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Flame-Retardant Additives as Possible Cancer Hazards

The main flame retardant in children's pajamas is a mutagen and should not be used.

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Thousands of chemicals to which humans have been exposed have been introduced into the environment without adequate toxicological testing. The toxicological and biological properties of food additives and drugs have been monitored by the U.S. Food and Drug Administration and now pesticides are monitored by the U.S. Environmental Protection Agency, but most other new substances are tested only superficially.

Some chemical flame retardants provide a good example of a technological innovation where adverse environmental effects may outweigh some of the benefits. Recent federal regulations, requiring that children's sleepwear, mattresses, mattress pads, and carpets meet flammability standards, are said to have resulted in a decrease in the number of burn injuries and deaths (*1*). As a result, flammability standards to cover all children's and adults' clothing, tents, sleeping bags, curtains, and upholstered furniture are being considered. Currently about 300 million pounds of flame-retardant chemicals are being produced mainly for use in fabrics, plastics, and carpets (*2*, *3*). Those added directly to textiles are often present in amounts as high as 10 to 20 percent of the weight of the fabric. Further extension of the scope of the standards may increase their production and usage even more.

Inevitably, some fraction of the many millions of pounds of flame retardants that are being produced will find their way into people. The chemicals are rubbing off on children's skins, may be inhaled from furniture, rugs, and tents, and, after "disposal" into the environment, may enter the food chain. The decision to further extend flame-retardant standards should not be based only on the benefit of a reduction in fire deaths and injuries. The possible risk to the population and environment of the widespread production, use, and dispersal of these potentially hazardous flame-retardant compounds should also be taken into account.

Until recently, little attention was paid to the long-term biological effects of these flame-retardant compounds. The main organic chemicals used in flame retardants contain bromine or chlorine or they are phosphate esters. Some have chemical structures (discussed below) that are closely related to compounds known to cause cancer or to be toxic to animals. Several compounds previously used as flame retardants have been shown to be teratogenic, carcinogenic, mutagenic, or highly toxic (*4*). In this article, we discuss the implications of the finding that tris-(2,3-dibromopropyl) phosphate (tris-BP) the main flame retardant currently used in children's pajamas, is a mutagen (see Fig. 1).

History of Flammable Fabric Standards

The history (*5*) of the use of chemical flame retardants goes back more than 300 years to a treatment for canvas used in Parisian theaters in 1638 and a report from Oxford on a piece of unburnable cloth in 1684 (*6*). The French king Louis XVIII commissioned Gay-Lussac to find a way of protecting fabrics used in the theater. In 1820 Gay-Lussac found that ammonium salts of sulfuric, hydrochloric, or phosphoric acid were effective in reducing fabric flammability (*6*). This work remains valid and applicable today.

The Flammable Fabrics Act in the United States was passed on 14 December 1953 to regulate the manufacture of highly flammable clothing such as brushed rayon sweaters, which were first sold during the 1940's. The act was intended to protect the public from the "unreasonable risk" of fires leading to death, personal injury, or significant property damage. A general wearing-apparel standard, effective 1 July 1954, established minimum flammability standards to keep highly flammable apparel out of the marketplace. The act was amended in 1967 to allow flammability standards to be set for many additional consumer products. Standards for carpets and rugs became effective in 1971, and for mattresses and mattress pads in 1973. The first children's sleepwear standard (DOCFF3-71) for sizes 0 to 6X became effective on 28 July 1972. Children's sleepwear fabric exposed to a gas flame along its bottom edge for 3 seconds is required to exhibit a char length no greater than 7 inches (1 inch = 2.54 cm), even after the fabric has been laundered 50 times.

In 1972, the Consumer Product Safety Commission was established and assumed jurisdiction over the regulation of flammable fabrics. A children's sleepwear standard for sizes 7 to 14 became effective on 1 May 1975. The requirements of this standard are similar to, but slightly less stringent than those for the sleepwear sizes 0 to 6X.

The Consumer Product Safety Commission is in the process of establishing uniform federal standards for upholstered furniture and tents. The National Bureau of Standards has carried out feasibility studies for a standard (based on both garment design and flame-retardant fabrics and treatments) to regulate all articles of adults' and children's clothing. Various state laws are being instituted to regulate upholstered furniture, curtains, tents, and sleeping bags although these may be preempted by federal regulations.

Consequences of Flammable Fabric Standards

The ever-increasing scope of government regulations is leading to a vastly expanded market for chemical flame retardants. In 1971, a total of approximately 175 million pounds (1 kilogram = 2.2 pounds) of flame-retardant compounds were produced. In 1975, the amount had doubled to over 300 million pounds, and it is expected to reach 500 million pounds by 1980 (*2*) although about two-thirds of this is inorganic material, such as alumina trihydrate and antimony oxide used in the carpet industry (*2*, *3*). Large numbers of different organic chemicals, many of which are brominated and

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chlorinated, are being introduced for various applications (*3, 6, 7*).

The Flammable Fabrics Act has had a major influence on the type of fabrics used in children's sleepwear (*8*). For example, in 1971, 56 percent of children's sleepwear was constructed of cotton and 27 percent consisted of polyester-cotton blends. Four years later, in 1975, 87 percent of children's sleepwear was constructed of various synthetics. No sleepwear was made of polyester-cotton and only 13 percent was cotton. Untreated cotton and polyester-cotton do not meet the flammability standards, and treatments have not been commercially competitive. As a result, flame-retarded polyesters, acetates, triacetates, and inherently flame-resistant fabrics such as modacrylics and those containing polyvinyl chloride have replaced cotton.

Selection of Flame-Retardant Chemicals

In 1913, the chemist William Henry Perkin defined the requirements for a flameproofing process in terms that remain applicable (*6*, p. 166):

> A process, to be successful, must, in the first place, not damage the feel or durability of the cloth or cause it to go damp . . . or dusty. It must not affect the colors or the design woven into the cloth or dyed or printed upon it. Nothing (such as arsenic, antimony, or lead) of a poisonous nature or in any way deleterious to the skin may be used and the fireproofing must be permanent. That is to say it must not be removed even in the case of a garment which may be possibly washed 50 times or more. Furthermore in order that it may have a wide application, the process must be cheap.

One or more of six elements—bromine, chlorine, phosphorus, nitrogen, boron, and antimony—are currently used in compounds to reduce fabric flammability because of their effectiveness (*6*). There may be particular toxicological problems with organic bromine and chloride compounds (in addition to antimony). Organic bromides and chlorides are used as flame retardants in synthetic fibers and are thought to act (*6*) as free radical traps and thus to suppress combustion. Burning is oxidation in the vapor phase, involving H·, OH·, and O· free radicals. The halogen may work by a mechanism: $RBr + H\cdot \rightarrow HBr + R\cdot$.

For man-made fibers, tris-BP is by far the most important flame-retardant compound in use and perhaps 10 million pounds a year are used in fabrics and plastics (*9*). It is almost exclusively used in polyester, acetate, and triacetate fibers, as well as being the basis for a successful finish to acrylic carpets. The use of tris-BP is currently the most economical, convenient way to meet the children's sleepwear standards (*9*).

Textiles vary greatly in their flammability (Table 1), and each type presents a different problem in reducing flammability (*10*). Cotton and other cellulose-based fibers can be flame-retarded by impregnated cellulose phosphate esters formed by direct esterification of the cellulose molecule with a phosphate of the flame-retardant compound. Most treatments of cotton are based on tetrakis(hydroxymethyl)phosphonium (THP) compounds or phosphonates, which are polymerized in the fabric. These finishes can result in a loss of tear strength in the fiber of up to 30 percent (*9*). For cotton textiles, about 20 percent, by weight of flame-retardant compounds is added on in order to meet the standard (*9*). Cotton and synthetic blends present more of a problem. The synthetic part of the fabric melts, and the cotton serves as a support that keeps the synthetic burning. Flame-retardant strategies for such blends are being developed, but no economically successful flame-retardant treatment for them is yet available.

Ironically, wool, which is inherently fire resistant (Table 1) (*11, 12*), does not meet the children's sleepwear standard set up by the Consumer Product Safety Commission. The regulations require the fabric to be bone dry (desiccated in an oven at 105°C for 1 hour, followed by a cooling period) prior to the flammability test (*5*). Objections have been raised to this bone-dry regulation as discriminating against wool and cotton, which have high moisture contents (*11*).

Flame-retardant treatments require compromises in economy, esthetics, and wear properties. Consequently, extensive research, costing tens of millions of dollars, is still being done by government and industry to try to find better flame-retardant treatments, particularly for polyester-cotton blends.

Table 1. Burning characteristics of textile fibers (*10*).

Fiber	Characteristics
Cotton	Supports combustion, burns rapidly, afterglows
Rayon	Supports combustion, burns very rapidly, no afterglow
Acetate or triacetate	Supports combustion, melts ahead of flame
Nylon	Supports combustion with difficulty, melts and carries flame away in falling droplets
Nylon 66	Does not readily support combustion, melts and carries flame away in falling droplets
Acrylic	Burns readily with sputtering
Modacrylic	Melts, shrinks away from flame and sometimes burns very slowly
Polyester	Supports combustion with difficulty, melts and carries flame away in falling droplets
Polyolefin	Melts, burns slowly
Wool	Supports combustion with difficulty
Vinyon	Does not readily support combustion

Biological Properties of "Tris," the Main Flame Retardant in Pajamas

There is a growing realization that chemicals can be absorbed through the skin and that long-term toxicological effects of chemical additives to clothing should be characterized more thoroughly. A manufacturer typically carries out only short-term tests for toxicity, and until recently little attention was given to long-term effects, such as carcinogenicity, mutagenicity, and teratogenicity.

The need for studying these long-term effects is illustrated by the case of tris-BP, the flame retardant used in about half of children's sleepwear (*9*). Tris-BP is padded on to the surface of polyester fabrics in amounts up to 10 percent of the fabric's weight. As much as half of this is called "surface tris" and is susceptible to extraction and possible absorption through the skin (*13*). A pair of children's pajamas, weighing 200 g, could easily contain 6000 mg of surface tris-BP. Three launderings would reduce surface tris-BP appreciably (*13, 14*), while not altering the flame-retardant qualities of the garment. This is not done prior to sale reputedly because of the high cost and because consumers are said to value new-looking garments.

The absorption of tris-BP through skin is suggested by several studies. As part of short-term toxicity studies (*15*) by Michigan Chemical, tris-BP applied dermally to rabbits increased blood bromine concentrations. In another study, the urine from a rat wearing a gauze pad impregnated with tris-BP was found to contain high concentrations of a tris-BP metabolite, 2,3-dibromopropanol (*16*). In humans (*13*) tris-BP is a low-level allergen, an indication of some absorption through human skin (*17*). Tris-BP caused delayed hypersensitization in human beings as did fabrics containing large amounts of this compound on the surface. The degree of sensitization from various fabrics was related to the amount of surface tris-BP available. Its percutaneous absorption is not surprising as, in general, chemicals in contact with skin can be absorbed into the body (*18, 19*).

The most important question is whether tris-BP is likely to cause cancer or genetic defects. The "high purity–low volatile" tris-BP made by Michigan Chemical and used for textiles contains 0.05 percent of the impurity 1,2-dibromo-3-chloropropane (*15*). Dibromochloropropane caused a high incidence of squamous carcinoma of the stomach in both rats and mice as early as 10 weeks after initiation of feeding (oral intubation) (*20*). In addition, 50 percent of the female rats developed mammary adenocarcinomas. This study, by the National Cancer Institute (NCI), was published in 1973, before the recent widespread use of tris-BP.

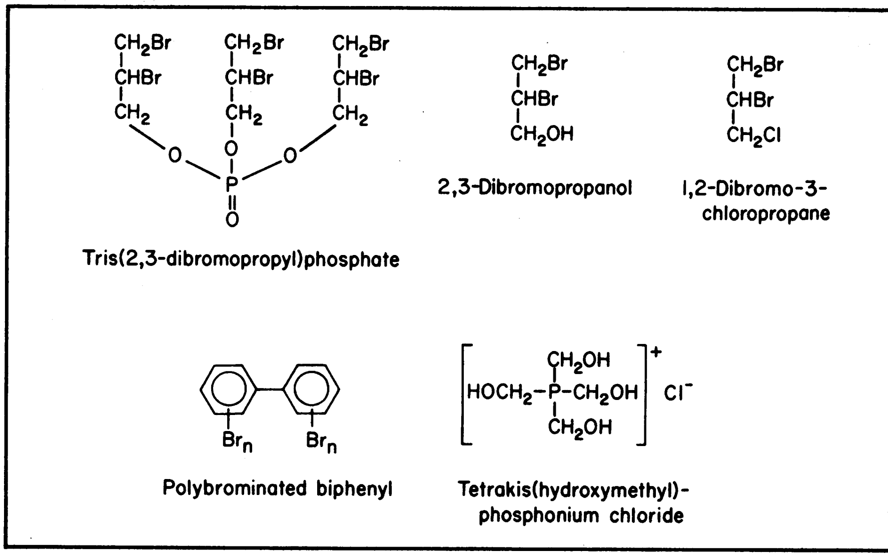

Fig. 1. Structures of flame retardants and related compounds.

Three impurities in commercial tris—dibromopropanol (also a metabolite of tris-BP), the carcinogen 1,2-dibromo-3-chloropropane, and 1,2,3-tribromopropane—as well as tris-BP itself are all related in structure to the known carcinogen 1,2-dibromoethane (ethylene dibromide). Ethylene dibromide is used (more than 200 million pounds in 1970) as a gasoline additive and grain fumigant (*20*). We reported that it is a mutagen in the *Salmonella* test (*21*) in 1971 (*22*) (it had previously been shown to be a mutagen in a variety of other microorganisms). Because of its widespread use and mutagenicity, the NCI tested it for carcinogenicity. Ethylene dibromide was found to be a potent carcinogen on feeding, producing squamous cell carcinomas early and in practically all the surviving male rats treated (*20*).

Tris-BP and the other brominated alkyl compounds discussed above are mutagens in our *Salmonella*/microsome test (*21*). This test shows an extremely high correlation (on the order of 90 percent) between carcinogenicity and mutagenicity (*21*), and has been used to predict a number of carcinogens. Liver microsomal enzymes that convert carcinogens to their active (and mutagenic) forms are combined with *Salmonella* bacteria that are used for detecting mutagenic compounds. Prival *et al*. and Rosenkranz first carried out such tests (*23*), showing the mutagenicity of tris-BP and some of its impurities.

Dose response curves for the mutagenecity of these five compounds are shown in Fig. 2. The mutagenic potency of tris-BP is considerably higher than that of the other chemicals shown. Tris-BP is more mutagenic in the test than several known human carcinogens (*21*). However, the use of the *Salmonella* test for predicting the rough potency of carcinogens remains to be validated, although preliminary results look promising (*21, 24*). Tris-BP and dibromopropanol, although more mutagenic than the carcinogens ethylene dibromide and dibromochloropropane, do differ in requiring activation by liver microsomal enzymes for efficient mutagenesis. Many of these microsomal activating enzymes are known to be present in human skin (*18, 19*).

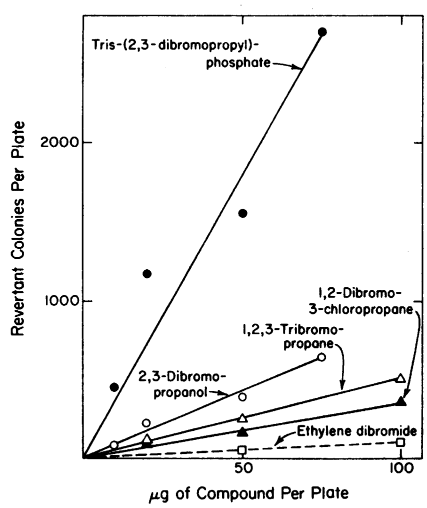

Fig. 2. All compounds were tested on *Salmonella* strain TA100 as described (*21*). The amount of ethylene dibromide added was 10 times that indicated on the scale. The data presented for tris-BP, 2,3-dibromopropanol, and dibromochloropropane were obtained in the presence of rat liver homogenate (20 μl S-9/plate, Aroclor induced) (*21*): human liver gave similar results. The potency (revertants per nanomole) (*21*) of the various chemicals is: tris-BP (0.1; 25 with S-9), 2,3-dibromopropanol (0.15; 1.9 with S-9), 1,2,3-tribromopropane (1.4; 1.4 with S-9), 1,2-dibromo-3-chloropropane (0.5; 0.9 with S-9), ethylene dibromide (0.02; 0.02 with S-9).

Bacterial tests showing that tris-BP is a mutagen suggest that it is likely to be a carcinogen, but animal studies are necessary for more conclusive evidence. Feeding studies (in which tris-BP was added to the animal chow) with rats and mice, at two dose levels, are being carried out at the NCI. The results should be known in 1977.

Recently tris-BP has been found to damage human DNA in vitro, to be a potent mutagen in *Drosophila*, and to cause unscheduled DNA synthesis in human cells in tissue culture (the latter test is quite effective in detecting carcinogens and is an indicator of a chemical's ability to damage DNA) (*25*).

The possible consequences of the widespread use of tris-BP are serious. It does come off fabric, is at least topically absorbed, is known to be a strong mutagen, and may contain a potent carcinogen as an impurity. Infants' and young children's habit of sucking their clothing could lead to its ingestion. Therefore, tris-BP poses a potential hazard as a human carcinogen and mutagen.

In addition to the hazard posed by tris-BP and its impurities to those who make, work with, and wear fabrics treated with it, an environmental hazard may, or may not (*15*), be posed by its disposal in large quantities into water and soil. The simulated washing of six treated sheets in a total volume of 30 gallons of water yielded about 6 parts per million (ppm) of tris-BP in the wash water. A concentration of 1 ppm in water is sufficient to kill goldfish within 5 days (*26*).

Biological Properties of Other Flame Retardants

The safety of a treatment for flame-retarding cotton fabrics has also been questioned although it is not clear that there is a significant problem with the current technology. Tetrakis(hydroxymethyl)phosphonium chloride (THPC) is polymerized and oxidized in cotton as a flame retardant, and this fabric has been reported to release formaldehyde and chloride when it is wet (*27, 28*). This is causing some concern (*9, 27, 28*) as there exists the theoretical possibility that these ingredients could form bis-chloromethyl ether, an extremely potent carcinogen in rats that has also caused cancer in factory workers. Bis-chloromethyl ether can be formed under certain acidic conditions from formaldehyde and chloride (*29*). To avoid any possibility of exposure of workers during the curing process (and to minimize free chloride in the garment) the American industry has switched to a salt that does not contain chloride, tetrakis(hydroxymethyl)phosphonium sulfate (*30*). It has been suggested that this could still be a problem in the wearing of treated cotton because appreciable amounts of formaldehyde can be extracted by synthetic sweat from cloth flame retarded with a THP salt, and sweat contains appreciable chloride ion (*28*). No bis-chloromethyl ether was found in this extract, however (*28*); as its formation requires acidic conditions, it probably is not a serious problem in nightwear.

A more obvious example of the hazards of flame-retardant chemicals is the polybrominated biphenyl (PBB) tragedy occurring in Michigan (*31*). Inadvertently 500 to 1000 pounds of a polybrominated biphenyl–based retardant were packed into bags similar to those in which Michigan Chemical Company packs the magnesium oxide feed additive known as Nutrimaster. The contents of these bags—the flame-retardant Firemaster—were mixed into a cattle feed mixture at the Farms' Services Bureau in Battle Creek, Michigan, and distributed throughout the state. Soon, Michigan dairy farmers noticed that their animals were beginning to suffer from loss of appetite, lowered milk production, excessive spontaneous abortion, birth defects among offspring, and eventual death of affected stock. After the cause was discovered to be chemical contamination, about 30,000 cattle, 6000 pigs, 1500 sheep, and 1,500,000 chickens were destroyed because their tissues contained PBB at concentrations greater than 1 ppm. At least 365 tons of feed, 18,000 pounds of cheese, 2600 pounds of butter, 34,000 pounds of dry milk products, and nearly 5,000,000 eggs were also destroyed.

Farmers and their families from all over the state who have eaten large amounts of dairy products and eggs from the affected animals have PBB's in their blood and fat, and some have begun to report a variety of illnesses, although the connection to the PBB ingestion has yet to be proved (*31*).

PBB has been reported to concentrate in fat (*32*). Caged fish kept on the Pine River below the Michigan Chemical Plant were reported to accumulate PBB (1 mg/kg) in their fat tissue. This represents a concentration factor greater than 10,000-fold within 2 weeks of exposure to very low concentrations of PBB (*32*).

The long-term carcinogenic and mutagenic effects of PBB's remain to be determined. Cancer tests in animals are in progress and teratogenicity in mice has been reported (*33*). The PBB's are close relatives of the carcinogenic and teratogenic polychlorinated biphenyls (PCB's), which are a worldwide health problem, in that they have been spread throughout the biosphere and have become concentrated in the food chain. The fact that less than a thousand pounds of the brominated PBB flame retardant has caused such widespread and persistent damage raises the question of the eventual consequences of the millions of pounds of PBB's that were produced in the past. It also shows the type of hazards that may be incurred in producing hundreds of millions of pounds of flame retardants (much of it containing organic bromine and chlorine) that will eventually end up somewhere in the environment.

The environmental bioaccumulation of these and other flame-retardant compounds may be a problem. Simple leaching of flame retardants from fabrics during manufacturing, laundering, and disposal could lead to their presence in water supplies and sewage. For example, the flame-retardant pentabromotoluene was found in a sewage plant in Sweden (*34*). Mirex (Dechlorane), a close relative of Kepone (it also often contains some Kepone), has been used as a flame retardant in plastics for many years, and is a carcinogen and teratogen (*4*), and bioaccumulates in fish and people. The environmental effects of the flame-retardant chemicals must be considered as well as the effects of the products of these chemicals after they have undergone oxidation and photochemical breakdown by sunlight or microorganisms in sludge, soil, water, or compost. Furthermore, studies should be carried out on the uptake, storage, accumulation, biochemical change, and elimination of the major flame-retardant compounds in fish and other aquatic organisms, in birds, and in mammals.

Alternatives to Preventing Burns Without Chemical Additives

1) *Self-extinguishing cigarettes*. The major single cause, accounting for about one-third to one-half (*35*), of the approximately 12,000 fire deaths and $11 billion in losses in the United States each year (*36*) is tobacco-smoking materials (*35*). The most common fire death scenario was found to be the residential furnishing fire started by tobacco-smoking materials; alone it accounts for 27 percent of fire deaths. The next largest single cause was residential furnishing fires started by open flames, which accounted for 5 percent of the United States fire deaths. All other single causes were 4 percent or less.

Most American cigarettes when put down will continue to smolder (some even more than 20 minutes), apparently because of additives and cigarette design. This long smoldering is the key factor in starting fires (*37*). Cigarettes are available that self-extinguish in a few minutes and are much less likely to start fires. We have tested a large variety of cigarettes and have determined that a few brands will go out in less than 5 minutes while the majority of brands burn from 15 to 22 minutes (*38*). One possibility for this is stated on the package of one brand. "Light an ordinary cigarette . . . there's a chemical in it to keep it burning." In contrast, this brand claims that its cigarettes have "*NO* flavorings, saltpeter, or tars added."

The major cause of fire deaths and losses could thus be attacked at its source by the introduction of self-extinguishing cigarettes. As an added benefit a significant number of forest fires might also be eliminated if cigarettes were to self-extinguish in a few minutes instead of smoldering for 15 or 20 minutes. Unfortunately one piece of legislation to give the Consumer Product Safety Commission jurisdiction over the flammable properties of cigarettes was defeated in the House of Representatives recently after its passage in the Senate (*39*).

The Consumer Product Safety Commission does have jurisdiction over matches and is developing standards for self-extinguishing matches (*30*). The major single cause of fires of children's clothing is due to children playing with cigarette lighters and matches (*35*). Book matches have been designed that are practical and yet child-proof (*40*), and their adoption might have a major effect.

2) *Fire prevention*. Some of the effort and expense that is being put into extensive flame retarding should be put into fire prevention. More effort could be put into additional consumer education on the causes and prevention of fires. The Public Education Office of the Fire Administration is set up to do this, but has a minimal budget (*41*). Improvements in design also could be encouraged for nightwear because loose, flowing garments have been shown to be involved in many more fires than more tightly woven, close fitting garments (*42*). Stove design could be modified so children could not easily turn on the burners. Space heaters could be changed so that it would be more difficult for people to get close enough to them to ignite their clothing. Gas heaters should not be put in garage workrooms where solvents are used.

3) *Inherently fire-resistant fabrics*. These provide possible safer alternatives to the addition of chemical flame retardants. Modacrylics and matrix fabrics based on polyvinyl chloride and polyvinyl alcohol are inherently flame retardant without the addition of chemicals. Multimillion-pound-capacity vinyl bromide plants are being built to provide monomer for flame-retardant fabric production (*43*). It is to be hoped the type of problems caused by the carcinogen vinyl chloride, such as monomer residues in the polymer and worker exposure, will not reoccur in the textile industry with vinyl chloride and vinyl bromide. Flame-retardant additives that are covalently bonded to the fabric or those that are polymerized and entrapped within the fibers may also be safer than those that are padded on, such as tris-BP.

4) *Standards for fabrics*. These should be examined to see whether technicalities could be changed to minimize the need for additives. For example, a "melt-drip" provision is in force for sleepwear sizes 0 to 6X, but not for sizes 7 to 14 (*44*). Because of this technicality, tris-BP addition is necessary for polyester in the sizes 0 to 6X despite the fact that polyester is relatively flame resistant. There is evidence that the "melt-drip" phenomenon does not constitute a significant burn hazard (*44*). In addition, several examples are discussed (below) where it appears that standards could be redrafted so as to not require additives in certain fabric types (nylon tents) or in items (sleepwear of infants, who are less than 6 months of age) in which the benefit seems to be relatively small.

Benefit and Risk

A federal report published in 1972 states that about 200,000 burn injuries and 4000 deaths are associated annually with flammable fabrics (*42*). This report is often cited by proponents of stricter clothing flammability standards. However, a recent study (*45*) for the National Advisory Committee for the Flammable Fabric Act suggests that these numbers may be about ten times too high, and estimates that there are about 16,000 annual textile-related burns and about 500 deaths in the United States (*45*). About 20 percent of these burn injuries and deaths might be associated with nightwear in children; that is, the standards might possibly prevent 3000 burn injuries and 100 deaths per year among 50,000,000 children. These numbers are only very approximate because of uncertainties in the burn statistics and the recent estimate might be severalfold too low. In any case, burns are a serious problem. It also is relevant that healed burn tissue is at greater risk for developing an epidermoid carcinoma several decades afterward (*46*).

Adding flame-retardant chemicals to almost all children's pajamas, as a consequence of the Consumer Product Safety Commissions's standards, most probably is reducing the number of burns and deaths due to children's nightwear catching fire, although statistics are unavailable. As we have indicated, there are also other ways of reducing fire injuries.

The risk of the exposure of tens of millions of children to a large amount of a chemical must be balanced against the risk of fire. A calculation (*47*) suggests that the risk from cancer might be very much higher than the risk from being burned. Flame retardants (and most other large volume industrial chemicals) either have not been tested or have not been adequately tested for carcinogenicity. The use of an untested chemical as an additive to pajamas is unacceptable in view of the enormous possible risks.

Even if tris-BP is found not to show any statistically significant increase in tumors in the current NCI feeding study, possible absorption of a highly mutagenic chemical by millions of children still poses a considerable risk. Would tris-BP mutate human germ cells? Would tris-BP be a potent carcinogen if it were painted on the skin (the actual mode of exposure to people) rather than fed, as in the NCI study?

Even if a chemical were tested, and were found to be negative in a thorough animal cancer test in two species, this does not guarantee safety. A thorough animal cancer test usually involves a few hundred test animals at most (compared with millions of children in the case of tris-BP). This is an inherent statistical limitation in animal cancer tests, and high doses in the animal may only partially compensate. Thus, a chemical that would cause a tumor increase of less than 5 percent may easily go undetected. That sort of increase in a population of millions would result in tens of thousands of additional cases of cancer.

The National Commission on Fire Prevention and Control (*36*) has suggested that consumers be given a choice whether to buy flame-retarded fabrics or not.

> The Commission does not favor unbridled extension of flammability standards to all categories of fabrics. Only grossly hazardous fabrics and fabrics implicated in a very large number of fire accidents should be banned from the marketplace. A preferable direction of emphasis is toward labeling requirements as to combustion hazards. This would honor the cherished principle of free choice, while at the same time informing consumers of potential risks and reminding them of the importance of fire. If reinforced by consumer education on fire safety, labeling requirements would have the effect of spurring manufacturers to improve the flame-resistance of fabrics.

However, as flame retarding adds an additional 10 to 30 percent to the cost of the garment and often adversely affects the feel and ease of its care, many consumers, particularly those with lower incomes, would not choose to buy the flame-retarded garment (*48*). One of the main reasons that has been given for the decision of the Consumer Product Safety Commission to implement compulsory standards is to protect the poor.

The strictness of these standards, their compulsory nature, and their further extension should be critically reexamined. The benefits of flame retarding all children's clothing, adult sleepwear and clothing, and upholstered furniture (*49*) are arguable, as is the benefit of adding flame retardants to wool and other less flammable fabrics. Also unclear is the benefit of chemical additives in hospital garments for newborn babies, and in infants' clothing and sleepwear (*48*).

Another striking example of unnecessary flame-retarding treatment is in the area of light-weight nylon tents used for backpacking and mountaineering. Of 119 documented injuries and deaths in the United States in tent fires during the years 1971 to 1974 inclusive, none occurred in nylon tents (*50*). Only 2 of 75 fires reported in this study involved nylon tents. In addition to the possible biological hazards of the flame-retardant compounds, their addition markedly increases the weight and cost and decreases the fabric tear strength. Even untreated tents have been known to tear under severe conditions leading to injury and death of the occupants (*51*). Thus, treated nylon tents are both heavier and potentially less safe. Nevertheless, legislation to require flame-retarding treatment of all tents is in force in California, as well as several other states.

Flame retardants added to plastics are obviously of less concern as environmental hazards than those added to clothing, yet any that are going to be eventually released into the environment in large amounts (such as the PBB's) should be given thorough toxicological testing. A few do appear to have been tested fairly thoroughly (for example, decabromobiphenyl oxide).

Responsibility

It is not clear who has the responsibility and authority for the establishment of flame-retardant standards that are safe, both from a fire and a biological point of view. The Consumer Product Safety Commission says that it has the responsibility to set performance standards, but not the authority to require that flame retardants be pretested for carcinogenicity or mutagenicity (*52*). The responsibility for safely meeting these standards is left to the chemical industry. Many industries do not accept this responsibility for carrying out cancer tests on large-volume chemicals. Thus, there is a conflict between government and industry as to who should be responsible for meeting biological and environmental safety standards. At present, no government agency has the authority for ensuring long-term safety of textile additives such as flame retardants, although the toxic substances law might eventually solve this problem. The strict flammability standards vitally affect many industries that are caught in the middle.

Few cancer tests in animals have been carried out with the large number of chlorinated and brominated chemicals (*7*) that make up a good part of about 100,000,000 pounds of organic flame retardants used annually in the United States. A similar situation existed 20 years ago when billions of pounds of chlorinated and brominated chemicals were introduced as pesticides and industrial chemicals even though animal cancer tests had not been performed. Both situations are disturbing for several reasons. Organic chemicals containing chlorine and bromine (and fluorine) are not used in natural biochemical processes and have not been normally present in the diet. A large number of these halogenated and industrial chemicals to which humans have unwittingly been exposed are proving to be carcinogens in animals now that the cancer tests are being done. Many more compounds remain to be tested. As the 20- to 30-year lag time for chemical carcinogenesis in humans is almost over, a steep increase in the human cancer rate from these suspect chemicals may soon occur. While waiting for the effects of the large-scale human exposure to the halogenated carcinogens—polychlorinated biphenyls (PCB's), vinyl chloride, Strobane-toxaphene, aldrin-dieldrin, DDT, trichloroethylene, dibromochloropropane, chloroform, ethylene dibromide, Kepone-mirex, heptachlor-chlordane, pentachloronitrobenzene; and so forth—we might think about the avoidance of a similar situation with flame retardants (*53*).

References and Notes

1. A. McGuire, director, Northern California Burn Council, personal communication; G. F. Crikelair, Proceedings of the Information Council on Fabric Flammability, New York, 1975.
2. E. V. Anderson, *Chem. Eng. News*, 22 March 1976, p. 12.
3. E. M. Pearce and R. Liepins, *Environ. Health Perspect.* **11**, 59 (1975).
4. Mirex (dechlorane) is a teratogen and carcinogen and tris-aziridinyl phosphine oxide is a carcinogen and mutagen (NIOSH) [National Institute of Occupational Safety and Health, Washington, D.C. Registry of Toxic Effects of Chemical Substances]; pentachlorobenzene is a teratogen [K. S. Khera and D. C. Villeneuve, *Toxicology* **5**, 117 (1975)]. The highly toxic PBB's are suspected of being all of these and are discussed in this article.
5. Background information has been obtained from: Flammable Fabrics Act, Fed. Reg. **3**, (30 December 1975, pp. 59884–59957; Fact Sheet 25, U.S. Consumer Products Safety Commission, Washington, D.C., 1974).
6. J. W. Lyons, *The Chemistry and Uses of Fire Retardants* (Wiley-Interscience, New York, 1970).
7. O. Hutzinger, G. Sundstrom, S. Safe, *Chemosphere* **1**, 3 (1976); R. B. LeBlanc, *Textile Industries* (February 1976), p. 28; close to a hundred different flame retardants, from various manufacturers, are listed and available from RFR Corp. (EnChem Environmental Division), 1 Main Street, Hope, Rhode Island 02831.
8. B. A. Worley, (Spring Mills, P.O. Box 70, Fort Mill, S.C.); *Techniforum* **2**, Arlington, Va., April 1976.
9. T. J. McGeehan and J. T. Maddock, *A Study of Flame Retardants for Textiles* Office of Toxic Substances, EPA-560/1-76-004 (U.S. Environmental Protection Agency, Washington, D.C., 1976).
10. B. J. Eisenberg and E. D. Weil, *J. Am. Assoc. Textile Color* **6**, 257 (1974).
11. M. Friedman, in *Flame-Retardant Polymeric Materials*, M. Lewin, S. M. Atlas, E. M. Pearce, Eds. (Plenum, New York, in press). "I think that the oven-dry requirements should be eliminated for natural fibers, such as wool and cotton, that ordinarily have a high moisture content. All fibers should be tested at their normal moisture contents except for special uses which require low humidity. The present standard unreasonably favors certain synthetics, such as polyester, that have low normal moisture contents." The Consumer Product Safety Commission, however, has set these low humidity levels because of a concern for low humidity environments, such as homes without humidifiers and the drier regions of the country (R. Adler, personal communication).
12. One of us (B.N.A.) was not successful in trying to set fire to an old woolen bathrobe.
13. R. W. Morrow, C. S. Hornberger, A. M. Kligman, H. I. Maibach, *Am. Ind. Hyg. Assoc. J.* **37**, 192 (1976).
14. R. H. Harris, of the Environmental Defense Fund, Petition to the Consumer Product Safety Commission, 24 March 1976.
15. F. A. Daniher, "Toxicology of tris-(2,3-dibromo propyl) phosphate," *Proceedings of the 1975 and 1976 Symposia on Textile Flammability* (Le Blanc Research Corp., 1975); A. F. Kerst, *J. Fire Flammability, Fire Retardant Chem. (Suppl.)* **1**, 205 (1974). Tris-BP was found to be neither a skin nor an eye irritant. Rats fed doses in amounts between 0.01 and 0.1 percent of their feed for 28 days showed some reversible weight loss and also reversible accumulation of bromine in liver, fat, and muscle tissue. In a 30-day feeding study with dogs, at doses of 50 mg/kg and 100 mg/kg, an increase in blood bromine was noted. Dermal application, in amounts up to 2 g/kg, to rabbits resulted in increased bromine levels.
16. L. E. St. John, Jr., M. E. Eldefrawi, D. J. Lisk, *Bull. Environ. Contam. Toxicol.* **15**, 192 (1976).
17. H. I. Maibach, personal communication.
18. M. J. Bartek, J. A. LaBudde, H. I. Maibach, *J. Invest. Dermatol.* **58**, 114 (1972); D. R. Bickers, A. Kappas, A. P. Alvarez, *J. Pharmacol. Exp. Ther.* **188**, 300 (1974).
19. R. J. Feldmann and H. I. Maibach, *J. Invest. Derm.* **54**, 399 (1970).
20. W. A. Olson, R. T. Habermann, E. K. Weisburger, J. M. Ward, J. H. Weisburger, *J. Natl. Cancer Inst.* **51**, 1993 (1973); M. B. Powers, R. W. Voelker, N. P. Page, E. K. Weisburger, H. F. Kraybill, *Toxicol. Appl. Pharmacol.* **33**, 171 (1975).
21. J. McCann, E. Choi, E. Yamasaki, B. N. Ames, *Proc. Natl. Acad. Sci. U.S.A.* **72**, 5135 (1975); J. McCann and B. N. Ames, *ibid.* **73**, 950 (1976); B. N. Ames, J. McCann, E. Yamasaki, *Mutat. Res.* **31**, 347 (1975). The test assays the mutagenicity (ability to damage DNA, the genetic material) of chemicals. *Salmonella* are used for measuring DNA damage, combined with tissue homogenates from rodents (or humans) to provide mammalian metabolism of chemicals. The test measures back mutations in a special set of histidine-requiring tester strains. A number of genetic modifications have been introduced into the strains to further increase sensitivity. About 1 billion bacteria are treated on a single petri plate. Those bacteria that are mutated back to histidine independence are measured by counting the colonies appearing on the plate after an incubation period of 48 hours. Many carcinogens cause the bacteria to mutate because they are directly active. We have been able to detect the large class of carcinogens activated to mutagens by mammalian metabolism by adding rat (or human) liver homogenates to the test system. One of the main results to come out of this work, in addition to the test system itself, is that 90 percent of the carcinogens tested in the system can be detected as mutagens, whereas very few noncarcinogens are mutagenic. Consequently we have supported the theory that almost all chemical carcinogens cause cancer by somatic mutation. Mutations damaging normal regulatory mechanisms in a cell could result in uncontrolled growth in that cell and in its descendants, thus giving rise to a tumor.
22. B. N. Ames, in *Chemical Mutagens: Principles and Methods for Their Detection*, A. Hollaender, Ed. (Plenum, New York, 1971), p. 267.
23. M. J. Prival, E. C. McCoy, B. Gutter, H. S. Rosenkranz, *Science* **195**, 76 (1977); H. S. Rosenkranz, *Bull. Environ. Contam. Toxicol.* **14**, 8 (1975).
24. M. Meselson and K. Russell in *Origins of Human Cancer*, J. D. Watson and H. Hiatt, Eds. (Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., in press); ———, personal communication; C. Sawyer and B. N. Ames, unpublished results.

25. B. Gutter and H. S. Rosenkranz, in preparation; R. A. Valencia, R. C. Serman, Y. Buchholz, K. Houtchens, in preparation; H. F. Stich, personal communication.
26. W. H. Gutemann and D. J. Lisk, *Bull. Environ. Contam. Toxicol.* **14**, 61 (1975). We have been informed of several experiments where the immersion of pajamas in goldfish tanks caused the death of the goldfish. This acute toxicity could possibly reflect an anticholinesterase activity of tris-BP.
27. L. V. Afanas'eva and N. S. Evseenko, *Hyg. Sanit.* **36**, 450 (1971).
28. G. Loewengart and B. L. Van Duuren, Third International Symposium on Detection and Prevention of Cancer, New York City, 26 April 1976; *J. Toxical. Environ. Health*, in press. These studies also report a small-scale carcinogenicity study of THPC on mice showing that, when 2 mg were applied topically three times a week for more than a year to 20 mice, one squamous carcinoma was observed in the treated group. Since this sort of cancer has not been observed in control mice over the years (B. L. Van Duuren, personal communication), further work was suggested.
29. G. J. Kallos and R. A. Solomon, *Am. Indust. Hyg. Assoc. J.* **34**, 469 (1973).
30. *Textile Flammability Digest* (December 1975), (Address: 5454 Post Road, East Greenwich, R.I.).
31. L. J. Carter, *Science* **192**, 240 (1976); J. E. Brody, *New York Times*, 12 August 1976, p. 20.
32. J. L. Hesse, paper presented at the Second National Conference on Complete WateReuse, Palmer House, Chicago, 4 May 1975.
33. T. H. Corbett, A. R. Beaudoin, R. G. Cornell, M. R. Anver, R. Schumacher, J. Endres, M. Szwabowska, *Environ. Res.* **10**, 390 (1975).
34. P. E. Mattsson, A. Norstrom, C. Rappe, *J. Chromatogr.* **111**, 209 (1975).
35. F. B. Clarke III, and J. Ottoson, *Fire J.* **70**, 20 (1976); B. M. Halpin, E. P. Radford, R. Fisher, Y. Caplan, *ibid.* **69**, 11 (1975); Bureau of Epidemiology, U. S. Consumer Product Safety Commission, "Analysis of injuries associated with specified wearing apparel (Washington, D.C., 1975).
36. *America Burning*, Report of the National Commission on Fire Prevention and Control (U. S. Government Printing Office, 1973), pp. xi and 68.
37. C. Huggett, National Bureau of Standards, personal communication.
38. B. N. Ames and A. Blum, unpublished results.
39. Congressional Record, Defeat of Hart Amendment for Consumer Product Safety Commission authority over flammable properties of cigarettes. An amendment similar to the Hart Amendment had been proposed earlier in March 1975 by R. D. Pittle, Commissioner of the U.S. Consumer Product Safety Commission.
40. D. Byrd and J. Burgess, *Fire J.* **70**, 11 (1976).
41. A. McGuire, Director, Northern California Burn Council, personal communication.
42. Bureau of Product Safety, Food and Drug Administration, *Flammable Fabrics, 4th Annual Report* (U.S. Government Printing Office, Washington, D.C., 1972).
43. Ethyl Corporation, advertisement, *Chem. Eng. News* (20 January 1975) p. 28.
44. W. I. Langstaff, Proceedings 1976 Symposium on Textile Flammability (LeBlanc Research Corp., East Greenwich, R.I.).
45. L. M. Kushner (U.S. Consumer Safety Commissioner) in letter to D. S. Duke, 11 August 1975; see also (*48*); "Analysis of injuries, association with specified wearing apparel items," U.S. Consumer Product Safety Commission (30 May 1975). These estimates only include cases where clothing was the first item ignited.
46. D. Trunkey, personal communication.
47. It is instructive to try to estimate the dose of tris-BP that a child might absorb and to compare it with the dose of dibromochloropropane (the carcinogenic impurity in tris-BP) that was used in the carcinogenicity experiments (*20*) in rats. A cumulative dose of about 1600 mg of dibromo chloropropane resulted in gastric squamous carcinomas in 85 percent of the rats and mammary adenocarcinomas in 50 percent of the female rats. (Ethylene dibromide is a carcinogen of roughly similar potency.) We think that a cumulative dose of about 1600 mg is likely to be absorbed by a child during the course of a childhood wearing polyester pajamas treated with tris-BP. [We estimate about 4000 mg of surface tris-BP in a 150 g (new pair) of pajamas with a surface area of 8000 cm^2: 500 $\mu g/cm^2$ of surface tris-BP. Absorption of nonpolar chemicals through the skin at appreciable rates appears to be the rule. In a study of 11 nonpolar chemicals applied to human skin (at 4 $\mu g/cm^2$), Feldman and Maibach (*19*) have shown the total absorption was from 1.5 to 50 percent with a mean rate of about 0.25 percent per hour. If 1 μg of tris-BP was absorbed per night from each square centimeter of skin then 1600 mg could be absorbed in about half a year and even if the rate was only 10 percent of this, that dose could be absorbed in 5 years. One would expect a decrease in the level of surface tris-BP as the pajamas were repeatedly washed, until a new pair was substituted. Thus, one does not know exactly what level of tris-BP is available for absorption through the skin and at what rate it is absorbed. To get the same effect of a chemical in a rat and a child, however, it is estimated that the child should receive a 20-fold higher dose [D. G. Hoel, D. W. Gaylor, R. L. Kirschstein, U. Saffiotti, M. A. Schneiderman, *J. Toxicol. Environ. Health* **1**, 133 (1975)]. However, tris-BP is a considerably stronger mutagen in our test than dibromochloropropane (about tenfold). [From our previous work on mutagenicity it appears extremely likely that tris-BP is a carcinogen. Although there is a rough correlation between mutagenic and carcinogenic potency (*24*), we do not have enough experience to attempt to predict a carcinogenic potency for tris-BP.] All these calculations are based on an amount of dibromochloropropane sufficient to produce cancer in almost all of the rats. If our assumptions are correct, even 1 percent of that dose of tris-BP could lead to an unacceptable incidence of cancer, in view of the millions of children at risk. A study (*16*) attempting to find the tris-BP metabolite dibromopropanol (or its conjugates) in human urine from two volunteers wearing pajamas treated with tris-BP was negative. However, in view of the risk we are discussing, the analytical method was insensitive (less than 0.2 ppm of the metabolite would not have been detected), and we do not know what percentage of any absorbed tris-BP would appear as dibro mopropanol or its conjugates.
48. *TIPS* (Textile Industry Product Safety) **4**, 1 (1976), available at 1750 Pennsylvania Avenue, NW, Washington, D.C. 20006.
49. A standard for all clothing is being formulated at the Center for Fire Research at the National Bureau of Standards for the Consumer Product Safety Commission.
50. R. F. Johnson, *Proceedings of the 8th Annual Meeting of the ICFF, New York City* (1974).
51. *Accidents in North American Mountaineering (1948–1975)*, American Alpine Club, New York.
52. A. C. Shakin, of the U.S. Consumer Product Safety Commission, in a memorandum to S. Butts, 26 March 1976; The National Commission on Fire Prevention and Control has advised (*36*): "The impact of new materials, systems, and buildings on users and the community should be assessed during design stages, well before use."

53. Supported by ERDA grant E(04-3)34 PA156 (to B.N.A.). We thank L. Haroun for assistance in the mutagenicity assays and D. Gold for other help with the study; we also thank M. Prival and H. Rosenkranz for information concerning their unpublished mutagenicity results with flame retardants and for help in other aspects of this work; B. L. Van Duuren for a sample of tris-BP and other help; and numerous colleagues in government and industry for criticism of the manuscript. A.B. was supported in part by NIH grant 1-F32-CA-05731-0.

Nuclear Waste Disposal: Two Social Criteria

Technical irreversibility and site multiplicity are suggested as criteria for safe nuclear waste disposal.

Gene I. Rochlin

Del carratere degli abitanti d'Andria meritano di essere ricordate du virtú: la sicurezza in se stessi e la prudenza. Convinti che ogni innovazione nella città influisca sul disegno del cielo, prima de' ogni decisione calcolano i rischi e i vantaggi per loro e per l'insieme della città e die mondi.—ITALO CALVINO (*1*).

There is a consensus that radiologically hazardous wastes from the nuclear fuel cycle should be separated from the biosphere to a sufficient degree and for a long enough time so that they present no significant risk to life. But this consensus does not extend to the definitions of "sufficient," "long enough," or "significant risk." Our ability to predict material or geological stability over the containment times required for long-lived components has been questioned (*2–4*). Moreover, the impossibility of predicting socially relevant factors over such relatively short periods as a few hundred years precludes accurate estimation of either the probability of an accidental or deliberate breach of containment or the effects of such a breach on society (*5*).

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