UNITED STATES
CONSUMER PRODUCT SAFETY COMMISSION
WASHINGTON, DC 20207

Memorandum

Date: APR 1 2004

TO : The Commission
Todd Stevenson, Secretary

THROUGH: John Gibson Mullan, General Counsel
Patricia Semple, Executive Director

FROM : Jacqueline Elder, Assistant Executive Director for Hazard Identification and Reduction
Suzanne Barone, Ph.D., Project Manager for Poison Prevention, Directorate for Health Sciences

SUBJECT : Additional Information on Petition on Natural Rubber Latex (HP 00-2)

This memorandum responds to Commissioner Moore's written questions, dated January 6, 2004, to the staff of the Office of Hazard Identification and Reduction (HIR) concerning the petition HP 00-2 to declare natural rubber latex (NRL) a strong sensitizer under the Federal Hazardous Substances Act (FHSA). This memorandum also includes the staff analysis of the comments received in response to the Federal Register notice of November 14, 2003 (68 FR 64610) announcing the public meeting and soliciting additional comments on the petition and the staff's briefing package.

RESPONSE TO COMMISSIONER MOORE'S QUESTIONS

Question: The briefing package describes numerous pieces of information that are unknown with respect to NRL allergy and NRL-containing products, such as:

a. the threshold levels of protein allergens for sensitization and symptom development and how these may differ among different individuals;
b. the most accurate and sensitive test to determine the threshold level that will elicit allergic reactions in allergic individuals;
c. the role of NRL-containing consumer products in the development of allergy to NRL;
d. the protein or allergen content of most non-medical NRL–containing products;
e. how to distinguish consumer products which may contain hazardous levels of NRL allergens;
f. a universally-accepted safe approach for diagnosing NRL allergy;
g. a conclusive explanation for the apparent increase in reports of IgE-mediated hypersensitivity to NRL products;

NOTE: This document has not been reviewed or accepted by the Commission.
Initial rch Date 4/1/04

CPSA 6(b)(1) CLEARED FOR PUBLIC RELEASE
NO MFRS/PRVTLBLRS OR PRODUCTS IDENTIFIED 4/1/04
ACCEPTED BY: PETITION

h. a reliable national, annual estimate of the frequency and severity of allergic reactions to NRL products.

What type of research would have to be done to find the answers to these various unknowns? Which ones are currently being worked on and what, if any, timetables have been established for their resolution? Who should be responsible for the research necessary for finding these answers? Assuming that the prevalence of NRL allergy in the general population is, as estimated in the briefing package, to be less than 1%, could having the answers to any or all of these issues have made a difference in the staff recommendation?

Response: The CPSC staff is not actively involved in research in the area of latex allergy. Therefore the staff does not know the current state of research beyond the published literature. To address each of the areas listed above, staff would contract with consultant(s) with expertise in this area. This would involve significant staff resources and contract dollars.

Knowing the answers to the research questions would not necessarily change the staff recommendation. The staff is recommending denying the petition based largely on the available data indicating a low frequency of allergic reactions to latex in the general population (less than one percent). The staff believes that this information does not provide the evidence needed to declare NRL a strong sensitizer under the FHSA.

Question: Several commenters stated that the vast majority of consumer products made with rubber use DNR rather than NRL. Do we know that to be the case?

Response: The staff has no information that would contradict the commenters' statements about the majority of NR products being made of DNR. According to a publication of the Rubber Foundation Information Center for Natural Rubber, about 12 percent of the total natural rubber production has been NRL, the remainder is DNR.

Question: Should children with known allergies to the foods and plants that are cross-reactive to NRL be warned to stay away from latex balloons?

Response: In general, significant allergies require diagnosis and treatment by medical professionals. Treatment regimens include patient education on avoidance of substances that are likely to trigger an allergic reaction. When the patient is a child, the appropriate information is presented to an adult caregiver for implementation in the child's daily routine, and may be presented to the child depending on age.

Medical professionals are familiar with the cross-reactivity of fruit and latex (NRL). In the medical literature, Ortiz, et al., (1998) specifically recommend that patients with fruit allergy be screened for NRL allergy even though not all patients with fruit allergy are allergic to NRL. Children with known allergies to the foods and plants that are cross-reactive to NRL are likely to learn how to identify and avoid potential allergenic products from adults as part of the usual routines of child-rearing. This one-to-one approach to education, incorporated into a child's daily life, tends to be relatively effective.

Question: The definition of strong sensitizer in the FHSA speaks of considering the "frequency" of occurrence. Staff seems to equate frequency with prevalence, which is defined in the briefing package as "the percentage of existing cases of a given condition affecting a given population at a given point in time." If we were to use the percentage of the general population affected as the basis for our decision making in other rulemaking contexts, as opposed to actual incidents or estimated number of incidents, it might be difficult to make a case for many of our rulemakings. One percent of the population of the United States is roughly 3 million people, a number which puts latex allergy in a much different light than talking about percentages. Why is it appropriate to use a percentage to define the statutory term "frequency" in the FHSA?

Response: Nothing in the FHSA directs the staff to express frequency in a particular way. As stated in the question, prevalence is the percentage of **existing** cases of a given condition affecting a given population at a given point in time. In contrast, incidence is the number of **new** cases that occur during a specified time period in a given population. Although both prevalence and incidence are measures of frequency, the existing studies of NRL allergy in the general population assess prevalence. Therefore, when talking about the frequency of NRL allergy in the general population it is more appropriate to discuss the prevalence. The prevalence of NRL allergy in the general population, derived from three studies, varies from 0 percent (0/20) to 0.37 percent (1/272) to 0.7 percent (5/758). Because of variability in the results of these studies, it is more appropriate to state the prevalence as a percentage (less than 1 percent) rather than an absolute number. In addition, since exposure to natural rubber products is widespread within the general population (estimated 40,000 products) expressing prevalence of NRL allergy in terms of percentage of the general population is appropriate.

Question: What allergic symptoms, in addition to anaphylaxis, are relevant for purposes of the statutory definition of "strong sensitizer?"

Response: Regulations under the FHSA define the minimal severity of reaction for the purpose of designating a material as a "strong sensitizer" as a "clinically important allergic reaction." The FHSA regulations also include examples,

"strong sensitizers may produce substantial illness, including any or all of the following: physical discomfort, distress, hardship, and functional or structural impairment. These may, but not necessarily, require medical treatment or produce loss of functional activities."
(16 CFR § 1500.3(c)(5)(iii))

The staff briefing package of October 10, 2003, described the range of symptoms and acknowledged that reactions to NRL can be severe including anaphylaxis or death. The estimated prevalence of less than one percent latex allergy in the general population is not based on the severity of the reaction but includes persons who tested positive to NRL in the referenced studies regardless of the extent of their symptoms. Medical literature indicates that about 10 to 20 percent of NRL allergic individuals experience symptoms that extend beyond localized urticaria, conjunctivitis, sneezing, and rhinitis. The number of individuals experiencing more severe, potentially life threatening anaphylactic reactions, is estimated to be much lower.

Question: On page 72 of the briefing package the following statement appears: "Excluding the high risk populations (i.e., occupationally exposed, surgically exposed, and atopic individuals), NRL allergy in the general population is estimated to be less than 1%." How many people are estimated to be included in the high-risk populations?

Response: Groups considered at risk for developing NRL allergy include health care workers and people undergoing multiple surgeries, such as children with spina bifida. These groups are considered to be at risk because they have a high exposure to NRL. However, not all people within these groups have a high exposure or become allergic to NRL. Most sensitized healthcare workers appear to develop NRL allergy due to exposure from the increased use of gloves and other medical devices made of or containing NRL. It is not possible to quantify the "populations at risk" because the number of individuals within these populations is not easily measured. For example, it is unknown what percentage of the estimated two million nurses in the United States are at risk for NRL allergy because many of them do not wear NRL gloves on a regular basis (school nurses, nurses in a doctors' office, etc.).

In addition, the exposure to NRL and prevalence of NRL allergy in populations are changing due to changes in glove manufacture and primary prevention and avoidance programs. Primary prevention programs that substitute low-protein powder-free NRL gloves, synthetic gloves, or both, for powdered NRL gloves appear to reduce the prevalence of NRL allergy in health care workers. Primary prevention and avoidance of NRL-containing medical devices during surgery reduced the prevalence of NRL allergy in spina bifida patients in one preliminary study (Nieto et al., 2002).

Atopic individuals, those who have a genetic hypersensitivity to allergens, are another group thought to be at risk for allergy to NRL. The size of the atopic population is also difficult to quantify because different studies use different techniques and parameters for defining and determining atopy.

Question: Please provide me with a copy of the 1986 Feinman report on chemical additives in NRL that was mentioned in the briefing package.

Response: A copy of the 1986 report is at Tab A.

RESPONSE TO COMMENTS

The Commission published a Federal Register notice on November 14, 2003 (68 FR 64610) announcing a public meeting and soliciting additional comments on petition HP 00-2 and the staff's briefing package dated October 10, 2003. The CPSC received 18 comments, including two comments that were presented at the public hearing on December 10, 2003 (Tab B). Six of the comments were from individuals or groups who had previously commented. Twelve of the comments were from people who reported that they had NRL allergy or were commenting on behalf of someone else, usually a latex-allergic child. Four of the commenters oppose the petition. Eleven commenters support the petition and labeling.

Many of the comments reiterated concerns and information that the staff addressed previously in the October 10, 2003 briefing package. The commenters continue to request content labeling of latex products. The staff discussed CPSC's authority under the FHSA when it addressed this comment in the October 10, 2003 briefing package on pages 18-19. In addition, a commenter (CH03-4-15) reiterated the request that the Commission ban balloons and powdered gloves. The staff addressed both of these issues in the October 10, 2003 briefing package on pages 20-22. The staff has no additional information on these issues that would cause us to alter our previous responses.

Several of the comments provided different information or commented on issues not addressed by the staff in the October 10, 2003 briefing package. The comments and staff responses are given below.

Comment: One commenter (CH03-4-6) noted that, in contrast to the CPSC staff's position regarding the labeling of balloons (October 10, 2003 briefing package, page 116), the Food and Drug Administration (FDA) requires a warning label on latex condoms even though they may be generally known to be made of latex.

Response: The FDA ruled on medical devices as a single category of products, and declined to exempt condoms although they may be an obvious source of latex. Labeling on medical devices is relevant to patients who are allergic to latex, and to health care workers, who are exposed to NRL-containing products, putting them at

higher risk for allergic reaction to NRL. As part of its rationale for rejecting the request to exempt condoms from the warning label requirement, FDA responded that the warning statement "...would clearly provide important information to individuals who are sensitive to natural latex proteins" (62 FR 51025). To exempt one medical device could have caused confusion among latex-sensitive users. If all other latex-containing medical devices to which a latex-sensitive person is exposed are labeled with a warning, and one is not, he or she may mistakenly assume that the unlabeled device is safe to use.

The commenter focuses on balloons, and the hazard they pose to latex-sensitive children because they are not required to have cautionary labeling about latex allergy, in contrast to condoms, which must be labeled. Balloons are a known source of risk for those who are latex sensitive, and staff reiterates its belief that labeling them would not address the commenter's concern. Many commenters identified exposure to balloons as a problem. However, none claimed that the exposure occurred because the balloons were not labeled. Each comment instead reported the hazard of unexpected and difficult-to-avoid exposure to balloons already in use in places such as stores, restaurants, and schools. Package or product labeling would have no impact on exposure of this type.

Comment: One commenter (CH03-4-2) stated that the term "natural rubber latex" was too general and not appropriate because latex allergies were specific to *Hevea brasiliensis*. The commenter stated that labeling should be limited to NRL-containing products made from that rubber tree species and labeling should reflect the origin of the latex. The commenter suggests that 50 ug/dm^2 could be used to regulate the protein level in all natural rubber products to prevent sensitization but that all products with protein from *Hevea brasiliensis* should be labeled to protect allergic individuals.

Response: The staff agrees that the term NRL is general because only certain proteins are associated with sensitization and allergic reactions. Products made of NRL can have variable amounts of these proteins. The commenter is involved in the development and promotion of another species, *guayule*, which she states has none of the allergenic proteins of *Hevea brasiliensis*. The 50 ug/dm^2 extractable protein level that the commenter suggests will not result in sensitization is an upper limit of extractable protein level used by the Standard Malaysian Glove Program (SMGP) for powder free examination gloves. Since the thresholds for development of sensitization and allergic reactions are not known, the level of 50 ug/dm^2 is not a "safe" level. This protein level was chosen due to technical considerations related to gloves and the test methods. The SMGP states that some NRL allergic patients will not react to this level (Yip and Cacioli, 2002). The staff continues to recommend that the Commission deny the petition to declare NRL a strong sensitizer under the FHSA.

Comment: One commenter (CH03-4-4) stated that the focus on natural rubber latex was too narrow and that CPSC staff should expand the scope of the petition to be "rubber" and include all additives that are found to be sensitizers.

Response: Products that contain NRL have been linked to two different immunologically mediated responses, IgE-mediated hypersensitivity and cell-mediated hypersensitivity. In the briefing package of October 10, 2003, the staff limited the discussion of potential allergy to NRL IgE-mediated hypersensitivity caused by the soluble proteins in NRL. The causal agent(s) in cell-mediated hypersensitivity are chemicals added to NRL during the manufacturing process. Since these chemicals are also found in consumer products not made of NRL, the CPSC staff did not evaluate the potential of such additives for causing cell-mediated hypersensitivity as part of the review of NRL. The staff continues to take the view that the evaluation of all chemicals added to NR is beyond the scope of the petition.

Comment: One commenter (CH-03-4-6) stated that the staff used the term "medical personnel" instead of the term "healthcare workers." The commenter states that medical personnel is one subcategory of the Census Bureau's classification of Healthcare and Social Assistance implying that this could result in an underestimation of the population at risk.

Response: The CPSC staff used the terms, "medical personnel", and "healthcare workers" synonymously. The staff was not referring to the Census Bureau's classification system. The Healthcare and Social Assistance classification as defined by the Census Bureau includes social workers and other medically-oriented occupational groups that would not be expected to have a high exposure to medical gloves and therefore would not necessarily be at risk to develop an allergy to NRL. The staff focused its review of prevalence on the general population.

Comment: One commenter (CH03-4-15) requested that latex foam mattresses and pillows not carry a claim to be hypoallergenic.

Response: If NRL was declared to be a strong sensitizer, and foam mattresses and pillows made of NRL were determined to be hazardous substances under the FHSA, cautionary labeling, including the signal words "Caution" or "Warning" would be required. According to 16 CFR § 1500.122 deceptive use of disclaimers is prohibited. Statements that negate or disclaim any of the label statements required by the FHSA would not be permitted.

Comment: One commenter (CH03-4-4) requested that CPSC regulate the manufacturing of rubber.

Response: The CPSC has jurisdiction over products and not the manufacturing process of raw materials used in products.

Comment: One commenter (CH03-4-15) requested that CPSC conduct a national campaign to educate the public on the risks of latex allergy.

Response: The purpose of the commenter's request for a national education campaign is unclear. The general public is at relatively low risk of developing an allergy from

exposure to NRL proteins even though NRL is used to make many products. At present, there is no way to identify who is at risk of sensitization, and which sensitized persons are at risk of allergic reaction. If one knows they are allergic, avoidance of latex, as well as food items and plants that cross-react with latex, is the only method of prevention. These restrictions are unreasonable for those who are unlikely to suffer any negative effects from NRL. There is, therefore, no obvious message that staff believes would be appropriate for a national audience.

RECOMMENDATION AND DISCUSSION

There was no additional information presented at the public hearing held on December 10, 2003 or in the additional comments received in response to the Federal Register notice of November 14, 2003, that would change the staff's recommendation to deny the petition. The staff recommends that the Commission deny the petition because the available data, including the low frequency of latex allergy in the general population, do not support that NRL is a strong sensitizer according to the FHSA definition.

References

Nieto, A., Mazon, A., Pamies, R. et al. The efficacy of Latex Avoidance for Primary Prevention of Latex Sensitization in Children with Spina Bifida. J. Pediatr. 140:370-372, 2002.

Ortiz, G., Moyano, J., Alvarez, M., Bellido, J. Latex allergy in Fruit-Allergic Patients. Allergy 53(5):523-6, 1998.

Yip, E. and Cavioli, P. The manufacture of gloves from natural rubber latex. J Allergy Clin Immunol,110(2):S3-S14.

TAB A

15 pgs

UNITED STATES GOVERNMENT

Memorandum

U.S. CONSUMER PRODUCT SAFETY COMMISSION
WASHINGTON, D.C. 20207

DATE: 29 DEC 1986

6 (b) CLEARED: JR 7-23-87
No Mfrs Identified
Excepted
Mfrs Notified
Comments Processed

TO: Sandra Eberle, Chemical Hazards Program, OPM

THROUGH: Andrew G. Ulsamer, Ph.D., Acting AED, HS AGU

THROUGH: Murray Cohn, Acting Director, HSHE MSC

FROM: Susan E. Feinman, Ph.D. SF

SUBJECT: Sensitivity to Rubber Chemicals

The attached report summarizes data on certain common rubber sensitizers found in consumer products. Among the chemicals examined, mercaptobenzothiazole (MBT) appears to be a potential strong sensitizer, and can be released from consumer products. The thiurams and certain thioureas, although reported to cause severe reactions in some exposed individuals, lack consumer exposure data.

The contact allergen, MBT, shown to induce sensitization in animals and man, is widely used as an accelerator and vulcanizing agent in rubber found in shoes, gloves, rubberized fabrics such as wet suits or undergarment elastic, and waterproofing or rubber cement. Case histories have confirmed allergic dermatitis reactions from these products and a Johns Hopkins contract study sponsored by CPSC showed that MBT was leached from a rubber heel which had elicited foot dermatitis.

MBT has elicited positive patch tests in 1 - 5% of the patients screened by the North American Contact Dermatitis Group (NACDG) of the American Academy of Dermatology. Assuming that the 2.3% rate of confirmed positive patch tests to MBT observed in 1984-5 (among 1369 dermatitis patients examined in clinics) could be extrapolated to the 8 million U.S. dermatitis and eczema patients estimated on the basis of the 1980 Census, there may be about 220,000 persons potentially affected per year.

Seven of 11 MBT-sensitive patients tested under the CPSC contract had strong or extreme reactions to the standard 1% MBT diagnostic patch test. The minimum elicitation threshold in most of these patients lay below 0.1% MBT; at 0.01% one person presented with a classic positive reaction and 4 had erythema (redness); at 0.003% MBT there was no effect.

Thiurams are rubber accelerators found in rubber gloves, shoes, putty, and paints. They have been shown to induce sensitization in guinea pigs and in humans. Positive patch tests to thiurams were elicited in 3.8% of 1364 dermatitis patients screened by the NACDG in 1984-5; 1.8% were found to have been exposed to thiurams (in domestic products or occupationally.) Extrapolating to the 8 million estimated

U.S. persons with dermatitis in 1980, there may have been approximately 144,000 patients affected that year. Leaching from rubber consumer products has not, however, been demonstrated in CPSC contract studies. The extent to which nonoccupational exposure contributes to thiuram allergic dermatitis, therefore, may be small.

Ethylbutylthiourea (EBT), used in sneakers and swim goggles, has been associated with severe allergic reactions by some U.S. dermatologists. Although EBT leaching has been demonstrated from consumer products, quantitative elicitation tests using EBT in humans have not been performed by CPSC since significant amounts of a carcinogenic starting product, diethylthiourea, were present. Data on extent of EBT use are not available.

Prior to considering the potential designation of MBT as a strong sensitizer, there is a need to perform an in-depth assessment of the extent of MBT use in consumer products and the availability of acceptable non-sensitizing substitute rubber accelerators and vulcanizing agents. If there is widespread consumer exposure to MBT at concentrations above 0.01%, the Commission should designate MBT as a strong sensitizer. The labelling of MBT at concentrations greater than 0.01% would probably enable almost all MBT-sensitive consumers to avoid products which might produce prolonged and painful eczematous reactions.

It is also recommended that standards be established for testing the concentrations of MBT in consumer products, according to the protocol developed by the Johns Hopkins contract. These levels should be correlated with the concentrations eliciting reactions.

Additional data are needed on exposure to thiurams and ethyl butyl thiourea (EBT) in consumer products before consideration of whether they meet the criteria of being strong sensitizers. Although thiurams are important sensitizers, the extent of their use in consumer products is uncertain because of failure to demonstrate leaching from several products. The additional studies can be performed in the Health Sciences Laboratory. Further consideration should await proof of availability from consumer products. For rubber products (sneakers and goggles) containing EBT, an allergen producing severe skin reactions, limited data are available to demonstrate contact allergy in human patients. These products have been shown to leach an unreacted starting product, diethylthiourea (DET), which is an animal carcinogen. This finding rendered impossible further study under our contract to assess the threshold of sensitivity. An economic assessment, evaluating the extent of EBT use in consumer products would be very useful and would enable Health Sciences to decide whether to perform an in-depth evaluation of DET and EBT toxicity and the extent of consumer exposure to DET.

RUBBER SENSITIZERS

by

Susan E. Feinman, Ph.D.

I. INTRODUCTION

A. Purpose of Report

The purpose of this report is to evaluate whether certain rubber additives are bioavailable from consumer products in sufficient quantities to elicit allergic hypersensitivity responses and whether they should be labeled by the Commission as strong sensitizers under the Federal Hazardous Substances Act.

B. Summary

The report evaluates 20 common rubber sensitizers, grouped chemically, based on clinical reports, patch testing data from dermatitis patients, and bioavailability data from consumer products. The report indicates that there are several major sensitizers in consumer products, important either due to widespread use or potency. Mercaptobenzothiazole (MBT) appears to be an important sensitizer, widely used in shoes. While the data indicate that thiurams are important sensitizers, insufficient information is available to indicate bioavailability and exposure from consumer products. Ethyl, butyl, and ethylbutylthiourea are potent sensitizers, in that as little as .02 ppm elicits reactions. Although they appear to be found mainly in athletic shoe insoles containing neoprene, there are no data on frequency of use and no large population studies on frequency of reaction. Isopropylphenylparaphenylene-diamine (IPPD), another potent sensitizer, is used rarely in consumer goods in this country but imported items have elicited allergic reactions.

C. Rubber Sensitization

Natural rubber poses no hazard as a contact allergen (Cronin, 1980). During the manufacturing process, however, chemicals must be added to both synthetic and natural rubber to prolong product life and to confer special properties. Many of these additives are capable of sensitizing and can persist in the final product. Thus, consumers attributing allergic contact dermatitis to "rubber" are actually reacting to rubber additives.

Sensitizing rubber additives may cause contact dermatitis even when rubber is considered completely cured (Fisher, 1973, Adams, 1983). One reason may be that small quantities of unreacted accelerators or antioxidants may remain after curing and may "bloom" or migrate to the surface over time (Schwartz et al, 1957). Contact with skin may be enhanced by localized heat and perspiration. Other reasons may include incomplete curing, presence of exposed sidegroups, and the constant breakdown and degradation of rubber by heat, friction, ozone, and other forces (Taylor and Son, 1982).

It is helpful to organize sensitizing rubber additives according to their chemical classes. Cronin (1980) states that the dermatologist is concerned with: "(a) a knowledge of the various groups of potentially allergenic chemicals which may be present in rubber, and (b) the cross-reaction patterns of the individual chemical."

Commonly tested sensitizing classes of rubber additives used as accelerators, vulcanizing agents, antioxidants, and corrosion inhibitors are as follows:

(1) Thiurams

Tetramethylthiuram disulphide	(TMTD)
Tetraethylthiuram disulphide	(TETD)
Dipentamethylenethiuram disulphide	(PTD)
Tetramethylthiuram monosulphide	(TMTM)

(2) Mercapto-group

Mercaptobenzothiazole	(MBT)
Cyclohexylbenzothiazylsulphenamide	(CBS)
Dibenzothiazyldisulphide	(MBTS)
Morpholinylmercaptobenzothiazole	(MMBT)

(3) Paraphenylenediamine (PPD) group

Phenylcyclohexyl-PPD	(CPPD)
Isopropylphenyl-PPD (Isopropylamino-diphenylamine)	(IPPD)
Diphenyl-PPD	(DPPD)
Diaminodiphenylmethane	(DDM)

(4) Naphthyl group

Phenyl-beta-naphthylamine	(PBN)
sym-Di-beta-naphthyl-PPD	(DBNPD)

(5) Carbamates

Zinc diethyldithiocarbamate	(ZDC)
Zinc dibutyldithiocarbamate	(ZBC)

(6) Miscellaneous

Diphenylguanidine	(DPG)
Dithiodimorpholine	(DOD)
Thiourea compounds	
Monobenzyl ether of hydroquinone	

Chemically related rubber chemicals are usually combined in initial patch tests to screen patients suspected of being rubber sensitive. The patch test mixtures are: 1% thiuram mix (0.25% each of TMTD, TETD, TMTM, PTD); 1% mercapto mix (0.33% each of CBS, MBTS, MMBT); 0.6% black rubber PPD mix (CPPD and DPPD at 0.25%, IPPD at 0.1%); and 3% carbamix (1% each of DPG, ZBC and ZDG). In addition, 1% MBT is tested alone because of the high number of reactions attributed to it (Cronin, 1980).

Standard patch tests on dermatitis patients provide data on the frequency of specific reactions in a selected population. These results are based on screening tests performed for diagnosis of consecutive dermatitis patients by the North American Contact Dermatitis Group (NACDG) of the American Academy of Dermatology, consisting of 13 geographically distributed North American

dermatologists who recommend patch testing standards for the United States. These patch tests have been performed on about 2,000 patients per year. In some cases the NACDG has not performed large-scale patch tests, as with the newly emerging sensitizer, ethyl butyl thiourea, which contains the residues of the potentially carcinogenic starting product, diethylthiourea (NTP, 1979).

II. MERCAPTOBENZOTHIAZOLE (MBT) AND MERCAPTOMIX

MBT, widely used in gloves and shoes, is commonly classified as an important contact allergen based on its being a common cause of positive responses in dermatitis clinics and a sensitizer in predictive studies in animals and in humans. MBT is among the 20 contact allergens most frequently causing patch test reactions.

A. Frequency of Reaction

Patch test studies are performed to estimate the frequency of MBT sensitization and to confirm its diagnosis; these use standardized test solutions and quantities, are applied to avoid irritation, and are read according to established criteria. MBT elicits positive patch test reactions in 1 to 5% of dermatitis patients tested by the NACDG annually; in general, the NACDG has observed that the most important contact allergens elicit positive patch tests in 1 to 11% of dermatitis patients per year (Storrs, 1986; Taylor, 1982). The rate of positive patch tests to MBT in 1984-5 was 2.6% (1,369 patients) in the United States (Storrs, 1986). Almost all of these patients (2.3%) were found to have relevant case histories and exposures. Assuming that the NACDG patients were average dermatitis patients, if these data were extrapolated to the population of 8 million dermatitis and eczema patients (Center for Health Statistics, 1980), there would be 218,700 people affected. Earlier patch test data are shown in Table 1.

B. Use

MBT is the most utilized contact allergen found in shoes, based on data from manufacturers/importers; almost all shoes contain it (Podmore, 1986). It can migrate and persist in hosiery (Rietschel, 1984). MBT foot dermatitis may resemble athlete's foot and may prevent the sensitive person from wearing shoes. The dermatitis may become generalized, spreading to the hands and elsewhere. MBT is the most commonly used contact allergen in rubber gloves (Cronin, 1980; Storrs, 1986). It also has been found in rubberized fabrics (wet suits, girdles) and waterproofing or rubber cements.

TABLE 1

Prevalence of Positive Patch Test Reactions to MBT in
North American Dermatitis Patients
#Positive patch tests/#Patients tested

Year	Male	Female	Total
1981-82*	36/913 (3.0%)	25/1327 (1.0%)	61/2240 (2.7%)
1980-81	32/849 (3.0%)	17/1231 (1.0%)	49/2080 (2.4%)
1979-80	50/834 (5.0%)	26/1263 (2.0%)	76/2097 (3.6%)
1977-78	51/943 (5.0%)	48/1299 (4.0%)	99/2242 (4.4%)

*Unpublished data from J.S. Taylor (1982), Task Force on Contact Dermatitis, American Academy of Dermatology, Evanston, Ill. Date for 1982-4 are not available.

C. Reactions to Consumer Products

In a recent small study of 23 patients with shoe dermatitis at the Oregon State Medical Center, two reacted to MBT (Podmore, 1986). In addition, CPSC sponsored a quantitative patch test study (Emmett et al, 1986) at the Cleveland Clinic/Johns Hopkins in 12 MBT-positive volunteer subjects, noting demographic characteristics. Two of the 12 subjects had acquired their dermatitis before the age of nine, two when over fifty, and the remainder between 20 and 50 years of age. At the time of study the dermatitis had lasted for 2-5 years in 4 subjects, 6-10 years in 4 subjects, and 11-20 years in 4 subjects. The dermatitis had been located in one or multiple sites: on the hands in eight patients, on the feet in six, on the trunk in two, and on the face in one. The age of the patients ranged from 18-76, with a mean of 46. Eleven were white and one was black; seven were male and five female. Only 2 of the subjects could identify by brand name any product causing reactions. The consumer products to which the 12 patients had ever reacted are listed in Table 2.

TABLE 2

Rubber Items to Which Reactions Have Occurred [1]

Any rubber product	3
Rubber gloves	4
Shoes	4
Elastic underwear	3
Rubber bands	2
Eraser	1
Rubber diaphragm	1
Rubber stamp	1
Rubber seals	1
Rubber contact cement	1

All of the patients had other contact allergies. Four were not employed (student, housewife, retired) and the others were employed in diverse occupations. At the time of study eight had no dermatological disease but four had eczematous dermatitis on the hands or arms (Tests are performed on the back).

The definitive patch test reading was recorded 96 hours after MBT patch application according to the following scheme.

+	papular erythema without vesicles
++	vesicular reaction
+++	extreme (spreading, bullous, ulcerative) reactions
?	doubtful reaction (erythema only)
-	negative reaction
NT	not tested

Emmett et al (1986). [1] individual subject's reaction may be noted more than once.

In the preliminary diagnostic patch test to 1% MBT three subjects had extreme reactions (bullous), four had strong reactions (erythema, infiltration, papules, and vesicles), and four had weak positive reactions (erythema, infiltration, possible papules). Upon repetition of the test after a time interval, reactions varied somewhat and, at lower concentrations of MBT, fewer subjects reacted and more patients had weaker reactions (Table 3).

TABLE 3

Results of Patch Testing with Serial Dilutions of MBT & MBTS in Petrolatum in Twelve Rubber Sensitive Subjects

Test Substance	Total No. Positive	++ to +++	+	Erythema only
1% MBT	11	9	2	1
0.316% MBT	10	6	4	2
0.1% MBT	7	3	4	4
0.0316% MBT	2	1	1	1
0.01% MBT	1	0	1	4
0.00316% MBT	0	0	0	0

At 0.1% MBT, three patients gave a strong positive reaction, four gave weak positive reactions, and four had erythema. The minimum elicitation threshold in most patients, therefore, lies below this level. At 0.01% (4.5ug/cm^2 *) MBT 1 patch, one patient reacted and four had erythema (redness). There was no effect at 0.003% (1.45 ug/cm^2) MBT. These tests were performed in a blind Latin Square to eliminate differences in location of patches (e.g., irritative interactions), differences in individual reactivity among patients, and differences in applied dilutions.

An earlier study reports that allergic contact dermatitis was induced in seven workers exposed to 0.01-0.05% MBT in a cutting oil for 3-8 months (Fregert and Skog, 1972). Although the induction of sensitization may have been facilitated by irritants in the cutting oil, the threshold (less than 0.01%) does not differ greatly from the elicitation concentration observed in the CPSC study. In the CPSC study, eight patients had dermatitis on the hands and six on the feet - sites of irritation from gloves and shoes. Four patients were known to react to gloves and four to shoes.

D. Induction of Sensitivity

Kligman (1966) demonstrated induction of sensitivity in nine of 24 human volunteers. Exaggerated test conditions were used to speed up induction and to lessen the number of volunteers required. Subjects were given a high (25%) dose MBT topically at a site previously inflamed with sodium lauryl sulfate; they were challenged with 10% MBT. The Kligman study demonstrated that MBT sensitization could be induced. Similar results were obtained with optimal conditions for induction in guinea pigs, using an occluded patch of 25% MBT and a challenge concentration of 15% MBT. Eight of 20 animals were sensitized. These numbers cannot be compared with elicitation percentages.

* See attached contract report for calculations.

MBT leaches from consumer products. Allergic reactions on the sole of the foot have developed when MBT was 3-4 layers below the sole of shoes or in the heel of a boot (Jordan, 1972; Storrs, 1985). Leaching studies were performed at Johns Hopkins on a consumer product (shoe heel) which had elicited allergic contact dermatitis (ACD) and one (rubber glove) which contained MBT but was not known to have elicited ACD. Although little MBT leached from the rubber glove sample (less than 4 ug/cm^2), 17-25 ug/cm^2 leached from the rubber heel (Emmett et al, 1986). This amount greatly exceeded the MBT threshold on the intact skin between 1.45 and of 4.5 ug/cm^2 (see attached report).

Dibenzothiazyl disulfide (MBTS), a closely related chemical, was also measured in the samples. Although apparently present (based on Soxhlet extraction), it was not extracted from the rubber heel by normal saline or synthetic solutions. Use of MBT is more common than that of other mercapto sensitizers. The rate of reaction to mercapto mix compounds alone (14 of 171 reactions to a 4-part mercaptomix) is relatively small (Mitchell et al, 1976) and there are no known case reports of allergic reactions to consumer products containing MBTS.

These data indicate that MBT is important as a strong sensitizer, with a threshold below 0.01% (100 ppm). MBT is frequency used in shoes. Identifying MBT as an ingredient would assist consumers who suffer from MBT shoe allergy. Sensitive customers could be advised about the availability of MBT-free footwear.

III. THIURAM CHEMICALS

Thiurams are rubber accelerators found in rubber gloves and shoes, especially crepe soles. They are also used in putty, paints and rubber bands. Although thiurams appear to be important sensitizers, bioavailability from consumer products has not been shown. Thiurams have been shown to be one of the ten most common contact allergen compounds in patch test screening (NACDG, 1975).

In a sample group of North American dermatitis patients, 3.6% to 5.4% per year had positive patch tests to a thiuram mix from 1977 to 1982 (Taylor, 1983). Rates do not differ greatly in men and women (Table 4). In 1984-5, there were 52 allergic reactions among 1,364 persons (3.8%) in the United States. Relevancy (shown by case history and clinical symptoms) was ascertained for only 1.8%, however. Canadian and British patients have rates similar to U.S. patients.

TABLE 4

Positive Patch Test Reactions to Thiuram Mix in A Group of North American Dermatitis Patients

#Positive patch tests/#Patients tested

Year	Male	Female	Total
1981-82	32/833 (3.0%)	55/1198 (4.0%)	87/2031 (4.3%)
1980-81	30/726 (4.0%)	55/1105 (4.0%)	88/1831 (5.4%)
1979-80	26/696 (3.0%)	48/1063 (4.0%)	74/1759 (4.2%)
1977-78	40/811 (5.0%)	61/1133 (5.0%)	101/1944 (5.2%)

Predictive tests in humans and guinea pigs have demonstrated that tetramethyl thiuram disulfide (TMTD) induced sensitization of 50% of guinea pigs (Zeigler et al, 1972) and 16% of humans (Kligman, 1966), using an exaggerated induction procedure.

In CPSC-sponsored studies, thiurams could not be detected in consumer products which were thought to have elicited allergic contact dermatitis in thiuram-positive patients (Emmett, 1986). No data could be found on leaching. It is presumed that much exposure is occupational and that household products containing thiurams do not present a special hazard to consumers. Most large studies abroad confirm that the majority of cases are work-related.

IV. THIOUREAS

Allergic contact dermatitis from thiourea-based rubber chemicals is being observed increasingly by dermatological specialists. Thioureas are used as accelerators and corrosion inhibitors in rubber. Most of the data available involve ethylbutylthiourea (EBTU) which is used in black neoprene rubber as a accelerator. Many clinicians have associated EBTU with severe allergic reactions from sneakers. It is also found in swim goggles.

Most EBTU foot dermatitis has resulted from its use in the neoprene inner sole of a popular U.S. jogging shoe. It was first reported in ten patients who had a severe and persistent dermatitis. Six patients had been exposed to insoles containing EBTU from 2 weeks to 3 months before treatment; the dermatitis lasted from 3 weeks to 2 years after ceasing use of the shoes (Roberts and Hanifin, 1979). Since a mild dermatitis persisted in some cases after removal of the exposure source, patients were patch tested with other thioureas. Cross-reactions occurred with ethyl-, butyl-, and diethylthioureas (Roberts and Hanifin, 1979). This type of foot dermatitis has again occurred in many other patients (Taylor, 1986) although shoe manufacturers allegedly ceased use of these sensitizers. In an unpublished study two out of 23 patients with shoe dermatitis reacted to thioureas from neoprene containing insoles (Podmore, 1986).

Chemical analysis of the foam rubber inner sole of a common running shoe and of black neoprene swim goggles confirmed the leaching of substantial amounts of EBTU and of the starting products, diethylthiourea (DET) and dibutylthiourea (DBT). Both inner soles and swim goggles released substantial amounts of DET, EBT, and DBT, the amount varying with the leaching media (Emmett et al, 1986). Quantities are shown in Table 5.

TABLE 5

Percentage of Available Dialkyl Thioureas Leached by Solvent Systems
(Total ug/g rubber sample)

Solvent Tennis Shoe Insole	DET	EBT	DBT
Normal Saline	64% (47)	66% (92)	38% (47)
Synthetic Sweat pH 5.4	71% (108)	74% (31)	41% (88)
Synthetic Sweat pH 6.6	69% (112)	65% (29)	32% (99)
Synthetic Sweat pH 7.8	67% (132)	69% (31)	28% (114)
Human Plasma	82% (242)	79% (37)	47% (90)

Goggles

Normal Saline	60% (7)	48% (10)	22% (5)
Synthetic Sweat pH 5.4	44% (12)	34% (37)	13% (10)
Synthetic Sweat pH 6.6	62% (8)	56% (10)	19% (7)
Synthetic Sweat pH 7.8	42% (17)	31% (19)	08% (16)
Human Plasma	37% (10)	19% (9)	00% (6)

Human studies were not performed because of the presence of DET (Emmett, 1986) because DET (CAS #105-55-5) has been found to produce cancer in male rats upon ingestion (NCI, 1979). Commercially sold EBTU contains about 25% DET (Emmett et al, 1986) and DBT.

These thiourea compounds are used as corrosion inhibitors as well as rubber accelerators. Positive patch tests have been elicited at concentrations as low as of 0.1% DET in one case (Adams, 1982) and 0.1% DBT in another (Kanerva et al, 1984). In the first case a severe widespread dermatitis had been elicited by DBT in an American rubber wet suit (Adams, 1982) and in the other case by DBT in a paint remover (Kanerva et al, 1984). There are little data on reaction frequencies to this group of sensitizers since they have only recently become the subject of investigation.

V. PHENYLENEDIAMINE-BLACK RUBBER COMPOUNDS

The phenylenediamine (PPD) group of antidegradant rubber compounds (IPPD, CPPD, and DPPD) are important sensitizers but rarely have been noted in consumer products (shoe, cushion, clothing elastic, watersports equipment). They are closely related to paraphenylenediamine which is already designated as a "Strong Sensitizer" in the current FHSA regulation. At least one, IPPD, induced sensitization in 49 persons wearing rubber fingerstalls; these reactions occurred at levels as low as 0.01%, upon frequent exposure (Roed-Peterson et al, 1977).

The PPD Mix chemicals have been shown to induce sensitization in guinea pigs (Magnusson and Kligman, 1970). Positive patch tests were elicited in 1.4% to 2.7% of dermatitis patients screened between 1972 and 1981 (Taylor, 1986). Positive patch tests were elicited in 1.3% of 1,366 U.S. patients in 1984-5; almost all were clinically relevant (Storrs, 1986). The reaction mix contained only 0.1% IPPD, compared to 0.25% CPPD, and 0.25% DPPD to avoid active sensitization since IPPD is a stronger allergen than the other PPD mix components (Cronin, 1980).

PPD chemicals tend to leach to the surface of rubber (Schonning and Hjorth, 1969). Several cases have been described of persons who became sensitized and/or developed ACD by contacting tires where IPPD leached to the surface (Fregert, 1973; Jordan, 1971). Although IPPD is not used by major U.S. tire manufacturers, it was present on Volkswagon tires, producing hand dermatitis in a man exposed by washing his car (Jordan, 1971). IPPD also caused ACD on faces of California skin divers exposed to swim masks (Maibach, 1975) and on the hands of two windsurfers gripping masts (Tennstedt and LaChapelle, 1981).

Emmett et al 1986)

VI. MISCELLANEOUS SENSITIZING RUBBER ADDITIVES

A. Carbamates

Carbamates constitute another important group of sensitizing chemicals; they are used as fast accelerators in rubber. In patch tests done with the carbamix (1% DPG, 1% ZDC, 1% ZBC), the NACDG reaction rates ranged from 2.7% to 5.4% from 1972 to 1982. In 1984-5, 43 of 1,362 NACDG (3.1%) patients reacted to the mix. Although DPG is used occupationally, there may be consumer exposure to ZBC and ZDC. Dithiocarbamates which elicit ACD may be present in gloves, clothing and boots (Wilson, 1969). In an interesting study, Jordan and Bourlas (1975) found six patients who were sensitive to their old underwear but not to new samples. ZDC was found to be changed chemically by the sodium hypochlorite bleach to a new potent sensitizer.

B. Other sensitizers

Among the other rubber chemicals less frequently eliciting sensitization are 4,4'dithiodimorpholine, 2-naphthalene, phenyl beta naphthylamine (PBN), sym-di-beta-naphthyl-para-phenylenediamine (Nonox C1) and the monobenzyl ether of hydroquinone.

VII. CONCLUSION

Although there are many sensitizing chemicals in rubber, only certain ones are important ingredients in consumer products. Thiurams are widely used contact allergens; however, there are insufficient data to indicate availability/exposure from consumer products. MBT has widespread use in shoes as well as being a common contact allergen in rubber gloves, fabrics, shoes, girdles and wet suits. MBT induces sensitization in predictive tests in guinea pigs and humans. Graded concentrations in patch tests suggest an elicitation threshold between 4 and 13 ug/cm^2 (0.01% MBT). Leaching studies on one consumer product eliciting reactions indicated that up to 25 ug/cm^2 could be released, greatly exceeding the elicitation threshold. In contrast, a product which had not elicited a reaction contained less than 4 ug/cm^2 product.

Although frequency data are not available on ethyl butyl thiourea, it has recently been associated with the elicitation of ACD from contact with the inner sole of a popular brand of sneaker. Ethyl butylthiourea and its starting chemicals, diethyl-and dibutylthiourea, appear to be able to cause severe and persistent reaction. Similarly, IPPD, a contact allergen with a threshold of less than 0.01%, has elicited sensitizing reactions, although it is rarely used in consumer products.

BIBLIOGRAPHY

Adams, R.M. (1982). Contact allergic dermatitis due to diethylthiourea in a wetsuit. Contact Dermatitis 8:277-8.

Center for Health Start, 1980.

Cronin, E. (1980). Contact Dermatitis. Churchill Livingstone, Edinburgh.

Fisher, A.A. (1973). Contact Dermatitis. Lea & Febiger, Philadelphia.

Fregert, S. and Skog, E. (1962). Allergic contact dermatitis from mercaptobenzothiazole in cutting oil. Acta Derm.-Venereol. 42:235-8.

Jordan, W.P. (1972). Clothing and shoe dermatitis recognition and management. Postgrad. Med. 52:143-8.

Jordan, W.P. and Bourlas, M.C. (1975). Allergic contact dermatitis to underwear elastic, chemically transformed by laundry bleach. Arch. Dermatol. 111: 593-5.

Kanerva, L. et al (1984). Contact dermatitis from dibutylthiourea. Contact Dermatitis 10:158-162.

Kligman, A. (1966). The identification of contact allergens by human assay. III. The maximization test: a procedure for screening and rating contact sensitizers. J. Invest. Dermatol. 47:393-410.

Magnusson, B. and Kligman, A.M. (1970). Allergic Contact Dermatitis in the Guinea Pig. Identification of Contact Allergens. Thomas, Springfield, Ill.

Maibach, H.I. (1975). Scuba diver facial dermatitis: Allergic contact dermatitis to N-isopropyl-N'-phenylparaphenylene diamine. Contact Derm. 1:330.

Mitchell, J.C., Clendenning, W.E., Cronin, E., Fregert, S., Kanof, N.B., and Maibach, H.I. (1976). Patch testing with mercaptobenzothiazole and mercapto-mix. Contact Dermatitis 2:123-4.

NACDG. North American Contact Dermatitis Group (1982b). Personal communication from James Taylor, Cleveland Clinic, unpublished data, American Acad. of Dermatol. Evanston, Ill. 1975-1982.

NCI. Tech. Report Services #149. NCI-CG-TR-149.

Podmore, P. 1986. Royal Victoria Hospital, Belfast, Letter to Susan E. Feinman, 15 April.

Rietschel, R. (1984). Role of socks in shoe dermatitis. Arch. Dermatol. 120:398.

Roberts, J.L. and Hanifin, J.M. (1979). Athletic shoe dermatitis. J.A.M.A. 241:275-6.

Roed-Peterson, J., Horth, N., Jordan, W.P., and Bourlas, M. (1977). Postsorters' rubber fingerstall dermatitis. Contact Derm. 3:143-147.

Schonning, L. and Hjorth, N. (1969). Cross-sensitization between hair dyes and rubber chemicals. Berufsdermatosen 17:100-6.

Schwartz, L., Tulipan, L., and Birmingham, D.J. (1957). Occupational Diseases of the Skin. Lea & Febiger, Philadelphia.

Shelley, W.B. (1967). Golf-course dermatitis due to thiuram fungicide. J.A.M.A. 188:415-7.

Stankevich, V.V., Vlasyuk, M.G., and Prokof'eva, L.G. (1980). Hygienic assessment of organosulfur accelerators for vulcanization of rubber for the food industry. Gig. Sanit. 10:88-89.

Stoll, D. and King, L.E. (1980). Disulfiram-alcohol skin reaction to beer-containing shampoo. J.A.M.A. 244:2045.

Storrs, F. 1985. Personal Communication.

Storrs, F. 1986. Dermatitis from Clothing and Shoes, In. Contact Dermatitis.3rd Ed. (Ed. Fisher, A.) Lea and Febisher, Phila., pp. 283-337.

Storrs, F. 1986. Oregon Health Sciences University. Letter to Susan E. Feinman, May 9.

Sugai, T. Takagi, T. Yamamoto, S., and Takahashi, Y. (1979). Age distribution of the incidence of contact sensitivity to standard allergens. Contact Derm. 5:383-8.

Sun, C.C. (1980). Two-year experience with patch testing. J. Formosan Med. Assoc. 79:220-9.

Sunderman, F.W. (1981). Chelation Therapy in nickel poisoning. Ann. Clin. Lab. Sci. 11:1-8.

Tannenbaum, M.H. (1967). Spandex dermatitis. J.A.M.A. 200:899.

Taylor, R. and Son, P.N. (1982). Rubber chemicals. In the Kirk-Othmer Encyclopedia of Chemical Technol., Vol. 20, 337-364.

Taylor, J.S. (1986). Rubber In Contact Dermatitis (Ed. Fisher, A.) Lea and Febisher, Phila., pp. 603-643.

Tennstedt, D. and Lachapelle, J.M. (1981). Windsurfer dermatitis from black rubber components. Contact Dermatitis 7:160-1.

Themido, R. and Menezes Brandao, F. (1984). Contact allergy to thiurams. Contact Derm. 10:251.

van Dijk, E. (1986). Contact dermatitis due to Spandex. Acta Dermato-vernereol. 48:589.

Van Hecke, and Vermander, F. (1984). Allergic contact sensitivity by oral disulfiram. Contact Derm. 10:254.

van Ketel, W.G. (1984). Sensitization to hydroguinone and the monobenzyl ether of hydroquinone. Contact Derm. 10:253.

van Ketel, W.G. (1968). Rubber, alcohol, in eczema. Ned Tijdsch Geneeskd 112:406-8.

van Ketel, W.G. (1976). Thiuram-mix. Contact Dermatitis 2:232-3.

Van der Waale, H.B., Delbreivine, L.P.C., and Seutter, E. (1982). Concomitant sensitization from hydroquinone and p-methoxyphenol in the guinea pig:inhibitors in acrylic monomers. Contact Derm. 8:147-154.

Varelzides, A., Katsambas, A., Georgala, S. and Capetanakis, J. (1974). Shoe dermatitis in Greece. Dermatologica 149:236.

Varigos, G.A. and Dunt, D.R. (1981). Occupational dermatitis. An epidemiological study in the rubber and cement industries. Contact Derm. 7:105-10.

Veien, N.K., Hattel, T., Justesen, O., and Norholm, A. (1982). Contact dermatitis in children. Contact Derm. 7:373-5.

Vollum, D.I. and Marten, R.H. (1968). Contact dermatitis from 4-isopropyl-amino-diphenylamine. Trans. St John's Hosp. Derm. Soc. 54:73-74.

Webb, P.K. (1979). Allergy to Antabuse and rubber. J.A.M.A. 241:2061.

Weinstein, L.H. and Fellner, M.J. (1979). Rubber band dermatitis. Int. Soc. Trop. Derm. 18:558.

Weston, J.A., Hawkins, K., and Weston, W.L. (1983). Foot dermatitis in children. Pediatrics 72:824-827.

White, W.G. and Vickers, H.R. (1970). Diethylthiourea as a cause of dermatitis in a car factory. Brit. J. Indust. Med. 27:167-9.

Wilkinson, D.S., Bandmann, H.J., Calnan, C.D., Cronin, E., Fregert, S., Hjorth, N. Magnussen, B. et al. (1970). The role of contact allergy in hand eczema. Trans. St. Johns' Hosp. Dermatol. Soc. 56:19.

Wilkinson, D.S. and Wilkinson, J.D. (1979). Acta Derm-venereol. 59:189-92.

Williams, E.E. (1937). Queries and minor notes: Effects of alcohol on workers with carbon disulfide. J.A.M.A. 109:1472-3.

Wilson, H.T.H. (1969). Rubber dermatitis: An investigation of 106 cases of contact dermatitis caused by rubber. Br. J. Dermatol. 81:175-9.

Wilson, H.T.H. (1960). Rubber-glove dermatiis. Br. Med. J. 2:21-3.

Wilson, W.B. (1962). Side effects of disulfiram. Br. Med. J. III:1610-1611.

Ziegler, V. and Suss, E. (1974-5). The allergenic effect of rubber accelerators, tetramethylthiuram disulfide (TMTD) and mercaptobenzothiazole (MBT). Allerg. Immunol. (Leipz.) 20-21:281-5.

Zugerman, C. (1981). Allergy to zinc dimethyldithiocarbamate in rubber gloves. Contact Dermatitis :337-8.

TAB B

United States
CONSUMER PRODUCT SAFETY COMMISSION
Washington, D.C. 20207

MEMORANDUM

DATE : January 13, 2004

TO : HS

Through: Todd A. Stevenson, Secretary

FROM : Martha Kosh

SUBJECT: Petition to Declare Natural Rubber Latex a Strong Sensitizer Under the Federal Hazardous Substance Act

ATTACHED ARE COMMENTS ON THE CH 03-4

COMMENT	DATE	SIGNED BY	AFFILIATION
CH03-4-1	11/17/03	Jack Trautman CEO	Allergen Reduction, Inc. 3017 Dianne Dr. Middleton, WE 53562
CH03-4-2	11/20/03	Katrina Cornish Ph.D, FAAAS	US Department of Agriculture Western Regional Research Center 800 Buchanan Street Albany, CA 94710
CH03-4-3	11/26/03	John Friar II	537 Montgomery St. Fall River, MA 02720
CH03-4-4	12/01/03	Carol Kuczora	P.O. Box 536 Grass Valley, CA 95945
CH03-4-5	12/03/03	P. Rourke-Nichols	P.O. Box 2242 Arnold, CA 95223
CH03-4-6	12/04/03	Debra Adkins (Speaker)	Latex Allergy Information Service 176 Roosevelt Ave Torrington, CT 06790
CH03-4-7	12/10/03	Dr. Esah S. Yip	Malaysian Rubber Export Promotion Council 3516 Intern'l Ct, NW Washington, DC 20008

Petition to Declare Natural Rubber Latex a Strong Sensitizer Under the Federal Hazardous Substance Act

CH03-4-8	12/18/03	Margaret Brewster	mrsbrewster@earthlink.net
CH03-4-9	12/18/03	Rhonda Weber	RWeber@irgresources.com
CH03-4-10	12/30/03	Mara Ellingson	rodelling@charter.net
CH03-4-11	01/10/04	William Stone	kstone@sbcglobal.net
CH03-4-12	01/06/04	Judy Hoffman	1311 SE 41 Street, Unit A Cape Coral, FL 33904
CH03-4-13	01/08/04	Rachel Subler Manager of Government Relations and Communications	American Apparel & Footwear Association 1601 N. Kent St, Suite 1200 Arlington, VA 22209
CH03-4-14	12/21/03 **Rec'd 1/8/04**	Noreen Worsnet	376 Bayview Dr. Avon Lake, OH 44012
CH03-4-15	01/08/04	Karen Jakpor Md, MPH	6649 Oakmeadow Dr. Riverside, Ca 92506
CH03-4-16	01/09/04	Linda Shaw	107 Silverwood Lane Cary, NC 27511
CH03-4-17	01/09/04	Laura St George	9237 W Parkview Terrace Loop Eagle River, AK 99577
CH03-4-18	01/09/04 **Rec'd 1/29/04**	Barbara Blakeney President	American Nurses Assoc. 600 Maryland Ave, SW Suite 100 West Washington, DC 20024