Precautionary Statements" shall consist of the label statements selected for use on the container or placard. Additional information on any aspect of safety or health not covered in other sections should be inserted in Section IX. The lower block can contain references to published guides or in-house procedures for handling and storage.

Department of Transportation markings and classifications and other freight, handling, or storage requirements and environmental controls can be noted.

(j) Signature and Filing

Finally, the name and address of the responsible person who completed the MSDS and the date of completion are entered. This will facilitate correction of errors and identify a source of additional information.

The MSDS shall be filed in a location readily accessible to workers potentially exposed to the hazardous material. The MSDS can be used as a training aid and basis for discussion during safety meetings and training of new employees. It should assist management by directing attention to measures to ensure safe handling and use of the material. It will aid the safety and health staff in planning a safe and healthful work environment and suggesting appropriate emergency procedures and sources of help in the event of harmful exposure of employees.

|  |  |
|--|--|
|  |  |
|  |  |
|  |  |

# MATERIAL SAFETY DATA SHEET

| I PRODUCT IDENTIFICATION              |   |  |
|---------------------------------------|---|--|
| MANUFACTURER'S NAME                   |   | REGULAR TELEPHONE NO.<br>EMERGENCY TELEPHONE NO. |
| ADDRESS                               |   |  |
| TRADE NAME                            |   |  |
| SYNONYMS                              |   |  |
| II HAZARDOUS INGREDIENTS              |   |  |
| MATERIAL OR COMPONENT                 | % | HAZARD DATA                                      |
|                                       |   |  |
|                                       |   |  |
|                                       |   |  |
|                                       |   |  |
|                                       |   |  |
|                                       |   |  |
|                                       |   |  |
| III PHYSICAL DATA                     |   |  |
| BOILING POINT, 760 MM HG              |   | MELTING POINT                                    |
| SPECIFIC GRAVITY (H <sub>2</sub> O=1) |   | VAPOR PRESSURE                                   |
| VAPOR DENSITY (AIR=1)                 |   | SOLUBILITY IN H <sub>2</sub> O, % BY WT          |
| % VOLATILES BY VOL                    |   | EVAPORATION RATE (BUTYL ACETATE=1)               |
| APPEARANCE AND ODOR                   |   |  |



| IV FIRE AND EXPLOSION DATA              |  |       |                             |  |
|---|--|-------|-----------------------------|--|
| FLASH POINT<br>(TEST METHOD)            |  |       | AUTOIGNITION<br>TEMPERATURE |  |
| FLAMMABLE LIMITS IN AIR, % BY VOL.      |  | LOWER | UPPER                       |  |
| EXTINGUISHING<br>MEDIA                  |  |       |                             |  |
| SPECIAL FIRE<br>FIGHTING<br>PROCEDURES  |  |       |                             |  |
| UNUSUAL FIRE<br>AND EXPLOSION<br>HAZARD |  |       |                             |  |
| V HEALTH HAZARD INFORMATION             |  |       |                             |  |
| HEALTH HAZARD DATA                      |  |       |                             |  |
| ROUTES OF EXPOSURE                      |  |       |                             |  |
| INHALATION                              |  |       |                             |  |
| SKIN CONTACT                            |  |       |                             |  |
| SKIN ABSORPTION                         |  |       |                             |  |
| EYE CONTACT                             |  |       |                             |  |
| INGESTION                               |  |       |                             |  |
| EFFECTS OF OVEREXPOSURE                 |  |       |                             |  |
| ACUTE OVEREXPOSURE                      |  |       |                             |  |
| CHRONIC OVEREXPOSURE                    |  |       |                             |  |
| EMERGENCY AND FIRST AID PROCEDURES      |  |       |                             |  |
| EYES                                    |  |       |                             |  |
| SKIN                                    |  |       |                             |  |
| INHALATION:                             |  |       |                             |  |
| INGESTION                               |  |       |                             |  |
| NOTES TO PHYSICIAN                      |  |       |                             |  |

|  |
|--|
| <b>VI REACTIVITY DATA</b>                            |
| CONDITIONS CONTRIBUTING TO INSTABILITY               |
| INCOMPATIBILITY                                      |
| HAZARDOUS DECOMPOSITION PRODUCTS                     |
| CONDITIONS CONTRIBUTING TO HAZARDOUS POLYMERIZATION  |
| <b>VII SPILL OR LEAK PROCEDURES</b>                  |
| STEPS TO BE TAKEN IF MATERIAL IS RELEASED OR SPILLED |
| NEUTRALIZING CHEMICALS                               |
| WASTE DISPOSAL METHOD                                |
| <b>VIII SPECIAL PROTECTION INFORMATION</b>           |
| VENTILATION REQUIREMENTS                             |
| SPECIFIC PERSONAL PROTECTIVE EQUIPMENT               |
| RESPIRATORY (SPECIFY IN DETAIL)                      |
| EYE  |
| GLOVES   |
| OTHER CLOTHING AND EQUIPMENT                         |

## IX SPECIAL PRECAUTIONS

PRECAUTIONARY  
STATEMENTS

OTHER HANDLING AND  
STORAGE REQUIREMENTS

PREPARED BY \_\_\_\_\_

ADDRESS \_\_\_\_\_

DATE \_\_\_\_\_

### XIII. APPENDIX V

#### First Aid and Treatment Kits

Two physician's treatment kits should be immediately available to trained medical personnel at each plant where there is a potential for the release of, accidental or otherwise, or for contact with, hydrogen cyanide or cyanide salts. One kit should be portable in order that it may be carried by medical personnel while accompanying a patient to the hospital. The other kit should be kept under lock and key to assure that it is intact and available when and if needed. The key should be readily available at all times to the work supervisor on duty and the storage place should be of such construction as to allow accessibility in the event of loss of the key.

Both kits for use by the medical personnel servicing each firm should contain the following as a minimum.

(1) Two (2) boxes (2 dozen) ampules; each ampule containing 0.3 ml of amyl nitrite.

(2) Two (2) ampules of sterile sodium nitrite solution (10 ml of a 3% solution in each).

(3) Two (2) ampules of sterile sodium thiosulfate solution (50 ml of a 25% solution in each).

(4) 2 sterile 10-ml syringe with intravenous needles.

(5) 1 sterile 50-ml syringe with intravenous needle.

(6) 1 tourniquet

(7) 1 gastric tube (rubber).

(8) 1 non-sterile 100 ml syringe.

The medical personnel servicing a firm where there is a potential for hydrogen cyanide release or a potential for exposure to inorganic cyanide should be familiarized with the use of these kits.

First-aid kits should be immediately available at work places where there is a potential for the release, accidental or otherwise, of hydrogen cyanide or a potential for exposure to inorganic cyanide. This kit should contain as a minimum two (2) boxes of ampules ( 2 dozen), each containing 0.3 ml of amyl nitrite. Ampules should be replaced biannually or sooner if needed to ensure their potency. The amyl nitrite ampules should be protected from high temperatures. In all cases, the contents of the medical and first-aid kits should be replaced before the manufacturer's assigned expiration dates.

#### First-Aid Procedure

Speed in the rendering of first-aid treatment is of the utmost importance. The patient should be removed at once to an area free from HCN. The rescuer should wear respiratory protective equipment in order not to be overcome or weakened by the gas.

Many victims will have stopped breathing. In this case, it is imperative that efforts at resuscitation be instituted at once and continued without interruption even while other treatment is being administered.

A physician should be summoned immediately.

First-aid kits should be readily available at all times. They should be quickly accessible but should not be kept only in operating areas

where they may not be available in case of a spill.

(1) Contact with Skin and Mucous Membranes

(A) If liquid HCN or a cyanide salt (solid or solution) has contaminated the skin or clothing, the clothing should be removed and the skin flushed with copious amounts of water. Careful attention should be paid to underwear, shoes, and socks.

(B) Carry out the specific actions recommended in (3), below.

(2) When Taken Internally

(A) If the victim is conscious, induce vomiting by having the victim drink a glassful of lukewarm salt water, soapy water, or mustard water. If the victim is unconscious, omit this step. NEVER GIVE ANYTHING BY MOUTH TO AN UNCONSCIOUS PERSON.

(B) Carry out the specific actions recommended in (1), above, and (3), below.

(3) Inhalation

(A) Administer amyl nitrite

A pearl (ampule), if not provided with a fabric sleeve, should be wrapped lightly in a handkerchief or gauze pad, broken, and held about 1 inch from the patient's mouth and nostrils for 15 seconds. Repeat 5 times at 15-second intervals. Use a fresh pearl every 5 minutes until 3 or 4 pearls have been administered.

WARNING: First-aiders should keep the pearls away from their own mouths and noses lest they become weak and dizzy and unable to give proper assistance to the victim. Amyl nitrite is flammable and

mixtures with air may be explosive if a source of ignition is present.

(B) Resuscitation

Before instituting artificial resuscitation, dentures and foreign objects, such as gum and tobacco, and any accumulated oropharyngeal fluids (saliva, etc) should be removed from the patient's mouth and pharynx and the tongue pulled forward.

If the patient's breathing is weak or has stopped, artificial resuscitation should be started at the earliest possible moment and continued without interruption until normal breathing has been established or the patient is pronounced dead.

Mouth-to-mouth resuscitation is the method of choice because of its simplicity and effectiveness. It is, however, impossible to administer amyl nitrite while using this method. Therefore, it is advisable to switch to other methods of artificial respiration, such as the Holger-Nielsen arm-lift back pressure method, during the periods when the amyl nitrite is being given.

If a mechanical resuscitator and personnel skilled in its use are available, this equipment may be used instead of other forms of resuscitation.

(C) The patient should be kept comfortably warm but not hot. Other drugs and stimulants are rarely necessary and should be administered only by a physician or trained medical personnel under the direction of a physician.

TABLE XIV-1

## PROPERTIES AND CHARACTERISTICS OF HYDROGEN CYANIDE\*

---

|  |   |
|--|---|
| Molecular Formula                                  | HCN   |
| Molecular Weight                                   | 27.03   |
| Physical state                                     | Liquid or gas   |
| Explosive limits                                   | 6% to 41% by volume in air,<br>horizontal propagation                         |
| Flashpoint (closed cup)                            | -17.8 degrees C   |
| Autoignition temperature                           | 538 degrees C (1000 F)  |
| Boiling point                                      | 26 degrees C (27.7 for 96% solution)  |
| Color  | Clear and colorless or bluish tinted<br>liquid                                |
| Freezing point                                     | -16.8 degrees C (for 96% solution)  |
| Odor   | Sweetish, not unpleasant, like<br>bitter almond to some people                |
| Reactivity   | When not pure or stabilized, it<br>can polymerize with explosive<br>violence. |
| Specific gravity                                   | 0.703 (for 96% solution)  |
| Vapor density                                      | 0.93 (Air = 1.0)  |
| Conversion Factors:                                |   |
| For HCN at 25 degrees C and 1 atmosphere pressure: |   |
| ppm equals   | (mg/cu m) x (0.90)  |
| mg/cu m equals                                     | (ppm) x (1.11)  |

---

\*Derived from references 2,8,33,107,254



TABLE XIV-2

## CHEMICAL AND PHYSICAL PROPERTIES OF SOME CYANIDE SALTS

| Compound              | Molecular Formula                      | Formula Weight | Melting Point, °C                    | Boiling Point, °C | Solubility: g/100 cc |                  |                          | Available Cyanide and Reference   |
|-----------------------|--|----------------|--------------------------------------|-------------------|----------------------|------------------|--------------------------|---|
|                       |  |                |                                      |                   | Density              | Cold Water       | Hot Water                |   |
| Ammonium cyanide      | NH <sub>4</sub> CN                     | 44.06          | Decomposes 36°                       | Sublimes 40°      | 1.02                 | Very soluble     | Decomposes               | At 36 degrees C decomposed to NH <sub>3</sub> and HCN 28                                |
| Calcium cyanide       | Ca(CN) <sub>2</sub>                    | 92.12          | Decomposes over 350°                 | ....              | ....                 | Decomposes       | "                        | Forms Ca(OH) <sub>2</sub> and HCN in presence of H <sub>2</sub> O or humid air 31,42,89 |
| Copper (I) cyanide    | CuCN                                   | 89.56          | 473° (in N <sub>2</sub> )            | Decomposes        | 2.92                 | Insoluble        | Insoluble                | K <sub>sp</sub> = 3.2 x 10 exp(-20) 34  |
| Copper (II) cyanide   | Cu(CN) <sub>2</sub>                    | 115.58         | Decomposes                           | ....              | ....                 | "                | ....                     | Decomposes to CuCN on boiling or drying 255   |
| Gold (III) cyanide    | Au(CN) <sub>3</sub> 3 H <sub>2</sub> O | 329.07         | Decomposes 50°                       | ....              | ....                 | Very soluble     | Decomposes, very soluble | ....  |
| Lead cyanide          | Pb(CN) <sub>2</sub>                    | 259.23         | ....                                 | ....              | ....                 | Slightly soluble | Soluble                  | ....  |
| Magnesium cyanide     | Mg(CN) <sub>2</sub>                    | 76.35          | Decomposes 300° to MgCN <sub>2</sub> | Decomposes 600°   | ....                 | Soluble          | Decomposes               | ....  |
| Mercury (II) cyanide  | Hg(CN) <sub>2</sub>                    | 252.63         | Decomposes                           | ....              | 3.996                | 9.3              | 33                       | "Virtually non-ionized" 256   |
| Potassium cyanide     | KCN                                    | 65.12          | 634.5°                               | ....              | 1.52                 | 50               | 100                      | Kh (25C) = .0000254 28  |
| Potassium cyanoaurite | K[Au(CN) <sub>2</sub> ]                | 288.10         | ....                                 | ....              | 3.45                 | 14.3             | 200                      | Forms complex cyanides in aqueous solution 35   |
| Silver cyanide        | AgCN                                   | 133.84         | Decomposes 320°                      | ....              | 3.95                 | 0.000023         | ....                     | K <sub>sp</sub> (20 degrees C) = 1.2 x 10 exp(-16). 34                                  |
| Sodium Cyanide        | NaCN                                   | 49.01          | 563.7°                               | 1496°             | ....                 | 48               | 82                       | Kh (25 degrees C) = 0.0000251 28  |
| Sodium cyanoaurite    | Na[Au(CN) <sub>2</sub> ]               | 271.99         | ....                                 | ....              | ....                 | Soluble          | ....                     | Forms complex cyanides in aqueous solution 35   |
| Zinc cyanide          | Zn(CN) <sub>2</sub>                    | 117.41         | Decomposes 800°                      | ....              | 1.852                | .0005            | ....                     | "Insoluble in water" 257  |

Taken in part from Weast [1].

TABLE XIV-3

## OCCUPATIONS WITH POTENTIAL EXPOSURE TO CYANIDES

---

|                             |                                    |
|-----------------------------|------------------------------------|
| Acid dippers                | Gilders                            |
| Acrylate makers             | Gold extractors                    |
| Acrylonitrile makers        | Gold refiners                      |
| Adipic acid makers          | Heat treaters                      |
| Adiponitrile makers         | Hexamethylenediamine makers        |
| Aircraft workers            | Hydrocyanic acid makers            |
| Almond flavor makers        | Hydrogen cyanide workers           |
| Ammonium salt makers        | Insecticide and rodenticide makers |
| Art printing workers        | Jewelers                           |
| Blacksmiths                 | Laboratory technicians             |
| Blast furnace workers       | Metal cleaners                     |
| Bone distillers             | Metal polishers                    |
| Bronzers                    | Methacrylate makers                |
| Browners, gun barrel        | Mirror silverers                   |
| Cadmium platers             | Mordanters                         |
| Case hardeners              | Nylon makers                       |
| Cellulose product treaters  | Organic chemical synthesizers      |
| Cement makers               | Oxalic acid makers                 |
| Coal tar distillery workers | Phosphoric acid makers             |
| Coke oven operators         | Photoengravers                     |
| Cyanide workers             | Photographers                      |
| Cyanogen makers             | Pigment makers                     |
| Disinfectant makers         | Plastic workers                    |
| Dyemakers                   | Polish makers                      |
| Electroplaters              | Rayon makers                       |
| Executioners                | Rubber makers                      |
| Exterminators               | Silver extractors                  |
| Fertilizer makers           | Silver refiners                    |
| Fire fighters               | Solderers                          |
| Fulminate mixers            | Steel carburizers                  |
| Fumigant makers             | Steel hardeners                    |
| Fumigators of fruit trees,  | Steel galvinizers                  |
| apiaries, soil, ships,      | Tannery workers                    |
| railway cars, warehouses,   | Temperers                          |
| stored foods                | Tree sprayers                      |
| Galvanizers                 | White cyanide makers               |
| Gas purifiers               | Zinc platers                       |
| Gas workers, illuminating   | Zinkers                            |

---

Taken in part from references 44,58,237,258,259,260,261.

TABLE XIV-4

MECHANISM OF ACTION OF ACUTE OR SUBACUTE CYANIDE POISONING  
AS POSTULATED BY RIEDERS [58]

---

Step 1 - Through the formation of a relatively stable coordination complex with ferric iron, cyanide tends to keep this metal in its higher oxidation state and thus reduces its efficacy as an electron carrier in ferric to ferrous iron transitions.

By such a complexation of iron, the respiratory enzyme ferricytochrome oxidase is changed to ferricytochrome oxidase-cyanide and its ability to catalyze the reaction of reduced cytochrome with oxygen is inhibited, with consequent impairment of cellular oxygen utilization

Step 2 - Since numerous metabolic pathways converge at the cytochrome system, the impairment of the cells' ability to utilize oxygen reduces or even stops aerobic metabolism. True histotoxic (cytotoxic) hypoxia results with a shift to anaerobic metabolism with accumulation of lactate, pyruvate, and glucose.

Step 3 - The cells are thus unable to use the oxygen brought to them as O<sub>2</sub>Hb by the arterial blood. The oxyhemoglobin continues into the veins, the arteriovenous oxygen difference diminishes, and the venous blood is almost as bright a red as the arterial blood.

Step 4 - The chemoreceptors in the carotid and aortic bodies, which are the tissues most sensitive to cellular hypoxia, trigger an inspiratory gasp and hyperpnea as an almost instantaneous pathophysiologic effect of cyanide absorption.

---

TABLE XIV-5

## REPORTED (ESTIMATED) HUMAN RESPONSES TO VARIOUS CONCENTRATIONS OF HCN VAPOR

| Responses   | Airborne HCN Concentration | Primary Reference | Secondary Reference |
|---|----------------------------|-------------------|---------------------|
| Estimated LC50 for 1 minute exposure  | 3,404 ppm                  | 68                | ---                 |
| Some nausea and difficulty in concentrating after 91 sec  | 500-625 ppm                | 86                | ---                 |
| No serious consequences in 1 minute   | 500 ppm                    | 142               | 262                 |
| No injury in 1 minute   | 500 ppm                    | 115               | 145                 |
| No injury in 1.5 minutes  | 375 ppm                    | 115               | 145                 |
| Immediately fatal   | 270 ppm                    | Lehmann*          | 118                 |
| Rapidly fatal   | 300 ppm                    | 240               | 263                 |
| Fatal in 6-8 minutes  | 270 ppm                    | 118               | ---                 |
| No injury in 2 minutes  | 250 ppm                    | 115               | 145                 |
| Fatal after 30 minutes  | 200-480 ppm                | **                | 149                 |
| Fatal after 10 minutes  | 181 ppm                    | 118,264           | 29                  |
| Fatal after 30 minutes  | 135 ppm                    | 118,264           | 29                  |
| Fatal after 30-60 minutes   | 110-135 ppm                | Lehmann*          | 118                 |
| Dangerous to life after 30-60 minutes   | 110-135 ppm                | Hess*             | 118                 |
| Fatal after 30-60 minutes   | 100-240 ppm                | **                | 149                 |
| Death after 60 minutes  | 90 ppm                     | 142               | 262                 |
| Fatal or immed. dangerous to life   | 90 ppm                     | 118               | ---                 |
| Numbness, weakness, vertigo, nausea, rapid pulse, flushing of face, headache, and gastric distress  | More than 50 ppm           | 27                | ---                 |
| Tolerated for 30-60 min without immediate or late effects   | 45-54 ppm                  | Lehmann*          | 118                 |
| Complaints of headache, nausea, vomiting, and cardiac symptoms  | 45 ppm                     | 118               | ---                 |
| Minimal symptoms after several hours of exposure  | 20-40 ppm                  | 118               | 149                 |
| "Effective after several hours of exposure"   | 18-36 ppm                  | Hess*             | 118                 |
| No symptoms after 6 hours   | 18-36 ppm                  | Lehmann*          | 118                 |
| Some headache, vertigo  | 5-18 ppm                   | 143               | 262                 |
| No observed effect  | 0-17 (Mean 4.9)            | 150               | ---                 |
| Fatigue, headache, body weakness, tremor, pain, nausea  | 5-13 ppm                   | 79                | ---                 |
| Headache, weakness, changes in taste and smell, throat irritation, nausea, effort dyspnea, enlarged thyroids, changes in blood chemistry    | 4.2-12.4 ppm (Mean 8.3)    | 110               | ---                 |
| Increased SCN excretion in urine, but to a lesser extent than in cigarette smokers; no other effects noted                                  | 2-8 ppm, (Mean 5)          | 76                | ---                 |
| None  | 0.1-0.9 ppm                | ***               | 262                 |
| Slight decrease in leukocytic activity of cytochrome oxidase, peroxidase, and succinyldehydrogenase after an average 5.4 years of exposure? | 0.23 ppm                   | 23                | ---                 |

\* The work of investigator cited appears only in the compilation of Flury and Zernick [118] or Kobert [240]

\*\* Primary author not given in citation by Henderson and Haggard [149]

\*\*\* Attributed to Lazareff by Czechoslovak Committee of MAC [262]

TABLE XIV-6

PHYSIOLOGIC RESPONSES OF ANIMALS TO VARIOUS  
CONCENTRATIONS OF HYDROGEN CYANIDE IN AIR

| Animal | <u>Concentration</u> |            | Responses   | Reference |
|--------|----------------------|------------|---|-----------|
|        | mg/cu m              | ppm        |   |           |
| Mouse  | 1450                 | 1300       | Fatal after 1-2 min   | 118       |
| "      | ---                  | 323        | LC50 for 5-min exposure   | 133       |
| "      | ---                  | 250        | First effects in as little as 20 sec, death within 40 min         | 115       |
| "      | ---                  | 200        | Not fatal with 5-min exposure                                     | 133       |
| "      | 140                  | 127        | Fell down in 45 sec   | 118       |
| "      | ---                  | 120        | Fatal in 30 min   | 115       |
| "      | 130                  | 118        | Fell down in 3 min  | 118       |
| "      | 125                  | 113        | Fell down in 8 min  | 118       |
| "      | 120                  | 110        | Fatal in 45 min   | 118       |
| "      | 90                   | 82         | Fell down in 7.5 min  | 118       |
| "      | 70                   | 63         | Fell down in 14 min   | 118       |
| "      | 60                   | 54         | Fell down in 14 min   | 118       |
| "      | 50                   | 45         | Fell down in 30 min   | 118       |
| "      | 50                   | 45         | Fatal after 2.5-4 hrs   | 118       |
| "      | 44                   | 40         | No serious symptoms in 7 hrs                                      | 118       |
| "      | ---                  | 10         | Impaired movement and respiration in 2 hrs                        | 84        |
| Rat    | ---                  | About 1500 | Fatal within 10 min   | 114       |
| "      | ---                  | 503        | LC50 for 5-min exposure   | 133       |
| "      | ---                  | About 500  | 31% died in 3 min   | 119       |
| "      | ---                  | About 590  | Fatal in 5-13 min   | 114       |
| "      | ---                  | About 480  | First effect in 2 min, death in 15 min                            | 115       |
| "      | ---                  | About 350  | First effect in 4 min, death in 40 min                            | 115       |
| "      | ---                  | 283        | Not fatal in 5 min  | 133       |
| "      | ---                  | About 250  | First effect in 5-12 min, most survived exposures of 1 hr or less | 115       |
| "      | 225                  | 204        | Fell down in 5 min  | 118       |
| "      | ---                  | About 180  | First effects at 10 min, removed at 25 min, and recovered         | 115       |
| "      | 140                  | 127        | Fell down in 9.5 min  | 118       |
| "      | ---                  | About 120  | No effect in 1 hr   | 115       |
| "      | 120                  | 110        | Fatal in 1.5 hrs  | 118       |
| "      | 100                  | 90         | "Safe" indefinitely?  | 86        |

TABLE XIV-6 (CONTINUED)

PHYSIOLOGIC RESPONSES OF ANIMALS TO VARIOUS  
CONCENTRATIONS OF HYDROGEN CYANIDE IN AIR

| Animal | Concentration |           | Responses  | Reference |
|--------|---------------|-----------|--|-----------|
|        | mg/cu m       | ppm       |  |           |
| Rat    | ---           | 100       | Fatal in 5.5 min   | 124       |
| "      | ---           | Around 50 | Minimum lethal dose  | 124       |
| "      | ---           | 30-40     | Rapid respiration; survived  | 124       |
| "      | ---           | 25        | No observable effects  | 124       |
| "      | 11            | 10        | Motor disturbances in 2-5 hrs  | 84        |
| Cat    | 1000          | 900       | Fell down in 55 sec  | 118       |
| "      | 700           | 635       | Fell down in 1 min   | 118       |
| "      | 430           | 390       | Fell down in 2 min   | 118       |
| "      | ---           | About 350 | First effect in 3 min  | 115       |
| "      | 350           | 315       | Respiratory paralysis in 2 min   | 264       |
| "      | Above 350     | Above 315 | Quickly lethal   | 118       |
| "      | ---           | About 250 | First effect 5-9 min, one death in 33 min, one recovery after 1 hr   | 115       |
| "      | 200           | 181       | Fell down in 3 min, some as long as 12-27 min  | 118       |
| "      | 200           | 180       | Fatal  | 118       |
| "      | 180           | 162       | Safe indefinitely?   | 86        |
| "      | 140           | 125       | Markedly toxic in 6-7 min  | 264       |
| "      | 140           | 127       | Fell down in 5 min   | 118       |
| "      | 130           | 118       | Fell down in 6 min   | 118       |
| "      | ---           | 120-150   | Death after 30 min   | 113       |
| "      | 100           | 91        | Fell down in 7.5 min   | 118       |
| "      | 90            | 82        | Fell down in 10 min  | 118       |
| "      | 70            | 63        | Fell down in 11.5 min  | 118       |
| "      | 60            | 54        | Fell down in 22.5 min  | 118       |
| "      | 50            | 45        | Fell down in 25 min  | 118       |
| "      | 50-60         | 45-54     | Most died in 2.5-5 hrs   | 113       |
| "      | 50            | 45        | Respiratory distress, increased flow of saliva, vomiting, dilation of pupils, and convulsions after 1.5 hrs exposure | 113       |

TABLE XIV-6 (CONTINUED)

PHYSIOLOGIC RESPONSES OF ANIMALS TO VARIOUS  
CONCENTRATIONS OF HYDROGEN CYANIDE IN AIR

| Animal     | Concentration |           | Responses   | Reference |
|------------|---------------|-----------|---|-----------|
|            | mg/cu m       | ppm       |   |           |
| Rabbit     | ---           | About 450 | 12% died in 3 min                                     | 119       |
| "          | 360           | 325       | Fell down in 4 min                                    | 118       |
| "          | 350           | 315       | Fatal   | 118       |
| "          | 300           | 272       | Fell down in 15 min                                   | 118       |
| "          | 284           | 256       | Death with 30-min exposure                            | 123       |
| "          | 225           | 204       | Fell down in 7.5 min                                  | 118       |
| "          | 200           | 181       | Fell down in 3.75 min                                 | 118       |
| "          | 185           | 168       | Fell down in 16 min                                   | 118       |
| "          | 180           | 162       | Safe indefinitely?                                    | 86        |
| "          | 140           | 127       | Fell down in 20 min                                   | 118       |
| "          | 130           | 120       | No symptoms of poisoning                              | 118       |
| Guinea pig | 1100          | 1000      | Fell down in 2 min                                    | 118       |
| " "        | 1000          | 900       | Fell down in 3 min                                    | 118       |
| " "        | ---           | About 900 | 40% died within 6 min                                 | 119       |
| " "        | ---           | About 480 | First effect in 5 min, fatal in 20 min                | 115       |
| " "        | ---           | About 360 | First effect in 35 min, recovered after 1-hr exposure | 115       |
| " "        | 350           | 315       | Fell down in 10.5 min                                 | 118       |
| " "        | 350           | 315       | Fatal   | 118       |
| " "        | 320           | 290       | Fell down in 10 min                                   | 118       |
| " "        | 300           | 272       | Fell down in 5 min                                    | 118       |
| " "        | ---           | About 240 | 25% died after 1-hr exposure, no effects on others    | 115       |
| " "        | 230           | 200       | Tolerated for 1.5 hrs without symptoms                | 118       |
| Pigeon     | ---           | About 240 | First effect in 8 min, death in 9 min                 | 115       |
| "          | 160           | 145       | Fell down in 9 min                                    | 118       |
| "          | 150           | 136       | Fell down in 9 min                                    | 118       |
| "          | 130           | 118       | Fell down in 5 min                                    | 118       |
| "          | 125-150       | 115-135   | Lethal in 15 min or less                              | 118       |
| Monkey     | 180           | 162       | Safe indefinitely?                                    | 86        |
| "          | 140           | 127       | Fell down in 12 min                                   | 118       |

TABLE XIV-6 (CONTINUED)

PHYSIOLOGIC RESPONSE OF ANIMALS TO VARIOUS  
CONCENTRATIONS OF HYDROGEN CYANIDE IN AIR

| Animal  | <u>Concentration</u> |           | Responses  | Reference |
|---------|----------------------|-----------|--|-----------|
|         | mg/cu m              | ppm       |  |           |
| Dog     | 350                  | 315       | Quickly fatal  | 118       |
| "       | About 300            | About 270 | Pretreated with sodium thiosulfate and sodium nitrite and survived   | 121       |
| "       | 225                  | 204       | Fell down in 5 min   | 118       |
| "       | 200                  | 181       | Fell down in 8 min   | 118       |
| "       | 160                  | 145       | Fell down in 10.5 min  | 118       |
| "       | 140                  | 127       | Fell down in 6.5 min   | 118       |
| "       | 125                  | 113       | Fell down in 7 min   | 118       |
| "       | 100                  | 90        | Fell down in 3 min   | 118       |
| "       | 100                  | 90        | Safe indefinitely?   | 86        |
| "       | 60                   | 54        | Fell down in 35 min  | 118       |
| "       | 50                   | 45        | Dyspnea, nausea, exaggerated intestinal peristalsis, diarrhea, then nervousness, tremor, unsteadiness, convulsions, weight loss, 1 death | 126       |
| "       | 50                   | 45        | Fell down in 15 min  | 118       |
| "       | About 50             | About 45  | Onset of convulsions   | 121       |
| Sparrow | ---                  | About 240 | First effect in 45 sec, death in as little as 2.5 min  | 115       |
| "       | ---                  | About 180 | First effect in 13 min, death in 20 min  | 115       |
| "       | ---                  | About 120 | Death in 40 min  | 115       |

Note: reference 264 may be an interpretation of data presented in reference 118



TABLE XIV-7

PHYSIOLOGIC RESPONSES OF ANIMALS TO VARIOUS  
CONCENTRATIONS OF CYANIDE SALTS

| Animal | Compounds<br>Given | Route* | Dose<br>(mg/kg)     | Responses   | Reference |
|--------|--------------------|--------|---------------------|---|-----------|
| Cat    | NaCN               | iv     | 0.05-0.10<br>mg/cat | Bradycardia   | 265       |
| "      | "                  | "      | 0.2-0.35            | Hyperpnea, unconsciousness,<br>pupil dilation, nystagmus,<br>flaccidity, defecation<br>and urination, vomiting,<br>and confusion; recovery                  | 266       |
| "      | "                  | "      | 0.38-0.52           | Hyperpnea, loss of con-<br>sciousness, motor disturb-<br>ances, pupil dilation,<br>respiratory pause, seizure,<br>prolonged state of confusion;<br>recovery | 266       |
| "      | "                  | "      | 0.4                 | Reversible increase in brain<br>lactic acid concentration;<br>no convulsions.   | 267       |
| "      | "                  | "      | 0.5-1.2             | Altered EEG patterns  | 268       |
| "      | "                  | "      | 0.8                 | Convulsions. Increased brain<br>lactic acid concentration   | 267       |
| "      | "                  | "      | 0.8                 | Altered ECG patterns  | 269       |
| "      | "                  | "      | 1.2                 | Fatal   | 267       |
| "      | "                  | "      | 1.4-1.6             | Altered ECG patterns in<br>paralyzed animals supported<br>by artificial ventilation   | 270       |
| "      | KCN                | sc     | 2-35 mg/cat         | Increased respiration, bowel<br>movement, twitch, head<br>tremor, nystagmus, and leg<br>spasm at lower doses; paraly-<br>sis, blindness, and convulsions    | 271       |

TABLE XIV-7 (CONTINUED)

PHYSIOLOGIC RESPONSES OF ANIMALS TO VARIOUS  
CONCENTRATIONS OF CYANIDE SALTS

| Animal | Compounds<br>Given                                      | Route*                    | Dose<br>(mg/kg)              | Responses   | Reference |
|--------|---|---------------------------|------------------------------|---|-----------|
| Dog    | NaCN  | iv                        | 1.0                          | Increased SCN in urine  | 272       |
| "      | "   | "                         | 1.5                          | Apnea, gasping respirations,<br>muscle incoordination;<br>alive after 14 days           | 125       |
| "      | KCN   | "                         | 1.0-2.5                      | Poisoning symptoms plus<br>increased adrenaline<br>secretion                            | 273       |
| "      | NaCN  | "                         | 2.25                         | Death in 48 hrs   | 125       |
| "      | KCN   | Infusion                  | Approx<br>0.012<br>mg/kg/min | Sodium resorption in kidney<br>decreased linearly with<br>increased CN, (ie, with time) | 274       |
| "      | "   | Oral<br>(stomach<br>tube) | 10.7                         | Death in 21 min   | 120       |
| "      | NaCN  | sc                        | 5.36                         | LD50  | 99        |
| "      | NaCN  | sc                        | 6                            | Lethal  | 275       |
| "      | "   | "                         | 6                            | Minimum lethal dose   | 276       |
| "      | KCN   | Oral<br>(stomach<br>tube) | 20.3                         | Death in 8 min  | 120       |
| "      | NaCN +<br>methylene<br>blue                             | sc                        | 12                           | Survived  | 276       |
| "      | NaCN  | "                         | 6-18                         | Recovery when treated with<br>Na <sub>3</sub> Co(NO <sub>2</sub> ) <sub>6</sub>         | 275       |
| Dog    | NaCN +<br>Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub> | sc                        | 18                           | Survived  | 276       |
| "      | NaCN +<br>Na <sub>2</sub> S <sub>4</sub> O <sub>6</sub> | "                         | 18                           | "   | 276       |

TABLE XIV-7 (CONTINUED)

PHYSIOLOGIC RESPONSES OF ANIMALS TO VARIOUS  
CONCENTRATIONS OF CYANIDE SALTS

| Animal | Compounds<br>Given   | Route* | Dose<br>(mg/kg)    | Responses   | Reference |
|--------|--|--------|--------------------|---|-----------|
| Dog    | NaCN +<br>Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub>                        | "      | 18.4               | LD50  | 99        |
| "      | NaCN +<br>amyl<br>nitrite  | "      | 24.5               | "   | 99        |
| "      | NaCN +<br>NaNO <sub>2</sub>  | "      | 24                 | Survived  | 276       |
| "      | "  | "      | 27.1               | LD50  | 99        |
| "      | NaCN +<br>methylene<br>blue +<br>Na <sub>2</sub> S <sub>4</sub> O <sub>6</sub> | "      | 36                 | Survived  | 276       |
| "      | NaCN +<br>amyl nitrite<br>+ Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub>      | "      | 60                 | "   | 276       |
| "      | "  | "      | 60.9               | LD50  | 99        |
| "      | NaCN +<br>NaNO <sub>2</sub> +<br>Na <sub>2</sub> S <sub>4</sub> O <sub>6</sub> | "      | 78                 | Survived  | 276       |
| "      | NaCN +<br>NaNO <sub>2</sub> +<br>Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub> | "      | 96.7               | LD50  | 99        |
| "      | "  | "      | 120                | Survived  | 276       |
| Monkey | NaCN   | iv     | 0.8                | Altered ECG patterns,<br>similar to those seen in<br>humans   | 269       |
| "      | KCN  | sc     | 2-35 mg/<br>animal | Increased respiration,<br>vomiting, bowel movement,<br>twitch, tremor of head,<br>nystagmus, and leg spasms<br>at lower doses; transitory<br>leg paralysis, blindness,<br>convulsions, and death at<br>higher doses | 271       |

TABLE XIV-7 (CONTINUED)

PHYSIOLOGIC RESPONSES OF ANIMALS TO VARIOUS  
CONCENTRATIONS OF CYANIDE SALTS

| Animal | Compound<br>Given          | Route*                             | Dose<br>(mg/kg)                            | Responses  | Reference |
|--------|----------------------------|------------------------------------|--|--|-----------|
| Mouse  | KCN +<br>HgCl <sub>2</sub> | iv?                                | 0.005 as CN                                | No changes   | 277       |
| "      | KCN                        | "                                  | 0.0005 as Hg                               |  |           |
| "      |                            |                                    | 0.25 as CN                                 | Rise in reticulocytes in<br>3rd and 4th mon of<br>5-mon experiment; 50%<br>inhibition of blood catalase;<br>changes in reflex activity       | 277       |
| "      | KCN +<br>HgCl <sub>2</sub> | "                                  | 0.25 as CN<br>0.05 as Hg                   | Rise in reticulocytes in<br>3rd and 4th mon of<br>a 5-mon experiment; 50%<br>inhibition of blood catalase<br>changes in reflex-arc activity. | 277       |
| "      | KCN                        | Oral<br>(in drink-<br>ing water)   | 0.5 mg/ml                                  | Inhibition of liver catalase   | 278       |
| "      | "                          | Intra-<br>neural<br>injec-<br>tion | 0.6-4.0<br>μ g into<br>one nerve<br>bundle | Morphologic changes to<br>nerve tissue visible under<br>electron microscopy  | 279       |
| "      | "                          | iv?                                | 3.2-3.4<br>as CN                           | 4/30 dead within a few hours   | 277       |
| "      | KCN +<br>HgCl <sub>2</sub> | "                                  | 3.2-3.4<br>as CN                           | 9/30 dead within a few hours   | 277       |
| "      | KCN                        | ip                                 | 30-35 as Hg<br>5                           | 70-72% inhibition of liver<br>cytochrome oxidase   | 57        |
| "      | "                          | "                                  | 5  | 40-50% inhibition of spleen<br>cytochrome oxidase  | 57        |
| "      | "                          | "                                  | 5.5-8                                      | Death; mortality decreased<br>by iv injection of hydroxo-<br>cobalamin   | 280       |

TABLE XIV-7 (CONTINUED)

PHYSIOLOGIC RESPONSES OF ANIMALS TO VARIOUS  
CONCENTRATIONS OF CYANIDE SALTS

| Animal | Compound Given  | Route*                   | Dose (mg/kg)               | Responses  | Reference    |
|--------|---|--------------------------|----------------------------|--|--------------|
| Mouse  | KCN   | Oral                     | 8.5                        | LD50   | 281          |
| "      | "   | "                        | 10.8                       | "  | 282          |
| "      | "   | sc                       | 12.0                       | "  | 283          |
| "      | "   | Oral                     | 15.8                       | "  | 282          |
| Pigeon | NaCN with and without various antidotes                                 | iv                       | Various multiples of LD50? | 1-6 times LD50 (3 mg/kg) survived with methemoglobin-producing agents  | 284          |
| Rabbit | KCN   | sc                       | 1-3.3                      | Increased red cell count and hemoglobin values   | 285          |
| "      | "   | im                       | 1.23 as CN                 | LD50 males   | 134,         |
| "      | "   | sc                       | 1.31 as CN                 | LD50 females   | 135,136      |
| "      | "   | im                       | 8                          | Increased tolerance with dosing  | 285          |
| "      | "   | im                       | 8                          | All dead; increased cyanide concentration in blood and nerve tissue  | 134,135, 136 |
| Rat    | KCN   | Oral (in drinking water) | 1 mg/ml                    | Reduced clearance of inhaled labeled Fe <sup>203</sup> after 5 mon of CN in water                            | 286          |
| "      | "   | ip                       | 2                          | Reversible changes in ultra-structure of heart muscle  | 287          |
| "      | KCN + NaNO <sub>2</sub> + Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub> | sc                       | 3-14                       | Cerebral changes in 10% of animals can be produced by SCN  | 288          |
| "      | KCN   | ip                       | 8                          | 70-75% inhibition of liver cytochrome oxidase  | 57           |
| "      | NaCN  | "                        | 5                          | Rapid respiratory stimulation followed by agitation, incoordination, convulsions, and cessation of breathing | 289          |
| "      | "   | "                        | 5                          | 53% inhibition of brain cytochrome oxidase   | 289          |

TABLE XIV-7 (CONTINUED)

PHYSIOLOGIC RESPONSE OF ANIMALS TO VARIOUS  
CONCENTRATIONS OF CYANIDE SALTS

| Animal | Compound Given           | Route*   | Dose (mg/kg)   | Response   | Reference |
|--------|--------------------------|----------|--|--|-----------|
| Rat    | NaCN                     | sc       | 8  | Comatose with seizures within 15 min; some died  | 290       |
| "      | KCN                      | ip       | 10   | Death within 5-15 min  | 287       |
| "      | NaCN                     | sc       | 83.3 mg/kg/day                                       | Retarded growth rate in growing rats. (Quantification of dose is suspect)  | 138       |
| "      | NaCN + NaNO <sub>2</sub> | iv or im | 6  | Survived   | 284       |
| "      | KCN                      | Oral     | 15   | 19/20, 15/20, 7/20 deaths with solution volumes corresponding to 5%, 2.5%, and 1.25% of bodyweight, respectively | 282       |
| "      | NaCN                     | sc       | 8 incremented to cumulative dose of 104.6 over 3 mon | 10/12 dead; survivors blind and ataxic with necrotic callosal and optic nerve lesions                            | 290       |
| "      | "                        | "        | 4 incremented to cumulative dose of 222.9 over 3 mon | 72/104 dead; 42/104 dead within 3 weeks; survivors blind and ataxic with callosal and optic nerve lesions        | 290       |
| "      | "                        | "        | 8 incremented to cumulative dose of 291.6 over 3 mon | 77/92 dead; 65/92 dead within 3 weeks. Survivors blind and ataxic with callosal and optic nerve lesions          | 290       |

\* Key to abbreviations:

iv - intravenous injection  
 sc - subcutaneous injection  
 im - intramuscular injection  
 ip - intraperitoneal injection

TABLE XIV-8  
HYDROGEN CYANIDE STANDARDS IN FORCE

| Country                     | Standard |      | Type*          | Reference        |
|-----------------------------|----------|------|----------------|------------------|
|                             | mg/cu m  | ppm  |                |                  |
| USA 1) Federal Standard     | 11       | 10   | TWA            | 29 CFR 1910.1000 |
| 2) ACGIH TLV                | 11       | 10   | "              | 291              |
| Bulgaria                    | 0.3      | --   | Ceiling        | 292              |
| Czechoslovakia              | 3        | 2.7  | TWA            | 262              |
|                             | 15       | 13.5 | Ceiling        | 262              |
| Finland                     | 11       | 10   | "              | 292              |
| Germany Federal Republic    | 11       | 10   | TWA            | 262              |
| Germany Democratic Republic | 5        | --   | Ceiling        | 262              |
| Great Britain               | 11       | 10   | "              | 262              |
| Hungary                     | 0.3      | --   | "              | 292              |
| Japan                       | 11       | 10   | "              | 292              |
| Poland                      | 0.3      | --   | "              | 292              |
| Romania                     | 0.3      | --   | "              | 292              |
| UAR                         | --       | 10   | "              | 292              |
| USSR                        | 0.3      | --   | "              | 292              |
| Yugoslavia                  | 11       | 10   | "              | 292              |
| USA - Florida               | --       | 10   | "              | 292              |
| - Hawaii                    | --       | 20   | "              | 292              |
| - Massachusetts             | --       | 10   | "              | 292              |
| - Mississippi               | --       | 10   | "              | 292              |
| - Pennsylvania              | --       | 10   | TWA            | 292              |
| - Pennsylvania (short)      | --       | 20   | 30-min ceiling | 292              |
| - South Carolina            | --       | 10   | Ceiling        | 292              |

\*Those specified as only MAC are assumed to be ceiling values.

TABLE XIV-9

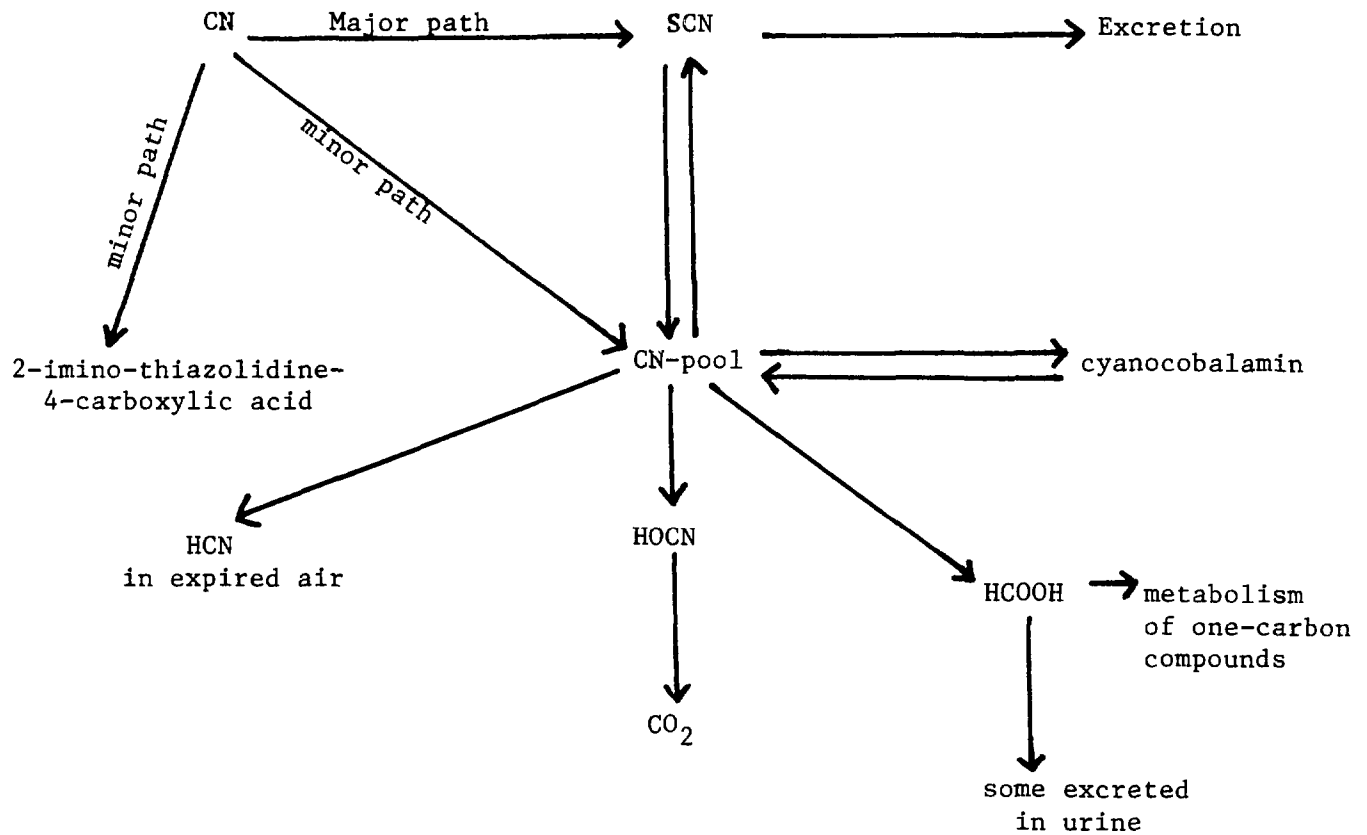
## INORGANIC CYANIDE STANDARDS IN FORCE

| Country                     | Standard |                | Reference        |
|-----------------------------|----------|----------------|------------------|
|                             | mg/cu m  | Type*          |                  |
| USA 1) Federal Standard     | 5        | TWA            | 29 CFR 1910.1000 |
| 2) ACGIH TLV                | 5        | "              | 291              |
| Bulgaria                    | 0.3      | Ceiling        | 292              |
| Czechoslovakia              | 3        | TWA            | 262              |
|                             | 15       | Ceiling        | 262              |
| Finland                     | 7        | "              | 292              |
| Federal Republic of Germany | 5        | TWA            | 292              |
| Hungary                     | 0.3      | Ceiling        | 292              |
| Poland                      | 0.3      | "              | 292              |
| Romania                     | 0.3      | "              | 292              |
| USSR                        | 0.3      | "              | 292              |
| Yugoslavia                  | 5        | "              | 292              |
| USA - Florida               | 5        | "              | 292              |
| - Massachusetts             | 5        | "              | 292              |
| - Mississippi               | 5        | "              | 292              |
| - Pennsylvania              | 5        | TWA            | 292              |
| - " (Short time limit)      | 5        | 30-min Ceiling | 292              |
| - South Carolina            | 5        | Ceiling        | 292              |

\*Those specified as only MAC are assumed to be ceiling values.



FIGURE XIV-1  
CYANIDE METABOLISM



Adapted from references 66, 67

DEPARTMENT OF  
HEALTH, EDUCATION, AND WELFARE  
PUBLIC HEALTH SERVICE

CENTER FOR DISEASE CONTROL

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

ROBERT A. TAFT LABORATORIES

4676 COLUMBIA PARKWAY CINCINNATI, OHIO 45226



POSTAGE AND FEES PAID  
U.S. DEPARTMENT OF HEALTH

HEW 369

OFFICIAL BUSINESS

PENALTY FOR PRIVATE USE, \$300