criteria for a recommended standard....

OCCUPATIONAL EXPOSURE
TO
BENZOYL PEROXIDE

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
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PREFACE

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

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

I am pleased to acknowledge the contributions to this report on benzoyl peroxide by members of the NIOSH staff, by the Review Consultants on Benzoyl Peroxide, by the ad hoc committees of the American Medical Association and the American Conference of Governmental Industrial Hygienists, and by Robert B. O'Connor, M.D., NIOSH consultant in occupational medicine. The NIOSH recommendations for standards are not necessarily a consensus of all the consultants and professional societies that reviewed this criteria document on benzoyl peroxide. A list of Review Consultants appears on page vi.

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The Division of Criteria Documentation and Standards Development, National Institute for Occupational Safety and Health, had primary responsibility for development of the criteria and recommended standard for benzoyl peroxide. The division review staff for this document consisted of Keith H. Jacobson, Ph.D. (Chairman), Douglas L. Smith, Ph.D., Frank L. Mitchell, D.O., with Thomas L. Anania (Division of Surveillance, Hazard Evaluations, and Field Studies), Thomas F. Bloom (Division of Technical Services), and Charles C. Hassett, Ph.D. Stanford Research Institute (SRI) developed the basic information for consideration by NIOSH staff and consultants under contract No. CDC-99-74-31. C. Ilana Howarth served as criteria manager.

The views expressed and conclusions reached in this document, together with the recommendations for a standard, are those of NIOSH, after review of the evidence and consideration of the comments of reviewers; these views and conclusions are not necessarily those of the consultants, other federal agencies, professional societies, or the contractor.

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CRITERIA DOCUMENT:
RECOMMENDATIONS FOR AN OCCUPATIONAL
EXPOSURE STANDARD FOR BENZOYL PEROXIDE

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I. RECOMMENDATIONS FOR A BENZOYL PEROXIDE STANDARD

The National Institute for Occupational Safety and Health (NIOSH) recommends that employee exposure to benzoyl peroxide in the workplace be controlled by adherence to the following sections. The standard is designed to protect the health and provide for the safety of employees for up to a 10-hour work shift, 40-hour workweek, over a working lifetime. Compliance with all sections of the standard should prevent adverse effects of benzoyl peroxide on the health and safety of employees. Sufficient technology exists to permit compliance with the recommended standard. Although the workplace environmental limit is considered to be a safe level based on current information, it should be regarded as the upper boundary of exposure and every effort should be made to maintain the exposure as low as is technically feasible. The criteria and standard will be subject to review and revision as necessary.

These criteria and the recommended standard apply to employees exposed to any form of the diacyl organic peroxide $(C6H5CO)2O2$, which is referred to as "benzoyl peroxide" throughout this document. Synonyms for benzoyl peroxide include benzoyl superoxide and dibenzoyl peroxide.

Pure benzoyl peroxide is a granular solid, greater than 95% benzoyl peroxide by weight, usually containing less than 5% water. Wet benzoyl peroxide, also a granular solid, contains 66-85% benzoyl peroxide by weight and 34-15% water. Pastes consist of approximately 50% benzoyl peroxide and 50% of a plasticizer or other diluent. Flour bleach usually contains 32% benzoyl peroxide and 68% cornstarch.

An action level is defined as equal to the environmental limit. Occupational exposure to benzoyl peroxide is defined as any work involving handling, storage, use, or manufacture of benzoyl peroxide at a concentration above the action level. Exposure at lower concentrations will not require adherence to the following sections, except for Sections 2(a,c), 3(a), 4(a), 5, 6(b,c,d,e), 7, and 8(a,d).

The major concerns from occupational exposure to benzoyl peroxide are the hazards arising from its instability, flammability, and explosive properties. In addition, benzoyl peroxide may cause local irritation of the eyes and skin.

Section 1 - Environmental (Workplace Air)

(a) Concentration

Exposure to benzoyl peroxide shall be controlled so that employees are not exposed at a concentration greater than 5 milligrams per cubic meter (mg/cu m) of air, determined as a time-weighted average (TWA) concentration for up to a 10-hour work shift in a 40-hour workweek.

(b) Sampling and Analysis

Sampling and analysis of airborne benzoyl peroxide shall be performed by the methods described in Appendices I and II or by other methods at least equivalent in precision and sensitivity.

Section 2 - Medical

Medical surveillance shall be made available to employees as outlined below.

(a) Preplacement medical examinations shall include at least:

(1) Comprehensive medical and work histories with emphasis on skin conditions.

(2) A complete physical examination giving special attention to the skin for evidence of dermatitis.

(b) Periodic examinations shall be made available at a frequency to be determined by the responsible physician, but at least every 3 years. These examinations shall include at least:

(1) Interim medical and work histories.

(2) A physical examination as described for the preplacement examination.

(c) During examinations, applicants or employees having medical conditions that could be directly or indirectly aggravated by exposure to benzoyl peroxide or formulations containing benzoyl peroxide shall be counseled on the increased risk of impairment to their health from working with these substances.

(d) Initial medical examinations shall be made available to all employees within 6 months of the promulgation of a standard based on these recommendations.

(e) Pertinent medical records shall be maintained for all employees occupationally exposed to benzoyl peroxide. Such records shall be kept for at least 30 years after termination of employment. These records shall be made available to the designated medical representatives of the Secretary of Health, Education, and Welfare, of the Secretary of Labor, of the employer, and of the employee or former employee.

Section 3 - Labeling and Posting

All labels and warning signs shall be printed both in English and in the predominant language of non-English-reading workers. Illiterate workers and workers reading languages other than those used on labels and posted signs shall receive information regarding hazardous areas and shall be informed of the instructions printed on labels and signs.

(a) Containers

All containers of benzoyl peroxide shall have a label containing the following information, in addition to such other information as may be required by other statutes, regulations, or ordinances or believed needed by the employer:

BENZOYL PEROXIDE
(TRADE NAME)*

DANGER! FLAMMABLE
ORGANIC PEROXIDE

EXPLOSION OR FIRE MAY RESULT FROM HEAT,
SHOCK, OR CONTACT WITH SOME MATERIALS

Store in a cool place in closed original container.
Protect from direct sunlight.
Keep away from heat, sparks, and open flame.
Prevent contamination with readily oxidizable materials and polymerization accelerators.
Avoid contact with skin and eyes.

First Aid: In case of eye contact, flush eyes thoroughly with copious amounts of water. Consult a physician.

*State % of benzoyl peroxide in product.

(1) In addition to the above information, labels for containers of pure benzoyl peroxide shall add the following: Do not add to

hot materials; do not grind or subject to friction or shock--explosive decomposition may result.

(2) Labels for containers of pastes containing benzoyl peroxide shall add the following: Do not freeze.

(3) Labels for containers of wet benzoyl peroxide shall add the following: Keep container tightly closed to prevent drying out.

(b) Work Areas

Areas where benzoyl peroxide is used, manufactured, or stored shall be posted with a sign reading:

BENZOYL PEROXIDE
(TRADE NAME)

NO SMOKING

KEEP AWAY FROM SOURCES OF
IGNITION AND OPEN FLAMES

MAY BE IRRITATING TO SKIN AND EYES

EXPLOSION OR FIRE MAY RESULT FROM CONTACT WITH SOME
MATERIALS, HEAT, OR SHOCK

Do not allow product to dry out.
Avoid breathing dust.
Avoid contact with skin and eyes.
Provide adequate ventilation.

Section 4 - Personal Protective Clothing and Equipment

(a) Protective Clothing and Equipment

(1) The employer shall provide chemical safety goggles, glasses, or face shields (8-inch minimum) with goggles and shall ensure that employees wear them during any operation in which benzoyl peroxide may enter the eyes. The applicable regulation is 29 CFR 1910.133.

(2) The employer shall provide fire-resistant clothing treated with an antistatic agent to employees using or handling pure benzoyl peroxide. Additional protective clothing shall be worn when needed. The employer shall ensure that precautions are taken to protect personnel who launder clothing contaminated with pure benzoyl peroxide.

(3) Protective gloves and aprons shall be worn during operations where pure benzoyl peroxide is handled and may contact the skin.

(4) Measures, such as the wearing of conductive shoes, designed to dissipate static electricity should be required by the employer when large amounts of pure benzoyl peroxide are handled.

(5) The employer shall ensure that all personal protective devices, including conductive shoes, and conductive flooring are inspected regularly, cleaned, and maintained in working condition.

(b) Respiratory Protection

Engineering controls shall be used when needed to maintain airborne benzoyl peroxide concentrations at or below the recommended environmental limit. Compliance with the permissible exposure limit by the use of respirators is permitted only during installation and testing of engineering controls, during performance of nonroutine maintenance or repair, when working in confined spaces, or during emergencies. When use of a respirator is permitted, it shall be selected and used in accordance with the following requirements:

(1) To determine the type of respirator to be used, the employer shall measure, when possible, the concentrations of airborne benzoyl peroxide in the workplace initially and thereafter whenever control, process, operation, worksite, or climatic changes occur that are

likely to increase the concentration of airborne benzoyl peroxide. This provision does not apply when only atmosphere-supplying positive pressure respirators are used.

(2) The employer shall ensure that no employee is exposed to benzoyl peroxide above the recommended limit because of improper respirator selection, fit, use, or maintenance.

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

(4) The employer shall provide respirators in accordance with Table I-1 and shall ensure that the employees properly use the respirators provided when wearing respirators is required. The respiratory protective devices provided in conformance with Table I-1 shall be those approved by NIOSH and the Mining Enforcement and Safety Administration (MESA) as specified under the provisions of 30 CFR 11.

(5) Respirators specified for use in higher concentrations of airborne benzoyl peroxide may be used in atmospheres with lower concentrations.

(6) When an emergency involving benzoyl peroxide requires evacuation, the employees shall leave the area immediately, stopping to put on respirators only if absolutely necessary.

(7) Respirators shall be easily accessible, and employees shall be informed of their location.

TABLE I-1

RESPIRATOR SELECTION GUIDE

Maximum Use Concentration or Condition	Respirator Type Approved under Provisions of 30 CFR 11
25 mg/cu m or less	Dust and mist respirator, except single-use respirator*
50 mg/cu m or less	(1) Dust and mist respirator except single-use or quarter-mask respirator* (2) Fume or high-efficiency particulate respirator* (3) Supplied-air respirator (4) Self-contained breathing apparatus
250 mg/cu m or less	(1) High-efficiency particulate filter respirator with full facepiece* (2) Supplied-air respirator with full facepiece, helmet, or hood (3) Self-contained breathing apparatus with full facepiece
1,000 mg/cu m or less	Type C supplied-air respirator with full facepiece operated in pressure-demand or other positive pressure mode or with full facepiece, helmet, or hood operated in continuous-flow mode
Greater than 1,000 mg/cu m or entry into area of unknown concentration	(1) Self-contained breathing apparatus with a full facepiece operated in pressure-demand or other positive pressure mode (2) Combination respirator which includes a Type C supplied-air respirator with full facepiece operated in pressure-demand or other positive pressure or continuous-flow mode and an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive pressure mode

*Benzoyl peroxide is a strong oxidizer and should not come in contact with oxidizable materials. Some cartridges and canisters may contain activated charcoal and shall not be used to provide protection against benzoyl peroxide. Only nonoxidizable sorbents are allowed.

Section 5 - Informing Employees of Hazards from Benzoyl Peroxide

(a) The employer shall ensure that each employee working in areas where benzoyl peroxide is used, handled, manufactured, or stored is informed at the beginning of employment, and at least annually thereafter, of the presence of benzoyl peroxide in the workplace, including the trade-name substances, if any, that contain benzoyl peroxide, the hazards, relevant symptoms, appropriate emergency procedures, and proper conditions and precautions for the safe use of benzoyl peroxide.

(b) The employer shall institute a continuing education program, conducted by persons qualified by experience or training, to ensure that all employees have current knowledge of job hazards, proper maintenance and cleaning methods, and proper respirator use. Employees engaged in maintenance and repair activities shall be included in these training programs. The instructional program shall include a description of the general nature of the medical surveillance procedures and of the advantages to the employee of undergoing these examinations. Each employee shall be advised of pertinent information, including that required for the material safety data sheet prescribed by paragraph (c) of this section, which shall be kept on file and shall be readily accessible to employees at all places of employment where there is occupational exposure to benzoyl peroxide.

(c) Required information shall be recorded on the "Material Safety Data Sheet" shown in Appendix III or on a similar form approved by the Occupational Safety and Health Administration, US Department of Labor.

Section 6 - Work Practices

(a) Control of Airborne Benzoyl Peroxide

Engineering controls, such as process enclosure or local exhaust ventilation, shall be used where needed to maintain benzoyl peroxide concentrations at or within the limit recommended in Section 1(a). All engineering controls shall be sparkproof. Ventilation systems shall be designed to prevent recirculation of benzoyl peroxide into the workplaces. Dead airspaces that would allow accumulation of benzoyl peroxide shall be minimized. Consideration must be given to applicable local, state, and federal air pollution regulations in designing exhaust ventilation systems discharging into outside air so that they do not constitute a hazard to the employees or to the general public. Ventilation systems shall be subject to regular preventive maintenance and cleaning to ensure effectiveness, which shall be verified by airflow measurements taken at least every 3 months.

(b) Storage, Handling, and General Work Practices

(1) Containers of benzoyl peroxide shall be kept tightly closed at all times. Containers shall be handled carefully to minimize accidental breakage or spillage and stored in a cool, well-ventilated area away from heat, combustible substances, acids, and oxidizers. No screw-top or metal containers may be used for pure benzoyl peroxide.

(2) Employers shall ensure that shipping containers of benzoyl peroxide are not reused unless they have been properly cleaned.

(3) Employers shall take precautions to minimize benzoyl peroxide contact with the skin and eyes of employees. Equipment, walls, and floors should be kept clean to limit employee exposure.

(4) Before maintenance work, sources of benzoyl peroxide shall be eliminated to the maximum extent feasible. If concentrations of airborne benzoyl peroxide cannot be maintained at or below the limit recommended in Section 1(a), respiratory protective equipment as described in Section 4 shall be used during such maintenance work.

(5) Sources of ignition, such as smoking materials and open flames, shall be prohibited in areas where benzoyl peroxide is used, handled, manufactured, or stored.

(6) All spills of benzoyl peroxide shall be wetted down and cleaned up immediately.

(7) Spills of pure benzoyl peroxide and solid formulations containing benzoyl peroxide shall be thoroughly wetted down or mixed with water-wetted vermiculite, perlite, sand, clay, or other suitable material before being placed in closed containers made of polyethylene or other suitable material and used exclusively for benzoyl peroxide wastes.

(8) Transportation and use of benzoyl peroxide shall comply with all applicable federal, state, and local regulations.

(c) Waste Disposal

(1) Pure benzoyl peroxide may be burned if local, state, and federal regulations permit. It shall be mixed with an inert material, such as vermiculite, and only 1 pound or less shall be burned at one time. The material shall be placed in a trench and ignited from a distance.

(2) Employers shall ensure that no pure benzoyl peroxide is flushed into sewage systems.

(3) Water slurries of benzoyl peroxide wastes and dry, solid, or powder formulations shall be mixed with 4-10 times their weight

of a 10% aqueous sodium hydroxide solution and neutralized before being flushed into any sewage system.

(d) Vessel Entry

(1) Entry into confined spaces, such as tanks, pits, tank cars, and process vessels which have contained benzoyl peroxide, shall be controlled by a permit system. Permits shall be signed by an authorized employer representative, certifying that preparation of the confined space, precautionary measures, and personal protective equipment are adequate and that prescribed procedures will be followed.

(2) Confined spaces which have contained benzoyl peroxide shall be thoroughly ventilated, cleaned, washed, inspected, and tested for oxygen deficiency and for the presence of benzoyl peroxide and other contaminants before entry.

(3) All efforts shall be made to prevent release of benzoyl peroxide into the confined space while work is in progress.

(4) Confined spaces shall be ventilated while work is in progress to keep concentrations of airborne benzoyl peroxide at or below the recommended environmental limit and to prevent oxygen deficiency.

(5) Individuals entering confined spaces where they may be exposed to benzoyl peroxide shall wear respirators as outlined in Section 4(b) and lifelines tended by another employee outside the space who shall also be equipped with the necessary protective equipment and who has contact with a third party. Communication (visual, voice, signal line, telephones, radio, or other suitable means) with the employee inside the confined or enclosed space shall be maintained by the standby person. The

third employee, equipped to aid the other two if necessary, shall have general surveillance of their activities.

(6) Hatch openings shall be large enough for two people to enter or exit simultaneously.

(e) Emergency Procedures

For all work areas where there is a reasonable potential for emergencies involving benzoyl peroxide, employers shall formulate in advance the procedures specified below and any others appropriate for the specific operation or process and shall instruct employees in their implementation.

(1) The employees shall be trained by periodic drills that simulate emergencies in a work situation. These drills shall involve evacuation procedures with a method of accounting for all personnel present in case of fire or explosion, handling of spills and leaks, location of remote controls for sprinkler systems, location and use of emergency water supplies and equipment and shutoff valves, and entry procedures for restricted areas. Procedures and emergency phone numbers for obtaining firefighting assistance, emergency medical care, and transportation of injured personnel shall be included.

(2) Approved eye, skin, and respiratory protective devices as specified in Section 4 shall be used by personnel essential to emergency operations.

(3) Employees not essential to emergency operations shall be evacuated from hazardous areas where benzoyl peroxide inhalation, skin or eye contact, or explosions may occur. The perimeters of these areas shall be delineated, posted, and secured.

(4) Spills of benzoyl peroxide shall be cleaned up immediately.

(5) If benzoyl peroxide or any of its formulations enters the eyes, the eyes shall be flushed immediately with copious amounts of water. Eyewash fountains and safety showers shall be provided. The applicable regulation for them is 29 CFR 1910.151.

(6) Alarms activated by heat or smoke shall be provided in all areas where benzoyl peroxide or its formulations are manufactured, used, or stored.

Section 7 - Sanitation Practices

(a) The employer shall develop and maintain a continuing program for plant sanitation. The applicable regulation covering plant sanitation is 29 CFR 1910.141.

(b) Eating and food preparation and dispensing (including vending machines) shall be prohibited in work areas where benzoyl peroxide is used, manufactured, handled, or stored.

(c) Smoking shall be prohibited in areas where benzoyl peroxide is used, manufactured, handled, or stored.

(d) Employees who handle benzoyl peroxide or equipment contaminated with benzoyl peroxide shall be instructed to wash thoroughly with soap or mild detergent and water before eating or using toilet facilities.

Section 8 - Monitoring and Recordkeeping Requirements

(a) Within 6 months of the promulgation of a standard based on these recommendations, employers shall conduct an industrial hygiene survey at locations where there is benzoyl peroxide in the workplace air to determine if there is exposure to airborne benzoyl peroxide at concentrations greater than the limit recommended in Section 1a. Records of these surveys, including the basis for concluding that concentrations of airborne benzoyl peroxide are at or below the action level, shall be maintained. Surveys shall be repeated at least annually and within 30 days of any change likely to result in increased concentrations of airborne benzoyl peroxide.

(b) If it has been determined that the concentration of benzoyl peroxide exceeds or may exceed the limit recommended in Section 1a, then the employer shall fulfill the following requirements:

(1) A program of personal monitoring shall be instituted to identify and measure, or permit calculation of, the exposure of each employee occupationally exposed to airborne benzoyl peroxide. Source and area monitoring may be used to supplement personal monitoring.

(2) In all personal monitoring, samples representative of the exposure to airborne benzoyl peroxide in the breathing zone of the employee shall be collected.

(3) For each determination of the TWA concentration, a sufficient number of samples shall be taken to characterize employee exposure during each work shift. Variations in the employee's work schedule, location, or duties and changes in production schedules shall be considered in deciding when samples are to be collected.

(4) Each operation in each work area shall be sampled at least once every 6 months or as otherwise indicated by a professional industrial hygienist. If an employee is found to be exposed to benzoyl peroxide at concentrations above the limit recommended in Section 1a, the exposure of that employee shall be measured at least once every week, control measures necessary to reduce the concentration of benzoyl peroxide in the employees' environment to less than or equal to the limit recommended in Section 1a shall be initiated, and the employee shall be notified of the exposure and of the control measures being implemented. Such monitoring shall continue until two consecutive determinations, at least 1 week apart, indicate that the employee's exposure no longer exceeds the recommended environmental limit. At that point, semiannual monitoring may be resumed.

(c) Environmental monitoring records shall be maintained for at least 30 years. These records shall include the name of the employee being monitored, duties performed and job locations within the worksite, dates of measurements, sampling and analytical methods used, the number, duration and results of samples taken, TWA concentrations estimated from these samples, and the type of personal protection used, if any, by the employee. Each employee shall be able to obtain information on his or her own environmental exposures. Environmental records shall be made available to designated representatives of the Secretary of Labor and of the Secretary of Health, Education, and Welfare.

Pertinent medical records shall be retained for 30 years after termination of employment. Records of environmental exposures applicable to an employee should be included in that employee's medical records.

These medical records shall be made available to the designated medical representatives of the Secretary of Labor, of the Secretary of Health, Education, and Welfare, of the employer, and of the employee or former employee.

(d) In the case of employees exposed to benzoyl peroxide at concentrations equal to or less than the action level, records of industrial hygiene surveys, including the basis for concluding that environmental concentrations are equal to or less than the action level, shall be kept until the next survey is conducted. Moreover, for these employees, records of preplacement medical examinations shall be maintained for at least 30 years after termination of employment involving work with benzoyl peroxide.

II. INTRODUCTION

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

The National Institute for Occupational Safety and Health (NIOSH), after a review of data and consultation with others, formalized a system for the development of criteria upon which standards can be established to protect the health and to provide for the safety of employees exposed to hazardous chemical and physical agents. The criteria and recommended standards should enable management and labor to develop better engineering controls resulting in more healthful work environments and should not be used as a final goal.

These criteria for a recommended standard for benzoyl peroxide are part of a continuing series of documents published by NIOSH. The recommended standard applies to workplace exposure to benzoyl peroxide arising from the handling, processing, manufacture, use, or storage of the substance as applicable under the Occupational Safety and Health Act of 1970. The standard was not designed for the population-at-large, and any extrapolation beyond occupational exposures is not warranted. It is intended to (1) protect against fires, explosions, and consequent injuries, (2) protect against the development of local effects on the eyes, skin, and mucous membranes of the nose and throat, (3) be measurable by techniques that are valid, reproducible, and available to industry and government agencies, and (4) be attainable with existing technology.

The major concerns in occupational exposure to benzoyl peroxide are the hazards arising from its flammability and explosive properties. More information is required regarding the types of conditions and circumstances in which benzoyl peroxide and its formulations can be handled without risk of an explosion. Experiments should be conducted to provide information that can be extrapolated to cover full-scale decompositions, fires, and explosions.

More information on how benzoyl peroxide can be handled without risk of explosion is needed. Experimental, epidemiologic, or other information on toxic effects of benzoyl peroxide and on concentrations at which toxic effects might occur is deficient. The information that is available suggests little toxic action by benzoyl peroxide that is inhaled or ingested or that contacts the skin. No reports were found on investigations that would clearly demonstrate whether short or long-term exposures to benzoyl peroxide cause adverse effects, so no definitive conclusions about the toxicity of the compound can be drawn. While neither tumorigenesis nor serious effects on reproduction would be expected from presently known structure-activity relationships, appropriate research is needed to resolve any doubts.

III. BIOLOGIC EFFECTS OF EXPOSURE

Extent of Exposure

Benzoyl peroxide, $(C_6H_5CO)_2O_2$, also called dibenzoyl peroxide, is a rhombic crystalline solid at room temperature [1,2]. Benzoyl peroxide is a flammable, solid, diacyl organic peroxide, which may decompose explosively if subjected to excessive heat, friction, or sudden shock [3-5]. If benzoyl peroxide is exposed to temperatures of 75-80 C for prolonged periods, it becomes unstable and may spontaneously decompose [4]. This type of sudden decomposition, a deflagration, is the rapid spreading of fire through a mass of reactive material [6]. This decomposition is accompanied by a 200-fold increase in volume [5] and yields a dense white smoke consisting of benzoic acid, phenyl benzoate, terphenyls, biphenyls, benzene, and carbon dioxide [7]. The resulting biphenyls promote the further decomposition of benzoyl peroxide [5,7] into products which can catch fire and ignite the remaining benzoyl peroxide. If this happens, or if the benzoyl peroxide itself ignites, a dense black smoke results [8].

The peroxide reacts violently with various organic and inorganic acids, amines, alcohols, metallic naphthanates, and other chemicals that are easily oxidized. Benzoyl peroxide also reacts violently with polymerization accelerators [4].

The presence of small quantities of water diminishes some of the hazardous properties of benzoyl peroxide [9]. During a series of tests on the ease of ignition of pure benzoyl peroxide and benzoyl peroxide with various proportions of water, pure benzoyl peroxide was shown to ignite violently with a loud noise, but benzoyl peroxide containing 5% water did not ignite at all. It was also observed that during this ignition test [9] it did not make any difference whether the total moisture content of the sample was equally divided between each granule or concentrated in 10-20% of the granules, as long as those granules were uniformly dispersed throughout the sample. Additional chemical and physical properties of benzoyl peroxide are presented in Table XIV-1 [1,2].

Benzoyl peroxide is synthesized commercially by a reaction of benzoyl chloride, sodium hydroxide, and hydrogen peroxide [10 (pp 14,85,187),11]. Excess water is removed to obtain pure benzoyl peroxide; the trace impurities remaining are benzoic acid and water. Water, plasticizers, corn starch, or other diluents are added to make the numerous commercial products containing benzoyl peroxide. Benzoyl peroxide has been produced commercially in the United States since 1927 [12]. By 1954, its yearly production was 1,768,000 pounds [13]; 8,829,000 pounds, 9,092,000 pounds, and 7,885,000 pounds were produced in 1973 [14], 1974 [15], and 1975 [16], respectively.

Since benzoyl peroxide is a good source of free radicals, it is used in a number of industrial processes, particularly in the manufacture of plastics [5]. Benzoyl peroxide is a curing agent for silicone rubber [17], a source of free radicals in the resin cements used in dentistry [18], automobile body putty [10 (p 283),19], and roof bolting systems in the mining industry [20], and an initiator in the synthesis of polyvinyl chloride [3]. It is also a component of flour and cheese bleaches [21,22]. In the early 1900's, benzoyl peroxide was used to bleach edible oils, but this practice is now rare [10 (p 276)]. In the past, textiles and paper were also treated with it [11]. In medicine, it now is used in the treatment of acne [23] and of decubitus ulcers (bed sores) [24]. Formerly, it was applied as an aid in the treatment of poison ivy [25].

NIOSH estimates that 25,000 workers in the United States are potentially exposed to benzoyl peroxide or its formulations. Occupations involving possible exposure to benzoyl peroxide are listed in Table XIV-2.

Historical Reports

Little was known about benzoyl peroxide until the end of the 19th century. In the *Encyclopedia of Chemical Technology*, Hooft [11] noted that Brodie synthesized benzoyl peroxide in 1858. One of the earliest references to benzoyl peroxide appeared in 1899 when Nencki and Zaleski [26] reported that it was converted to benzoic acid in the intestines of dogs. As early as 1921, benzoyl peroxide was used in Germany as a fixing agent in light microscopy [27]. It was also used at that time as an antiseptic and local anesthetic in the treatment of burns and ulcers, as reported by Farmer [27]. Benzoyl peroxide had previously been taken internally, but that practice was discontinued because of its poisonous action on the blood, which was not specifically described. However, in 1964, Tiunov [28] noted that Smirnova, using unspecified chemical methods, found that benzoyl peroxide had almost no hemolytic action.

In 1930, Lamson [25] stated that powdered benzoyl peroxide was a theoretically ideal treatment for skin lesions caused by poison ivy because it reduced the spread of the rash and relieved itching. The flammability hazard of benzoyl peroxide treatment was not mentioned in the literature until 1931 when it was reported that a man whose poison ivy rash was being treated with benzoyl peroxide was injured by the ignition of bandages that were covering the powdered benzoyl peroxide on his hands [29,30]. When the bandages were ignited by a lighted cigarette, the benzoyl peroxide exploded, and the skin and several muscles of his right hand were destroyed. The author [29] retracted his recommendation of powdered benzoyl peroxide as a useful therapeutic agent, emphasizing its explosive properties; he recommended, instead, an ointment of an unspecified concentration of benzoyl peroxide in lubricating jelly, which he considered neither explosive nor extremely flammable. No references have been found indicating further use of benzoyl peroxide for the treatment of poison ivy.

Effects on Humans

The effects of occupational exposure to and treatment with benzoyl peroxide have been examined. Inhalation and skin contact are the most frequent routes of exposure.

In 1950, Moskowitz and Burke [31] described the inspection of a factory that used benzoyl peroxide in the production of flour bleach. The powdered bleach contained 32% benzoyl peroxide; the remaining 68% consisted of unspecified proportions of potassium aluminum sulfate (alum) and magnesium carbonate. Over a 3-day period, standard (Greenburg-Smith) impingers containing water collected nine air samples at six different work areas in the factory. The sampling was performed for 20 minutes, 2 to 3 times/shift, on all 3 days. The water from the impingers was analyzed by unspecified methods for benzoyl peroxide and alum. No analyses for magnesium carbonate were performed. Two air samples were taken near grinders on the 1st day. One reportedly contained 1.34 mg of benzoyl peroxide and 2.58 mg of alum/cu m, and the other had 5.17 mg of benzoyl peroxide and 5.33 mg of alum/cu m. Nose and throat irritation were experienced by the two inspectors who were taking the air samples.

On the 2nd day, another air sample taken during a bag-changing operation at one of the grinders contained 2.91 mg of benzoyl peroxide and 3.12 mg of alum/cu m [31]. Another air sample taken on the 2nd day, near a worker emptying a tumbling barrel from one of the grinders, contained 17.0 mg of benzoyl peroxide and 18.8 mg of alum/cu m. In the same location 16 minutes after the barrel had been emptied, the concentrations of benzoyl peroxide and alum were 1.45 mg/cu m and 1.96 mg/cu m, respectively. A fourth sample taken during a bag-changing operation at a grinder contained 5.25 mg of benzoyl peroxide and 5.4 mg of alum/cu m. Again the inspectors had symptoms of nose and throat irritation. The factory workers wore cotton-pad dust respirators during potentially dusty operations and did not complain of nose or throat irritation.

On the 3rd day, during the filling of 100-lb fiber drums at a tumbling barrel, an air sample contained 12.2 mg of benzoyl peroxide and 8.26 mg of alum/cu m [31]. A second air sample taken near a worker emptying a tumbling barrel contained 82.5 mg of benzoyl peroxide and 44.9 mg alum/cu m. The inspectors reported nose and throat irritation at these higher concentrations of airborne dust. A third sample was taken near the grinders 6 minutes after the tumbling barrel had been emptied; also, the floor was being swept near the impinger during the sampling operation, and this action may have increased the airborne dust concentrations. The concentrations in this sample were 2.58 mg of benzoyl peroxide and 3.05 mg of alum/cu m. Nose, eye, and throat irritation occurred during the changing of bags and the emptying and filling operations at the grinders when the concentrations of airborne benzoyl peroxide were between 2.58 mg/cu m and 82.5 mg/cu m. These dust levels could have caused some of the irritation experienced by the inspectors. There was natural ventilation in the plant from open windows, especially when there were strong winds. On days when no wind blew through the working areas, the dustiness increased, and the workers experienced eye irritation. Alum has astringent properties and could have possibly caused the irritation.

The authors [31] made no specific conclusions about the possible irritating effects of benzoyl peroxide. They indicated that the airborne dust was irritating on all 3 days when it contained benzoyl peroxide at concentrations between 1.34 and 82.5 mg/cu m. The reported concentrations of airborne benzoyl peroxide and alum are questionable because no data were given which defined the efficiency of standard impingers containing water for collecting benzoyl peroxide and alum, and there was insufficient analytical information to assess the reliability of the determinations. In addition, it was noted that the proportions of benzoyl peroxide to alum were extremely variable and did not reflect the proportion of the two chemicals in the flour bleach being processed.

In 1945, Baird [32] reported that a young male baker suffered from asthmatic wheezing and severe dermatitis of the face, neck, chest, shoulders, and arms. Although the author was not certain whether these symptoms were caused by occupational skin contact or ingestion of benzoyl peroxide-treated flour, when wheat flour was removed from the baker's diet, he improved rapidly. When wheat flour without improving agents was reintroduced in his diet, he had no further allergic reactions. However, he later worked with treated wheat flour, and the dermatitis reappeared.

Patch tests with different kinds of flour performed on the baker gave positive results if the flours contained improving agents; areas tested with unimproved flours showed no reaction [32]. Patch tests performed on the baker with potassium bromate and benzoic acid in water gave no definitive reaction. A patch test of 6% benzoic acid in liquid petrolatum was positive; a control patch with petrolatum alone was negative.

Baird [32] concluded from information provided by the Canadian Department of Agriculture that the use of benzoyl peroxide in flour produced a benzoic acid residue of 18-45 ppm. Perhaps this is the reason that no patch tests were performed with benzoyl peroxide. However, in 1953, Knight and Kent-Jones [33] stated that, although most of the benzoyl peroxide used to bleach flour decomposes to benzoic acid within a few days, a small amount remains unchanged for several weeks.

Two years after being seen, the baker used benzoyl peroxide-treated flour again and promptly developed dermatitis [32]. Baird concluded that the baker's allergy was the result of benzoic acid, the residue remaining from benzoyl peroxide, but he did not develop data to rule out the role of some other chemical allergen in the diet.

In 1957, Malten [34] outlined a dermatologic study of aircraft factory workers in the Netherlands who suffered from occupational dermatitis. Patch tests were performed with many agents, including benzoyl peroxide, as test materials. Three of 30 polyester processors had hypersensitive skin responses to the benzoyl peroxide patch tests. The total number of workers or the percentage of workers having occupational dermatitis was not specified. Malten stated that no new cases of dermatitis were reported after improved ventilation and changes in work practices went into effect.

In 1960, Jirasek and Kalensky [35] evaluated 34 of an unspecified number of workers in Czechoslovakia who had been exposed to various epoxy resins and had experienced some degree of irritation from at least one of the epoxy resins or the materials used to make the resins. Benzoyl peroxide was used as a hardener and was one of the compounds tested on the workers. Eight of the 34 showed an unspecified toxic reaction to benzoyl peroxide. The authors also observed that patients with sensitive skin showed signs of slight irritation when tested with benzoyl peroxide at concentrations of 20-100% in an unspecified solvent. Work histories of the patients were not provided.

Morley [24] treated 180 patients who had decubitus ulcers with repeated applications of what was described as a water-in-oil emulsion containing 20% benzoyl peroxide. The benzoyl peroxide-treated dressing was applied to the ulcer, covered with a sheet of plastic, and held in place with an elastic net or body stocking. The dressing was changed every 12 hours. This treatment was continued until the ulcer was healed. Treatment was discontinued in one patient because of irritation. It was necessary to surgically repair only one of the treated ulcers.

A number of cases of skin reactions to benzoyl peroxide-containing formulations used in the treatment of acne have been described [36-38]. In 1968, Eaglstein [37] described two patients with allergic dermatitis from benzoyl peroxide. One, a 15-year-old girl, who had previously used a topical antiacne preparation containing benzoyl peroxide and had experienced severe skin irritation, redness, and edema, tried another ointment, which contained 5% benzoyl peroxide and 2% sulfur. It produced severe edema, redness, and a burning sensation in about 12 hours. She had positive patch-test reactions to all tested preparations containing benzoyl peroxide; the preparations were not described.

The other patient, a 21-year-old woman, was treated for superficial acne lesions with a lotion containing 5% benzoyl peroxide; the other ingredients were not specified [37]. After the second overnight facial application, the patient noted marked erythema and a burning sensation on the face. Patch tests with 5% benzoyl peroxide in petrolatum were positive.

To evaluate the meaning of these positive reactions, Eaglstein [37] conducted patch tests with 5% benzoyl peroxide in petrolatum, with petrolatum alone, and with untreated control patches on 41 patients hospitalized for various skin conditions. After 48 hours, only one patient, who had not used benzoyl peroxide previously, had a positive reaction to benzoyl peroxide. It is unlikely that responses in this control group made up of patients with dermatologic conditions would be representative of the general population.

In 1970, Poole et al [36] conducted a three-part study of experimental contact sensitization with benzoyl peroxide. In the first test, 10 volunteers underwent patch tests for irritation from benzoyl peroxide at 3 concentrations. Each was given single applications of an unspecified amount of polyethylene glycol containing 1% sulfur and 1%, 5%, or 10% benzoyl peroxide on separate sites on the arms. Because it had sufficiently low potential for causing irritation, the ointment containing 10% benzoyl peroxide and 1% sulfur was selected for a large-scale repeated-insult patch test. In a second test, each of 69 volunteers received on 1 arm, during a 3-week period, nine 24-hour applications of 0.25 g of polyethylene glycol containing 10% benzoyl peroxide and 1% sulfur. They were tested simultaneously with polyethylene glycol alone.

Two of the 69 subjects had minor reactions to the test materials during the first 24-hour treatment period [36]. By the 3rd week of the testing period, an unspecified number of subjects had positive reactions to the test materials but not to the control vehicle, polyethylene glycol. If there was a positive reaction at the test site and benzoyl peroxide was applied once to another site on the same person, it also showed a positive reaction, demonstrating general skin sensitivity. At the end of the 3-week period, 25 of 69 subjects showed severe, eczematous skin reactions when challenged with the test material. Another six subjects had responses stronger than those seen on the single induction exposures but which were not classified as sensitization.

The third part of the study occurred 2 months after the conclusion of the repeated patch tests when 10 subjects who had shown moderate sensitivity to the benzoyl peroxide and sulfur test material were tested with a single 24-hour patch test of each of the following: (1) polyethylene glycol, (2) polyethylene glycol containing 1% sulfur, (3) polyethylene glycol containing 10% benzoyl peroxide, and (4) polyethylene glycol containing 1% sulfur and 10% benzoyl peroxide [36]. All the subjects reacted to the benzoyl peroxide whether or not sulfur was present, but none reacted to the polyethylene glycol or sulfur.

In 1973, Ede [38] discussed a double-blind study of 196 acne patients who were randomly divided into 4 groups. Three acne lotions and a placebo were tested. The lotions contained 5.5% benzoyl peroxide, 0.25%

chlorohydroxyquinoline, and 0.5% hydrocortisone; 5.5% benzoyl peroxide and 0.25% chlorohydroxyquinoline; or 5.5% benzoyl peroxide. The placebo contained only the base lotion. The lotion was applied to affected areas 1 to 4 times daily for 4 weeks; however, the mean number of applications/day for the groups ranged from 2.2 to 2.5. The lotion was left on the skin for at least 3-4 hours. None of the patients exhibited any skin sensitivity to the lotions containing benzoyl peroxide at the end of the 4 weeks; however, 10 patients dropped out of the study for unspecified reasons.

The following laboratory tests were performed during the study [38] on the blood and urine of 20 of the patients, 10 men and 10 women, to determine whether there were any systemic effects of the lotions: calcium, inorganic phosphorus, glucose, blood urea nitrogen, uric acid, cholesterol, total protein, albumin, and total bilirubin concentrations; activities of alkaline phosphatase, lactate dehydrogenase, and serum glutamic-oxaloacetic transaminase; complete blood count (hemoglobin, hematocrit, RBC, WBC with differential count) and urinalysis (specific gravity, pH, color, appearance, sugar, microscopic examination, albumin, and acetone). The results were within the normal ranges and indicated no systemic effects from any of the lotions.

Bloom [19], in 1975, reported that welders employed in the manufacture of diesel locomotives were exposed to a plastic body filler made of a talc-polyester resin and benzoyl peroxide. Two of four welders who were interviewed thought that the coughing they experienced during the day was caused by exposure to welding fumes and to plastic body filler dust. There was no evidence of skin irritation or sensitization.

A NIOSH Health Hazard Evaluation Determination discussed by Kingsley [39], indicated that telephone repair workers were exposed to a styrene hardener containing 50% benzoyl peroxide and 50% butyl benzoyl phthalate when new and replacement telephone cables were installed. A worker who was wearing disposable gloves would add the hardener to the polyester, manually knead the mass until it was the right consistency, and drop it down into a vault where another gloved worker would shape the compound around the splice. Each such operation required two or three tubes of hardener and took about 30 minutes. One crew normally coated splices once or twice a week. The vaults were naturally ventilated through the manhole covers. The workers did not report adverse effects from using the compound.

Accidents

Hazardous properties of benzoyl peroxide, such as explosion and flammability, have resulted in accidents and serious injuries or death. The following incidents demonstrate that injuries were usually caused by ignorance of the hazards or by negligent handling. Other accidents that did not produce injury are discussed in Chapter V.

Twelve pounds of pure benzoyl peroxide being added through a stainless steel funnel into a polymerization kettle exploded, killing the operator [3]. There were three possible reasons for the explosion: (1) the funnel may have become heated during the operation, so that excessive heat may have caused the peroxide to explode; (2) the peroxide may have become contaminated with residual vinyl acetate from the polymerization reaction; or (3) a static discharge may have occurred.

In another case, an employee escaped serious injury when a flash fire erupted in a 1-pound container of benzoyl peroxide and covered his safety glasses with melted benzoyl peroxide [3]. He was using a glass spatula to transfer benzoyl peroxide from the container to a laboratory scale [3]. As the spatula, which had just been cleaned and dried, was inserted into the container, the benzoyl peroxide burst into flame. The account of the accident indicated that contamination of the benzoyl peroxide may have caused the fire. It is also possible that the friction from the insertion of the spatula may have started it.

In still another case, the owner of a plant that manufactured benzoyl peroxide sustained second degree burns from a fire started by an unknown quantity of benzoyl peroxide dust exposed to an arcing electric light switch [3]. The fire generated smoke and chemical fumes; eventually, there was an explosion.

Lappin [40] found that a laboratory worker received hand injuries and lacerations when benzoyl peroxide in a 4-ounce, brown-glass container exploded as the plastic screwcap was being removed. The author thought that some benzoyl peroxide, along with other organic dust present in the laboratory, was caught in the threads and, as the cap was unscrewed, the friction caused the top layer of peroxide in the bottle to explode.

The explosiveness of benzoyl peroxide was further illustrated when several thousand pounds of the compound exploded in a truck, causing severe property damage within a radius of several city blocks and injuring four people, one seriously [41]. A fire was seen seconds before the explosion occurred, but the exact cause of the accident was unknown. Investigators speculated that perhaps other chemicals had come in contact with the cargo of benzoyl peroxide or that an all-day exposure to hot sun had caused drying of the benzoyl peroxide. Another possibility was that the truck might have been bumped, dislodging the cargo.

Animal Toxicity

There are few data on the effects of benzoyl peroxide on animals. The effects of inhalation, ingestion, skin painting, and injection of benzoyl peroxide have been examined.

Two eye irritation tests with granular 78% benzoyl peroxide were conducted on eight albino rabbits by Wazeter and Goldenthal [42]. Though not specified in the report, 78% benzoyl peroxide granules commonly consist of 22% water and benzoic acid. Sodium fluorescein was put into the eyes when they were examined under ultraviolet light so that corneal damage could be detected. The eyes were examined before treatment with benzoyl peroxide and periodically afterwards. In the one test, 111.4 mg of 78% benzoyl peroxide (0.1 ml measured by volume) was put in the cupped conjunctival sac of the right eye of each of five rabbits; the eyelid was held shut for 1 second. The left eyes served as controls. After 5 minutes, the test eyes were washed with a gentle stream of water, regulated to deliver 300 ml in 2 minutes.

The corneas showed no ulceration or opacity after 1, 24, 48, or 72 hours or after 7 days [42]. The irises appeared unaffected. The conjunctivae of two rabbits showed slight redness 1 hour and 24 hours after the washing, but this disappeared in 48 hours. Three of five rabbits exhibited conjunctival edema 1 hour after the washing, but this was not apparent at 24 hours. The authors concluded that, under these test conditions, benzoyl peroxide was not irritating or corrosive to the eyes.

In another eye irritation test [42], 120.7 mg of 78% benzoyl peroxide was placed in the cupped conjunctival sac of the right eye of each of three rabbits where it remained for 24 hours; the left eyes were controls. After 24 hours, the benzoyl peroxide was washed out with 300 ml of water for 2 minutes. The eyes were examined under ultraviolet light as described in the first test. The irises appeared normal after 1, 24, 48, and 72 hours and after 7 days. The conjunctivae of the rabbits exhibited various degrees of redness and conjunctival edema at 1, 24, 48, and 72 hours, but all adverse effects disappeared in 7 days. One rabbit had blanched conjunctival tissue at 1 hour, but normal color had returned within 24 hours. Examinations under ultraviolet light showed corneal opacity in the three rabbits after 24 hours but no corneal opacities at 48 hours. The only corneal damage in this experiment was revealed in one rabbit by the eye examinations done at 72 hours, and it had disappeared by the 7th day.

Wazeter and Goldenthal [42] concluded that benzoyl peroxide was neither irritating nor corrosive to the eyes of albino rabbits if it was washed out within 5 minutes after being placed in the conjunctival sac; however, if 78% benzoyl peroxide was not washed out until 24 hours later, it proved to be a strongly irritating substance. It was not considered corrosive because corneal opacity lasted less than 6 days.

In a third experiment, Wazeter and Goldenthal [42] tested the skin irritation potential of benzoyl peroxide on three male and three female New Zealand white rabbits. No control animals were mentioned. The hair was shaved from an area on the back of each rabbit, and the skin was then abraded with a scalpel blade. Five hundred milligrams of 78% benzoyl peroxide was applied to each patch of skin and held in place for 4 hours with a gauze bandage. After 4 hours, the bandages were removed and the exposed areas washed with lukewarm water. The skin was examined for any injury or irritation from benzoyl peroxide at 4, 24, and 72 hours. The skin on the six rabbits appeared unaffected. The authors concluded that 78% benzoyl peroxide was neither a primary skin irritant nor a corrosive substance.

Wazeter and Goldenthal [42] also performed a short-term inhalation study on 10 male Spartan rats housed in groups of 2 or 3. The rats were exposed at an atmospheric concentration of 24.3 mg/liter of 78% benzoyl peroxide added to a 59.1-liter glass test chamber supplied by two Wright dust feeders with a regulated airflow.

None of the rats died during the test or the subsequent 14-day observation period [42]. The rats showed the following signs during the 4-hour exposure period: eye squint, increased and decreased respiratory rates, difficulty in breathing, salivation, lacrimation, erythema (location unspecified), and an increase followed by a decrease in motor activity. All of the rats appeared normal at 24 and 48 hours. An unspecified number of rats exhibited signs of eye irritation consisting of corneal opacity and ulceration from the 5th to the 14th day. The authors concluded that 78% benzoyl peroxide was not highly toxic by the inhalation route of administration under the conditions of the experiment.

A short-term oral toxicity test was performed by Wazeter and Goldenthal [42] with 78% benzoyl peroxide in water on five male Spartan albino rats. Each rat received one 5,000 mg/kg dose of 78% benzoyl peroxide suspended in corn oil. The rats took food and water ad libitum and were maintained in temperature- and humidity-controlled quarters during the 14-day study. No control animals were reported. Body weights of all the rats were recorded initially and at 14 days. None of the rats died during the study, and all exhibited normal weight gain. Under the test conditions, 78% benzoyl peroxide was not toxic by the oral route of administration.

In 1958, Kuchle [43] described an experiment in which 15 organic peroxides, including benzoyl peroxide, were tested for their effects on rabbits' eyes. A "lentil-sized" amount of an undefined paste containing 50% benzoyl peroxide was placed in the conjunctival sacs of each of several rabbits, and unspecified amounts of a 93% benzoyl peroxide powder were placed in the conjunctival sacs of several other rabbits. No controls were mentioned. After 1 minute, the eyes were rinsed with tapwater, and any solid residues were removed with a cotton swab. The eyes were then examined after 20 minutes, after 24 hours, then every other day for 1 week, and finally twice a week for 6 weeks. Neither form of benzoyl peroxide was considered to have had harmful effects on the rabbits' eyes; no evidence of burning or irritation was observed, and the corneas of the test animals were clear and had no opacities.

Radomski et al [44] published, in 1948, a study in which three dogs were given a diet containing benzoyl peroxide-treated flour for 6 weeks. The purpose of the experiment was to determine the toxicity of candidate replacements, including benzoyl peroxide, for agene, an improving agent used to treat flour, which consisted of 1% nitrogen trichloride in air saturated with water vapor. Benzoyl peroxide was added to the flour (1 oz benzoyl peroxide/100 pounds flour or 0.625 g/kg). A short time before it was fed to the dogs, the mixture was steamed for 90 minutes, and nutrients were added to it. The nutritionally balanced diet contained 71.6% treated flour on a dry-weight basis. Because the authors did not state the amount of food consumed by each dog, the actual intake of benzoyl peroxide is unknown. The effects of steaming on benzoyl peroxide were not considered.

The authors [44] stated that, since the 1920's, canine hysteria, sometimes called running fits, had been observed in dogs that had eaten agene-treated flour. No canine hysteria was observed in the dogs given the diet containing benzoyl peroxide, and, unlike dogs fed agene-treated flour, they behaved in a normal manner.

In 1949, Arnold [45] described a study in which dogs were provided with a diet in which flour had been treated with 0.8 g of benzoyl peroxide/100 pounds of flour (0.02 g/kg). Chlorine at 20 g/100 pounds (0.44 g/kg), ammonium persulfate at 15 g/100 pounds (0.33 g/kg), and potassium bromate at 5 g/100 pounds (0.11 g/kg) were also used to treat the flour; the amounts were greater than those used commercially in flour bleaching. The diet contained about 80% treated flour on a dry-weight basis. This diet and other experimental diets were given intermittently to six dogs for periods ranging from 21 to 38 days with intervening times of 3-16 days. The dogs were observed for canine hysteria, but it was not seen in those dogs fed benzoyl peroxide-treated flour.

One group of investigators [46] attempted to determine the oral LD50 of benzoyl peroxide in rats. Groups of two fasted rats each were given oral doses of benzoyl peroxide placed on a small amount of pea soup concentrate at 200, 400, and 950 mg/kg. None died. One of the rats that received 400 mg/kg had some vasodilatation, and one that received 950 mg/kg showed slight muscular weakness. The investigators concluded that the oral LD50 of benzoyl peroxide in rats is greater than 950 mg/kg.

Skin irritation by benzoyl peroxide in an unspecified number of guinea pigs was also tested [46]. Patches of skin were chemically depilated, and pure benzoyl peroxide, in doses ranging from 0.25 to 1.0 g/kg, was held against the depilated skin under patches for 24 hours. The skin under the benzoyl peroxide was examined for any irritation or other injury. Slight erythema with some delayed scarring of the epidermis resulted. There were no deaths. A similar test was run on guinea pigs with a 10% solution of benzoyl peroxide in propylene glycol. The doses ranged from 5 to 20 ml/kg. Only slight erythema was observed; no deaths occurred.

An inhalation test also described in this study [46] showed that an unspecified number of rats had no observable ill effects after being exposed to airborne benzoyl peroxide at an unspecified concentration for 3 hours.

In 1957, Horgan et al [47] gave 12- to 14-week-old female R and CBA hybrid hairless albino mice intraperitoneal (ip) injections of benzoyl peroxide. The injections consisted of 0.1-0.4 ml of unspecified concentrations of benzoyl peroxide in ethyl palmitate. The LD50 was reported to be 20 μmoles (4.8 mg)/mouse.

In 1959, Philpot and Roodyn [48] found the LD50 of benzoyl peroxide in 13- to 14-week-old female R hybrid mice to be 17.1 μmoles (4.1 mg)/mouse or 167 mg/kg.

In 1964, Sharratt et al [49] reported the results of a series of tests to determine the effects of benzoyl peroxide incorporated in the diet or administered by subcutaneous injection or by skin painting on rats and mice. Each test lasted 120 weeks for rats and 80 weeks for mice; moribund animals were killed during the study. The age and weight of the animals at the start of the experiment were not reported.

Three experimental groups, each composed of 25 male and 25 female rats and 25 male and 25 female mice, were given nutritionally balanced diets of wholemeal flour that was treated with a commercial flour bleach consisting of 18% benzoyl peroxide, 78% calcium sulfate, and 4% magnesium carbonate [49]. The control group contained the same number of animals as the experimental group but received untreated flour in their diet. The resulting benzoyl peroxide concentrations in the diet were 2,800 ppm, 280 ppm, and 28 ppm. These concentrations were selected because they were estimated to be 1,000, 100, and 10 times the normal human intake based on a yearly consumption of 200 pounds of flour/person. How much the animals actually ate was not reported, so exact dosages cannot be determined. Weight gains were recorded only for the rats during the first 16 months of the test.

The rats whose diets contained flour treated with 2,800 ppm and 280 ppm benzoyl peroxide gained weight at a slower rate than the controls; the authors reported that this effect was not seen when the rats were caged singly in a diet preference test and an individual caging test [49]. Seventeen mice that received the 280-ppm diet were killed accidentally, and a large number of rats and mice in the entire colony showed signs of infection, the nature of which was not specified by the investigators. For these reasons, the statistical significance of the results cannot be accurately evaluated.

A diet preference test and an individual caging test were conducted with 10 pairs of male rat littermates to determine if any differences in weight gain in the animals were the result of greater food intake with 1 of the diets [49]. One of each pair of the male littermates was given a flour-based diet containing benzoyl peroxide at 2,800 ppm, and the other was given the same diet without any benzoyl peroxide. Each rat was caged singly.

The weight gain for the two groups was reported to be similar [49]. After 30 weeks, each of the control rats had gained an average of 355 g and had consumed an average of 4,870 g of the supplied diet; the experimental group had gained 350 g each and eaten 4,902 g of the supplied diet. Rats caged singly tended to increase food intake slightly. On the basis of the diet preference test and the caging test, they concluded that concentrations of 1,000 and 100 times the normal human daily intake of benzoyl peroxide in the diets may have reduced the nutritional value of the diet; whereas the diet containing 10 times the normal daily intake of benzoyl peroxide did not.

Sharratt et al [49] provided diets of breadcrumbs made from flour treated with benzoyl peroxide to two groups of animals. The breadcrumbs given to 100 male and 100 female mice and 100 male and 100 female rats were prepared from bread made with flour containing benzoyl peroxide at 28 ppm. A group of 25 male and 25 female mice and 25 male and 25 female rats received a breadcrumb diet in which the flour had contained 2.8 ppm benzoyl peroxide. A control group of 100 male and 100 female mice and 100 male and

100 female rats was given a breadcrumb-based diet made from flour containing no benzoyl peroxide. Weight gains were reported only for the rats during the first 16 months of the test.

There were no significant differences in the body weights of the rats given treated breadcrumbs made with treated flour and those of the controls except at 16 months, when the male rats that received the breadcrumbs made from flour containing 2.8 ppm of benzoyl peroxide weighed significantly more than the male control rats [49]. The authors considered this of doubtful importance, since all rats began to gain and lose weight erratically because of chronic infection in the colony.

In another part of the study [49], rats and mice were given a single subcutaneous injection of what was described as a freshly prepared 20% suspension of benzoyl peroxide in starch solution. The dose for 25 male and 25 female rats was 120 mg of benzoyl peroxide, and, for 25 male and 25 female mice, it was 50 mg of benzoyl peroxide. Control rats and mice, 25 of each sex of each species, were each given an injection of the starch solution. All the rats and mice were provided with a commercial pellet diet. Body weights were reported only for the rats for the first 16 months. There was no difference in the rate of weight gain in the rats administered benzoyl peroxide and in their controls. No tumors were found at the injection sites in any of the rats or mice; there was no significant difference in the tumor incidence in the experimental animals and in the controls.

Sharratt et al [49] also painted benzoyl peroxide on the back of the neck of 25 male and 25 female mice for 6 consecutive days. One drop (about 50 mg) of a freshly prepared 50% suspension of benzoyl peroxide in flour paste was applied to each animal. A similar number of control mice were painted with only the flour paste. Both groups of mice were fed a commercial pellet diet. No tumors appeared at the sites of painting, and there was no significant difference in the overall tumor incidence between the experimental animals and the controls.

Sharratt et al [49] also administered a multiple treatment to groups of 25 male and 25 female rats and 25 male and 25 female mice. There were no control animals for this part of the experiment. The rats and mice received the flour-based diet containing 2,800 ppm benzoyl peroxide and subcutaneous injections of benzoyl peroxide as in the previously described tests. The mice were also painted with flour paste containing benzoyl peroxide in the manner described previously. Body weights were reported only for the rats for the first 16 months. Except for a slight decrease at the 8th month, the weight gain of the rats in this multiple treatment group was not significantly different from that of the controls in the other tests described previously. No tumors were found at the sites of injection or painting.

Sharratt et al [49] observed that the entire colony of mice and rats used in their experiments with benzoyl peroxide had many abnormal changes irrespective of the test performed on the animal. There was a statistically significant incidence of atrophy of the testicles in the rats given the diet based on flour treated with benzoyl peroxide at 2,800 ppm and in the rats receiving diets of breadcrumbs made with flour treated with benzoyl peroxide at 28 ppm and 2.8 ppm. The authors suggested that this atrophy was caused by benzoyl peroxide, which probably marginally decreased the amount of vitamin E in the diet. This conclusion was not supported by any analyses of the diets, and the degree of testicular atrophy in each rat was not stated; therefore, no definitive conclusion can be made. While the authors [49] concluded that benzoyl peroxide was not carcinogenic in rats or in mice under the test conditions, it does not seem that this was a definite experiment of carcinogenicity or of other types of chronic toxicity. The length of the observation periods and the experimental design were probably adequate; however, there may have been insufficient numbers of animals to detect carcinogenicity. In addition, it is uncertain how much benzoyl peroxide remained unchanged after it was added to the diets.

Other investigators have studied the action of benzoyl peroxide in animals to ascertain whether it is carcinogenic. Hueper [50] conducted a study to determine if benzoyl peroxide, when used as a polymerization catalyst for silicone rubber, had carcinogenic properties. According to the manufacturer, benzoyl peroxide was totally destroyed in the rubber curing process. A piece of silicone rubber that had been cured with benzoyl peroxide was implanted subcutaneously in the neck of each of 21 male and 14 female Bethesda black rats. In another group of Bethesda black rats, a gelatin capsule containing 50 mg of benzoyl peroxide was implanted subcutaneously in the nape of the neck of 20 males and 15 females. No control animals were used. The rats were observed for 24 months.

In the rats with silicone rubber implants, 10 sarcomas occurred at the implantation sites, and there were neoplasms at other sites, viz, 4 round cell sarcomas of the ileocecal lymph nodes, 3 mesotheliomas of the peritoneum, and 1 carcinoma of the bladder [50]. There were no tumors at the implantation sites in the rats with the encapsulated benzoyl peroxide, although seven of these rats had malignancies at other sites, including four round cell sarcomas of the ileocecal lymph nodes, one mesothelioma of the peritoneum, one epidermoid carcinoma of the snout, and one myxosarcoma of the anal region. Benign tumors, including two adenofibromas of the breast and one cystic cholangioma, appeared in three other rats in the group with the benzoyl peroxide implants. Hueper concluded that the absence of tumors at the sites of implantation provided conclusive evidence that benzoyl peroxide was not implicated in the induction of polymer cancers.

Van Duuren and his colleagues [51] studied the carcinogenicity of a group of epoxides, lactones, and peroxides including benzoyl peroxide. The backs of 30 male Swiss-Millerton mice were painted 3 times weekly with about 100 mg of a 5% benzene solution of benzoyl peroxide. Controls were similarly painted 3 times weekly with 100 mg of benzene alone. The median survival times were 292 days for the mice exposed to benzoyl peroxide and 264, 262, 412, and 292 days for the four control groups. The animals were examined regularly for tumors. None of the mice developed carcinomas; one mouse exposed to benzoyl peroxide developed a benign tumor. The authors concluded that benzoyl peroxide showed no carcinogenic activity in this experiment.

In 1972, Epstein et al [52] tested 174 agents, including benzoyl peroxide, for dominant lethal mutations in ICR/Ha Swiss mice. Benzoyl peroxide at doses of 54 and 62 mg/kg was administered by intraperitoneal (ip) injection to seven and nine male mice, respectively. Each animal was then caged with three untreated virgin female mice for 1 week. The females were replaced each week for a total of 8 weeks and then killed and examined for pregnancy (total implants), early fetal deaths, and late fetal deaths. Since late fetal deaths were very rare, total implants and early fetal deaths were the only implant features analyzed.

The results obtained in the experimental mice were not significantly different from the results in the control mice [52]. Benzoyl peroxide, in the dose range and in the strain of mice used, met none of the screening criteria for these dominant lethal mutations. The authors recommended additional tests to confirm the apparent lack of mutagenicity of benzoyl peroxide.

An evaluation of the mutagenic properties of 78% benzoyl peroxide was reported in 1975 [53]. The yeast Saccharomyces cerevisiae, strain D4, and the bacterium, Salmonella typhimurium, strains TA-1535, TA-1537, and TA-1538, were used in modified Ames assays. Tissue homogenates from mice, rats, and monkeys were added to the culture media to see if benzoyl peroxide might be activated to a mutagenic compound. It was concluded that benzoyl peroxide exhibited no mutagenic activity in any of the in vitro microbial assays performed; this conclusion is consistent with the data presented. However, the benzoyl peroxide was added in dimethylsulfoxide, a solvent in which it is not soluble, although it did, nevertheless, allow the benzoyl peroxide to come in contact with the yeast and bacteria.

Correlation of Exposure and Effect

The one report [31] on the effects of inhalation of airborne dust containing benzoyl peroxide on humans stated that two plant inspectors had symptoms of nose and throat irritation on 2 days when the concentrations of benzoyl peroxide ranged from 1.34 to 17.0 mg/cu m. On the 3rd day, when the concentrations of airborne benzoyl peroxide were 2.58-82.5 mg/cu m, they had symptoms of eye irritation, as well as of nose and throat irritation. However, no definite conclusions can be made from this report because the analytical information provided is insufficient for the reliability of the determinations to be assessed, so the concentrations of airborne benzoyl peroxide are questionable. Also, the presence of alum in the airborne dusts may have caused or contributed to the irritation.

Eye irritation tests in rabbits [42,43] and skin irritation tests on rabbits [42] and guinea pigs [46] have indicated that benzoyl peroxide is a low-grade irritant. There is some evidence that contact with benzoyl peroxide can cause sensitization in humans, although the incidence of this appeared low. Baird [32], Malten [34], and Jirasek and Kalensky [35] observed cases of occupational or contact dermatitis in humans, which were attributed to exposure to benzoyl peroxide. Benzoyl peroxide has been reported to be an allergen [34]; however, because it is unstable when in solution or in contact with flour and reacts to yield benzoic acid, it is not clear whether benzoic acid or benzoyl peroxide might be the allergen.

Benzoic acid itself is an allergen [32] and, perhaps because of its acid nature, an irritant. Redness and skin irritation occurring after exposure to benzoyl peroxide may be caused by primary irritation or by an allergic response. Baird [32] observed an allergic skin reaction and asthmatic wheezing in a baker who was exposed to benzoyl peroxide-treated flour. Malten [34] and Jirasek and Kalensky [35] diagnosed skin reactions as occupational contact dermatitis in workers who had become sensitized to benzoyl peroxide.

Some patients who used benzoyl peroxide for acne therapy were sensitized after repeated applications [36,37]; others had redness, which could have been primary skin irritation as well as a sensitization, but the authors [37,38] did not differentiate between the two. Morley [24] observed that only 1 of 180 patients treated with benzoyl peroxide could not tolerate the treatment. It was not stated whether this patient had an allergic response or a skin irritation.

There has been no evidence of systemic toxicity caused by benzoyl peroxide. Dogs given diets containing flour treated wih 0.8-28 g of benzoyl peroxide/100 pounds of flour had no apparent adverse effects [44,45]. No data were presented that would indicate the amount of benzoyl peroxide that remained in their diets after they were prepared, which involved steaming the flour treated with the compound. Sharratt and his colleagues [49] noted that male and female rats given benzoyl peroxide at concentrations of 280 or 28 ppm in a flour-based diet gained weight at a slower rate than the control rats; male rats given a diet with breadcrumbs made from flour treated with benzoyl peroxide at a concentration of 2.8 ppm gained weight at a rate similar to that of the controls. In another study [46], single dietary doses of 950, 400, or 200 mg/kg produced no ill effects. Ingestion of benzoyl peroxide in amounts far greater than those normally used to treat commercial flour had no apparent toxic effects in rats and dogs [42,44-46,49]. However, much of the benzoyl peroxide in the diets of these animals may have decomposed to benzoic acid by the time it was consumed.

Horgan et al [47] reported that, in mice, the LD50 of benzoyl peroxide administered through ip injection was 4.8 mg/mouse; later, Philpot and Roodyn [48] calculated an LD50 in mice of 4.1 mg/mouse for benzoyl peroxide given by ip injection. Sharratt et al [49] reported that a subcutaneous injection of 50 mg of benzoyl peroxide/mouse (2,500 mg/kg) caused an abscess that healed in several weeks; no deaths occurred. Sharratt et al [49] also gave rats 120 mg of benzoyl peroxide by subcutaneous injection with no apparent adverse effects. The absorption of benzoyl peroxide in mice appears to vary greatly depending on the site of injection.

Laboratory tests reported by Ede [38] on 10 men and 10 women using acne medications containing benzoyl peroxide were normal, indicating no systemic effects from dermally applied benzoyl peroxide. No data were found that dealt specifically with absorption of benzoyl peroxide through the skin or from different sites of injection in humans or animals.

The flammability and explosiveness of pure benzoyl peroxide have been the cause of accidents involving serious injuries and fatalities [3,40]. Accidents involving only property damage are summarized in Chapter V.

Carcinogenicity, Mutagenicity, Teratogenicity, and Effects on Reproduction

The results of experiments designed to show if benzoyl peroxide has any carcinogenic activity when it is implanted [50], painted on skin [49,51], or injected [49] were negative. The results of tests to detect mutagenic effects of benzoyl peroxide in a modified dominant-lethal assay with mice [52] and in Ames assays with bacteria and yeast [53] were also negative. No data on teratogenesis or other effects of benzoyl peroxide on reproduction were found.

TABLE III-1

EFFECTS OF BENZOYL PEROXIDE EXPOSURE ON HUMANS

Route of Exposure	Exposure Concentration and Duration	Effects	Reference
Dermal	20%	Irritation in 1 of 180	24
"	1%, 5%, and 10% 9 24-hr applications	Severe eczematous skin reactions in 25 of 69 at end of experiment	36
"	5 % 12 hr	Marked erythema and burning	37
"	5% 48 hr	Severe irritation	37
"	Unknown	Positive patch test and dermatitis in 3 of 30	34
"	20 - 100%	Slight skin irritation	35
Respiratory	1.34-17.0 mg/cu m	Nose and throat irritation	31
"	2.58-82.5 mg/cu m	Eye, nose, and throat irritation	31
Dermal and respiratory	Unknown	Severe dermatitis, asthmatic wheezing	32

TABLE III-2

EFFECTS OF BENZOYL PEROXIDE EXPOSURE ON ANIMALS

Route of Exposure	Species	Exposure Concentration and Duration	Effects	Reference
Inhalation	Rats	Unknown concentration 3 hr	None	46
"	"	24.3 mg/l 4 hr	Eye squint, increased and decreased respiratory rates, salivation, lacrimation, erythema; no effects after 48 hr except lingering eye irritation	42
Oral	"	5,000 mg/kg	None during 14-d observation period	42
"	"	950 mg/kg	Slight muscular weakness in 1 of 2	46
"	"	400 mg/kg	Vasodilatation in 1 of 2	46
"	"	200 mg/kg	None	46
"	"	2,800 ppm in diet 120 wk	Testicular atrophy	49
"	"	280 ppm in diet 120 wk	None	49
"	"	28 ppm in diet 120 wk	"	49
"	"	28 ppm in breadcrumb diet 120 wk	Testicular atrophy	49

TABLE III-2 (CONTINUED)

EFFECTS OF BENZOYL PEROXIDE EXPOSURE ON ANIMALS

Route of Exposure	Species	Exposure Concentration and Duration	Effects	Reference
Oral	Rats	2.8 ppm of breadcrumb diet 120 wk	Testicular atrophy	49
"	Dogs	Benzoyl peroxide-treated* flour 71.6 % of diet for 6 wk	None	44
"	"	Benzoyl peroxide-treated** flour 80% of diet for 21 - 38 d	"	45
ip	Mice	62 mg/kg	"	52
"	"	54 mg/kg	"	52
sc	Rats	120 mg	"	49
"	Mice	50 mg	"	49
Eye contact	Rabbits	111.4 mg of 78% benzoyl peroxide 5 min	Redness of conjunctivae in 2 of 5 lasting up to 48 hr	42
"	"	120.7 mg of 78% benzoyl peroxide 24 hr	Slight opacity of cornea in 3 of 3 lasting up to 48 hr; redness of conjunctivae in 3 of 3 lasting up to 7d	42
"	"	Unknown amount of 93% benzoyl peroxide 1 min	None	43

TABLE III-2 (CONTINUED)

EFFECTS OF BENZOYL PEROXIDE EXPOSURE ON ANIMALS

Route of Exposure	Species	Exposure Concentration and Duration	Effects	Reference
Eye contact	Rabbit	Unknown amount of 50% benzoyl peroxide 1 min	None	43
Dermal	"	500 mg of 78% benzoyl peroxide 4 hr	"	42
"	Guinea pigs	0.25 - 1.0 g/kg 24 hr	Slight erythema, delayed scarring	46
"	"	5 - 20 ml/kg of 10% benzoyl peroxide in propylene glycol 24 hr	Slight erythema	46
"	Mice	50 mg of 50% suspension	No tumors	49
"	"	100 mg of 5% solution	"	51
sc implants	Rats	50 mg 24 mon	No tumors at site of benzoyl peroxide implant; no tumors attributed to benzoyl peroxide	50

*28 g of benzoyl peroxide/100 lb of flour

**0.8 g of benzoyl peroxide/100 lb of flour

IV. ENVIRONMENTAL DATA

Environmental Levels

The information available on atmospheric concentrations of benzoyl peroxide in industry is limited. One manufacturer of benzoyl peroxide reported the results of an analysis of breathing zone air samples containing benzoyl peroxide from two different operations within the plant [10 (p 16)]. At the dry packing station, the total dust concentration was 0.10 mg/cu m. Another sample taken during another packing operation indicated that the total dust concentration was 0.16 mg/cu m. Both of these dust concentrations were below the existing federal environmental limit for benzoyl peroxide of 5 mg/cu m.

Sampling and Analysis

During industrial operations, benzoyl peroxide may escape into the environment as airborne dust [10 (p 16)]; however, there currently are no validated sampling and analytical methods specific for airborne benzoyl peroxide.

Kaznina [54] used a method for sampling and analysis in which the air samples were drawn through a filter into an absorber containing 5 ml of ethyl alcohol. Analyses of the samples for benzoyl peroxide were performed by ultraviolet spectrophotometry. The method was sensitive for benzoyl peroxide to a concentration of 1.0 μg/ml. Benzoyl peroxide, styrene, and dimethylaniline are present simultaneously where styrene-containing plastics are prepared [54]. The method was reported to have limited use because of interference by dimethylaniline and styrene, which were also present in the operation. Therefore, an analysis based on ultraviolet spectrophotometry would be of limited value because much of the benzoyl peroxide produced each year in the United States is used in the production of polystyrene [5].

Dugan [55] and Dugan and O'Neil [56] determined benzoyl peroxide by an analytical colorimetric method. A colored complex resulted when benzoyl peroxide was used to accelerate the reaction between methanol and N,N-dimethyl-p-phenylene diamine sulfate. The relationship of the color intensity and the amount of benzoyl peroxide present in solution followed Beer's Law at peroxide concentrations of 5-30 µg/ml but deviated at 40 µg/ml. For this analytical method to be accurate, time and temperature must be held constant because the reaction proceeds slowly without the addition of peroxide [57]. The authors [56] stated that molecular oxygen might interfere with the reaction as it does with many colorimetric methods. The time and temperature requirements, as well as the possible interference of molecular oxygen, make this method undesirable for analysis.

Banerjee and Budke [58] also used a colorimetric method of analysis for benzoyl peroxide. Benzoyl peroxide was dissolved in a mixture of acetic acid and chloroform; potassium iodide was then added. The absorption of the liberated iodine was measured at 470 nm, and the amount of benzoyl peroxide in the sample was determined from a standard curve. This method may be hazardous because explosions have occurred when chloroform and benzoyl peroxide were mixed and then heated above room temperature [59-61]. Furthermore, NIOSH has concluded that chloroform is carcinogenic (letter from Director, NIOSH, to Assistant Secretary of Labor, OSHA, June 1976). This analytical method is not specific for benzoyl peroxide but determines total peroxides.

Airborne methylethylketone peroxide (MEKO) was analyzed by a colorimetric method (T Anania, written communication, January 1977). A known volume of air containing MEKO was drawn through a U-tube filled with dimethyl phthalate in which the benzoyl peroxide dissolved. The solution was transferred to a test tube, and diphenylcarbohydrazide, a color reagent, was added. This solution was compared to a standard solution in a spectrophotometer. When benzoyl peroxide was analyzed by this method, at the lowest level, 50 μg/sample, the color intensity was equivalent to that produced by 1.5 μg of MEKO. After an initial relative linearity in the range of 0-100 μg/sample, benzoyl peroxide, in increasing quantities, developed a progressively lower color intensity/unit and gave a curvilinear standard curve. Although no recommendations were made by the author, this degree of curvature is undesirable for a quantitative analysis.

Dolin [62] used methods for sampling and analysis that were not specific for benzoyl peroxide. One cubic foot of air/minute was drawn through a Greenburg-Smith impinger containing 75 ml of doubly distilled water for times varying from 13 to 37 minutes. Aliquots of the sampling solution were added to flasks containing a mixture of 0.75% aqueous potassium iodide and a freshly prepared 0.50% starch solution, which were then allowed to stand from 1 hour to overnight. The color intensity was measured in a spectrophotometer or visually compared with a set of color standards prepared from known concentrations of benzoyl peroxide. The relationship of the developed color in the standards to the concentration of benzoyl peroxide followed Beer's Law, and a standard curve was constructed. The concentrations of benzoyl peroxide in the samples were read from the standard curve. Dolin found that, unless the standards were prepared at the same time as the sample solutions, the measurement error was as high as 25%. With this method, a spectrophotometer can detect as little as 1 μg of benzoyl peroxide; as little as 3 μg can be detected visually. The method was not specific for benzoyl peroxide but indicated total peroxides. Dolin used a standard impinger in his sampling method but gave no data on the collection efficiency of the impinger with distilled water as an absorbent.

Sampling and analytical methods have been developed that allow specific analysis for benzoyl peroxide. A known volume of air is drawn through a membrane filter. The benzoyl peroxide is subsequently extracted from the filter and analyzed by high pressure liquid chromatography [63]. When an air sample size of 90 liters was collected, by drawing air at a rate of 1.5 liters/minute through a 37-mm diameter mixed cellulose ester membrane filter with a pore size of 0.8 μm, a collection efficiency of 1.00 was determined. Storage stability studies on samples collected from a test atmosphere at a concentration of 7.30 mg/cu m indicated that, after 1 week with the samples held in the filter cassettes at room temperature, there was a 9.3% decrease in the amount of benzoyl peroxide recovered from the filter.

Benzoyl peroxide was extracted from the filter with ethyl ether [63]. Tests showed that benzoyl peroxide is stable in ethyl ether at room temperature for at least 1 week. Thus, there may be up to a 9.3% loss of benzoyl peroxide if the samples are not extracted immediately or refrigerated.

Analysis of the samples by high pressure liquid chromatography is subject to interference from any compound that has the same retention time as benzoyl peroxide at the operating conditions used [63]. Although retention time data on a single column cannot be considered proof of chemical identity, an interfering compound can be eliminated as an interference by altering operating conditions, using a different column packing, or using a selective detector. The coefficient of variation for the total sampling and analytical method in the range of 3.12-19.10 mg/cu m was 0.060, which corresponds to a standard deviation of 0.30 mg/cu m at an air concentration of benzoyl peroxide of 5 mg/cu m. The sampling device is small and portable, and it involves no liquids. The samples collected on membrane filters are analyzed by means of a quick instrumental method. This method has been shown to provide sufficient accuracy, sensitivity, and precision within the range required to determine compliance with this standard for benzoyl peroxide.

Other methods have been reported for the determination of benzoyl peroxide in pharmaceuticals [64,65], flour [66], cheese [22], fats [67], and oils [67]. In 1967, Gruber and Klein [64] reported the comparison of spectrophotometric, titrimetric, and polarographic techniques in testing the stability of pharmaceuticals containing benzoyl peroxide. The results of the polarographic and spectrophotometric methods, when they were used to show the degradation of benzoyl peroxide at high temperatures, were in good agreement. The titrimetric method was far less sensitive than the other two and did not differentiate between benzoyl peroxide and some of its decomposition products. All three methods are colorimetric, and none is specific for benzoyl peroxide. In 1975, Daly et al [65] reported difficulty in reproducing the results of Gruber and Klein [64] and suggested another titrimetric method as a more accurate means for determining the content of benzoyl peroxide in pharmaceuticals. The authors [65] noted that, although alkylhydroperoxides and dialkyl peroxides would interfere with this method, commercial pharmaceutical creams and lotions containing benzoyl peroxide would probably not contain these other classes of peroxides. The American Oil Chemists Society (AOCS) [67] published their official method for analyzing total peroxide in fats and oils in 1960; it was reapproved in 1973. The described method was a titrimetric procedure that was not specific for benzoyl peroxide.

It is recommended that total dust concentrations be monitored routinely by collecting breathing zone samples on a preweighed glass-fiber filter as detailed in Appendix I. Glass-fiber filters have been selected for sampling because they will efficiently collect airborne dust particles. In addition, being relatively free of organic matter, they are less likely to form explosive mixtures with benzoyl peroxide than filters like cellulose paper.

After the sample is collected, the weight of total dust is determined by gravimetric analysis. The filter is reweighed with the same balance that was used for the preweighing, and the difference between the tare and final weights is determined. Before each weighing, the filter should be equilibrated in a constant humidity chamber, and a static charge neutralizer should be used to improve the reproducibility of the weight determinations and thus enhance gravimetric accuracy. The recommended gravimetric method is described in detail in Appendix II.

In many applications, one should not have to do more than measure total dust. However, if the total airborne dust exceeds the recommended benzoyl peroxide environmental limit of 5 mg/cu m, the gravimetric analysis must be followed by a colorimetric analysis for total peroxide developed from a method by Dolin [62]. The filter is placed in a flask containing a mixture of potassium iodide and starch solution which is oxidized by benzoyl peroxide and other peroxides to form a blue iodide-starch complex. The filter should remain in the solution for 12 hours to permit the blue color to develop from the iodide-starch complex. The color intensity is measured in a spectrophotometer or visually compared with a set of color standards. The concentration of total peroxides should be calculated as benzoyl peroxide. Other oxidizing agents would also produce the iodide-starch complex and give erroneously high concentrations when they are present with benzoyl peroxide in the sample. This interference, however, would never produce a calculated benzoyl peroxide concentration lower than the actual concentration. The recommended analytical method is described in detail in Appendix II.

Engineering Controls

Benzoyl peroxide should be protected from contact with sparks, shocks, friction, and excessive heat. Electrical installations in all areas where pure benzoyl peroxide or formulations containing benzoyl peroxide are manufactured, used, or stored should conform to the National Electrical Code, NFPA No. 70-1975 [68]. Where benzoyl peroxide is used in spray applications, electrical installations and other engineering controls, including ventilation, should conform to the Standard for Spray

Application Using Flammable and Combustible Materials, NFPA No. 33-1973 [69]. Where it is used in the manufacture of organic coatings, electrical installations and other engineering controls, such as ventilation, should conform to the Standard for the Manufacture of Organic Coatings, NFPA No. 35-1971 [69].

Descriptions of two hazard classification systems, one under consideration by the NFPA (O Mageli, written communication, January 1977) and the other recommended by Factory Mutual Research Corporation [70], a loss prevention research and engineering organization, are found in Chapter XII, Appendix IV. The NFPA classification system provides a general description of the burning characteristics of organic peroxides. The Factory Mutual Research Corporation provides a more detailed description of the physical reactions to the tests used to generate the hazard classifications.

Nuclear static eliminators can be used to remove any static electric charge which might build up where benzoyl peroxide flows through an aperture [10 (p 7)]. All metal surfaces that benzoyl peroxide comes in contact with should be grounded and bonded [4]. Conductive flooring or mats will also aid in the control of static electricity [4].

Benzoyl peroxide and its formulations should be stored where there are no sources of excessive heat or ignition, [4] such as open flames, electrical devices [71], and exposed steam lines or wall radiators, in the storage area [4]. Futhermore, benzoyl peroxide should not be exposed to direct sunlight [4,71].

Buildings or facilities intended specifically for the storage of organic peroxides should be constructed in conformance with any applicable local, state, or federal requirements [4] and any additional recommendations of manufacturers and insurance authorities [71]. Depending on the amount of organic peroxides stored at one time, manufacturers and users should provide detached storage buildings or storage rooms separated by fire-resistant walls [71]. Explosion venting should be provided where benzoyl peroxide is manufactured, used, or stored; the Factory Mutual Research Corporation [72] has recommended that there should never be less than 1 sq ft of venting area/30 cu ft of volume. However, supporting data were not included with this recommendation. In process areas where there are numerous operations, partitioning with fire- and explosion-resistant materials should be installed where needed.

All buildings where large quantities of pure benzoyl peroxide are stored should have automatic sprinkler systems [4]. Appropriate building codes should be consulted for specific requirements for installing these sprinkler systems.

Any area or room where pure benzoyl peroxide is manufactured and stored should have at least two exits; no part of the room should be more than 75 feet from an exit [4]. The doors should open outward, and they should be equipped with a "panic bar" if they are latched [4].

Respiratory protective equipment and protective clothing are not acceptable substitutes for proper engineering controls but should be available for emergency purposes and for nonroutine maintenance and repair situations.

If ventilation is necessary, it should conform to the National Electric Code, NFPA No. 70 [68]. The NIOSH Recommended Industrial Ventilation Guidelines [73] should also be consulted for guidance in design. Recommendations in *Industrial Ventilation--A Manual of Recommended Practice* [74] and *Fundamentals Governing the Design and Operation of Local Exhaust Systems*, ANSI Z9.2 -1971 [75] should also be considered. Exhaust air should not be recirculated into workrooms. Ventilation ducts should be maintained so benzoyl peroxide does not accumulate.

The Factory Mutual Research Corporation [72] has recommended that stored flammable liquid peroxides and solid benzoyl peroxide formulations that are explosive or flammable should be provided with natural ventilation through permanent roof- and floor-level openings having at least 1 sq ft of free inlet and outlet opening/500 sq ft of floor area. Individual ventilators should be no more than 72 sq inches and covered with screen to prevent wastes, embers, or small animals from entering. Trapped drains leading to a safe, outdoor disposal point should be installed and, where waste water containing benzoyl peroxide could enter the drains, they should be flushed to prevent an accumulation of material in the trap.

V. WORK PRACTICES

The work practices and sanitation needs appropriate to the manufacture, handling, and storage of benzoyl peroxide differ for each benzoyl peroxide formulation. Improper use or negligent handling and storage of benzoyl peroxide formulations can lead to a separation or precipitation of benzoyl peroxide from the diluents [3,76]. If a formulation separates or dries out, the more stringent work practices appropriate for pure benzoyl peroxide should be observed.

Pure benzoyl peroxide is a very flammable solid which may decompose explosively if subjected to excessive heat, shock, sparks, or friction [4]. If benzoyl peroxide is exposed to temperatures of 75-80 C for prolonged periods of time, it becomes unstable and may spontaneously decompose; if heated to just above its melting point (104 C), it will instantaneously and violently decompose [4]. When benzoyl peroxide must be mixed with other materials, the temperature of these other materials should be below 50 C [4]. Benzoyl peroxide may react violently with various organic and inorganic acids, amines, alcohols, metallic naphthanates, polymerization accelerators, and other chemicals that are easily oxidized [4]. Benzoyl peroxide will decompose at room temperature in the presence of small amounts of tertiary arylalkylamines which are used in curing polyester resins. Many transition metal ions also catalyze the decomposition of benzoyl peroxide [77]. Direct or reflected sunlight may cause decomposition of benzoyl peroxide [71]. Decomposition of benzoyl peroxide is accompanied by a 200-fold increase in volume [5] and yields a dense white smoke consisting of benzoic acid, phenyl benzoate, terphenyls, biphenyls, benzene, and carbon dioxide [7]. The decomposition of benzoyl peroxide may be preceded or followed by fire [5]. If benzoyl peroxide or its decomposition products catch fire, dense black smoke is produced [8]. The resulting biphenyls promote the further decomposition of benzoyl peroxide [5,7].

Formulations of benzoyl peroxide are generally less hazardous than the pure compound [9,77]. In safety tests, the burning rate of a benzoyl peroxide formulation containing 25% water was not as intensive as that of pure benzoyl peroxide [7]. Formulations containing plasticizers also generally burn slower than does pure benzoyl peroxide; however, a 50% benzoyl peroxide paste with tricresyl phosphate decomposed at a lower temperature than that required to explode pure benzoyl peroxide [78]. Appendix IV explains two hazard classification sytems that relate to the physical properties of all organic peroxides and indicate the precautions that should be observed for their safe handling, use, and transporation; they give no indication of toxicity. Tests that evaluate the total energy release of a compound, the rate at which the energy is released, and the ease of ignition and decomposition are the basis for such hazard classifications. Employers should be aware of the appropriate hazard classification of the benzoyl peroxide formulations used in the workplace and should institute pertinent work practices.

Accidents

The flammability and explosiveness of benzoyl peroxide have caused accidents; those which resulted in injuries or fatalities are discussed in Chapter III. Other accidents, involving damage, have been described.

Knowledge of the physical properties of benzoyl peroxide and correct work practices might have prevented some of the accidents or at least lessened their severity. Malkemus [5] reported that 1 pound of benzoyl peroxide exploded after it had been removed from its original shipping container, placed in an open 1-quart can, and set under a window exposed to the sun. He [5] stated that the heat from the sunlight contributed to the explosion and that the can may have been contaminated with a reactive chemical.

A report from the American Insurance Association [3] included accounts of several accidents. A tractor-trailer carrying 300 pounds of benzoyl peroxide in 1-pound containers sideswiped another trailer, and the benzoyl peroxide exploded. All of the benzoyl peroxide was consumed in the explosion, and no fire resulted.

In another accident, an unspecified quantity of benzoyl peroxide caught fire because friction was generated by a broom used to sweep it off the floor. The fire spread to benzoyl peroxide stored on the second floor of the building.

A third accident reported by the American Insurance Association [3] occurred at a reinforced-plastics manufacturing plant. There was an explosion in a warehouse where 1,000 pounds of organic peroxides were stored. The report implied that benzoyl peroxide was present. The resulting fire spread to several adjoining buildings. Spilled peroxide and careless smoking were given in the report as possible causes of the accident.

A blended mixture of 30% benzoyl peroxide and unknown quantities of magnesium carbonate, hydrogen peroxide, sodium hydroxide, and oleic acid exploded while being dried in a steam-heated continuous drying oven [3].

There was a secondary explosion and flash fire in the building. The benzoyl peroxide apparently decomposed inside the oven, releasing what was described as a white, copious, flammable gas. Three sides and the top of the oven were blown out as much as 2 feet.

In 1974, Bolt and Joyce [79] described explosions which occurred during the alkylation of polyhalomethanes by alkanes and alkadienes in the presence of catalytic amounts of benzoyl peroxide. A reactor was charged with 100 g of carbon tetrachloride and 0.40 g of benzoyl peroxide. The reactor was then pressurized with ethylene and heated with agitation. Twenty minutes after the reaction had started, when the temperature was 94 C and the pressure was about 14,230 pounds per square inch (psi), an explosion occurred which blew out the gas inlet line near the reactor. An increased ratio of water to carbon tetrachloride resulted in no further explosions when the reactor was operated at 9,600 psi and 110 C; 100 g of carbon tetrachloride, 100 g of water, and 0.23 g of benzoyl peroxide were used.

The investigators [79] stated that the reaction can occur without incident at a lower pressure, such as 1,400 psi with a temperature as high as 120 C when 0.45 g of benzoyl peroxide and 200 g of carbon tetrachloride are used. However, a violent reaction occurred when equal weights of water and carbon tetrachloride were used at 1,400 psi and 165 C, although there was no explosion.

Storage, Handling, and Transportation

All areas, rooms, and buildings where benzoyl peroxide and its formulations are stored should be inspected frequently. Any area where benzoyl peroxide is manufactured or stored should have smoke and heat detectors. Any conditions that may cause benzoyl peroxide to burn or explode should be eliminated. Unopened containers should be returned to a central storage area; opened containers may be kept in a special dispensing or premixing area, although they are safer in an isolated building. Benzoyl peroxide formulations containing more than 75% benzoyl peroxide should be stored alone. Other benzoyl peroxide formulations should not be stored with chemicals, such as explosives, reactive metals, and acclerators, that will readily react with benzoyl peroxide [3].

Benzoyl peroxide and its formulations should always be stored in their original containers. In addition, because of possible contamination, no benzoyl peroxide which has been removed should be returned to its original container. Benzoyl peroxide containers should be kept closed when not in use to prevent contamination [71]. Contamination of benzoyl peroxide may result in decomposition or fire [3]. No screw tops should be permitted on containers used for formulations of benzoyl peroxide if pure benzoyl peroxide could accumulate in the screw threads [78]; an accident occurred when a screwcap bottle of benzoyl peroxide was being opened [40]. Precautions should be taken so that wet benzoyl peroxide formulations do not dry out.

Ultraviolet radiation will, like heat, increase the rate of decomposition of benzoyl peroxide [80]. Sufficient open space should be left between stacks of peroxide containers in storage areas. When hazardous benzoyl peroxide formulations must be refrigerated, explosion-proof refrigerators should be used for this purpose [72].

Only clean, properly designed equipment should be used for benzoyl peroxide and its formulations; containers should be made of polyethylene or stainless steel. The use of copper, brass, lead, zinc, and galvanized equipment should be avoided because reactions in such equipment may accelerate decomposition of organic peroxides [71]. Benzoyl peroxide should be brought into the process area in the original shipping container and in quantities limited to the amounts required for daily use. Only small quantities of pure benzoyl peroxide, definitely not more than 1 pound, should be handled at a time [5]. If large quantities of the peroxide start to decompose, the decomposition of the outside layer confines the inner mass and increases the rate of decomposition, causing an explosion [5].

A separate area should be provided for premixing benzoyl peroxide with resins [72]. The accelerator should be mixed with the resin before benzoyl peroxide is added to prevent violent decomposition [71]. Work practices for fibrous glass and plastic fabricators have been recommended to minimize the hazardous properties of benzoyl peroxide [81,82].

No pure benzoyl peroxide, without diluents, should be allowed in any grinding operation because explosive decomposition may occur [71]. Benzoyl peroxide may explode if it is recrystallized from hot chloroform [59-61]. The peroxide can be safely recrystallized from chloroform at room temperature if methanol is added to the solution [59]. However, as was mentioned in Chapter IV, Sampling and Analysis, chloroform has been implicated as a carcinogen, so an alternative solvent should be considered.

All containers of benzoyl peroxide and its formulations should be properly labeled. Labels for benzoyl peroxide formulations should follow the regulations in Hazardous Industrial Chemicals, ANSI, Z129.1. Shipping labels should comply with the US Department of Transportation regulations and other applicable statutes, regulations, and ordinances [4].

Warnings should be posted in places where benzoyl peroxide is used and stored. The warnings should briefly and concisely state the important safety precautions to be adhered to within the area [4]. These warning placards should also indicate that these areas are accessible only to authorized personnel. Exits should be easily accessible and clearly marked. The location of emergency and first-aid equipment should also be easily accessible and clearly marked.

The Department of Transportation regulations, 49 CFR 173.157 and 178.58, specify that benzoyl peroxide wet with at least 30% water by weight should be packaged in quantities not to exceed 1 pound. It is important that fire-resistant material separates the individual bags so that the decomposition of benzoyl peroxide in one bag is less apt to affect the other bags in the box [5].

Housekeeping and Maintenance

The hazardous nature of benzoyl peroxide makes it imperative that housekeeping duties be performed continually under adequate supervision. Failure to follow these procedures has caused fires and accidents [71]. Even small amounts of benzoyl peroxide are potentially dangerous, and they may unpredictably decompose if subjected to any friction, heat, or shock [4]. Benzoyl peroxide formulations, such as pastes or the wet peroxide, may separate into their respective components through evaporation or freezing [6,76,83]. Thus, these small amounts of benzoyl peroxide formulations may be dangerous if not cleaned up from the floor and from the equipment in the process areas. The accidental decomposition of these traces of benzoyl peroxide could initiate the decomposition of all the benzoyl peroxide in the surrounding area [61]. Wet mops or other implements that will minimize sparks and friction should be used to clean up spills; a fire has resulted when the friction between a broom and benzoyl peroxide on the floor ignited the peroxide [3].

All equipment should be cleaned meticulously to avoid possible violent reactions between benzoyl peroxide and reactive chemicals. Ducts should be cleaned and inspected regularly to prevent the accumulation of benzoyl peroxide. Benzoyl peroxide should either be removed or covered during maintenance and repair work [71]. Where benzoyl peroxide formulations are used to bleach flour or catalyze certain organic reactions, the proportion of benzoyl peroxide is generally so small in relation to other chemicals present that the nature of these chemicals, rather than that of benzoyl peroxide, may dictate the housekeeping and maintenance procedures [4].

The grounds surrounding process and storage buildings must be kept cleared of vegetation and all other combustible materials, such as trash, to prevent the spread of fire if one should occur [71,72]. Maintenance and repair work in areas where benzoyl peroxide is used, stored, or manufactured should be authorized by the appropriate supervisor [3,71].

Spills and Waste Disposal

Spills should be wetted with water and cleaned up immediately with a wet mop or other nonsparking implements [10 (p 9)]. Vacuum units should be operated from a remote location away from electrical contacts; filter bags, as well as the vacuum lines, should be grounded to prevent static charge buildup. Care should be taken that benzoyl peroxide wastes are not mixed with other materials or chemicals, such as oxidizing or reducing agents, that might create hazardous conditions. A nonreactive container, such as one made of polyethylene, reserved only for benzoyl peroxide wastes, should be used to store the wastes until their disposal.

Benzoyl peroxide should not be disposed of by burning unless it has been thoroughly wetted down or mixed with water-wetted vermiculite, perlite, or another inert substance [84]. Water slurries of benzoyl peroxide wastes may be destroyed by gradually adding small amounts of the slurry to 10 times its weight of 10% sodium hydroxide solutions [4,84]. There should be sufficient agitation or stirring of the mixture so that there is no lump formation or settling. Water may be added to prevent thickening of the mixture that would make stirring difficult. The resulting slurry of sodium benzoate should be checked for neutrality and may be flushed into the sewage system if local regulations permit. Pure benzoyl peroxide itself should never be flushed into the sewage system [78]. Additional details of inactivating and disposing of benzoyl peroxide are described in Appendix V.

If wetted vermiculite or perlite has been added to a benzoyl peroxide spill, the water should be drained off and the waste water added to the waste slurry. The remaining material may be burned in an open incinerator or otherwise disposed of in accordance with local, state, and federal laws. If the material is burned, it should be placed in a shallow trench and ignited from a distance of at least 6 feet. When benzoyl peroxide becomes mixed with an unknown material, it should be considered contaminated and disposed of properly [72].

If bags and cartons that formerly contained benzoyl peroxide are to be destroyed, they should be placed in a special waste collection drum provided for that purpose. The contents of the drum should be kept wet until they can be carefully burned in an area reserved for that purpose [4]. When the bags and cartons are ready for disposal, they should be burned in open piles or disposed of in accordance with local, state, and federal regulations. Empty 1-pound bags and cartons should not be recycled unless properly cleaned of all traces of benzoyl peroxide.

Disposal containers made of plastic or other flexible material should be used because, while they may rupture thereby releasing the contents, they are unlikely to explode [85]. Extreme caution should be taken to ensure that wet benzoyl peroxide wastes and other wastes containing pastes and liquid solutions of benzoyl peroxide are not allowed to dry out and thus increase the hazards of fire and explosion. The waste containers should be placed in a cool, well-ventilated place and disposed of frequently.

Protective Clothing and Equipment

Protective clothing and safety glasses with side shields or safety goggles should be worn by employees to reduce the possibility of skin contact and eye irritation. Such protection is especially important where benzoyl peroxide and other powder or granular benzoyl peroxide formulations may become airborne or where liquid or paste formulations of benzoyl peroxide might be spattered or spilled.

Protective clothing should be fire resistant. Any fabric that generates static electricity is not recommended. To prevent the buildup of static electricity, appropriate conductive footwear should be worn [4,10 (p 6)]. Gloves made of rubber, leather, or other appropriate material should be worn by employees for protection when they are opening shipping boxes of pure benzoyl peroxide [4] or otherwise handling pure benzoyl peroxide. Aprons made of rubber or another appropriate material are recommended for added protection when handling benzoyl peroxide and its formulations. Plastic aprons that generate static electricity should not be used [4].

All personal protective clothing and equipment should be cleaned, inspected on a regular schedule, and replaced when worn out or broken. The employer is responsible for ensuring that such clothing and equipment are stored in suitable designated containers or locations when not in use.

When the protective clothing is laundered, an antistatic rinse should be used to reduce static electricity [10 (p 6)]. Employers should inform launderers of the hazards of benzoyl peroxide, including the danger of smoking in the vicinity of the soiled clothing.

Workers must not carry sources of ignition, such as lighters and matches, into areas where benzoyl peroxide is being used or stored [10 (p 86)]. Workers whose uniforms become grossly contaminated with benzoyl peroxide should remove them before going to areas where smoking is permitted, where chemicals that may react explosively with benzoyl peroxide are present, or where there are any sources of ignition, such as soldering irons or welding equipment. In addition, employees should work behind a safety shield made of a transparent shatterproof material when they are performing particularly hazardous tasks, such as packaging benzoyl peroxide [10 (p 6)].

Respiratory protection as specified in Chapter I must be used whenever airborne concentrations of benzoyl peroxide cannot be controlled to the recommended workplace environmental limit by either engineering or administrative controls.

Sanitation

Protective clothing should be kept apart from the workers' street clothing in lockers with two compartments provided for that purpose.

To minimize the potential for explosion or fire, workers must not eat or smoke where benzoyl peroxide is manufactured, used, or stored. Workers should also wash their hands before eating, smoking, or using the lavatory. A supply of potable water must be available near all places where there is potential contact with benzoyl peroxide and its formulations. A water supply may be provided by a free-running hose at low pressure or by emergency showers. Soap should be available at emergency showers. Where contact with the eyes is likely, eyewash fountains or bottles should be provided [10 (p 6)].

Emergency Procedures

Drills and training for all personnel should be an integral part of on-the-job training [10 (p 8)], and the employer should continually update emergency procedures. The employer should provide all emergency equipment and ensure that it is clearly marked, located in an easily accessible place, and maintained in working order.

Firefighters should be informed that the dense smoke produced by benzoyl peroxide necessitates the use of a lifeline and a self-contained breathing apparatus [4,10 (p 86)] in addition to their standard firefighting clothing [4].

Local fire units and rescue squads should be apprised of the types of emergencies that may arise before any emergencies occur. The necessary phone numbers for such emergency assistance must be prominently posted in areas where emergencies are likely to occur.

Areas where pure benzoyl peroxide is manufactured, packaged, and stored should not contain firefighting equipment; if a fire occurs, these areas should be evacuated immediately; employees should not attempt to control this type of fire. However, firefighting equipment should be well marked and located in every room and area where formulations of benzoyl peroxide are stored. If a fire occurs near an organic peroxide storage area, the containers within the storage area should be kept continually wetted to prevent overheating.

Appropriate warning alarms that are automatically activated by heat or smoke should be installed in all benzoyl peroxide storage and work areas. In addition, an independent alarm system that can be controlled manually and whose controls are readily accessible to employees is advisable if smoke or heat is considered insufficient to trigger the automatic alarms.

VI. DEVELOPMENT OF STANDARD

Basis for Previous Standards

In 1964, the American Conference of Governmental Industrial Hygienists (ACGIH) [86] proposed 5 mg/cu m as a tentative Threshold Limit Value (TLV) for benzoyl peroxide. The TLV is a TWA concentration for an 8-hour workday, 40-hour week. This 5 mg/cu m limit was adopted by the ACGIH in 1966 and has remained unchanged [87]. In 1976, the ACGIH reported a tentative short-term exposure limit (STEL) of 5 mg/cu m for benzoyl peroxide. The ACGIH defines the STEL as the maximum allowable concentration, or absolute ceiling, not to be exceeded at any time during the 15-minute excursion period [88].

The 1974 revision of the 1971 documentation [89] and the 1966 documentation [90] cited inhalation data from the unpublished industrial hygiene survey [31] of a benzoyl peroxide manufacturer in November 1950. The two plant inspectors experienced pronounced nose and throat irritation when the concentration of benzoyl peroxide in airborne dust was 12.2 mg/cu m, but they noted no adverse symptoms at 1.34-5.25 mg/cu m. Potassium aluminum sulfate and magnesium carbonate were also present simultanously with the airborne benzoyl peroxide. The authors, Moskowitz and Burke [31], failed to isolate a single component of the dust as the irritant.

In 1966, the Pennsylvania Department of Health [91] listed an 8-hour TWA concentration of 5 mg/cu m for benzoyl peroxide. This value was based on the ACGIH TLV [87]. Pennsylvania also listed a short-term exposure limit of 10 mg/cu m for 15 minutes for airborne benzoyl peroxide. The Pennsylvania Department of Health [91] cited a report by Kayanovich et al

[92] that exposure to starting materials in the manufacture of benzoyl peroxide or to benzoyl peroxide itself caused respiratory tract irritation, increased numbers of monocytes, and disturbances in ventilatory function. However, Kayanovich et al [92] indicated that the production of benzoyl peroxide was carried out in an enclosed system and was not accompanied by the release of any toxic substance into the air. Benzoyl chloride and phosgene were starting materials to which the workers were exposed. The authors [92] indicated that the toxic effects seen in workers were consistent with those that would be expected with exposure to phosgene and benzoyl chloride.

In 1968, a report of the International Labour Office [93] listed 5 mg/cu m as the maximum allowable concentration for benzoyl peroxide in the Federal Republic of Germany. Winell [94], in a summary of hygiene standards in different countries for chemicals in the work environment, wrote that the Committee of the German Research Association based this value on the ACGIH TLV. The Maximale Arbeitplatzkonzentrationen 1976 stated that benzoyl peroxide has very little effect on skin [95]. The International Labour Office [96], in a 1976 tabulation of permissible levels of toxic substances, listed 0.05 mg/cu m as the limit for benzoyl peroxide in Bulgaria and 5 mg/cu m in Belgium, Finland, the Netherlands, and Switzerland. The International Labour Office did not provide the bases for these values.

The present federal standard (29 CFR 1910.1000) for exposure to benzoyl peroxide in the workplace is an 8-hour TWA concentration limit of 5 mg/cu m. This was based on the 1968 ACGIH TLV [97].

Basis for the Recommended Standard

(a) Permissible Exposure Limits

Inhalation of airborne dust containing benzoyl peroxide has caused irritation in humans [31] and animals [42]. Nose, eye, and throat irritation were reported by two state inspectors at a plant where benzoyl peroxide was used [31]. They experienced this irritation on 3 days when the concentration of airborne benzoyl peroxide ranged between 1.34 and 82.5 mg/cu m. The interpretation by the ACGIH TLV Committee indicated that no irritation occurred when the concentration of benzoyl peroxide in air was 5.25 mg/cu m or lower. Although this view may be correct, the lack of details in the report makes verification of this interpretation impossible. The inspection report did not specifically state that benzoyl peroxide was the cause of the discomfort or whether potassium aluminum sulfate or magnesium carbonate in the dust caused or contributed to the irritating effects. The methods of analyses were not described. Since there is no validated method of sampling and analysis for benzoyl peroxide, the method used to analyze the collected samples was probably not specific for this compound. The possible toxic effects of airborne benzoyl peroxide on humans cannot be accurately assessed because the report lacks essential data.

Studies have indicated no carcinogenic [49-51] or mutagenic [52,53] effects from benzoyl peroxide. Sharratt et al [49] found that benzoyl peroxide had no carcinogenic activity from skin painting of mice, subcutaneous injection in mice and rats, and feeding studies in mice and rats. Van Duuren et al [51] reported that benzoyl peroxide showed no carcinogenic activity when used in skin painting experiments in mice.

Hueper [50] found that rats implanted with encapsulated benzoyl peroxide developed no tumors at the site of implantation. Epstein et al [52] observed that benzoyl peroxide demonstrated no mutagenic activity when tested in a modified dominant lethal assay. Benzoyl peroxide exhibited no mutagenic activity in bacteria and yeast [53]. No teratogenic studies or epidemiologic surveys were found.

The ACGIH [90] documentation of 5 mg/cu m as the recommended limit is primarily based on the report by Moskowitz and Burke [31] which, the ACGIH interpreted, indicated that no adverse symptoms were observed by two plant inspectors when the concentration of airborne benzoyl peroxide remained under 5.25 mg/cu m. (As commented above, verification of this interpretation is impossible because the report had insufficient detail.) Few pertinent toxicologic data on humans have been found in the literature. The animal data in the literature suggest that benzoyl peroxide is not a toxic compound, although no definitive studies have been found. The major hazard is injury or death resulting from fires and explosions caused by benzoyl peroxide [3,40,41].

The available epidemiologic and toxicologic evidence on benzoyl peroxide is insufficient to allow derivation of a new environmental limit or to warrant a change in the present environmental limit. It is recommended, therefore, that the present permissible exposure limit of 5 mg/cu m as a TWA concentration be retained. Because of the apparently low degree of toxicity of benzoyl peroxide, the action level is defined as equal to the environmental limit.

(b) Sampling and Analysis

It is recommended that airborne dust containing benzoyl peroxide be collected on a glass-fiber filter and analyzed gravimetrically. If the total airborne dust concentration is 5 mg/cu m or less, no further analysis need be done. If the total airborne dust concentration is greater than 5 mg/cu m, a total peroxide analysis should be performed on the material collected on the filter. A colorimetric analysis, developed from a method by Dolin [62], was selected for benzoyl peroxide because it is simple, reliable, and sensitive. However, the selected method is not specific for benzoyl peroxide; other peroxides can interfere. A method [63] specific for benzoyl peroxide, involving high pressure liquid chromatography, as described in Chapter IV, should be used if other, nonspecific methods, such as total peroxide analysis, show concentrations greater than 5 mg/cu m.

(c) Medical Surveillance and Recordkeeping

Little information has been found on the toxicity of benzoyl peroxide, so frequent comprehensive medical examinations are not proposed as a requirement. However, there is some evidence that benzoyl peroxide and its degradation products, including benzoic acid, cause sensitization. This sensitization should especially be looked for in the preplacement examinations, which should include an examination of the skin.

(d) Personal Protective Equipment and Clothing

Clothing worn and equipment used by employees while working with benzoyl peroxide and its formulations should be constructed of materials that will not cause sparks, friction, heat, or shock. Because there is some evidence that benzoyl peroxide and its breakdown products cause irritation and sensitization, protective clothing and equipment, such as gloves, aprons, and goggles or safety glasses with side shields, are recommended.

Respirators with cartridges or canisters containing activated charcoal or other oxidizable material should not be used because benzoyl peroxide is a strong oxidizer. On respirators, holders of replaceable filters should not have threads.

(e) Informing Employees of Hazards

The employer should initiate a continuing education program to ensure that employees have current knowledge of job hazards and of proper work practices and emergency procedures. Employees also should be informed that irritation and sensitization can possibly be caused by benzoyl peroxide and its breakdown products.

(f) Work Practices

Work practices are discussed in Chapter V. In operations involving the manufacture, use, or storage of pure benzoyl peroxide, the potential for skin, eye, throat, and nose irritation and for fire and explosion is greater than that for any of its formulations; protective clothing and equipment should be worn whenever required to prevent inhalation of benzoyl peroxide or eye and skin contact with it. Protective clothing, conductive shoes and floors, grounded machinery, and other engineering controls used to ensure a spark- and shock-proof environment will minimize the dangers from fire and explosion. Smoking, open flames, or any other source of ignition should be prohibited in benzoyl peroxide exposure areas to prevent fires and explosions. Engineering controls must be used when needed to keep concentrations of airborne benzoyl peroxide below the recommended limit.

(g) Monitoring and Recordkeeping Requirements

The workplace environment should be monitored semiannually and the records retained for 30 years. Since no chronic effects of benzoyl peroxide have been found, retention of environmental and medical records of employees for more than 30 years after termination of a worker's employment is unnecessary.

VII. RESEARCH NEEDS

Further study is needed to properly assess the toxicity of benzoyl peroxide and to evaluate its potential hazard to the working population. Presently, little is known about its toxic effects. The effects of long-term exposure to benzoyl peroxide, particularly those caused by ingestion and inhalation, should be studied, especially to determine if there are any carcinogenic, mutagenic, teratogenic, or other systemic changes.

Little information has been found concerning the possibility of absorption benzoyl peroxide through the skin, although skin contact is the most common route of human exposure. Studies should determine if benzoyl peroxide is altered during specific manufacturing processes and if the resulting residues can cause skin irritation or other adverse effects. Metabolic studies might provide information about the extent to which metabolites of benzoyl peroxide are responsible for toxic effects.

Research is necessary to assess the explosiveness and other hazards of exposure to benzoyl peroxide and its formulations. Laboratory experiments should be designed to provide information that can be extrapolated to full-scale decompositions, fires, and explosions and thus aid the development of a standard hazard classification system which would facilitate safe, consistent labeling, handling, and storage of benzoyl peroxide and its formulations. The sampling and analytical techniques used should be ascertained to be safe and reliable.

More specific work practices should be developed. The most appropriate protective clothing and respirators for particular processes should be determined, and waste disposal procedures that are safe and effective and that comply with current pollution control regulations should be formulated.

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IX. APPENDIX I

SAMPLING METHOD FOR AIRBORNE BENZOYL PEROXIDE

The sampling method for airborne benzoyl peroxide is adapted from general particulate sampling methods [98,99, R O'Gee, written communication, August 1976].

General Requirements

Collect breathing zone samples representative of the individual employee's exposure. Collect enough samples to permit calculation of a TWA concentration for every operation or location in which there is exposure to benzoyl peroxide. At the time of sample collection, record the sampling location and conditions, equipment used, time and rate of sampling, individual performing the sampling, and any other pertinent information.

Air Sampling

(a) Collect breathing-zone samples as close as practicable to the employee's face, without interfering with the employee's freedom of movement. This may be accomplished by use of a glass-fiber filter mounted in a personal cassette attached to the employee's clothing. The samples should characterize the exposure from each job or specific operation dealing with the manufacture, formulation, or application of benzoyl peroxide. Sampling flow rates should be checked frequently. If filters become clogged so that airflow is too restricted, change the filters and initiate the collection of new samples.

(b) Collect samples using a portable, explosion-proof sampling pump whose flow can be determined to an accuracy of ± 5% at 1-2 liters/minute. Connect the pump to the filter unit, which consists of a preweighed glass-fiber filter (Type A, 37 mm in diameter) mounted in a polystyrene, 37-mm, two-piece cassette holder and supported by a backup pad. The filter should be weighed to the nearest 0.01 mg after being brought to a constant weight in a chamber that is kept at a constant humidity by a 42.5% aqueous sulfuric acid solution [100].

(c) Static charges should be dissipated on the balance and filter with a nuclear static eliminator during all weighing operations.

(d) Operate the pump at a known flow rate of 2 liters/minute for a maximum of 1 hour/sample. Record the total sampling time. A sample size of 90 liters is recommended. Before reweighing the filter after sampling, bring it to constant relative humidity (50%) in a chamber containing an aqueous sulfuric acid solution (42.5%).

(e) With each batch of 10 samples, submit one filter from the same lot used for sample collection, subjecting it to exactly the same handling as the samples except that no air is drawn through it. Label this as a blank.

Calibration of Sampling Trains

The accurate calibration of a sampling pump is essential for the correct interpretation of the volume indicated. The frequency of calibration is dependent on the use, care, and handling to which the pump is subjected. Pumps should be recalibrated if they have been misused or if they have just been repaired or received from a manufacturer. If the pump receives hard use, more frequent calibration may be necessary. Regardless of use, maintenance and calibration should be performed on a regular schedule, and records of these operations should be kept.

Ordinarily, pumps should be calibrated in the laboratory both before and after they are used in the field. The accuracy of calibration is dependent on the type of instrument used as a reference. The choice of calibration instrument will depend largely on where the calibration is to be performed. For laboratory testing, a 1- or 2-liter buret for a soapbubble calibration or wet-test meter is recommended, although other standard calibrating instruments, such as a spirometer, Marriott's bottle, or dry-gas meter, can be used.

Instructions for calibration with the soapbubble meter follow. If another calibration device is selected, equivalent procedures should be used. Since the flow rate is dependent on the pressure drop of the sampling device, the pump must be calibrated while being operated with a representative filter and backup pad in line.

(a) While the pump is running, check the voltage of the pump battery with a voltmeter to assure that it is adequate for calibration. Charge the battery if necessary.

(b) Turn on the pump and immerse the buret in the soap solution; draw bubbles up the inside until they are able to travel the entire length of the buret without bursting.

(c) Adjust the pump flow controller to provide the desired flow rate.

(d) Start a soapbubble up the buret and measure with a stopwatch the time the bubble takes to move from one calibration mark to another.

(e) Repeat the procedure in (d) at least three times, average the results, and calculate the flow rate by dividing the volume between the preselected marks by the time required for the soapbubble to traverse the distance. If, for the pump being calibrated, the volume of air sampled is the product obtained by multiplying the number of strokes times a stroke factor (given in units of volume/stroke), the stroke factor is the quotient obtained by dividing the volume between the two preselected marks by the number of strokes.

(f) Data for the calibration include volume measured, elapsed time or number of strokes, pressure drop, air temperature, atmospheric pressure, serial number of the pump, date, and the name of the person performing the calibration.

X. APPENDIX II

ANALYTICAL METHOD FOR BENZOYL PEROXIDE

An initial gravimetric analysis for total dust should be performed with a preweighed glass-fiber filter [98,99, R O'Gee, written communication, August 1976]. If the total airborne dust exceeds the environmental limit for benzoyl peroxide, a colorimetric analysis, adapted from the method described by Dolin [62], should be performed on the particles trapped in the filter.

Principle of the Method

(a) Air samples are drawn through glass-fiber filters; the filters are then analyzed by a general gravimetric method.

(b) If the total airborne dust exceeds the environmental limit for benzoyl peroxide, a chemical analysis should be performed, using the filter(s) that collected airborne dust in excess of the environmental limit.

(c) The preferred chemical method, a colorimetric analysis, is based on the development of color in an aqueous solution of starch and potassium iodide.

(d) The intensity of the blue color resulting from the released iodine is read in a spectrophotometer. The concentration of benzoyl peroxide in the sample is read from a standard curve prepared from standard solutions of benzoyl peroxide treated the same as the sample solutions.

The concentration of benzoyl peroxide in the sample can also be determined visually by comparing the color of the sample to standard solutions of known concentrations.

Range and Sensitivity

With a spectrophotometer, the lower limit of the working range is 1 µg/sample; when visual comparisons are made, the lower limit is 3 µg/sample. There is no upper limit because the sample solutions can always be sufficiently diluted to allow spectrophotometric readings within the limits set by standard curves or to match the absorption of standard solutions.

Interferences

Other peroxides will also react in the colorimetric analysis to release the iodine, and other oxidizing or reducing agents present in the sample may interfere.

Advantages of the Method

(a) It provides a method suitable for determination of total peroxides in the air.

(b) The sampling device is small and portable and involves no liquids.

(c) The analysis is readily accomplished.

(d) No elaborate equipment is required.

Disadvantage of the Method

The method is not specific for benzoyl peroxide.

Precision and Accuracy

(a) The precision and accuracy of the gravimetric sampling method is defined by the limits of sensitivity of the balance used to weigh the filter.

(b) It is important that the standard and sample solutions are prepared and used at the same time. An error of as high as 25% may occur if the standard solutions have been prepared as little as 1 day before the sample solution. No further data were given on the accuracy or precision of this method.

Apparatus

(a) Spectrophotometer.

(b) Cuvettes that allow the reading of solutions in the spectrophotometer.

(c) Balance for gravimetric analysis.

Reagents

(a) Standard aqueous solutions of known concentrations of benzoyl peroxide, 0.5-10 μg in increments of 0.5 μg are suggested.

(b) Aqueous potassium iodide, 0.75% (w/v).

(c) Aqueous starch solution, 0.5% (w/v).

Analysis of Samples

(a) Gravimetric analysis

(1) A glass-fiber filter is placed in a chamber over an aqueous sulfuric acid solution for 24 hours to bring the filter to a constant weight at 50% relative humidity.

(2) The initial weight of the glass-fiber filter is recorded to the nearest 0.01 mg. A nuclear static eliminator on the balance will remove static charges that might interfere with obtaining accurate, reproducible weights of the filter.

(3) A known volume of air is drawn through the preweighed glass-fiber filter to collect airborne dust, including airborne benzoyl peroxide.

(4) After sampling, the filter is replaced in the chamber for 24 hours and again brought to a constant weight at 50% humidity.

(5) The filter is reweighed on the balance used for the preweighing, and the weight is recorded to the nearest 0.01 mg. If the difference in the initial and final weights of the filter, divided by the known volume of air sampled, equals or is less than the environmental limit for benzoyl peroxide, nothing further need be done.

Filter(s) found to contain a dust concentration higher than the environmental limit should be analyzed by the following colorimetric procedure.

(b) Colorimetric analysis

(1) Put each glass-fiber filter that was used for the sampling of total dust in a clean, dry flask with 10 ml of double-distilled water, 1 ml of potassium iodide solution, and 1 ml of starch solution. Mix

the contents of the flask and allow it to stand for 12 hours.

(2) Treat portions of each of the standard aqueous benzoyl peroxide solutions in a similar manner.

(3) Determine the absorption of the sample solution and of the standards at the absorption band maximum in the spectrophotometer. Make dilutions of the sample solutions if necessary.

(4) Construct a standard curve of the percent transmittance versus μg benzoyl peroxide, using the data obtained from the standard solutions.

(5) Read the concentrations of the sample solutions from the standard curve, or visually compare the standard and sample solutions to obtain the closest color match and the corresponding concentration of benzoyl peroxide. This visual comparison can be performed instead of steps (c) and (d) when less sensitivity is needed.

(6) The concentration of benzoyl peroxide in air can be expressed as milligrams of benzoyl peroxide/cu m of air, which is numerically equal to micrograms of benzoyl peroxide/liter of air:

$$\text{mg benzoyl peroxide/cu m} = \mu\text{g benzoyl peroxide}/V$$

where:

μg benzoyl peroxide = micrograms of benzoyl peroxide (from the calibration curve)
V = volume of air sampled (in liters) at 25 C and 760 mmHg

XI. APPENDIX III

MATERIAL SAFETY DATA SHEET

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

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

(a) Section I. Product Identification

The manufacturer's name, address, and regular and emergency telephone numbers (including area code) are inserted in the appropriate blocks of Section I. The company listed should be a source of detailed backup information on the hazards of the material(s) covered by the MSDS. The listing of suppliers or wholesale distributors is discouraged. The trade name should be the product designation or common name associated with the material. The synonyms are those commonly used for the product, especially formal chemical nomenclature. Every known chemical designation or competitor's trade name need not be listed.

(b) Section II. Hazardous Ingredients

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

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

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

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

(c) Section III. Physical Data

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

(d) Section IV. Fire and Explosion Data

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

(e) Section V. Health Hazard Information

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

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

> Skin Contact--single short contact, no adverse effects likely; prolonged or repeated contact, possibly mild irritation.
>
> Eye Contact--some pain and mild transient irritation; no corneal scarring.

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

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

(f) Section VI. Reactivity Data

The comments in Section VI relate to safe storage and handling of hazardous, unstable substances. It is particularly important to highlight instability or incompatibility to common substances or circumstances, such as water, direct sunlight, steel or copper piping, acids, alkalies, etc. "Hazardous Decomposition Products" shall include those products released under fire conditions. It must also include dangerous products produced by aging, such as peroxides in the case of some ethers. Where applicable, shelf life should also be indicated.

(g) Section VII. Spill or Leak Procedures

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

(h) Section VIII. Special Protection Information

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

(i) Section IX. Special Precautions

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

(j) Signature and Filing

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

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

MATERIAL SAFETY DATA SHEET

I PRODUCT IDENTIFICATION

MANUFACTURER'S NAME	REGULAR TELEPHONE NO. EMERGENCY TELEPHONE NO.

ADDRESS

TRADE NAME

SYNONYMS

II HAZARDOUS INGREDIENTS

MATERIAL OR COMPONENT	%	HAZARD DATA

III PHYSICAL DATA

BOILING POINT, 760 MM HG		MELTING POINT	
SPECIFIC GRAVITY ($H_2O=1$)		VAPOR PRESSURE	
VAPOR DENSITY (AIR=1)		SOLUBILITY IN H_2O, % BY WT	
% VOLATILES BY VOL		EVAPORATION RATE (BUTYL ACETATE=1)	
APPEARANCE AND ODOR			

IV FIRE AND EXPLOSION DATA

FLASH POINT (TEST METHOD)			AUTOIGNITION TEMPERATURE		
FLAMMABLE LIMITS IN AIR, % BY VOL.	LOWER		UPPER		
EXTINGUISHING MEDIA					
SPECIAL FIRE FIGHTING PROCEDURES					
UNUSUAL FIRE AND EXPLOSION HAZARD					

V HEALTH HAZARD INFORMATION

HEALTH HAZARD DATA

ROUTES OF EXPOSURE

INHALATION

SKIN CONTACT

SKIN ABSORPTION

EYE CONTACT

INGESTION

EFFECTS OF OVEREXPOSURE

ACUTE OVEREXPOSURE

CHRONIC OVEREXPOSURE

EMERGENCY AND FIRST AID PROCEDURES

EYES

SKIN:

INHALATION:

INGESTION

NOTES TO PHYSICIAN

VI REACTIVITY DATA

CONDITIONS CONTRIBUTING TO INSTABILITY

INCOMPATIBILITY

HAZARDOUS DECOMPOSITION PRODUCTS

CONDITIONS CONTRIBUTING TO HAZARDOUS POLYMERIZATION

VII SPILL OR LEAK PROCEDURES

STEPS TO BE TAKEN IF MATERIAL IS RELEASED OR SPILLED

NEUTRALIZING CHEMICALS

WASTE DISPOSAL METHOD

VIII SPECIAL PROTECTION INFORMATION

VENTILATION REQUIREMENTS

SPECIFIC PERSONAL PROTECTIVE EQUIPMENT

RESPIRATORY (SPECIFY IN DETAIL)

EYE

GLOVES

OTHER CLOTHING AND EQUIPMENT

IX SPECIAL PRECAUTIONS

PRECAUTIONARY STATEMENTS

OTHER HANDLING AND STORAGE REQUIREMENTS

PREPARED BY

ADDRESS

DATE

XII. APPENDIX IV

TWO TENTATIVE HAZARD CLASSIFICATION SYSTEMS

The following hazard classification system is adapted from a tentative NFPA definition of peroxide classes (O Mageli, written communication, January 1977).

Class I contains organic peroxide formulations which burn like Class II materials (ie, like nitrocellulose and Class 1A flammable liquids) and deflagrate. These materials do not detonate.

Class II contains moderately reactive organic peroxide formulations which burn rapidly like polystyrene and Class C flammable liquids.

Class III contains moderately reactive organic peroxide formulations which burn rapidly like cellular polyethylene and Class II combustible liquids.

Class IV organic peroxide formulations have a reactivity hazard and, like wood, paper, and Class II combustible liquids, will not sustain combustion.

Class V contains organic peroxide formulations that will not sustain combustion.

The following hazard classification system for organic peroxides was developed by the Factory Mutual Research Corporation and was published in March, 1972 [72]. A table with further information on commercial products containing benzoyl peroxide has been compiled by Factory Mutual Research Corporation [70].

> Hazard classifications are based on tests designed to evaluate the total energy release, the rate of energy release, and the ease of ignition and/or decomposition and storage containers when exposed to normal temperatures and when exposed to heat, fire, or mechanical shock.
>
> These tests include: burning rate (solids or pastes); flash point (liquids); impact sensitivity (drop weight test); self-accelerating decomposition temperature (temperature at which self-heating to decomposition is initiated) and the evaluation of the violence of this decomposition; heat exposure to a sample in a vented pressure vessel to evaluate rate and violence of decomposition; and lead block deformation test (exposure to heavy shock) to evaluate violence of decomposition.
>
> Peroxides frequently do not react consistently in the various tests. Therefore, a peroxide may be classified on the basis of the most hazardous rating attained in any one of the series of tests.
>
> Classification of each peroxide is based on its normal shipping container. If a peroxide is shipped in a different container or transferred to a different container, the normal hazard classification may no longer apply. In general, a stronger container will increase the hazard.
>
> Classification is also based on a specific product of a specific manufacturer. The same type product in the same type of container by various manufacturers will not necessarily be in the same class. Differences in manufacturing procedures may have an effect on the hazard of a peroxide which can be determined only by tests.
>
> The classifications are as follows:
>
> Class I. Class I peroxides present a high explosion hazard through easily initiated, rapid explosive decomposition. This group may include peroxides that are relatively safe under highly controlled temperatures or in a liquid solution where loss of temperature control or crystallization out of solution can result in severe explosive decomposition.
>
> Class II. Class II peroxides present an intermediate explosion hazard. That is, an explosive decomposition is not as rapid, violent or complete as that produced by a Class I

material. As with Class I materials, this group may also contain peroxides that are relatively safe under controlled temperatures or when mixed with a diluent.

Class III. Class III peroxides present moderate explosion and severe fire hazards. They have characteristics of rapid burning, high heat liberation or vapor-air explosion hazards of the products of decomposition.

Class IV. Class IV peroxides have moderate fire hazard characteristics that can be easily contained by normal sprinkler systems and fire walls.

Class V. Class V peroxides present a low or negligible fire hazard. With these peroxides, combustible packing materials may present a greater hazard than the peroxide itself.

XIII. APPENDIX V

INACTIVATION OF BENZOYL PEROXIDE

The following method for inactivating benzoyl peroxde for subsequent disposal is recommended for pure benzoyl peroxide (96-99%) and wet benzoyl peroxide formulations; "BPO-78" means 78% benzoyl peroxide plus 22% water.

> Pure benzoyl peroxide (98+%) and water-wet benzoyl peroxide formulations (70% or 78% wetted products) can be hydrolyzed with dilute sodium hydroxide to form sodium benzoate and a solution of hydrogen peroxide in caustic. The hydrogen peroxide decomposes in the caustic solution.
>
> Procedure
>
> Slowly add the BPO-98 (BPO-78 or BPO-70) in small portions to a rapidly stirred 10% sodium hydroxide solution, the amount of such solution being 10 times the weight of the actual benzoyl peroxide to be hydrolyzed. The sodium hydroxide solution must be no warmer than room temperature [25 C] at the time of addition. The reaction is only mildly exothermic, so cooling is not necessary. When all the benzoyl peroxide has been added, continue stirring until the solution is free of solids. The solution will be cloudy. When the temperature is maintained at about 25 C, the time for hydrolysis will be about three hours.
>
> When the solution is free of solids, the benzoyl peroxide has been hydrolyzed and the solution can be disposed of, in accordance with any regulations which apply to disposal of a dilute sodium hydroxide solution containing benzoic acid salts (O Mageli, written communication, January 1977).

XIV. TABLES

TABLE XIV-1

PHYSICAL AND CHEMICAL PROPERTIES OF BENZOYL PEROXIDE

Molecular formula	$(C_6H_5CO)_2O_2$
Formula weight	242.23
Autoignition temperature	80 C
Specific gravity (25 C)	1.3340
Melting point	104 C (with explosive decomposition above 105 C)
Boiling point	Explodes
Solubility	Soluble in ethanol, diethyl ether, acetone, benzene, and carbon disulfide; very slightly soluble in water and methanol

Adapted from references 1 and 2

TABLE XIV-2

OCCUPATIONS WITH POTENTIAL EXPOSURE TO BENZOYL PEROXIDE

- Automobile body repair workers
- Bakers
- Benzoyl peroxide makers
- Cheesemakers
- Dentists
- Dental assistants
- Flour-mill workers
- Miners
- Nurses
- Pharmaceutical products makers
- Pharmacists
- Physicians
- Plastic products makers
- Polyester makers
- Printers
- Silicone rubber makers
- Styrene makers
- Telephone repair workers

Adapted from references 10 (pp 277-284) and 20

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