From: Wava Truscott, PhD, MBA.

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Comments to: The California Environmental Protection Agency's Office of Environmental Health Hazard Assessment (OEHHA) addressing the intent to list 2-Mercaptobenzothiazole (MBT, CAS #149-30-4) as a chemical know to the state to cause cancer under the Safe Drinking Water and Toxic Environment Act of 1986 (California Proposition 65).

Listing MBT: The CA Office of Environmental Health Hazard Assessment (OEHHA) proposed the listing of 2-Mercaptobenzothiazole (MBT), CAS #149-30-4, based on the International Agency for Research on Cancer's (IARC 2016, Grosse *et al*. 2016) rating of the chemical as a 2A carcinogen. We understand that by definition this rating means the decision to list MBT was based on "limited evidence in humans" and "sufficient evidence in experimental animals". The World Health Organization (WHO) described those specific studies as follows:

> "In the studies evaluated by the IARC Monographs Working Group, exposure to high amounts of MBT in humans occurred in workers in the chemical industry, but workers in the rubber or tyre-manufacturing industries may also be exposed to MBT. The general public may be exposed to smaller amounts of MBT by skin contact with some rubber-containing goods, such as gloves and footwear. MBT has also been detected in urban air, probably because of tyre abrasion.
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> It is important to stress that the exposure of the general public to MBT from using rubber-containing goods is much smaller than the exposure of workers in chemical plants, and that the risk of developing cancer from exposure to rubber-containing goods has not been studied." *(World Health Organization: International Agency for Research on Cancer, Q&A on 2-Mercaptobenzothiazole [MBT] March 9, 2016)*

Additionally, it should be noted that 2-Mercaptobenzothiazole complies with the following US FDA regulations for indirect contact with food: 21 CFR 175.105 (adhesives used in articles contacting food), 21 CFR 176.300 (slimicides used to manufacture paper intended to contact food) and 21 CFR 177.2600 (rubber articles designed for repeat use in contacting food).

Testing for MBT

When testing for MBT, inappropriate test methods are often employed. For example, zinc mercaptobenzothiazole (ZMBT) is mistakenly identified as MBT if a non-distinguishing test method is used. ZMBT is classified as a different chemical with a separate CAS number (155-04-4). ZMBT is not a simple salt that easily separates into a mixture containing MBT. It is stable up to its melting point of 300°C (572°F). To distinguish the two, one must use gas chromatography-mass spectrometry (GC-MS). Methods using high- performance liquid chromatography (HPLC), or the EPA 8270C test method, read both chemicals as MBT and thus present an inaccurate identification. Additionally, any test that is used to determine what an individual might be exposed to from the use of an item, should be utilizing an extraction preparation method rather than a total content destructive assay that presents an inaccurate exposure level.

Critical Importance of ZMBT

Thin-filmed gloves are typically made from natural rubber latex or nitrile latex, are reacted with sulfur and other chemicals to "cure" or crosslink the rubber. This converts the final thin film product from a relatively weak, gummy material into a form that is much stronger and much more resistant to chemical penetration, permeation and degradation. This curing process is termed vulcanization. A group of chemicals used to make vulcanization more efficient and the crosslinks between the rubber and sulfur molecules more effective are called accelerators. There are several types of accelerators. Some accelerate the cross-linking faster than others increasing through-put for manufacturers.

However, when glove chemical resistance is important to prevent exposure to hazardous chemicals, slower vulcanization with increased cross-linking density and optimal orientation is critical to reduce the risk of chemical "break-through" in the manufactured glove. It is much more important than rapid production. ZMBT (zinc mercaptobenzothiazole; CAS 155-04-4), is not a rapid accelerator. It provides a higher density, optimally oriented cross-linking configuration that provides the wearer enhanced protection against chemical penetration and permeation. Optimizing the cross-linking process in this way also makes the glove physically stronger, more durable and more resistant to degradation. ZMBT is very reactive in vulcanization chemistry and, when formulated in accurate proportions, is consumed in the process becoming a permanent part of the glove structure. As noted above, ZMBT is thermally stable up to its melting temperature of 300°C. During glove production, temperatures reach a high of approximately 125°C during production.

Therefore, ZMBT will be found as one of the accelerators in most gloves used where exposure to hazardous chemicals is anticipated. For example, medical gloves worn when handling chemotherapy drugs will almost all (if not all) have been formulated with ZMBT to enable the glove to withstand incidental exposure to these aggressive carcinogenic chemicals. Gloves used for this protection are tested with chemo-drugs according to ASTM D6978 at treatment concentrations to establish drug-specific penetration and permeation breakthrough times over a 4-hour period. Similar testing is performed on gloves made to provide wearer protection against other hazardous chemicals.

Manufacturers cannot just remove ZMBT from a glove formulation. Doing so will result in very poor wearer protection. For example, just removing the ZMBT will cause the following.

1) The pre-cure maturation of the compound will be retarded resulting in less effective initial molecular cross-linking.
2) Reduced cross-linking density will continue during online production. This will be evidenced as the formulated latex gel coating the hand former swells with excessively absorbed leach water. This will result in finished gloves that will have more pinholes, rip more easily, and allow chemicals to more readily pass through the glove to the wearer's hands.
3) Stripping the finished gloves off the formers would more difficult. The suboptimal cross-linking would result in excessive glove elongation and reduced strength causing increased strip-tear (torn gloves).
4) Due to the lower cross-linking density, gloves will tend to be sticky during off-line handling. Those that are chlorinated will need to use higher chlorine concentrations. This will affect the glove's shelf life upon storage and could result gloves sticking together especially as they age. The stickiness also is an indicator of cure reversion as the gloves become weaker and more permeable.

For these and many more reasons, removing ZMBT is not a simple process. It will require extensive reformulation, many finished material evaluations, potential line modifications, production validation and

regulatory filings all culminating with a glove that may, or may not, be equivalently protective. To attempt to do so would require an estimated 2.5 to 3 years for manufacturers.

There are grades of purchased ZMBT that can contain left over MBT as a by-product of the ZMBT chemical manufacturing process ranging from 0% to 16%. Many glove manufacturers select ZMBT with no or trace levels of the MBT impurity. It is proposed that a threshold detection level of MBT be allowed while Chemical companies upgrade their purification processes.

Per the above information, the following requests are respectfully submitted:

1) Continue to permit ZMBT to be used in gloves where chemical splash protection is needed (e.g., protection from hazardous chemicals including those that are carcinogenic – as are a majority of the 200 therapeutic chemicals listed by the FDA). To address residual ZMBT or MBT levels or concerns:
    a. Glove extraction methods should appropriately represent the mode of potential exposure to the wearer. In this case, sweat from the hand would be the most common extracting fluid. Water or phosphate buffered saline would be the most realistic extracting fluid to leach any unbound chemicals from the glove.
    b. A test method that appropriately distinguishes between MBT (CAS 149-30-4) and ZMBT (CAS 155-04-4) must be used. This would be a GC-MS analysis, or any other method that provides the said differentiation.
2) Alternatively, exempt gloves from the proposed Prop 65 listing to avoid the differentiating test methods and apply a logical assessment of weighing the risk vs. benefit; or minimal, if any, risk vs. far greater proven risk of Chemo-drug carcinogen exposure.
3) If reformulation of all gloves containing any trace of MBT is required or mandated, a 3-year grace period is requested to enable manufacturers to ensure the safety and quality performance of the new glove formulations, and obtain the required pre-market authorization from the FDA.

Respectfully submitted,

Wava Truscott, PhD. MBA.
Truscott MedSci Associates, LLC.
wava.truscott@gmail.com
Office: 678-224-8335
Cell: 678-860-1550

I submit this comment and request as a contract consultant and educator with over 35 years of medical device, glove science, and focused patient and staff safety experience.

- Before my doctorate, I worked at MIDECO, an independent medical device contract-testing laboratory.
- I received my doctorate in Comparative Pathology (human and animal disease systems) with emphasis in microbiology, immunology and pathology from the University of California, School of Medicine, Davis campus.
- I worked at the bench with FDA's Office of Science and Technology (OST) to understand the potential for viral penetration in medical gloves during the emergence of HIV in 1987 through

1990. Then worked with standards committees to establish test methods and set glove requirements.

- I worked at the bench and in the field (Malaysia) with FDA, CDC, and international clinical researchers tracking down causes and solutions for Type I hypersensitivity to the *Hevea brasiliensis* (rubber tree) allergenic proteins found in medical gloves, dental dams, catheters, etc.
- As an AAMI/ANSI appointed delegate, I worked with regulatory and scientists on new ISO test methods and standards (ISO 10993) for medical device safety to be adopted by the then emerging European Union.
- I spent years working with others on an ASTM test method for quantifying glove powder, submitting case studies with scientific reasoning to the FDA, and authoring an extensive citizen's petition to the FDA in efforts to ban glove powder from all US healthcare facilities.
- My focus now is infection prevention in healthcare together with preventing medical staff, pharmaceutical staff and home caregiver safety from exposure to toxic and/or carcinogenic chemotherapy drugs.