Toxicological Profile for

BENZO[b]FLUORANTHENE

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
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16. Abstract (Limit: 200 words)

The ATSDR Toxicological Profile for Benzo(b)fluoranthene is intended to characterize succinctly the toxicological and health effects information for the substance. It identifies and reviews the key literature that describes the substances's toxicological properties. Other literature is presented but described in less detail. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced. The profile begins with a public health statement, which describes in nontechnical language the substance's relevant toxicological properties. Following the statement is material that presents levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine the substance's health effects is described. Research gaps in nontoxic and health effects information are described. Research gaps that are of significance to the protection of public health will be identified in a separate effort. The focus of the document is on health and toxicological information.

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FOREWORD

The Superfund Amendments and Reauthorization Act of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law (also known as SARA) directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The list of the 100 most significant hazardous substances was published in the *Federal Register* on April 17, 1987.

Section 110 (3) of SARA directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. Each profile must include the following content:

> "(A) An examination, summary, and interpretation of available toxicological information and epidemiologic evaluations on a hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects.
>
> (B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, and chronic health effects.
>
> (C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans."

This toxicological profile is prepared in accordance with guidelines developed by ATSDR and EPA. The guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary, but no less often than every three years, as required by SARA.

The ATSDR toxicological profile is intended to characterize succinctly the toxicological and health effects information for the hazardous substance being described. Each profile identifies and reviews the key literature that describes a hazardous substance's toxicological properties. Other literature is presented but described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

Each toxicological profile begins with a public health statement, which describes in nontechnical language a substance's relevant toxicological properties. Following the statement is material that presents levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Research gaps in toxicologic and health effects information are described in the profile. Research gaps that are of significance to protection of public health will be identified by ATSDR, the National Toxicology Program of the Public Health Service, and EPA. The focus of the profiles is on health and toxicological information; therefore, we have included this information in the front of the document.

The principal audiences for the toxicological profiles are health professionals at the federal, state, and local levels, interested private sector organizations and groups, and members of the public. We plan to revise these documents in response to public comments and as additional data become available; therefore, we encourage comment that will make the toxicological profile series of the greatest use.

This profile reflects our assessment of all relevant toxicological testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, EPA, the Centers for Disease Control, and the National Toxicology Program. It has also been reviewed by a panel of nongovernment peer reviewers and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.

James O. Mason

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1. PUBLIC HEALTH STATEMENT

1.1 WHAT IS BENZO[b]FLUORANTHENE?

Benzo[b]fluoranthene (B[b]F) is one of the polycyclic aromatic hydrocarbon (PAH) compounds. Because it is formed when gasoline, garbage, or any animal or plant material burns, it is usually found in smoke and soot. This chemical combines with dust particles in the air and is carried into water and soil and onto crops. Benzo[b]fluoranthene is found in the coal tar pitch that industry uses to join electrical parts together. It is also found in creosote, a chemical used to preserve wood.

1.2 HOW MIGHT I BE EXPOSED TO BENZO[b]FLUORANTHENE?

People may be exposed to B[b]F from environmental sources such as air, water, and soil and from cigarette smoke and cooked food. Workers who handle or are involved in the manufacture of PAH-containing materials may also be exposed to B[b]F. Typically, exposure for workers and the general population is not to B[b]F alone but to a mixture of similar chemicals.

The general population may be exposed to dust, soil, and other particles that contain B[b]F. The largest sources of B[b]F in the air are open burning and home heating with wood and coal. Factories that produce coal tar also contribute small amounts of B[b]F into the air. People may come in contact with B[b]F from soil on or near hazardous waste sites, such as former gas-manufacturing sites or abandoned wood-treatment plants that used creosote. At this time, B[b]F has been found at 46 out of 1,177 sites on the National Priorities List (NPL) of hazardous waste sites in the United States. As more sites are evaluated by the Environmental Protection Agency (EPA), this number could change. The soil near areas where coal, wood, or other products have been burned is another source of exposure. Exposure to B[b]F and other PAHs may also occur through skin contact with products that contain PAHs such as creosote-treated wood, asphalt roads, or coal tar.

People may be exposed to B[b]F by drinking water from the drinking water supplies in the U.S. that have been found to contain low levels of the chemical. Foods grown in contaminated soil or air may contain B[b]F. Cooking food at high temperatures, as occurs during charcoal-grilling or charring, can increase the amount of B[b]F in the food. Benzo[b]fluoranthene has been found in cereals, vegetables, fruits, meats, beverages, and in cigarette smoke.

The greatest exposure to B[b]F is likely to take place in the workplace. People who work in coal tar production plants; coking plants; asphalt production plants; coal-gasification sites; smoke houses; municipal trash incinerators; and facilities that burn wood, coal, or

oil may be exposed to B[b]F in the workplace air. Benzo[b]fluoranthene may also be found in areas where high-temperature food fryers and broilers are used.

1.3 HOW DOES BENZO[b]FLUORANTHENE GET INTO MY BODY?

The most common way B[b]F enters the body is through the lungs when a person breathes in air or smoke containing it. It also enters the body through the digestive system when substances containing it are swallowed. Although B[b]F does not normally enter the body through the skin, small amounts could enter if contact occurs with soil that contains high levels of B[b]F (for example, near a hazardous waste site) or if contact is made with heavy oils containing B[b]F.

1.4 HOW CAN BENZO[b]FLUORANTHENE AFFECT MY HEALTH?

Benzo[b]fluoranthene causes cancer in laboratory animals when applied to their skin. This finding suggests that it is likely that people exposed in the same manner could also develop cancer.

Because studies of B[b]F are not complete, we don't know if B[b]F that is breathed in or swallowed could cause cancer or if it can cause harmful effects other than cancer.

1.5 IS THERE A MEDICAL TEST TO DETERMINE IF I HAVE BEEN EXPOSED TO BENZO[b]FLUORANTHENE?

Very few tests are available that can tell if exposure to B[b]F has taken place. In the body, B[b]F is changed to related chemical substances called metabolites. The metabolites can bind with DNA, the genetic material of the body. The body's response after exposure can be measured in the blood. However, this test is still being developed. Benzo[b]fluoranthene can also be found in the urine of individuals exposed to PAHs. It is not possible to know from these tests how much B[b]F a person was exposed to or to predict what health effects may happen at certain levels. Also, none of these tests have been used in exposure situations outside the workplace.

1.6 WHAT LEVELS OF BENZO[b]FLUORANTHENE EXPOSURE HAVE RESULTED IN HARMFUL HEALTH EFFECTS?

No information has been found about specific levels of B[b]F that have caused harmful effects in people after breathing, swallowing, or touching the substance.

Skin cancer has developed in mice that had B[b]F on their skin throughout their lives. Skin cancer is the only harmful effect that can be predicted when animals are exposed to B[b]F. It is not known if similar levels could cause cancer in people. No information has been found about harmful effects of B[b]F in animals that breathed in or ate the chemical.

1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

Based on information from another PAH chemical, the federal government has developed standards and guidelines to protect individuals from the potential health effects of PAHs, including B[b]F, in drinking water. EPA has provided estimates of levels of total cancer-causing PAHs in lakes and streams associated with various risks of developing cancer in people. EPA has also determined that any release of PAHs of more than 1 pound should be reported to the National Response Center.

Pure B[b]F is produced in the United States only as a laboratory chemical. However, B[b]F is a PAH, and PAHs are found in coal tar and in the creosote oils and pitches formed from the production of coal tar. The government's goal has been to protect workers involved with the production of coal tar products. Although government standards are not for B[b]F alone, they are useful in controlling exposure to total PAHs.

The National Institute for Occupational Safety and Health (NIOSH) has determined that workplace exposure to coal products can increase the risk of lung and skin cancer in workers and suggests a workplace exposure limit for coal tar products of 0.1 milligram of PAHs per cubic meter of air (0.1 mg/m^3) for a 10-hour workday, 40-hour workweek. NIOSH has not suggested a specific workplace limit for B[b]F. The Occupational Safety and Health Administration (OSHA) has set a legal limit of 0.2 milligram of all PAHs per cubic meter of air (0.2 mg/m^3).

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2. HEALTH EFFECTS SUMMARY

2.1 INTRODUCTION

This section summarizes and graphs data on the health effects concerning exposure to B[b]F. The purpose of this section is to present levels of significant exposure for B[b]F based on key toxicological studies, epidemiological investigations, and environmental exposure data. The information presented in this section is critically evaluated and discussed in Sect. 4, Toxicological Data, and Sect. 7, Potential for Human Exposure.

This Health Effects Summary section comprises two major parts. Levels of Significant Exposure (Sect. 2.2) presents brief narratives and graphics for key studies in a manner that provides public health officials, physicians, and other interested individuals and groups with (1) an overall perspective of the toxicology of B[b]F and (2) a summarized depiction of significant exposure levels associated with various adverse health effects. This section also includes information on the levels of B[b]F that have been monitored in human fluids and tissues and information about levels of B[b]F found in environmental media and their association with human exposures.

The significance of the exposure levels shown on the graphs may differ depending on the user's perspective. For example, physicians concerned with the interpretation of overt clinical findings in exposed persons or with the identification of persons with the potential to develop such disease may be interested in levels of exposure associated with frank effects (Frank Effect Level, FEL). Public health officials and project managers concerned with response actions at Superfund sites may want information on levels of exposure associated with more subtle effects in humans or animals (Lowest-Observed-Adverse-Effect Level, LOAEL) or exposure levels below which no adverse effects (No-Observed-Adverse-Effect Level, NOAEL) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels) are of interest to health professionals and citizens alike.

Adequacy of Database (Sect. 2.3) highlights the availability of key studies on exposure to B[b]F in the scientific literature and displays these data in three-dimensional graphs consistent with the format in Sect. 2.2. The purpose of this section is to suggest where there might be insufficient information to establish levels of significant human exposure. These areas will be considered by the Agency for Toxic Substances and Disease Registry (ATSDR), EPA, and the National Toxicology Program (NTP) of the U.S. Public Health Service in order to develop a research agenda for benzo[b]fluoranthene.

2.2 LEVELS OF SIGNIFICANT EXPOSURE

2.2.1 Key Studies and Graphical Presentations

To help public health professionals address the needs of persons living or working near hazardous waste sites, the toxicology data summarized in this section are organized first by route of exposure--inhalation, ingestion, and dermal--and then by toxicological end points that are categorized into six general areas--lethality, systemic/target organ toxicity, developmental toxicity, reproductive toxicity, genetic toxicity, and carcinogenicity. The data are discussed in terms of three exposure periods--acute, intermediate, and chronic.

Two kinds of graphs are used to depict the data. The first type is a "thermometer" graph. It provides a graphical summary of the human and animal toxicological end points and levels of exposure for each exposure route for which data are available. The ordering of effects does not reflect the exposure duration or species of animal tested. The second kind of graph shows Levels of Significant Exposure (LSE) for each route and exposure duration. The points on the graph showing NOAELs and LOAELs reflect the actual dose (levels of exposure) used in the key studies. No adjustments for exposure duration or intermittent exposure protocol were made.

Adjustments reflecting the uncertainty of extrapolating animal data to man, intraspecies variations, and differences between experimental versus actual human exposure conditions were considered when estimates of levels posing minimal risk to human health were made for noncancer end points. These minimal risk levels were derived for the most sensitive noncancer end point for each exposure duration by applying uncertainty factors. These levels are shown on the graphs as a broken line starting from the actual dose (level of exposure) and ending with a concave-curved line at its terminus. Although methods have been established to derive these minimal risk levels (Barnes et al. 1987), shortcomings in the techniques reduce the confidence in the projected estimates. Also shown on the graphs under the cancer end point are low-level risks (10^{-4} to 10^{-7}) reported by EPA if available. In addition, the actual dose (level of exposure) associated with tumor incidence is plotted.

2.2.1.1 Inhalation

No information was found in the available literature concerning the effects of B[b]F following inhalation exposure.

Lethality and decreased longevity. No information is available.

Systemic toxicity. No information is available.

Developmental toxicity. No information is available.

Reproductive toxicity. No information is available.

Genotoxicity. No information is available.

Carcinogenicity. No reports directly correlating inhalation exposure to B[b]F and cancer induction in humans are available, although reports of cancer among individuals exposed to mixtures of PAHs

containing B[b]F lend qualitative support to its potential for carcinogenicity in humans. No inhalation experiments in animals are available, although B[b]F has elicited respiratory tract tumors in rats following intratracheal instillation.

2.2.1.2 Oral

No information was found in the available literature concerning the effects of B[b]F following oral exposure.

Lethality and decreased longevity. No information is available.

Systemic toxicity. No information is available.

Developmental toxicity. No information is available.

Reproductive toxicity. No information is available.

Genotoxicity. No information is available.

Carcinogenicity. No information is available.

2.2.1.3 Dermal

No information is available on the effects of B[b]F following short-term dermal exposure.

B[b]F has been shown to be carcinogenic following intermediate-term dermal exposure. This conclusion is based on observations of experimental animals because no data are available for human exposure; results are summarized in Figs. 2.1 and 2.2.

Lethality and decreased longevity. No information is available.

Systemic toxicity. No information is available.

Developmental toxicity. No information is available.

Reproductive toxicity. No information is available.

Genotoxicity. No information is available.

Carcinogenicity. No information directly correlating human dermal exposure to B[b]F and cancer induction is available, although reports of skin tumors among individuals exposed to mixtures of PAHs containing B[b]F lend some qualitative support to its potential for human carcinogenicity. The contribution of B[b]F to the overall carcinogenicity of the mixtures is not known.

Studies in experimental animals have demonstrated the ability of B[b]F to induce skin tumors following intermediate-term dermal exposure. Mice receiving a dose of 2.9 mg/kg (equivalent to an average daily dose of 1.2 mg/kg) and larger applied to their skin three times weekly developed an excess of malignant skin tumors following exposure for up to 1 year (Wynder and Hoffmann 1959). No estimate of human risk has been calculated based on the results of this study.

2.2.2 Biological Monitoring

The available biological monitoring techniques can be useful in predicting whether exposure to B[b]F or other PAHs has occurred, but they may not be useful in estimating body doses. Individual variability,

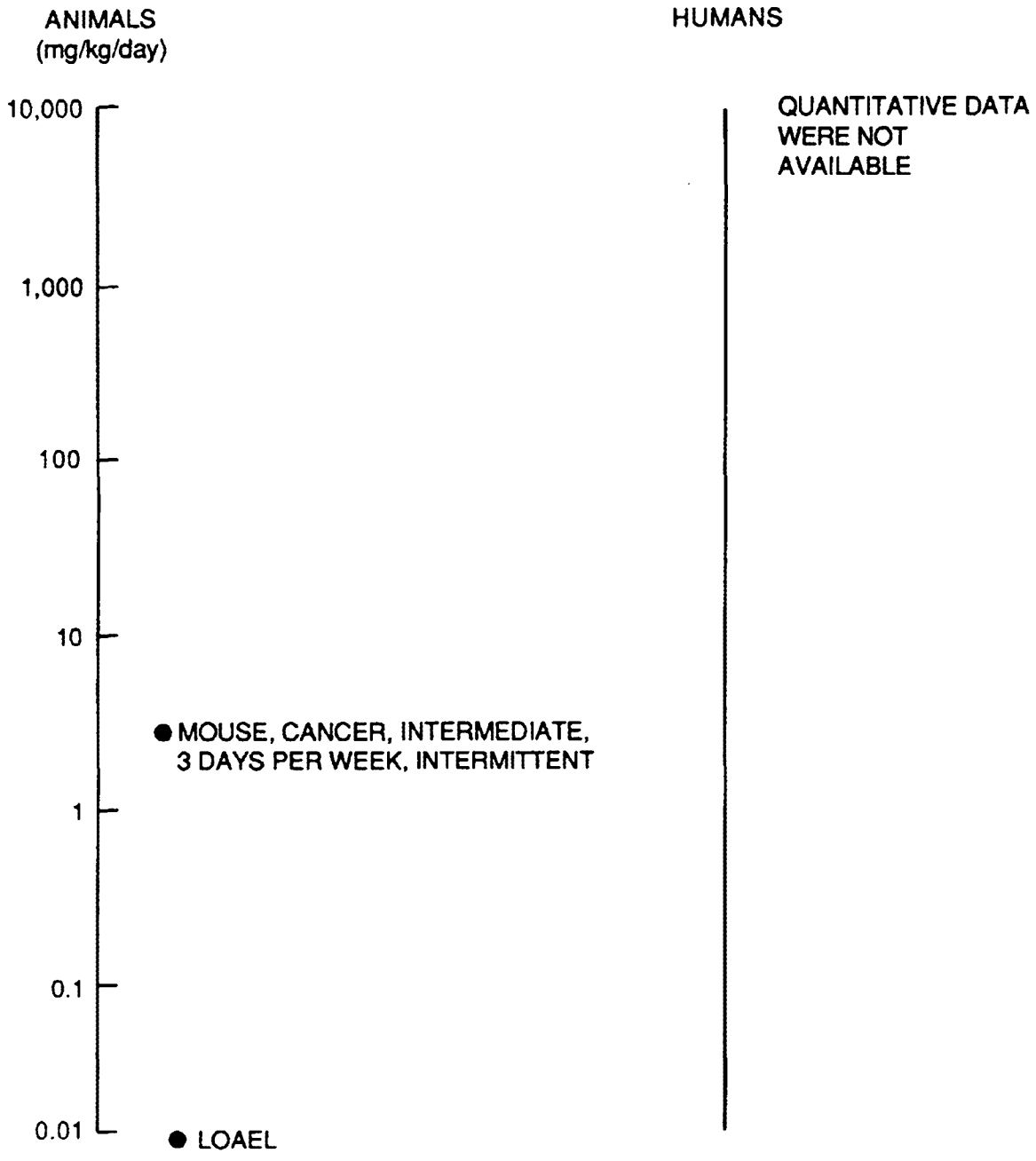


Fig. 2.1. Effects of benzo[b]fluoranthene—dermal exposure.

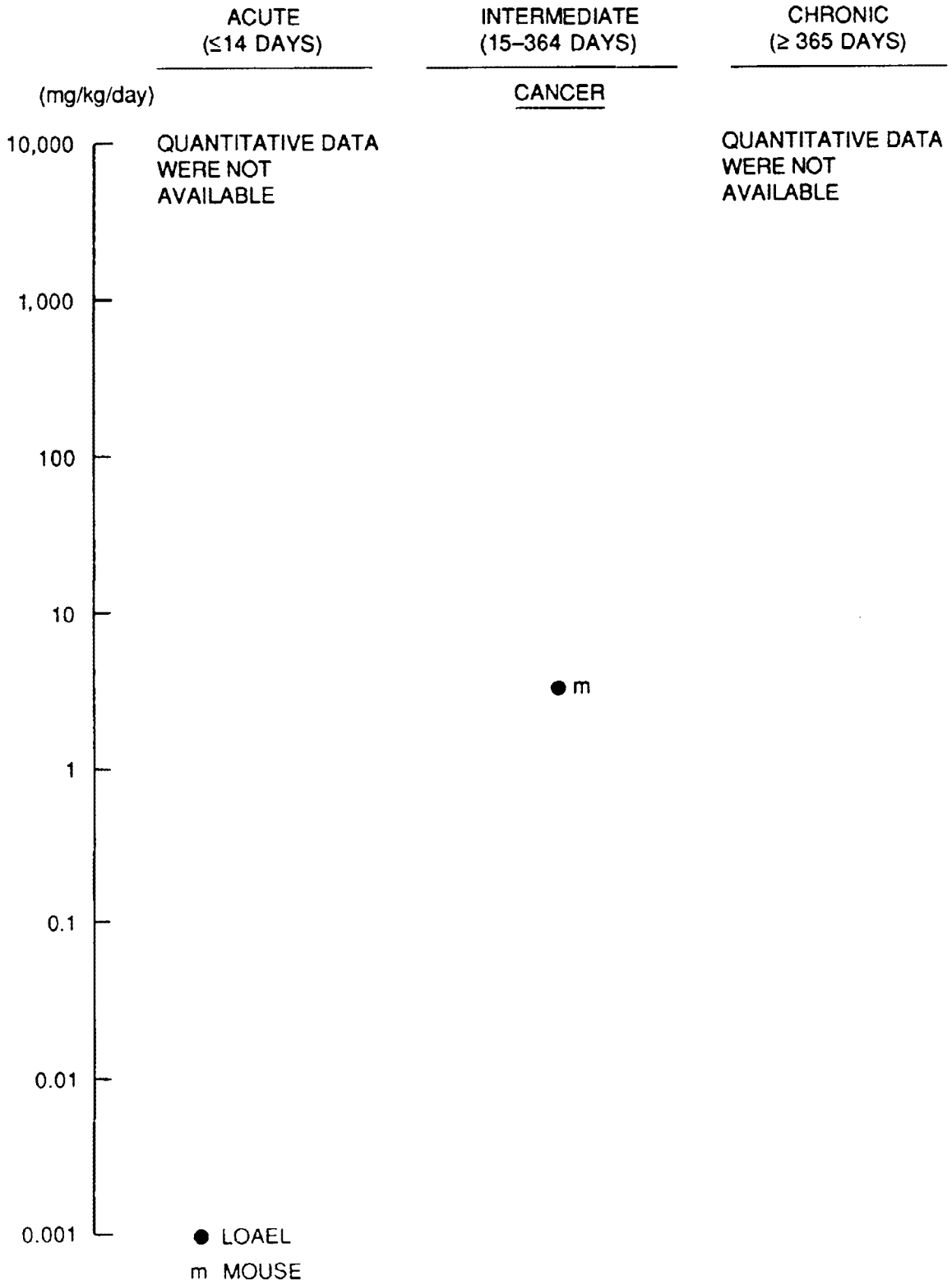


Fig. 2.2. Levels of significant exposure for benzo[b]fluoranthene—dermal.

confounding effects of drugs, and the specificity of the techniques are likely to complicate the association between B[b]F metabolites in the body and environmental exposure. The most common tests for determining exposure to PAHs include examination of tissues, blood, and urine for the presence of PAHs or PAH metabolites. Currently available biological monitoring techniques are discussed in detail in Sect. 8, Analytical Methods.

Modica et al. (1982) and Bartosek et al. (1984) used gas-liquid chromatography to determine the presence of PAHs in the blood, mammary and adipose tissue, liver, and brain of rats. However, no examples of examination of human tissue samples using this method were found in the available literature.

In the body, B[b]F can be converted by specific cellular enzymes (cytochrome 450 monooxygenase system and epoxide hydrolase) to a dihydrodiol and further metabolized to epoxides or dihydrodiols that can bind to DNA and form DNA adducts (Geddie et al. 1984). In the ^{32}P postlabeling technique, a tissue sample is taken from an exposed individual, and DNA from the exposed cells is digested and labeled with radioactive phosphorus (^{32}P). Thin-layer chromatography is then used to determine the presence of altered DNA, and scintillation counting is used to quantify the adducts (Randerath et al. 1985; Randerath et al. 1986; Weyand et al. 1987a,b). Although the structures of the B[b]F-DNA adducts are not known, structural analogs of potential B[b]F-DNA adducts have been synthesized and examined using high-performance liquid chromatography (Amin et al. 1985b). A technique using immunoassays (Harris 1985a,b; Harris et al. 1986) has been developed that tests for the presence of antibodies to the PAH-DNA adducts in human blood. A patent application has been submitted for a method and kit for detecting antibodies in human sera to diol epoxide-DNA adducts by immunoassay (Harris 1985b). This method has been used to examine exposure to benzo[a]pyrene and other PAHs.

PAHs have been detected in the urine of individuals occupationally exposed to atmospheric PAHs, in smokers, and in individuals treated with therapeutical coal tar for psoriasis (Becher and Bjorseth 1983, Becher et al. 1984, Becher 1986, Clonfero et al. 1986).

A recently developed biological monitoring technique using an antibody-based fiberoptics biosensor to detect PAHs has been tested. This technique has been investigated in sample solutions containing benzo[a]pyrene and may be useful for assessing an individual's exposure to other PAHs provided appropriate antibodies are used (Vo-Dinh et al. 1987).

2.2.3 Environmental Levels as Indicators of Exposure and Effects

2.2.3.1 Levels found in the environment

B[b]F has been detected in the environment, but the information available to characterize background exposures is inadequate. B[b]F air concentrations in U.S. cities have been reported in the range of 0.09 to 1.8 ng/m^3 (Gordon and Bryan 1973). B[b]F concentrations in finished drinking waters of the United States have been reported to be <2 ng/L

(Sorrell et al. 1981). No data are available on B[b]F levels in U.S. soil, but concentrations of total PAHs, including B[b]F, have been reported in the range of 4 to 13 mg/kg in relatively rural areas of the United States (summarized by Blumer et al. 1977).

B[b]F may occur in the soil and on particulate matter in the air surrounding waste sites, such as former manufactured-gas plants and creosote wood treatment plants. However, exposure levels at these sites have not yet been published.

Data are not available which relate environmental levels of B[b]F to significant health effects in humans following exposures.

2.2.3.2 Human exposure potential

Humans may be exposed to B[b]F in air, water, soil, and food. Each of these media constitutes a normal route of background exposure in the nonoccupational environment. Background exposures to B[b]F are expected to be at low levels. Much higher exposure concentrations are associated with tobacco smoke and with some occupational environments. At hazardous waste sites, exposure concentrations may also be higher, and humans may be exposed to B[b]F via contact with soil or inhalation of particulate matter in air. Estimates of body doses or tissue levels associated with B[b]F intake require (1) information on the chemical concentrations in soil and air, (2) certain assumptions about factors controlling intake, and (3) information on absorption of B[b]F from soil or particulate matter.

Information on the first two of these data needs is relatively site-specific and cannot be generalized. Quantitative toxicological information on the absorption of B[b]F and other PAHs from soil or particulate matter is limited, although absorption is expected to be low (Becher et al. 1984). Consequently, estimates of dose following exposure to B[b]F in soil or air are based on limited toxicological and epidemiological data and on assumptions regarding dermal absorption of B[b]F from soil and absorption of incidentally ingested B[b]F on soil or inhaled B[b]F on particulate matter. These assumptions lend uncertainty to any risk assessment of potential health effects following environmental exposures.

2.3 ADEQUACY OF DATABASE

2.3.1 Introduction

Section 110 (3) of SARA directs the Administrator of ATSDR to prepare a toxicological profile for each of the 100 most significant hazardous substances found at facilities on the CERCLA National Priorities List. Each profile must include the following content:

"(A) An examination, summary, and interpretation of available toxicological information and epidemiologic evaluations on a hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects.

(B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, and chronic health effects.

(C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans."

This section identifies gaps in current knowledge relevant to developing levels of significant exposure for B[b]F. Such gaps are identified for certain health effect end points (lethality, systemic/target organ toxicity, developmental toxicity, reproductive toxicity, and carcinogenicity) reviewed in Sect. 2.2 of this profile in developing levels of significant exposure for B[b]F, and for other areas such as human biological monitoring and mechanisms of toxicity. The present section briefly summarizes the availability of existing human and animal data, identifies data gaps, and summarizes research in progress that may fill such gaps.

Specific research programs for obtaining data needed to develop levels of significant exposure for B[b]F will be developed in the future by ATSDR, NTP, and EPA.

2.3.2 Health Effect End Points

2.3.2.1 Introduction and graphic summary

The availability of data for health effects in humans and animals is depicted on bar graphs in Figs. 2.3 and 2.4, respectively.

The bars of full height indicate that there are data to meet at least one of the following criteria:

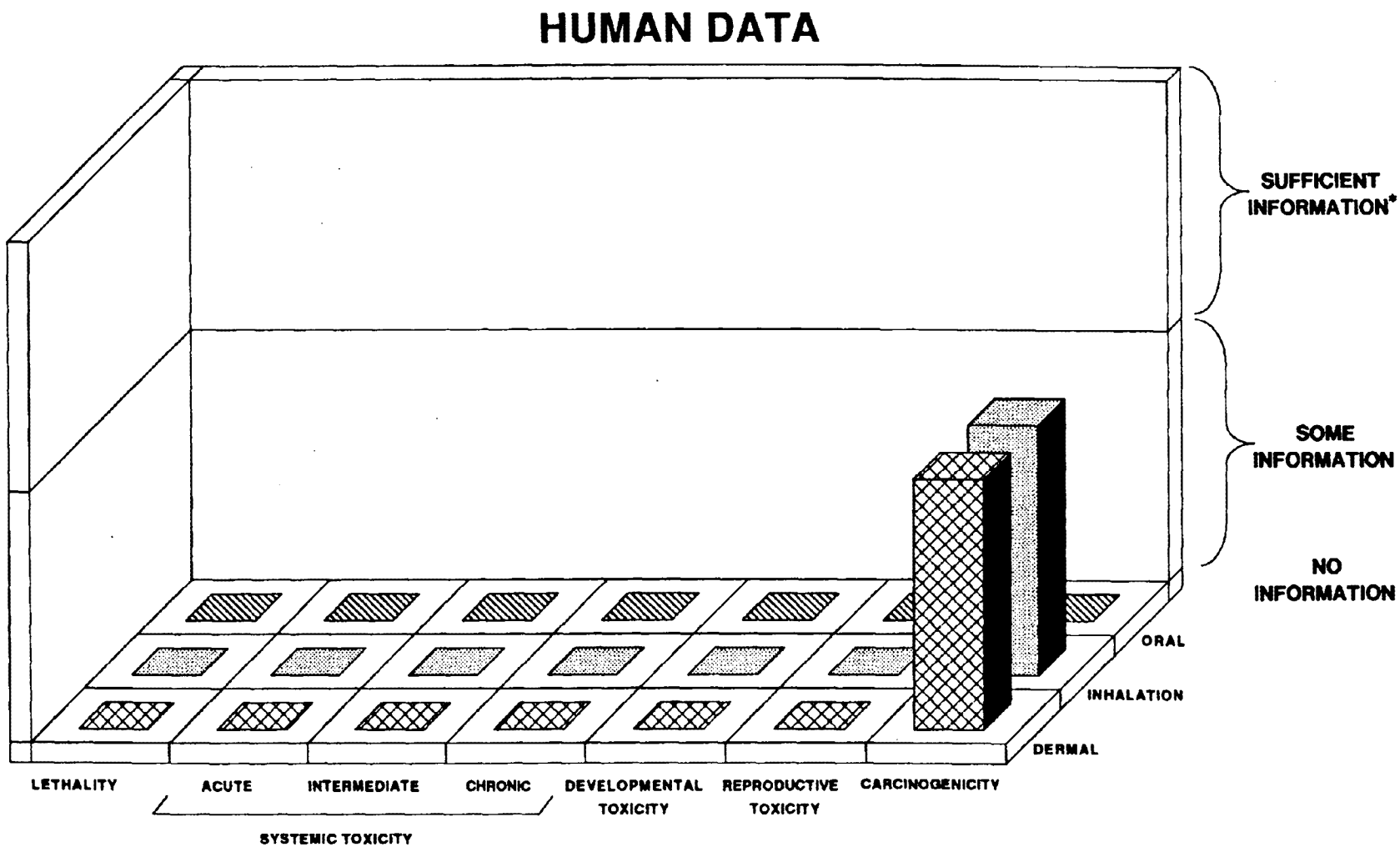
1. For noncancer health end points, one or more studies are available that meet current scientific standards and are sufficient to define a range of toxicity from no-effect levels (NOAELs) to levels that cause effects (LOAELs or FELs). For human carcinogenicity, a substance is classified as either a "known human carcinogen" or a "probable human carcinogen" by both EPA and the International Agency for Research on Cancer (IARC) (qualitative), and the data are sufficient to derive a cancer potency factor (quantitative).

2. For animal carcinogenicity, a substance causes a statistically significant number of tumors in at least one species, and the data are sufficient to derive a cancer potency factor.

3. There are studies which show that the chemical does not cause this health effect via this exposure route.

Bars of half height indicate that "some" information for the end point exists, but does not meet any of these criteria.

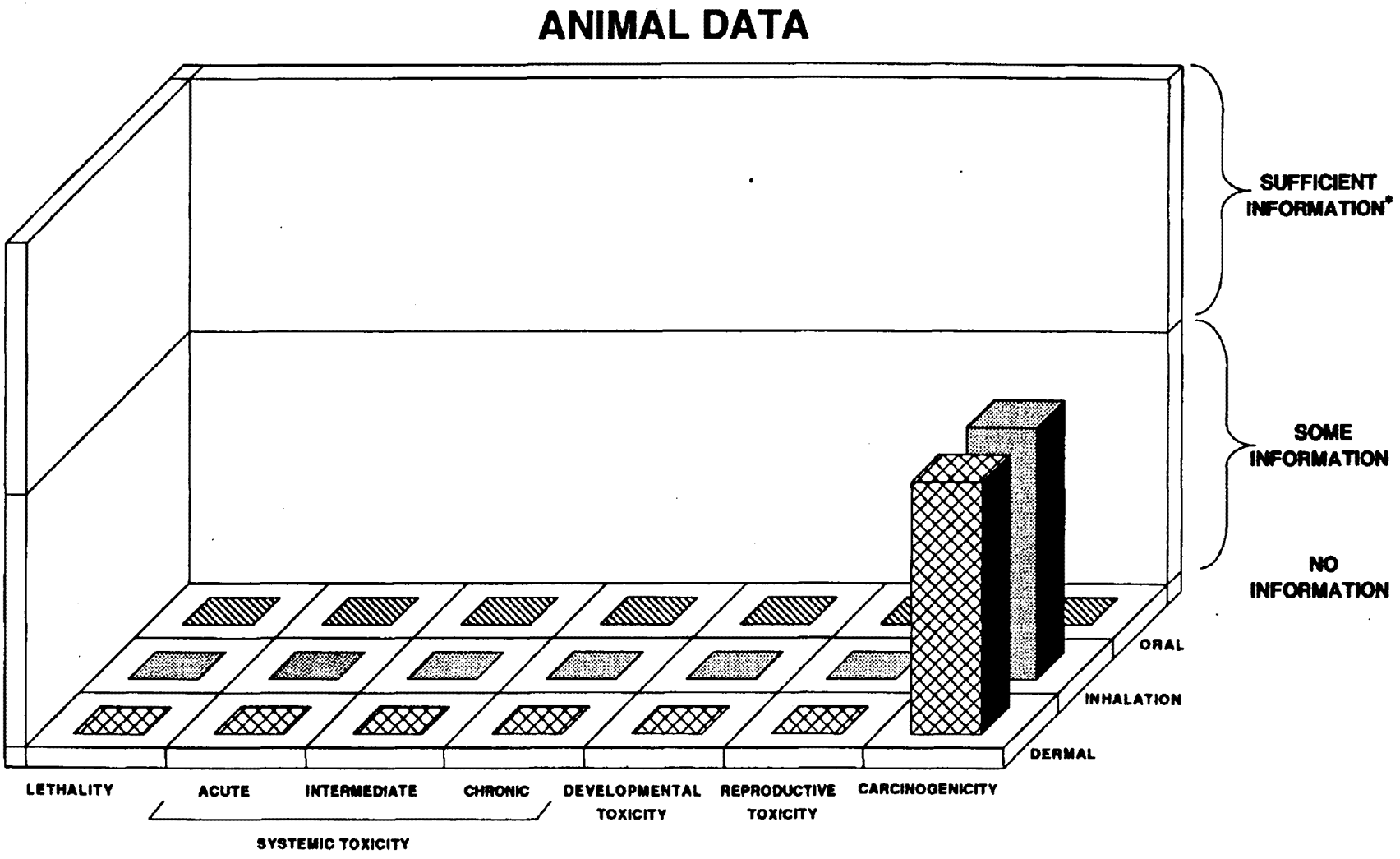
The absence of a column indicates that no information exists for that end point and route.



*Sufficient information exists to meet at least one of the criteria for cancer or noncancer end points.

Note: The adequacy of the database for the carcinogenicity of benzo[b]fluoranthene by the inhalation and dermal routes of exposure has been assessed on the basis of human exposure to complex mixtures of chemicals containing this compound, not on the basis of the compound alone.

Fig. 2.3. Availability of information on health effects of benzo[b]fluoranthene (human data).



*Sufficient information exists to meet at least one of the criteria for cancer or noncancer end points.

Note: The adequacy of the database for the carcinogenicity of benzo[b]fluoranthene by the inhalation route of exposure has been assessed on the basis of intratracheal instillation experiments using rats, in the absence of inhalation data.

Fig. 2.4. Availability of information on health effects of benzo[b]fluoranthene (animal data).

2.3.2.2 Description of highlights of graphs

Fig. 2.3 indicates that there are no data available to assess significant exposure levels of B[b]F alone for humans. Reports of adverse health effects such as carcinogenicity by the inhalation and dermal routes of exposure do exist for mixtures of chemicals that include B[b]F, thus providing some information to qualitatively assess the role of B[b]F as a human carcinogen.

As displayed in Fig. 2.4, some data are available in animals to assess only the dermal and inhalation carcinogenicity of B[b]F; however, in the absence of inhalation data, the latter are based on intratracheal instillation experiments. No information could be found on the effects of B[b]F following oral or inhalation exposure.

2.3.2.3 Summary of relevant ongoing research

Research is ongoing in the areas of the molecular dosimetry of B[b]F, as well as into its biological mechanisms of action such as those of DNA binding and repair. B[b]F has been listed in both the *National Toxicology Program (NTP) Fiscal Year 1986 Annual Plan* and the *NTP Review of Current DHHS, DOE, and EPA Research Related to Toxicology*. (DHHS is the acronym for the Department of Health and Human Services; DOE is the acronym for the Department of Energy.) This chemical is being tested in *Salmonella* (status C: test started in February 1986) for mutagenesis/genetic toxicity by the National Institute of Environmental Health Sciences. A comparative potency method to quantitatively assess the carcinogenic effects for PAHs is under development by the Carcinogen Assessment Group, the Office of Solid Waste, the Office of Drinking Water, and the Office of Air Quality Planning and Standards of the EPA (EPA Contract Number 68-02-4403) and is being applied to the data available for B[b]F.

2.3.3 Other Information Needed for Human Health Assessment

2.3.3.1 Toxicokinetics and mechanisms of action

There is no specific information available on the absorption, tissue distribution, and excretion of B[b]F in animals and humans.

There is limited information on the metabolism of B[b]F. Metabolic data on B[b]F have been derived from mouse skin and in vitro hepatic preparations. A clear mechanistic picture of the steps involved in the metabolic activation of B[b]F is lacking. The literature on B[b]F suggests that this hydrocarbon is the subject of active research in the area of metabolism.

2.3.3.2 Adequacy of data on biological monitoring

Many of the biological monitoring techniques have not been used to examine exposure to B[b]F specifically. Additional research should be focused on using these tests to examine exposure to other PAHs.

The biological monitoring techniques by which DNA adducts are quantified are limited because inborn factors, environmental chemistry, and drugs can alter the activity of the enzymes responsible for converting PAHs to the dihydrodiols or epoxides that bind to DNA. There

is limited information concerning the use of these techniques in occupationally or environmentally exposed individuals. Additional research should include further investigation of the formation of adducts following these exposure situations.

The technique that uses immunoassays to determine the presence of antibodies to adducts in blood has been tested in occupationally exposed humans and smokers (Harris 1985b, Harris et al. 1986). This technique has shown an association between sera positive for antibodies and occupational exposure or smoking. The reliability of this method needs to be further examined in other, nonoccupational, exposure situations.

The presence of PAHs or PAH metabolites in urine is an indication that exposure has occurred. However, in occupational studies, the amount of PAH concentrated in the urine did not adequately reflect environmental PAH concentrations (Becher and Bjorseth 1983, Becher et al. 1984, Becher 1986). The lack of a direct quantitative relationship may be the result of the nonbioavailability of particle-bound PAHs; therefore, this method should be further examined for its applicability in other exposure situations (Becher et al. 1984).

In addition, some occupationally related activities and cigarette smoking result in human exposure to PAHs; therefore, the determination of biological levels of PAHs in smokers and in the general population must be examined more fully to properly assess environmental exposure.

2.3.3.3 Environmental considerations

The accuracy and precision of the analytical methods used to measure ambient B[b]F are somewhat limited; but the current methods, if properly conducted, are sufficient to record ambient levels of B[b]F. However, some methods have limited sensitivity.

Inadequate data are available to characterize background levels of B[b]F and other PAHs, or levels typically found at hazardous waste sites. Comprehensive monitoring studies are being conducted by EPA at and around many hazardous waste sites, but the data are not yet available in a single database.

No quantitative data are available on the bioavailability of B[b]F in soil or sorbed onto particulate matter in air. This lack of information limits our understanding of potential health risks in humans following exposure to these media.

Information on the fate of B[b]F sorbed onto particulate matter in air is presently unclear. The role of photochemical oxidation in the removal of B[b]F from air needs to be elucidated. Also, additional information on biodegradation processes and rates in aquatic and terrestrial systems is needed.

Inadequate information is available on the interactions of B[b]F with other chemicals typically found in the environment and at hazardous waste sites. Consequently, risks associated with exposure to B[b]F in the environment are not completely understood.

3. CHEMICAL AND PHYSICAL INFORMATION

3.1 CHEMICAL IDENTITY

The chemical formula, structure, synonyms, and identification numbers for B[b]F are listed in Table 3.1.

3.2 PHYSICAL AND CHEMICAL PROPERTIES

Important physical and chemical properties of B[b]F are given in Table 3.2.

Table 3.1. Chemical identity of benzo[b]fluoranthene

Chemical name: Benzo[b]fluoranthene

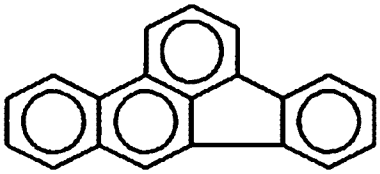
Synonyms: 3,4-benzofluoranthene; benz[e]acephenanthrylene; 2,3-benzfluoranthrene; 2,3-benzofluoranthene; 2,3-benzofluoranthrene; 3,4-benzfluoranthene; benzo[e]fluoranthene; B[b]F (IARC 1983)[a]

Trade name: Not applicable

Chemical formula: $C_{20}H_{12}$ (IARC 1983)

Wiswesser line notation: L C65 K666 1A TJ (HSDB 1987)

Chemical structure:



Identification numbers:

CAS Registry No.: 205-99-2
NIOSH RTECS No.: CU1400000
EPA Hazardous Waste No.: Not available
OHM-TADS No.: Not available
DOT/UN/NA/IMCO Shipping No.: Not available
STCC No.: Not available
Hazardous Substances Data Bank No.: 4035
National Cancer Institute No.: Not available

[a]Confusion exists in the literature concerning the naming of this compound, mainly because two different systems (Richter and IUPAC) of numbering ring structures have been used; the IARC reference, unfortunately, does not acknowledge that this confusion exists and that the nomenclature of some of the synonyms listed is incorrect.

Table 3.2. Physical and chemical properties of benzo[b]fluoranthene

Property	Value	Reference
Molecular weight	252.32 g/mol	IARC 1983
Color	Colorless	IARC 1983
Physical state	Needles (recrystallized from benzene)	CRC 1987
Odor	Unknown	
Melting point	167–168°C	CRC 1987
Boiling point	Unknown	
Autoignition temperature	Unknown	
Solubility		
Water	14 μg/L	EPA 1982
Organic solvents	Slightly soluble in benzene and acetone	IARC 1983
Biological fluids	Unknown	
Density	Unknown	
Partition coefficients		
Octanol-water (K_{ow})	1.15×10^6	EPA 1982
log K_{ow}	6.06	
Soil-organic carbon-water (K_{oc})	5.5×10^5	EPA 1982
Vapor pressure (20°C)	5×10^{-7} mm Hg	EPA 1982
Henry's law constant	1.22×10^{-5}	EPA 1982
Flash point	Unknown	
Flammability limits	Unknown	
Conversion factor (in air)[a]	1 ppm = 10.32 mg/m^3	Verschueren 1983

[a]Calculated using the ideal gas law, $PV = nRT$ at 25°C.

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4. TOXICOLOGICAL DATA

4.1 OVERVIEW

No data on the absorption, distribution, or excretion of B[b]F were identified. Evidence of dermal absorption in animals is found in skin carcinogenicity studies conducted with B[b]F. B[b]F is metabolized under in vitro incubation conditions to phenol and dihydrodiol metabolites.

B[b]F is thought to be metabolized to reactive derivatives other than diol epoxides that may be responsible for its mutagenic activity in experimental systems, although it is a weak mutagen. B[b]F is a weak experimental dermal carcinogen (compared to benzo[a]pyrene). Its carcinogenicity has not been studied by the inhalation or oral routes of exposure, although it is active following intratracheal instillation. Mutation is thought to be a necessary (albeit insufficient) step for the carcinogenic activity of B[b]F.

There is no information on other toxic effects of B[b]F in humans and experimental animals following inhalation, oral, or dermal exposures. Carcinogenic PAHs as a group, however, cause skin disorders and have an immunosupressive effect.

4.2 TOXICOKINETICS

4.2.1 Overview

No data on the absorption, distribution, or excretion of B[b]F were identified. Evidence of dermal absorption in animals is found in skin carcinogenicity studies conducted with B[b]F. B[b]F is metabolized under in vitro incubation conditions to phenol and dihydrodiol metabolites. No evidence for formation of bay-region diol epoxide metabolites or their corresponding dihydrodiol precursor intermediates was obtained under in vitro conditions. Under in vivo conditions, dihydrodiol metabolites have been identified, but only one has shown tumor-initiating activity comparable to that of B[b]F. The metabolic activation of B[b]F to a reactive intermediate is therefore thought to occur primarily via metabolites other than diol epoxides in a departure from the pathways established for benzo[a]pyrene and other carcinogenic PAHs with bay-region systems.

4.2.2 Absorption

4.2.2.1 Inhalation

Human. No information on the absorption of B[b]F via the respiratory tract was found. Absorption of B[b]F via this route may be

inferred from the identification of metabolites in individuals exposed to PAHs in an industrial environment (Becher and Bjorseth 1983).

Animal. No information was found on the absorption of B[b]F via the respiratory tract. By analogy to benzo[a]pyrene, pulmonary absorption of B[b]F is expected to be efficient and to be subject to similar controlling factors; specifically, the role of metabolism in absorption mechanisms (Kao et al. 1985), particle size matrix effects, and mucociliary clearance is anticipated to influence the rate of absorption via the respiratory tract (Creasia et al. 1976, Tornquist et al. 1985, Medinsky and Kampcik 1985).

4.2.2.2 Oral

Human. No data on the absorption of B[b]F via the gastrointestinal tract in humans were identified.

Animal. No data on the absorption of B[b]F via the gastrointestinal tract in animals were identified.

4.2.2.3 Dermal

Human. No data on the dermal absorption of B[b]F in humans were identified. The rate of dermal penetration of B[b]F may be expected to be reasonably close to that of benzo[a]pyrene. For the latter, under in vitro conditions, 3% of an applied dose of [^{14}C]benzo[a]pyrene (10 $\mu g/cm^2$) permeated human skin in 24 h (Kao et al. 1985).

Animal. No quantitative data on the dermal absorption of B[b]F in animals were identified. Evidence of dermal absorption in animals is found in skin carcinogenicity studies conducted with B[b]F (Amin et al. 1985a, IARC 1973).

4.2.3 Distribution

No data on the distribution of absorbed B[b]F were identified.

4.2.4 Metabolism

The metabolism of B[b]F has been investigated in vitro using hepatic S9 preparations (Amin et al. 1982). The general biotransformation pathways established for benzo[a]pyrene are also active on B[b]F (Cooper et al. 1983, Levin et al. 1982, Grover 1986) (see Fig. 4.1).

The metabolites isolated under the above conditions consisted of phenols and dihydrodiols. The major phenolic metabolites were identified as the 5-, 6-, and 4- or 7-hydroxy B[b]F. The predominant diol formed was the *trans*-11,12-dihydrodiol B[b]F, accompanied by smaller amounts of *trans*-1,2,-dihydrodiol B[b]F (Amin et al. 1982). No evidence was obtained to indicate the formation of *trans*-9,10-dihydrodiol B[b]F. The latter would be a precursor to a bay-region diol epoxide, a metabolite class implicated in the carcinogenic activity of other PAHs (Sims 1982, Thakker et al. 1985). Although the evidence is not conclusive at this point, it is possible that the reactive metabolites associated with the tumorigenic effects of B[b]F are not diol epoxides (Amin et al. 1982, Amin et al. 1985a).

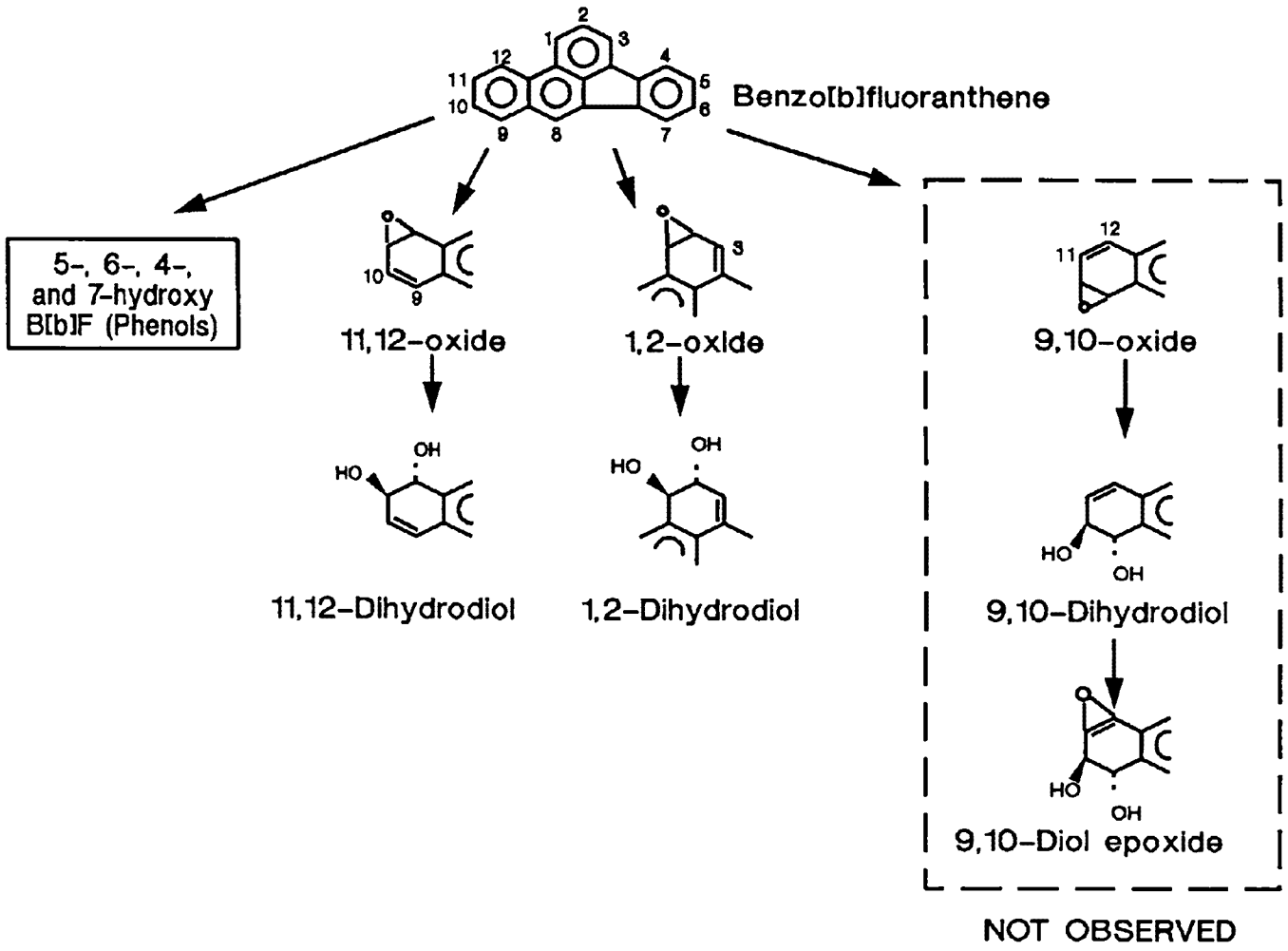

Fig. 4.1. Metabolic fate of benzo[b]fluoranthene.

4.2.5 Excretion

The steps involved in the excretion of B[b]F are likely to be those established for other PAHs. Metabolism, hepatobiliary excretion, and elimination through feces are the dominant features in this process (Schlede et al. 1970). As for other PAHs, the material excreted is expected to consist predominantly of dihydrodiol and phenol conjugates (e.g., glucuronide and sulfate esters) and glutathione conjugates (Grover 1986).

4.3 TOXICITY

4.3.1 Lethality and Decreased Longevity

Pertinent data regarding lethality and decreased longevity in humans or experimental animals following inhalation, oral, and dermal exposure to B[b]F could not be found in the available literature.

4.3.2 Systemic/Target Organ Toxicity

No information is available on the systemic effects of B[b]F in humans or experimental animals following inhalation, oral, and dermal exposures. The carcinogenic PAHs as a group cause skin disorders and have an immunosuppressive effect; however, specific effects of B[b]F have not been reported.

4.3.3 Reproductive and Developmental Toxicity

Pertinent data regarding the reproductive and developmental toxicity of B[b]F in humans or experimental animals following inhalation, oral, and dermal exposure could not be found in the available literature.

4.3.4 Genotoxicity

4.3.4.1 Overview

The genetic toxicity of B[b]F has been evaluated experimentally in a limited number of short-term bioassays utilizing two bacterial cell strains and a mammalian cell system as target organisms. The test systems used to evaluate the genotoxicity of B[b]F and the results obtained are summarized in Table 4.1.

4.3.4.2 General discussion

The genotoxicity of B[b]F has been demonstrated equivocally in three in vitro studies. B[b]F showed mutagenic activity in *Salmonella typhimurium* in the presence of an exogenous rat-liver preparation (LaVoie et al. 1979b). Some mutagenic activity was also reported by Hermann (1981) in a similar study, but negative results were reported by Mossanda et al. (1979). The data in these studies are inadequate to support a positive or negative determination for B[b]F mutagenicity. These studies cannot be used as primary evidence for B[b]F mutagenic activity. In the one available in vivo study, B[b]F exposure resulted in

Table 4.1. Genetic toxicity of benzo[b]fluoranthene

End points	Species (test systems)	Result[a]	References
Gene mutation (in vitro)	*Salmonella typhimurium* TA100 (his+/his−)	Positive-activation	LaVoie et al. 1979b
	Salmonella typhimurium TA98 (his+/his−)	Equivocal-activation	Hermann 1981
	Salmonella typhimurium TA98, TA100 (his+/his−)	Negative-activation	Mossanda et al. 1979
Sister chromatid exchange (in vivo)	Chinese hamster bone marrow cells	Positive	Roszinsky-Kocher et al. 1979
Chromosomal aberration (in vivo)	Chinese hamster bone marrow cells	Negative	Roszinsky-Kocher et al. 1979

[a]The results presented in Table 4.1 are based on activity profiles prepared by Waters et al. (1987), Gene-Tox data files supplied by John S. Wassom, and/or personal review of the original citation.

a weak induction of sister chromatid exchange (SCE) but no significant induction of chromosomal aberrations in Chinese hamster bone marrow cells (Roszinsky-Kocher et al. 1979). The SCE results are, at best, weakly or marginally positive, but the data are insufficient to assess the negative determination for chromosomal aberrations because no indices of toxicity are given (Roszinsky-Kocher et al. 1979).

There is inadequate evidence that B[b]F is active in short-term genetic assays. Further studies are needed in order to evaluate the genotoxic potential of B[b]F.

4.3.5 Carcinogenicity

4.3.5.1 Overview

The carcinogenicity of B[b]F has not been adequately studied. There are no reports directly correlating human B[b]F exposure and tumor development, although humans are likely to be exposed by all routes. There are a number of reports, however, associating human cancer with exposure to mixtures of PAHs that include B[b]F. There is experimental evidence that B[b]F is a skin carcinogen in animals following dermal application and a lung carcinogen following intratracheal instillation. It is likely that B[b]F would cause cancer in humans as well.

4.3.5.2 Inhalation

Human. No studies on the carcinogenicity of B[b]F in humans following inhalation exposure were found in the available literature. However, epidemiologic studies have shown an increased incidence of lung cancer in humans exposed to coke-oven emissions (Lloyd 1971, Redmond et al. 1972, Mazumdar et al. 1975), roofing tar emissions (Hammond et al. 1976), and cigarette smoke (Wynder and Hoffmann 1967, Maclure and MacMahon 1980, Schottenfeld and Fraumeni 1982). Each of these mixtures contains B[b]F as well as other carcinogenic PAHs and other potentially carcinogenic chemicals such as nitrosamines. It is thus impossible to evaluate the contribution of B[b]F to the total human carcinogenicity of these mixtures because of their complexity and the presence of other carcinogens. Reports of this nature nonetheless provide a qualitative suggestion of the potential for B[b]F-induced carcinogenicity.

Animal. No studies on the carcinogenicity of B[b]F in animals following inhalation exposure were found in the available literature. However, B[b]F has been shown to cause respiratory tract tumors in rats following intratracheal instillation (Deutsch-Wenzel et al. 1983). In this experiment, B[b]F was prepared in solution with trioctanoin and molten beeswax and injected into the left lobe of the lungs of female Osborne-Mendel rats. The mixture congealed into a pellet from which the test compound diffused over time into the surrounding tissue. Doses of 0, 0.1, 0.3, or 1.0 mg B[b]F were administered, eliciting 0/35, 1/35, 3/35, or 13/35 lung-tumor-bearing animals per group, respectively. Tumors were epidermoid carcinomas or pleomorphic sarcomas. This experiment indicates that B[b]F is a moderately active respiratory tract carcinogen.

4.3.5.3 Oral

Human. No studies on the carcinogenicity of B[b]F in humans following oral exposure were found in the available literature.

Animal. No studies on the carcinogenicity of B[b]F in animals following oral exposure were found in the available literature.

4.3.5.4 Dermal

Human. No studies on the carcinogenicity of B[b]F in humans following dermal exposure were found in the available literature. As with inhalation exposure, however, there are reports of skin cancer among individuals exposed dermally to mixtures of PAHs containing B[b]F. The earliest of these is the report of Pott (1775) of scrotal cancer among chimney sweeps. More recently, skin cancer among those exposed dermally to shale oils has been reported (Purde and Etlin 1980). These reports provide only qualitative suggestions pertaining to the human carcinogenic potential of B[b]F, however, because of the presence of other putative carcinogens in the mixtures.

Animal. B[b]F has been shown to cause skin tumors in mice following dermal application. The results of a key study by Wynder and Hoffmann (1959) are shown in Table 4.2. As part of a study of the carcinogenicity of tobacco and its constituents, these authors tested the benzofluoranthenes as carcinogens on mouse skin. Groups of 20 female Swiss mice had concentrations of 0.01, 0.1, or 0.5% B[b]F dissolved in acetone applied three times a week to their backs with a brush throughout their lifetimes. No solvent control group was reported; however, since no papillomas or carcinomas were obtained for several of the benzofluoranthenes tested, a solvent control group would most likely have been negative as well. A dose-response relationship for the dermal carcinogenicity of B[b]F was demonstrated over an order-of-magnitude dose range. Survival was also dose related. Although this study was designed as a long-term (chronic) bioassay, malignant tumors appeared as early as 4 months in the high-dose group and 5 months in the intermediate-dose group. As a result, this study is considered to provide evidence that B[b]F is carcinogenic following intermediate-term exposure. The lowest dose at which B[b]F elicited malignant tumors was 0.1%, which is approximately equal to a dose of 2.9 mg/kg received three times weekly, or an average daily dose of 1.2 mg/kg. This study had a number of weaknesses, including no reporting of compound purity and no statistical treatment.

The skin-tumor-initiating ability of B[b]F has also been demonstrated in mice using a standard initiation/promotion protocol with either croton oil or phorbol myristate acetate as a tumor promoter (Amin et al. 1985a; LaVoie et al. 1979a, 1982).

4.3.5.5 General discussion

The only end point of toxicity that has been established for B[b]F using routes of exposure that can be extrapolated to human environmental exposures is dermal carcinogenicity. There is evidence that intratracheal instillation in rats (Deutsch-Wenzel et al. 1983), intraperitoneal injection in newborn mice (LaVoie et al. 1987), and

Table 4.2. Carcinogenic activity of benzo[b]fluoranthene on mouse skin

Dose[a] (% concentration)	Dose (mg/kg/day)	Number with tumors/ effective number (%)	
		Papillomas	Carcinomas
0.01	0.12	1/20 (5)	0/20 (0)
0.1	1.2	13/19 (68)	17/19 (89)
0.5	6.0	20/20 (100)	18/20 (90)

[a]Solutions of B[b]F in 100 μL acetone were applied three times weekly to the backs of female Swiss mice throughout their lifetimes.

Source: Wynder and Hoffmann 1959.

subcutaneous injection in mice (Lacassagne et al. 1963) can lead to tumor formation as well. The mechanism of B[b]F-induced carcinogenicity appears to be somewhat different from that of other PAHs, involving metabolic activation to reactive metabolites other than bay-region diol epoxides that may form adducts with DNA that lead to mutation and tumor initiation under certain circumstances (IARC 1983).

4.4 INTERACTIONS WITH OTHER CHEMICALS

Most human exposures to B[b]F are not to the pure compound but to particle-bound B[b]F; the presence of particles is likely to affect its pharmacokinetics and carcinogenicity. Sun et al. (1982) showed that when the carcinogenic polycyclic aromatic hydrocarbon benzo[a]pyrene was particle-bound, it was cleared from hamster lungs much more slowly than a pure B[a]P aerosol, thus increasing the length of time the lungs were exposed and increasing the dose to the gastrointestinal tract as a result of mucociliary clearance. Respirable PAH-containing particulates such as diesel exhaust, when coated with the phospholipid component of a pulmonary surfactant, are genotoxic (Wallace et al. 1987). Dusts can increase the rates of pulmonary cell proliferation (Harris et al. 1971, Stenback et al. 1976, Stenback and Rowland 1979), which in turn increases the susceptibility of those cells to an initiation event in the presence of a carcinogen. Coadministration of B[a]P and particles greatly increases respiratory tract tumor yields in experimental animals (Stenback et al. 1976, Stenback and Rowland 1979). The effects of particles on potential B[b]F carcinogenesis is likely to be similar.

Human exposure to B[b]F in the environment seldom, if ever, occurs to B[b]F alone, but rather to B[b]F as a component of complex mixtures of PAHs and other chemicals. Interactions between B[b]F and other mixture components are likely to occur. In particular, interactions may play a large part in carcinogenesis resulting from experimental exposure to PAHs. For example, Mahlum et al. (1984) have shown that different temperature range distillates of coal liquids have different skin-tumor-initiating activities in mice despite the fact that they contain similar levels of known carcinogenic PAHs. This difference is believed to be due to the modifying effects of the spectrum of noncarcinogenic PAHs obtained at different temperatures. Most of the PAH components of coal liquid fractions obtained at different temperatures will vary both qualitatively and quantitatively; consequently, their abilities to modify carcinogenesis will vary accordingly. The relative roles of the PAH components of each of such mixtures is unknown, however, so that quantitative evaluation is not possible. Because human exposure occurs to mixtures of PAHs and not individual components, the quantitative evaluation of the toxicity of individual PAHs is probably insufficient.

Human exposure to complex mixtures of PAHs has been extensive, and some adverse effects are well-documented, particularly carcinogenic effects following long-term exposure. The extent of human exposures to well-defined PAH mixtures that are responsible for producing excess disease is generally not known in quantitative terms. Coke-oven emissions and related substances such as coal tar have probably been the most widely studied. Coal tar derivatives were most likely responsible for the first observation of occupational cancer, that of scrotal cancer among London chimney sweeps, made by Percival Pott in 1775. More recent

mortality studies have demonstrated strong associations between human exposure to coke-oven emissions and excess disease; specifically, significant increases in lung and genitourinary cancer mortality have been observed (IARC 1983). The earliest of these reports was made in 1936 by investigators in Japan and England (Kennaway and Kennaway 1936) who were studying lung cancer mortality among persons employed in coal carbonization and gasification processes. Subsequent studies conducted in the United States clearly demonstrated substantial increases in lung and genitourinary system cancer mortality among coke-oven workers (Lloyd 1971, Redmond et al. 1972, IARC 1984). Human tumorigenicity has also been reported to result from exposure to creosote. Creosote is a generic term that refers to wood preservatives derived from coal tar, creosote, or coal tar neutral oil, and includes extremely complex mixtures of liquid and solid aromatic hydrocarbons. Workers who engaged in activities such as dipping timbers in creosote were reported to have developed malignant and pre-malignant skin lesions of the face, arms, and scrotum (O'Donovan 1920, Cookson 1924, Henry 1947, Lenson 1956). Many of the individual PAH components of creosote, such as B[b]F, have been shown to be both mutagenic and carcinogenic in laboratory bioassays, supporting the evidence of its human carcinogenicity (IARC 1983).

Exposures to many other complex chemical mixtures that include PAHs have been associated with human disease incidence, such as the use of tobacco products and exposure to roofing tar emissions and shale oils. Although this discussion falls short of providing a thorough review of the extensive literature available on the experimental and epidemiological observations of the toxicity of PAH mixtures, its purpose has been to provide examples wherein such toxicity has been documented in order to emphasize that human exposure to multiple PAHs does occur.

Predicting the toxicity of a complex mixture on the basis of one or several of its components may be misleading because of the possibility of interactions among the components that may modify toxicity. For example, both carcinogenic and noncarcinogenic PAHs may compete for the same metabolic activating enzymes and thereby reduce the toxicity of carcinogenic PAHs. Exposure to other PAHs may induce enzyme levels leading to more rapid detoxification of B[b]F, thus reducing its carcinogenicity (Slaga and diGiovanni 1984, Weibel 1980). Naturally occurring compounds have been found to induce the enzymes that metabolize PAHs, leading to either increased or decreased toxicity. For example, plant flavonoids can induce microsomal monooxygenases and reduce the carcinogenicity of B[b]F (Weibel 1980). Environmental contaminants such as tetrachlorodibenzo-p-dioxin can also increase microsomal enzyme activity and consequently affect PAH toxicity (Kouri et al. 1978). Interactions can thus play important modulating roles in PAH toxicity that may not be adequately reflected in the identification of significant human exposure levels based on the toxicity of single PAHs, because human exposure to mixtures of PAHs does occur.

5. MANUFACTURE, IMPORT, USE, AND DISPOSAL

5.1 OVERVIEW

B[b]F occurs in fossil fuels and as a result of the incomplete combustion of fuel and wood and other organic matter. B[b]F is available as a research chemical from some specialty chemical firms. B[b]F is a PAH and may be found in coal tar and in the creosote oils and pitches formed from the distillation of coal tars. Coal tar pitch is primarily used as a binder for electrodes. Creosote is primarily used as a wood preservative. Coal tar is also used as a therapeutical treatment for skin diseases such as psoriasis. PAHs are also found in limited amounts in bitumens and asphalt.

5.2 PRODUCTION

The primary source of B[b]F in air is the incomplete combustion of fuel or wood for heating (EPA 1985).

Crude coal tar is produced as a by-product in the formation of coke from coal. Hot gases and vapors released from the conversion of coal to coke are collected in a scrubber that condenses these gases into ammonia, water, crude tar, and other by-products. A typical coke oven produces 80% coke, 12% coke-oven gas, 3% coal tar, and 1% crude benzene. The coal tar is then distilled to yield a number of chemical oils, creosote, and coal tar pitch. The coal tar pitch residue is 40.5% of the crude tar; creosote is ~11.5%. Heavy and light creosote also make up a small percentage of distillate (NIOSH 1977). Coal tar contains ~0.3% B[b]F (IARC 1985).

As of 1981, the world output of crude coal tar was 18×10^6 metric tons; 14×10^6 metric tons was of coke-oven origin. In 1980, the U.S. production of crude tar was 2.4×10^6 metric tons. Creosote oil production in the United States in 1981 was estimated to be 0.5×10^{-6} metric tons. The coal tar pitch production in the United States in 1974 was estimated to be 1×10^6 metric tons (McNeil 1983).

Bitumens and asphalt (a mixture of bitumen with mineral materials) are derived from crude oil. Bitumen samples have been reported to contain a number of PAHs (IARC 1985).

5.3 IMPORT

In 1985, the United States imported a total of almost 12×10^6 gal of creosote oil from the Netherlands, France, West Germany, and other countries and almost 185×10^6 lb of coal tar pitch, blast furnace tar, and oil-gas tar from Canada, Mexico, West Germany, Asian countries, Australia, and other countries (USDOC 1986).

5.4 USE

B[b]F has some use as a research chemical. It is available from some specialty chemical firms in low quantities (25-100 mg) (Aldrich Chemical Co. 1986).

Coal tar pitch is primarily used as a binder for electrodes in the aluminum reduction process; it is used to bind the carbon electrodes used in the reduction pots (NIOSH 1977). In North America, coal tar pitch is also used as the adhesive in membrane roofs (McNeil 1983).

Almost 99% of the creosote produced is sold to wood preservation plants; 0.1 to 0.2% is sold to individual customers (NIOSH 1977). Creosote is used in the preservation of railroad ties, marine pilings, and telephone and telegraph poles. Some creosote is also consumed as fuel by steel producers (NIOSH 1977).

Coal tar is also used in the clinical treatment of skin disorders such as eczema, dermatitis, and psoriasis. The use of dermatological coal tar preparations is extensive (NIOSH 1977).

Bitumens and asphalt are primarily used for paving roads, in waterproofing and roofing, for electrical and sound insulation, and for pipe coating (IARC 1985).

5.5 DISPOSAL

In 1978, following the release of small amounts of B[b]F present in coal tar creosote, a 0.39-mg/L concentration of B[b]F was found in aqueous raw discharges from timber product industries (EPA 1985).

6. ENVIRONMENTAL FATE

6.1 OVERVIEW

B[b]F in the environment is derived from both natural (e.g., wildfires, volcanoes) and man-made sources, but B[b]F originating from man-made sources is quantitatively the most significant. B[b]F, like all PAHs, is formed during high-temperature pyrolytic processes. Consequently, combustion is the major source of environmental B[b]F. Virtually all direct releases of B[b]F into the environment are to the air. Small amounts are released to water and land. B[b]F is removed from the atmosphere by photochemical oxidation and dry or wet deposition to land or water. B[b]F that reaches the surface will likely remain and be partitioned primarily to soil/sediment, where it is very persistent. The dominant degradation process for B[b]F in soil/sediment is most likely biodegradation. Biodegradation is a slow process, with a half-life of 610 days estimated for B[b]F in soil.

6.2 RELEASES TO THE ENVIRONMENT

Incomplete combustion of carbonaceous material is the major source of B[b]F in the environment. Residential heating and open burning (man-induced and natural) are the largest combustion sources. The large quantity of B[b]F released by these sources is a consequence of inefficient combustion processes and uncontrolled emissions. Of all home heating sources, wood heating is the greatest contributor to B[b]F emissions. In a recent assessment of B[b]F sources and release volumes across the United States, EPA (1985) estimated that home wood combustion contributed 92 metric tons, or 43% of all released volumes. Open-burning sources overall are responsible for 100 metric tons, or 47% of the total B[b]F releases; prescribed burning is responsible for 50 metric tons of that total, wildfire for 30 metric tons, and agricultural burning for 20 metric tons. Small amounts of B[b]F are likely formed and released into the environment during coal tar production and use and during gasoline and diesel fuel combustion. Also, PAH-containing products such as creosote-treated wood and asphalt roads may release small amounts of B[b]F and other PAHs into the environment. These other sources individually are estimated to contribute 1% or less to total B[b]F releases.

Ninety-seven percent of all estimated environmental releases of B[b]F are to air. Of the remaining 3%, approximately equal amounts of B[b]F are released to water and land.

Although they are the source of small amounts of B[b]F and other PAHs on a national scale, hazardous waste sites can be concentrated sources of PAHs on a local scale. For example, abandoned wood treatment plants are sources of high concentrations of creosote, and former

manufactured-gas plants (town gas sites) are sources of high concentrations of coal tar. Both creosote and coal tar are composed of a variety of PAHs, including B[b]F. PAHs at these sites are likely to occur on the soil and on suspended particulate matter in the air.

6.3 ENVIRONMENTAL FATE

Few data are available which describe the environmental fate of B[b]F specifically, and much of the understanding of the fate of B[b]F is based upon analogy to benz[a]anthracene (B[a]A), benzo[a]pyrene (B[a]P), and PAHs in general. The discussion below is based primarily on these generalizations. Fate information specific to B[b]F is identified when available.

The environmental fate of B[b]F is determined to a large degree by the chemical's low water solubility and high propensity for binding to particulate or organic matter. As a result, B[b]F in the atmosphere is expected to be associated primarily with particulate matter, especially soot, whereas most of the B[b]F in aquatic systems is expected to be strongly bound to suspended particles or bed sediments. Likewise, B[b]F will be strongly sorbed to surface soils. The dispersion of particle-bound B[b]F is the primary transport process within air, water, and land.

Based upon an analogy to benzo[a]pyrene, the dry deposition of particle-bound B[b]F is probably the most significant transport process between air and land or water (EPA 1979), although wet deposition is known to occur (Den Hollander et al. 1986). Because of a very low vapor pressure, B[b]F that reaches the surface will likely remain and be partitioned primarily to soils/sediments. Sediment/particle adsorption or biotic uptake are the primary transport processes for the removal of waterborne B[b]F. Desorption into water from soil is very unlikely, and erosion of contaminated soils by surface runoff is the most probable process for transport of soil-bound B[b]F to aquatic systems.

Information on the fate of particulate PAHs, including B[b]F, released to the atmosphere is presently unclear. It is generally assumed, however, that photochemical oxidation processes play an important role. Atmospheric half-lives on the order of days have been suggested (NAS 1972). PAHs strongly absorb solar radiation at wavelengths above 300 nm, and there is sufficient evidence to indicate that PAHs undergo photooxidation in solution, as pure solids, and when adsorbed onto certain solid substrates such as alumina (NAS 1972). Singlet oxygen has been implicated as the primary oxidant; endoperoxides and, ultimately, quinones have been implicated as the reaction products (NAS 1972).

It has been inferred that similar processes take place when the compounds are adsorbed on airborne particles. Kamens et al. (1986) reported that B[b]F and other PAHs adsorbed on soot particles rapidly decayed in the presence of sunlight. However, photooxidation of PAHs adsorbed on carbon black particles was extremely slow (Barofsky and Baum 1976). Similarly, Korfmacher et al. (1980a,b) found that benzo[a]pyrene and other PAHs adsorbed on fly ash are highly resistant to photodegradation. More research is needed to elucidate the rate and substrate dependency of atmospheric B[b]F degradation.

Data collected by Smith et al. (1978) indicate that within aquatic systems, most PAHs accumulate in the sediment and are transported with suspended sediment. PAHs in the water column also accumulate in aquatic organisms. However, many organisms metabolize and excrete PAHs rapidly; therefore, bioaccumulation is a short-term process. For example, in bluegill sunfish, an 89% loss of B[a]P was recorded 4 h after exposure (Leversee et al. 1981). Lee et al. (1972) reported rapid elimination of B[a]P in three species of California marine teleosts. Depuration rates in invertebrate species vary more widely. Some species, such as hard-shell clams, show little or no depuration, whereas others, such as many oysters, eliminate virtually all PAHs following exposure (Eisler 1987).

Aquatic organisms can also assimilate PAHs from food. For example, crustaceans and fish have been reported to readily assimilate PAHs from contaminated food (Eisler 1987). However, in many cases where assimilation of PAHs has been demonstrated, metabolism and excretion of PAHs were rapid (Eisler 1987). In laboratory aquatic ecosystem studies in which radiolabeled B[a]P was used, Lu et al. (1977) found that high levels of B[a]P can be accumulated through the food in the mosquito fish. After 3 days of exposure, the intact parent compound comprised over 50% of the extractable radiolabeled carbon in fish. However, after 33 days of exposure, the intact parent compound comprised only 7% of the total extractable radiolabeled carbon, indicating metabolism of B[a]P. The tendency of fish to metabolize PAHs may explain why PAHs are frequently undetected, or only detected in low concentrations in the livers of fish from environments heavily contaminated with PAHs.

A minimal amount of PAHs is dissolved in the water column and degraded rapidly by direct photolysis. Smith et al. (1978) calculated a half-life of 1.2 h for midday direct photolysis of dissolved B[a]P. Chemical oxidation may be a significant fate process for B[b]F in water when chlorine or ozone (both oxidants) exist in sufficient concentrations (EPA 1979).

The major fate of sediment-bound PAHs, including B[b]F, is most likely biodegradation (EPA 1979). In general, biodegradation processes are quite slow; a half-life of 7,000 h has been reported for benz[a]anthracene (EPA 1979), and it is possible that the degradation rate for B[b]F is similar. Biodegradation half-lives in contaminated streams can be 10 to 400 times longer. These long half-lives indicate that PAHs are relatively persistent in sediments and aquatic systems.

Within terrestrial systems, biodegradation is also the probable fate process. Since this process is very slow, B[b]F is very persistent in soils. Coover and Sims (1987) estimated a half-life of B[b]F in soil of 610 days.

At hazardous waste sites, half-lives may be longer, because other contaminants present at the site may be toxic to the degrading microorganism. Bossert and Bartha (1986) reported reduced biodegradation of PAHs in soil containing a chemical toxic to microorganisms.

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7. POTENTIAL FOR HUMAN EXPOSURE

7.1 OVERVIEW

As the previous discussions indicate, the greatest portion of B[b]F releases to the environment is directly into the atmosphere. Consequently, inhalation is one of the primary routes of background human exposure to B[b]F in the environment. Part of the B[b]F in the atmosphere returns to the surface via dry and wet deposition. This input leads to B[b]F in soil and water to which humans may be exposed. Humans may also be exposed to B[b]F in food, tobacco smoke, and certain occupational settings, and through contact with PAH-containing products such as coal tar, asphalt, and creosote-treated wood. At hazardous waste sites, humans most likely will be exposed to B[b]F in the soil and on particulate matter in the air. At this time, B[b]F has been found at 46 of the 1,177 hazardous waste sites on the National Priorities List (NPL) in the United States (View 1989).

7.2 LEVELS MONITORED IN THE ENVIRONMENT

7.2.1 Air

Very few data are available to characterize B[b]F levels in air, and estimates of ambient concentrations are limited to two relatively outdated monitoring studies in Los Angeles and a report of average concentrations in U.S. cities in 1958. Consequently, definitive statements about average background exposure levels cannot be made. In the most recent monitoring study, Gordon (1976) reported ambient B[b]F concentrations in Los Angeles County to range between 0.24 and 1.30 ng/m^3. Gordon and Bryan (1973) reported levels in the range of 0.09 to 1.8 ng/m^3 in Los Angeles County during the years 1971-1972. Hoffmann and Wynder (1976) summarized data on B[b]F levels across U.S. cities in 1958 and reported concentrations in the range of 2.3 to 7.4 ng/m^3.

7.2.2 Water

B[b]F has been detected in raw and finished drinking waters in the United States, but minimal data limit the degree to which background levels can be adequately characterized. Sorrell et al. (1981) reported B[b]F concentrations between 4 and 16 ng/L in raw water and less than 2 ng/L in finished drinking water. These data were based on a very small sample (10 cities) and may not be representative of drinking water concentrations in the United States.

Because of a high propensity to bind to organic matter, it is unlikely that B[b]F will occur to any appreciable extent in surface water or groundwater at hazardous waste sites or other sites.

7.2.3 Soil

No data are available on B[b]F levels in U.S. soils. However, Blumer et al. (1977) summarized information that indicated concentrations of total PAHs to be between 4 and 13 mg/kg in the soil from relatively rural areas of the eastern United States. Soil levels in more populated and industrialized areas may be higher. Butler et al. (1984) examined soil PAH levels in Switzerland and demonstrated that much higher soil PAH concentrations are found near complex road interchanges than in areas more distant. Also, the soils at waste sites, such as former manufactured-gas sites and creosote wood treatment plants, may contain high levels of PAHs, including B[b]F.

7.2.4 Food

Data on B[b]F levels in food are limited, primarily because the substance is not one of the PAHs commonly analyzed in food. However, B[b]F has been detected in vegetables and fruits grown in PAH-contaminated soil near areas of high vehicular traffic (Wang and Meresz 1982). Thus, the possible consumption of food grown in contaminated soil near hazardous waste sites, industrial areas, or highways may contribute to human exposure.

Humans may also be exposed to B[b]F and other PAHs in aquatic organisms that are typical components of the diet. Specifically, PAHs have been detected in bivalve mollusks (i.e., clams, oysters, mussels), crabs, and lobsters (Eisler 1987). PAHs have also been detected in fish; however, levels in fish are usually low, because this group rapidly metabolizes PAHs.

7.2.5 Cigarette Smoke

B[b]F has been reported to occur in cigarette mainstream smoke at between 4 and 22 ng per cigarette (IARC 1983). Concentrations in sidestream smoke may potentially be higher, because levels 2 to 4 times higher than those in mainstream smoke have been reported for other PAHs (DHHS 1986).

Today there is an increasing concern regarding indoor air pollution by environmental tobacco smoke. A report by the U.S. Surgeon General (DHHS 1986) concluded that environmental tobacco smoke can be a substantial contributor to the concentration of respirable particles of indoor air pollution. These higher concentrations of sidestream smoke constitutents, such as B[b]F, in conjunction with the fact that many people spend many hours in indoor polluted atmospheres, may lead to increased health risks to individuals passively exposed to cigarette smoke.

7.3 OCCUPATIONAL EXPOSURES

PAHs, such as B[b]F, have been isolated in numerous occupational situations, including coal-tar production and coking plants, coal gasification sites, smokehouses, aluminum production plants, bitumen and asphalt production plants, coal-tarring activities, and around municipal incinerators. Within these environments, B[b]F and other PAHs occur as a complex mixture; thus, exposure to B[b]F alone does not occur.

Historically, the highest level of human exposure to PAHs has occurred in industrial situations. B[b]F and other PAHs have been detected in the occupational environments of coke production plants, aluminum reduction plants, and coal gasification plants in the United States (IARC 1984). B[b]F and other benzofluoranthenes have been detected at a level of 140 $\mu g/g$ at the top of a fixed-bed gasifier of a U.S. coal gasification plant (IARC 1984). Concentrations of benzo[a]pyrene (often used as an indicator of total PAH concentration) have been reported to range from 0.8 to 23.1 $\mu g/m^3$ in the workroom air of coke-oven operations in the United Kingdom (Davies et al. 1986). Similarly, high values have been reported by Lindstedt and Solenberg (1982) in Swedish industries.

7.4 POPULATIONS AT HIGH RISK

At highest risk for cancer induced by PAHs are those people who are exposed to high levels of PAHs. Examples of high-risk populations include workers in certain occupations that have elevated PAH concentrations in the ambient work environment; smokers and involuntary (passive) smokers who receive elevated PAH intake via tobacco smoke; and populations living near industries, such as creosote and coal tar manufacturers, that generate PAHs as a by-product of production.

Individuals in these high-exposure groups may have varying susceptibility to PAH toxicity. Some of the available data on PAH carcinogenicity suggest a relationship between aryl hydrocarbon hydroxylase (AHH) activity and cancer risk. Genetic variation in AHH inducibility has been implicated as a determining factor for susceptibility to lung and laryngeal cancer (EPA 1980). Attempts have been made to demonstrate that persons with lung cancer have higher inducibility of AHH in cultured lymphocytes. A review by Calabrese (1984) indicates that several studies support this hypothesis, and some genetic data indicate that the human population can be segregated based on this trait (EPA 1980). Thus, individuals that are AHH-inducible may constitute a high-risk population. However, the data regarding genetic susceptibility are not yet conclusive.

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8. ANALYTICAL METHODS

8.1 ENVIRONMENTAL SAMPLES

The procedures used to sample and extract B[b]F in different media are very similar. In air and tobacco smoke, PAHs, including B[b]F, are adsorbed predominantly on particulate matter, which is collected on a filter. In water and soil, PAHs are extracted directly without filtration.

The extraction of PAHs from the filter can be accomplished by a variety of techniques with or without solvents. The following extraction techniques are most commonly used: soxhlet, sublimation at elevated temperatures, ultrasonic, and polytron extractions (Sawicki 1976).

A cleanup step is necessary to separate B[b]F and PAHs from other pollutants. Typically, this step involves liquid-liquid extraction of the dry organic particulate extract, followed by adsorption chromatography using silica gel or alumina columns (Sawicki 1976, Riggin and Strup 1984). These adsorbents selectively remove interfering compounds. Thin-layer chromatography (TLC) can also be used as a cleanup method (Sawicki 1976).

The most commonly used analytical methods for determining B[b]F in environmental samples are column gas chromatography (GC) and high-performance liquid chromatography (HPLC). Table 8.1 summarizes common analytical methods, detection limits, and accuracy (percent recovery) for the determination of B[b]F in air, water, soil, and food.

GC is an analytical technique in which components of a sample are separated by differential distribution between a gaseous mobile phase and a solid or liquid stationary phase (EPA 1983). Following separation in the GC column, sample components are identified and quantified by a detection system such as flame ionization detection (FID) or mass spectrometry (MS). These techniques are described in detail in NIOSH (1984) and EPA (1983, 1984a).

HPLC is an analytical method in which components are separated based on their polarity (EPA 1983). Reverse-phase HPLC, which is used more widely for the analysis of PAHs, uses a nonpolar stationary phase and a polar mobile phase; hydrophilic components are eluted earlier than hydrophobic components. The detection systems most appropriate for HPLC analysis of PAHs are UV absorption spectroscopy and fluorescence spectroscopy (FS). FS is useful for extremely dilute solutions; therefore, pretreatment by concentration and cleanup of the sample before HPLC is not necessary (Das and Thomas 1978).

Table 8.1. Methods for analysis of benzo[b]fluoranthene in environmental media

Media	Sample preparation	Analytical method[a]	Detection limit	Accuracy[b]	References
Air	Ultrasonic extraction with cyclohexane	HPLC	3 ng/m^3 (1500-m^3 sample)	95%	NIOSH 1984 (Method 5506)
	Ultrasonic extraction with benzene, pentane, or dichloromethane	HPLC/FS	10 pg	NA	Andersson et al. 1983
	Soxhlet extraction with benzene-methanol	GC/MS	0.05 ng/m^3	NA	Matsumoto and Kashimoto 1985
	Extraction with solvent	GC/MS	NA	NA	NIOSH 1984 (Method 5515)
Water	Extraction with methylene chloride	HPLC/FS	0.018 μg/L	Approx. 78%[c]	EPA 1984a (Method 610)
		UV	4 μg/L	76-135%	Riggin and Strup 1984
	Extraction with methylene chloride at pH < 2 and pH > 11	GC/MS	4.8 μg/L	Approx. 93%[c]	EPA 1984a (Method 625)
	Extraction with methylene chloride at pH 12-13 and	GC/MS	10 μg/L	NA	EPA 1984a (Method 1625)
	and pH < 2	GC/MS	NA	NA	EPA 1986a
	Extraction with dichloromethane	HPLC/UV	73 pg	NA	Ogan et al. 1979
	Extraction with cyclohexane	TLC/FS	0.5-1 ng/L	NA	Borneff and Kunte 1979
Soil	Extraction with *n*-pentane	TLC/UV	NA	NA	Butler et al. 1984
	Extraction with methylene chloride	GC/MS	NA	NA	EPA 1986a
Food	Extraction with isooctane	TLC/UV	0.2 μg/kg	NA	Howard 1979

[a]Abbreviations: HPLC, high-performance liquid chromatography; TLC, thin-layer chromatography; FS, fluorescence spectroscopy; QLL, quasi-linear luminescence; GC, gas chromatography; MS, mass spectrometry; UV, ultraviolet absorption spectroscopy.

[b]NA = not available.

[c]In large samples.

TLC has also been used to analyze for PAHs. With quasi-linear luminescence methods (QLL), quasi-linear spectra can be obtained for PAHs at liquid nitrogen temperatures (Sawicki 1976).

GC and HPLC are the chromatographic methods routinely used for determining 10 to 20 of the major PAHs in air and water samples. Detailed analysis of major and minor PAHs in a complex PAH mixture requires a combination of chromatographic techniques (Wise et al. 1986). GC/MS has a detection limit of greater than 10 pg; HPLC/FS has an approximate detection limit for PAHs of 25 to 50 pg (Santodonato et al. 1981).

HPLC (5506) or GC/MS (5515) are the methods recommended by NIOSH (1984) for analyzing PAHs in workplace air. These methods incorporate a sampling train consisting of a filter and a solid sorbent (NIOSH 1984). The use of a high-volume sampler to sample a large quantity of air allows for the detection of small amounts of PAH. The analytical methods required by EPA (1984a) for the analysis of B[b]F in water are procedures 610 (HPLC/FS), 625 (GC/MS), and 1625 (GC/MS). These are required test procedures under the Clean Water Act for municipal and industrial wastewater-discharging sites. GC/MS is also the method required by the EPA Contract Laboratory Program for analysis of B[b]F and other PAHs in water and soil. The contract required quantitation limit (CRQL) for B[b]F in water is 10 μg/L; in soil/sediment, the limit is 330 μg/kg (EPA 1986a).

8.2 BIOLOGICAL SAMPLES

The available biological monitoring techniques are useful for detecting whether occupational or environmental exposure to PAHs has occurred; however, because there have been no population-based studies to determine normal body levels of PAHs, it is not yet possible to predict environmental exposure from body PAH levels or to predict what health effects are likely to be associated with these levels. In general, techniques that measure PAH or PAH metabolite concentration in the urine are most appropriate for use in determining occupational exposure, since a high level of PAH exposure is necessary to result in the presence of these compounds in the urine. Methods that detect diol epoxide-DNA adducts are more sensitive to low exposure levels and are most appropriate for use in determining environmental exposure. The techniques presently available for determining exposure to PAHs are summarized in Table 8.2 and discussed in detail below.

Modica et al. (1982) and Bartosek et al. (1984) examined PAHs (specifically chrysene and benz[a]anthracene) present in blood, mammary, adipose, liver, and brain tissue from rats orally exposed to PAHs using gas-liquid chromatography with a flame-ionization detector. PAHs were determined in all tissues examined. No information concerning the use of this technique in determining PAH concentrations in human tissue samples was found in the available literature.

In mammalian systems, B[b]F is converted by specific cellular enzymes to dihydrodiols or diol epoxides that are capable of binding to DNA (Geddie et al. 1984). The structure of these adducts is not known. However, Amin et al. (1985b) used HPLC/FS to examine structural analogs of potential B[b]F-DNA adducts.

Table 8.2. Methods for analysis of PAHs in biological samples

Medium	Technique	Measured parameter	Reference
Tissue	Gas chromatography	PAH concentration	Modica et al. 1982, Bartosek et al. 1984
	Postlabeling of DNA	PAH diol epoxide-DNA adducts	Randerath et al. 1985, 1986; Weyand et al. 1987a,b
Blood	Immunoassay	Antibodies to diol epoxide-DNA adducts	Harris 1985a,b, Harris et al. 1986
Urine	Gas chromatography	PAH concentration	Clonfero et al. 1986
	High-performance liquid chromatography	PAH concentration	Becher and Bjorseth 1983, Becher et al. 1984

The degree of DNA adduct formation can be used as a measure of dose in target tissues or organs using the ^{32}P postlabeling technique. In this technique, radioactivity (^{32}P) is incorporated into the DNA removed from the exposed cells, and the digested DNA is separated using TLC or HPLC. Quantitation of the adducts is achieved by scintillation counting. Small amounts of DNA are needed for analysis. These techniques have not been examined in humans or in actual biological samples to determine whether abnormal levels can be detected. Randerath et al. (1985, 1986) examined PAH-DNA adducts in skin tissue from mice dermally treated with cigarette smoke condensate. Tissues from the placenta, bronchus, and larynx of smokers were also examined. Weyand et al. (1987a,b) evaluated the ability of B[b]F to bind to mouse skin following single dermal application.

Procedures are currently available to examine for the presence of antibodies to PAH-DNA adducts in the blood using enzymatic immunoassays (Harris 1985a, Harris et al. 1986). Harris (1985b) developed a technique for determining human exposure to PAHs by detecting antibodies, in sera, to diol epoxide-DNA adducts using an immunoassay. The technique was tested on coke-oven workers exposed to substantial amounts of benzo[a]pyrene and other PAHs in the work atmosphere and in smokers and nonsmokers. Antibodies to benzo[a]pyrene diol epoxide-DNA adducts were quantified by enzyme-linked immunosorbent assay (ELISA). Higher proportions of sera positive for antibodies were found in a group of smokers and in the occupationally exposed group. This technique may be applicable for determining exposure to B[b]F, but further investigation of the formation of B[b]F-DNA adducts is necessary.

The urine of exposed humans was examined for the presence of PAHs. PAHs and their metabolites can be extracted from urine and analyzed using HPLC/FS or GC/MS. PAHs were found in the urine of workers in an aluminum plant. However, the level of environmental exposure could not be determined from the chrysene content in urine, because high environmental concentrations of PAHs in the workplace were not found to be reflected to the same extent in the excretion of PAHs in urine (Becher and Bjorseth 1983, Becher et al. 1984, Becher 1986). This problem was suggested to result from the nonbioavailability of particle-bound PAHs, and this method may still be applicable in other exposure situations. Clonfero et al. (1986) detected PAHs using GC/MS in the urine of individuals treated therapeutically with crude coal tar. However, this is not necessarily a useful test for occupational exposure, because high levels of PAHs in the coal tar were necessary to concentrate PAHs in the urine.

Vo-Dinh et al. (1987) developed an antibody-based fiber-optic biosensor that can be used to detect benzo[a]pyrene or other PAHs in sample solutions. In this technique, antibodies to benzo[a]pyrene are covalently bound to the tip of the sensing probe. A helium-cadmium laser excites the molecules of benzo[a]pyrene bound to the antibodies, and the resulting fluorescence of these molecules is recorded by a photomultiplier; the intensity of the fluorescence signal is proportional to the amount of antigen bound to the sensor tip. The

fiber-optic device can detect 1 femtomole (fmol; one-quadrillionth of a mole) benzo[a]pyrene in a 5-μL sample drop. This technique can be useful in the assessment of an individual's exposure to benzo[a]pyrene and other PAHs, provided appropriate antibodies are used.

9. REGULATORY AND ADVISORY STATUS

Regulatory standards have been developed for the carcinogenic PAHs in the benzene- or cyclohexane-soluble fraction of coal tar pitch volatiles. B[b]F is not extracted in the benzene- or cyclohexane-soluble fraction. However, the regulatory standards were developed to regulate exposures to all PAHs in coal tar pitch volatiles and are appropriate for B[b]F. These standards and advisory guides are presented in Table 9.1.

B[b]F has been shown to be carcinogenic in experimental animals; similar to other PAHs, it likely undergoes metabolism to reactive electrophiles capable of binding covalently to DNA and inducing bacterial mutation and DNA damage. EPA has not classified B[b]F based on carcinogenicity data. IARC (1973) has classified B[b]F in Group 2B because of sufficient evidence of carcinogenicity in experimental animals. IARC (1985) has also concluded that there is sufficient evidence of the carcinogenicity of coal tars, creosote, and coal tar pitches in experimental animals. In addition, IARC (1985) concluded that there is sufficient evidence that occupational exposure to coal tar and coal tar pitch is associated with skin cancer, and limited evidence of the carcinogenicity of creosote in occupationally exposed individuals.

9.1 INTERNATIONAL

The World Health Organization European standards for drinking water recommend a concentration of PAHs not to exceed 0.2 μg/L. This is based on the composite of six PAHs in drinking water: fluoranthene, benzo[a]pyrene, benzo[g,h,i]perylene, B[b]F, benzo[k]fluoranthene, and indeno[1,2,3-cd]pyrene (WHO 1971). This limit was not chosen on the basis of potential health effects.

9.2 NATIONAL

9.2.1 Regulatory Standards

Coal tar, coal tar pitch, and creosote are considered by NIOSH and EPA to be human carcinogens (NIOSH 1977; EPA 1978, 1981, 1984c, 1986b). NIOSH reviewed epidemiologic and experimental toxicological evidence and concluded that inhalation exposure to these coal products, which contain a number of PAHs, increases the risk of lung and skin cancer in workers (NIOSH 1977). The Secretary of Labor has taken the position that no safe occupational exposure can be established for a carcinogen.

The current workroom air standard determined by the Occupational Safety and Health Administration (OSHA) is an 8-h time-weighted average permissible exposure limit (PEL) of 0.2 mg/m^3 for the benzene-soluble

Table 9.1. Regulatory standards and advisory levels

Regulatory standard or advisory level	Basis	Concentration	References
	Air		
Regulatory standard			
8-h Time-weighted average permissible exposure limit (PEL)	Benzene-soluble fraction of coal tar pitch volatiles	0.2 mg/m^3	OSHA 1985
Advisory levels			
8-h Time-weighted average threshold limit value	Benzene-soluble fraction of coal tar pitch volatiles	0.2 mg/m^3	ACGIH 1986
10-h Time-weighted average threshold limit value	Cyclohexane-soluble fraction of coal tar pitch volatiles	0.1 mg/m^3	NIOSH 1977
	Water		
Advisory levels			
Ambient water quality criterion	Benzo[a]pyrene	0 (28, 2.8, and 0.28 ng/L)[a]	EPA 1980

[a]The EPA recommended concentration for ambient water is zero. However, because attainment of this level may not be possible to achieve, the EPA recommended concentrations of total carcinogenic PAHs for ambient water corresponding to a 10^{-5}, 10^{-6}, and 10^{-7} upper-bound lifetime excess risk estimate, respectively, are presented.

fraction of coal tar pitch volatiles (OSHA 1985). The PEL was established to minimize exposure to those PAHs believed to be carcinogens.

9.2.2 Advisory Levels

9.2.2.1 Air advisory levels

ACGIH Time-Weighted Average Threshold Limit Value. The American Conference of Governmental Industrial Hygienists (ACGIH 1986) recommended a time-weighted average threshold limit value (TLV) for occupational exposure to coal tar pitch volatiles based on an 8-h workday and a 40-h week. The ACGIH time-weighted average TLV of 0.2 mg/m^3 is based on the benzene-soluble fraction of coal tar pitch volatiles (including benzo[a]pyrene, anthracene, phenanthrene, acridine, chrysene, and pyrene). The TLV is based on the ACGIH conclusion that at concentrations below 0.2 mg/m^3, any increase in the incidence of lung and other tumors caused by occupational exposure to coal tar pitch volatiles should be minimal.

NIOSH Time-Weighted Average Threshold Limit Value. The National Institute for Occupational Safety and Health (NIOSH) examined the epidemiologic and experimental toxicological evidence on coal tar, coal tar pitch, and creosote; conclusions were that these compounds are carcinogenic to experimental animals and potentially carcinogenic to humans (NIOSH 1977). PAHs have been identified in coal tar products. Because of the carcinogenic potential of these compounds, NIOSH recommended that the permissible exposure limit be set at the lowest concentration detected by the NIOSH-recommended method of environmental monitoring, that is, 0.1 mg/m^3 (NIOSH 1977). NIOSH proposed this time-weighted average threshold limit value to reduce the risk of cancer associated with exposure to coal tar products in the workplace.

9.2.2.2 Water advisory levels

Ambient Water Quality Criterion. EPA (1980) developed an ambient water quality criterion (AWQC) to protect human health from the potential carcinogenic effects caused by exposure to PAHs through ingestion of contaminated water and contaminated aquatic organisms.

B[b]F is an animal carcinogen. Because there is no recognized safe concentration for a human carcinogen, EPA (1980) recommended that the concentration of total carcinogenic PAHs in ambient water be zero. However, EPA (1980) recognized that a zero concentration level may not be possible to attain. The present criteria for total carcinogenic PAHs were based on the carcinogenicity assay reported by Neal and Rigdon (1967), in which a statistically higher incidence of stomach tumors developed in CFW-Swiss mice exposed to doses of 1 to 250 ppm benzo[a]pyrene in the diet than in controls. Assuming that an individual consumes 2 L of water and 6.5 g fish and shellfish each day, the sum of the concentrations of total carcinogenic PAHs corresponding to upper-bound lifetime excess cancer risks of 10^{-5}, 10^{-6}, and 10^{-7} are 28, 2.8, and 0.28 ng/L, respectively. These risk estimates may be revised by EPA depending on the ongoing reevaluation of the studies and methods of risk estimation.

9.2.2.3 Food advisory levels

No food advisory levels for B[b]F were located in the available literature.

9.2.2.4 Other guidance

Sections 103(a) and 103(b) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA) require that persons in charge of vessels or facilities from which a hazardous substance has been released in quantities that are equal to or greater than its reportable quantity (RQ) immediately notify the National Response Team of the release. Potential carcinogens are grouped into high-, medium-, or low-hazard categories on the basis of the biological information available. The RQ for B[b]F is 1 lb (EPA 1987).

9.2.3 Data Analysis

9.2.3.1 Carcinogenic potency

Although EPA previously published inhalation and oral risk estimates for carcinogenic benzo[a]pyrene (EPA 1984b) based on the studies of Thyssen et al. (1981) and Neal and Rigdon (1967), these numbers are currently under review and have not been included here pending recalculation.

9.3 STATE

The State of New York has recommended a guidance level of 0.2 μg/L for the sum of benz[a]anthracene, benzofluoranthene, benzo[a]pyrene, fluoranthene, indeno[1,2,3-cd]pyrene, methylbenz[a]anthracene, and pyrene in ambient water (NYSDEC 1984). Regulations and advisory guidance from the states were still being compiled at the time of printing.

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11. GLOSSARY

Acute Exposure--Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Bioconcentration Factor (BCF)--The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same time period.

Carcinogen--A chemical capable of inducing cancer.

Ceiling value (CL)--A concentration of a substance that should not be exceeded, even instantaneously.

Chronic Exposure--Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Developmental Toxicity--The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

Embryotoxicity and Fetotoxicity--Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurred. The terms, as used here, include malformations and variations, altered growth, and in utero death.

Frank Effect Level (FEL)--That level of exposure which produces a statistically or biologically significant increase in frequency or severity of unmistakable adverse effects, such as irreversible functional impairment or mortality, in an exposed population when compared with its appropriate control.

EPA Health Advisory--An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

Immediately Dangerous to Life or Health (IDLH)--The maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health effects.

Intermediate Exposure--Exposure to a chemical for a duration of 15-364 days, as specified in the Toxicological Profiles.

Immunologic Toxicity--The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

In vitro--Isolated from the living organism and artificially maintained, as in a test tube.

In vivo--Occurring within the living organism.

Key Study--An animal or human toxicological study that best illustrates the nature of the adverse effects produced and the doses associated with those effects.

Lethal Concentration(LO) (LC_{LO})--The lowest concentration of a chemical in air which has been reported to have caused death in humans or animals.

Lethal Concentration(50) (LC_{50})--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal Dose(LO) (LD_{LO})--The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals.

Lethal Dose(50) (LD_{50})--The dose of a chemical which has been calculated to cause death in 50% of a defined experimental animal population.

Lowest-Observed-Adverse-Effect Level (LOAEL)--The lowest dose of chemical in a study or group of studies which produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Lowest-Observed-Effect Level (LOEL)--The lowest dose of chemical in a study or group of studies which produces statistically or biologically significant increases in frequency or severity of effects between the exposed population and its appropriate control.

Malformations--Permanent structural changes that may adversely affect survival, development, or function.

Minimal Risk Level--An estimate of daily human exposure to a chemical that is likely to be without an appreciable risk of deleterious effects (noncancerous) over a specified duration of exposure.

Mutagen--A substance that causes mutations. A mutation is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

Neurotoxicity--The occurrence of adverse effects on the nervous system following exposure to a chemical.

No-Observed-Adverse-Effect Level (NOAEL)--That dose of chemical at which there are no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

No-Observed-Effect Level (NOEL)--That dose of chemical at which there are no statistically or biologically significant increases in frequency or severity of effects seen between the exposed population and its appropriate control.

Permissible Exposure Limit (PEL)--An allowable exposure level in workplace air averaged over an 8-h shift.

q_1^*--The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The q_1^* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually μg/L for water, mg/kg/day for food, and $\mu g/m^3$ for air).

Reference Dose (RfD)--An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

Reportable Quantity (RQ)--The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are: (1) 1 lb or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Sect. 311 of the Clean Water Act. Quantities are measured over a 24-h period.

Reproductive Toxicity--The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

Short-Term Exposure Limit (STEL)--The maximum concentration to which workers can be exposed for up to 15 min continually. No more than four excursions are allowed per day, and there must be at least 60 min between exposure periods. The daily TLV-TWA may not be exceeded.

Target Organ Toxicity--This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Teratogen--A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV)--A concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a TWA, as a STEL, or as a CL.

Time-weighted Average (TWA)--An allowable exposure concentration averaged over a normal 8-h workday or 40-h workweek.

Uncertainty Factor (UF)--A factor used in operationally deriving the RfD from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of humans, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10.

APPENDIX: PEER REVIEW

A peer review panel was assembled for benzo[b]fluoranthene. The panel consisted of the following members: Dr. Dietrich Hoffmann, Naylor Dana Institute for Disease Prevention; Dr. Roger O. McClellan, Lovelace Inhalation Toxicology Research Institute; and Dr. Alexander Wood, Roche Institute of Molecular Biology. These experts collectively have knowledge of benzo[b]fluoranthene's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in the Superfund Amendments and Reauthorization Act of 1986, Section 110.

A joint panel of scientists from ATSDR and EPA has reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply their approval of the profile's final content. The responsibility for the content of this profile lies with the Agency for Toxic Substances and Disease Registry.