701 Pennsylvania Avenue, Ste. 800
Washington, DC 20004–2654
Tel: 202 783 8700
Fax: 202 783 8750
www.AdvaMed.org

AdvaMed
Advanced Medical Technology Association

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Monet Vela
Office of Environmental Health Hazard Assessment
P. O. Box 4010
1001 I Street
Sacramento, CA 95812-4010

Sent Electronically to: P65PublicComments@oehha.ca.gov

SUBJECT: CLEAR AND REASONABLE WARNING REGULATIONS

Dear Ms. Vela:

On behalf of the Advanced Medical Technology Association (AdvaMed), thank you for the opportunity to submit comments regarding the Office of Environmental Health Hazard Assessment's ("OEHHA") Notice of Proposed Repeal of Article 6 and Adoption of New Article 6 Title 27 of the California Code of Regulations pursuant to the Safe Drinking Water and Toxic Enforcement Act ("Proposition 65").

AdvaMed is the world's largest trade association representing medical device and diagnostics manufacturers. AdvaMed's member companies produce the innovations that are transforming health care through earlier disease detection, less invasive procedures and more effective treatments. In 94 facilities located throughout the state, our member companies contribute over 84,000 jobs to California. Our member companies range from the largest to the smallest medical technology innovators and manufacturers and actively engage in policy discussions that are critical to the growth and development of the medical technology industry.

While AdvaMed applauds OEHHA's efforts to provide clarity to Proposition 65 and reduce frivolous lawsuits, we do not believe this revision successfully accomplishes these goals. Instead, we believe it 1) overreaches in its applicability to medical devices and could be preempted by federal law; 2) increases the labeling and financial burden on the medical device industry; and 3) has the potential to increase frivolous lawsuits, among other potential problems.

Safe Harbor for Medical Devices

As we have articulated in previous comments, we do not believe including warnings on medical devices is consistent with the underlying goals of Proposition 65 and that medical devices should be given a safe harbor similar to prescription drugs. We believe the main components within Proposition 65 - right to know and consent of the consumer - are properly achieved as some devices are dispensed via prescription and by medically licensed personnel (and such accreditation and mechanisms are recognized and controlled by the State of California). As such, we maintain medical

devices that are subject to the jurisdiction of the U.S. Food and Drug Administration (FDA) and approved for use by the Agency should be exempted.

Federal Regulation of Medical Devices

Medical Device Amendments ("MDA")[1], to the Food, Drug and Cosmetic Act ("FDCA")[2], establish a scheme for comprehensive federal regulation of prescription and other medical devices, while also protecting life-saving innovations in device technology from being stifled by unnecessary restrictions. Congress sought "national uniformity in product regulation" in enacting the MDA.

In order to legally market a FDA approved or FDA cleared medical device, the manufacturer must provide FDA with reasonable assurance that the device is both safe and effective.[3] For Class III devices, this is initially accomplished by completing a thorough review process known as Pre-Market Approval ("PMA"). For Class II, and as applicable Class I devices, this is accomplished by demonstrating that the product is substantially equivalent to a device previously cleared through the 510(k) process.[4] In any case, the FDA considers hazards to the user when considering whether to approve a device under the PMA requirements or clear it under the 510(k) review process.

Furthermore, FDA has established specific requirements pertaining to device labeling. The FDCA is the law under which the FDA takes action against regulated products related to labeling requirements. Labeling regulations related to medical devices are found in the following Parts of Title 21 of the Code of Federal Regulations (CFR):

- General Device Labeling -21 CFR Part 801
- In Vitro Diagnostic Products - 21 CFR Part 809
- Investigational Device Exemptions - 21 CFR Part 812
- Premarket Approval Application – 21 CFR Part 814
- Good Manufacturing Practices - 21 CFR Part 820
- General Electronic Products - 21 CFR Part 1010

Lastly, prior to FDA approval or clearance, medical devices must be demonstrated to be sufficiently biocompatible. This means biological evaluation of medical devices is performed to determine the potential toxicity resulting from contact of the component materials of the device with the body. Evidence is provided to FDA via direct testing or otherwise meeting international standards and/or Federal Guidelines. The FDA reviews this biocompatibility information prior to making a marketing authorization decision for medical devices, and if necessary, FDA may require additional warnings or disclosures in the medical devices' labeling.

In summary, we maintain that medical devices subject to the jurisdiction of the U.S. Food and Drug Administration (FDA) and approved for use by the Agency should be given a safe harbor from Proposition 65 requirements.

Preemption

[1] 21 U.S.C. § 360c, et. seq.
[2] 21 U.S.C. § 301, et seq.,
[3] 21 U.S.C. § 360e(d)(2).
[4] See 21 C.F.R. §§ 21 C.F.R. 807 et seq., 862.9, 864.9.

Further, we believe that Proposition 65, if applied to medical devices, is not only illegal per federal law, but is also preempted and unconstitutional. As outlined above, the FDA regulates the marketing and sale of medical devices throughout the United States and expressly preempts state law requirements governing medical devices. Per 21 United States Code Part 360k(a), "…no State… may establish or continue in effect with respect to a device intended for human use any requirement – (1) which is different from, or in addition to, any requirement applicable under this chapter to the device, and (2) which relates to the safety or effectiveness of the device..." This is to ensure national uniformity of medical device labeling. Good public policy would suggest avoiding a situation where only Californians are provided with the additional Proposition 65 labeling which result in some individuals being influenced to delay appropriate medical treatment.

Even if a court were not inclined to rule strictly on preemption grounds, we would like to reference the 2001 case where the Public Media Center brought a suit against tuna canning companies because their products contain methyl mercury. The court issued a decision based on three key rules including that Proposition 65's warning requirement conflicted with the FDA's "carefully considered" policy of advising consumers about both the benefits and risks, whereas Proposition 65 would communicate only the risks and thereby frustrate the FDA's more balanced approach. Food and medical devices are both regulated by the FDA and both include carefully considered wording to balance benefit and risk as overseen by this federal agency. We believe that any court case against medical devices would return a similar verdict, which would waste company, taxpayer, and California court system resources.

We strongly urge OEHHA to reexamine its previous stance on a safe harbor for medical devices. That said, we understand that, despite the concerns raised by medical device manufacturers and others, OEHHA may move forward without offering a safe harbor for medical devices. Should OEHHA take that path, with which we disagree, we nonetheless offer the following comments for consideration of other aspects of the proposed regulation:

Section 25600 – General

The proposed regulation does not retain the explanation for "clear and reasonable" language in warnings. Guidance will likely be sought through costly mechanisms or result in litigation. Providing clarity and certainty as to what constitutes a clear and reasonable warning will benefit all stakeholders. The language will be left for businesses to individually interpret and could lead to some manufacturers being out of compliance simply because they misinterpreted the requirements.

The proposed warning regulations will become effective two years after adoption, however, numerous medical devices circulate over several years through various distribution and commerce cycles. This type of change would be very difficult to implement in two years, leading to potential interruption of live-saving medical products to the citizens of California. As such, we recommend at least three years is for implementation, which would allow for appropriate labeling updates to be implemented within the confines of the regulated market of medical devices. This implementation period is consistent with the inventory depletion timeframe associated with the Unique Identifier Regulation, 21 CFR Part 801.30(a)(1), which was well-thought by FDA and should provide a precedent for similar regulations that impact product labels and/or labeling.

Section 25600.1 – Definitions

"Knowingly" -- Proposition 65 requires California businesses with 10 or more employees to provide a clear and reasonable warning before "knowingly and intentionally" exposing individual to

chemicals known to cause cancer and/or reproductive toxicity. Businesses often provide warnings on their products or facilities out of an abundance of caution and to avoid lawsuits, even if no chemical exposure is present or if the chemical exposure is occurring below specified threshold (safe harbor) levels. The Office of Environmental Health Hazard Assessment (OEHHA) should support efforts to further clarify the term "knowingly" in order to reduce the chances of a company being sued over whether they "knew" a chemical could cause exposure or not.

Section 25600.2 – Responsibility to Provide Product Exposure Warnings
Proposition 65 focuses more on content than exposure, and as such does not appropriately take into account the location of a substance within a product, the likelihood of a consumer actually coming into contact with the substance during conventional use, and the potential duration and route of exposure. These are all very important factors in assessing whether a true hazard exists. OEHHA should establish safe harbor levels for chemicals based on content (in parts per million) rather than exposure rates. Manufacturers should then only be required to provide additional information to consumers on how they will be exposed to those chemicals if the content threshold is exceeded and the consumer can come into contact with the chemical in a form that can enter the body through inhalation, ingestion or through the skin, thereby potentially causing harm to the consumer. A concentration of a chemical in a product should not be of concern if that chemical is not in a form that would facilitate it being absorbed into one's body (e.g., the chemical is contained within an internal component of the product for which the consumer will not come into contact with the chemical through conventional use of the product).

Should OEHHA not provide a content-based exposure threshold, the clear and reasonable warning requirements should, at a minimum, clarify that exposure is said not to occur if the substance *"is not accessible to an individual through normal and foreseeable use and abuse of such product or component part, nor is it in a chemical state that could cause it to be absorbed into the body."* Under this approach, OEHHA should also clarify the level of proof/evidence needed to show no significant exposure because the chemical is not accessible to the consumer. OEHHA should also require use of the word *"contains"* rather than the phrase *"can expose*" in the clear and reasonable warning and require manufacturers to explain how that content could become a hazard – such as identifying the routes for potential exposure to the Proposition 65 chemical.

Finally, chemicals should not be added to the Proposition 65 list until a method is developed to properly test for the chemical. Such test methods must maintain a consistent understanding of product usage to determine whether or not contact with the Proposition 65 chemical is even possible. The medical device industry has significant experience in developing proper test procedures to ensure that test results are consistent across manufacturers and that consumers can accurately compare products based on similar test methods. Lack of such testing leads to inconsistency in interpretation of the nature and degree of any hazard that may exist, which in turn leads to many frivolous lawsuits.

Section 25601 – Safe Harbor Clear and Reasonable Warnings – Methods and Content
We have significant concerns about the fluidity of the list of chemicals to be included in the text of a warning. Companies need predictability. Additionally, there are no criteria established for identification or to update the list of chemicals and we believe OEHHA may be overstepping its authority to create and impose this list (Gov't Code Section. 11342.2.).

Although OEHHA clarified that the proposal's intent was to only require at least one chemical on the

label, the regulatory text is far from clear on this matter. The phrase "one or more" can easily be interpreted to require all the chemicals for which a warning is being provided. In addition, OEHHA should clarify that a manufacturer can choose which chemical to identify in the warning.

Furthermore, we have concerns with the vague grouping of phthalates as part of the "dirty dozen" list of chemicals in this section. Phthalates are a family of chemicals that includes hundreds of chemicals – most of which are not currently listed under Proposition 65.

Some phthalates are specifically regulated across the globe. For example, pursuant to the *Phthalates Regulations* within the Canada Consumer Product Safety Act "phthalate" means di(2-ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), benzyl butyl phthalate (BBP), diisononyl phthalate (DINP), diisodecyl phthalate (DIDP) or di-n-octyl phthalate (DNOP). Similarly, the *EU Directive 2005/84/EC* since replaced by the REACH regulation identifies the specific phthalate chemical entities subject to the Directive.

OEHHA should list all the specific phthalates they want raised to the level of disclosure or give direction on whether it is sufficient to list "phthalates" on a warning.

Section 25602 – Product Exposure Warnings – Methods of Transmission
The issue of whether a warning can be placed in owner's manuals, instructions for use (IFUs) and/or accompanying documents to satisfy a manufacturer's labeling obligation under Proposition 65 is not clearly addressed in the proposed rule and may not even be allowed as currently drafted. The previous version of the regulation states a warning may be provided "*on a product's label or other labeling."* The term *labeling"* in the existing regulation includes communication accompanying a product (e.g., owner's manuals, IFUs), while the term *"label"* does not. To ensure that the current policy of providing warnings in the owner's manual where other warnings and information are contained (e.g., electric and drinking water safety) does not change, we strongly recommend the following revision to the proposed rule before it is finalized:

> *Section 25602(a)(3) A label OR OTHER LABELING that complies with the content requirements in Section 25603(a).*

It is critical for medical device manufacturers to be allowed to continue to provide required warnings in owner's manuals, IFUs and/or accompanying documents, rather than directly on product labels that are typically numerous, limited in size, and already highly populated with other state and/or federal consumer and medical device disclosure requirements. Furthermore, changes to labels for medical devices often require review and approval by the U.S. Food and Drug Administration (FDA) – an often costly process that can also significantly slow the time for newly labeled products to reach the marketplace.

Section 25602 (d)
Section 25603(d) states, "*If any label, labeling or sign about a product is provided in a language or languages other than or in addition to English, then a warning for that product meets the requirements of this Article only if the warning is also provided in the same language or languages on the label, labeling or sign."* This is concerning for multi-language (e.g., in French and English for Canada) medical device labels and owner's manuals, IFUs and/or accompanying documents, essentially requiring any related Proposition 65 warning to also be in multiple languages. We believe OEHHA is overstepping their boundary in requiring translation of a warning only applicable to the

State of California.

Section 25603 – Product Exposure Warnings – Content
Subsection (a)(1) indicates that one element that a warning must contain in order to meet the requirements of the product exposure warning is "*A symbol consisting of a black exclamation point in a yellow equilateral triangle with a bold black outline".* This pictogram requirement should be removed from the proposed rule before it is finalized because it is misleading. In ANSI Z535.4-2011 4.11, this particular symbol configuration means danger, warning or caution and states, "Safety alert symbol: A symbol that indicates a hazard. The safety alert symbol is only used on hazard alerting signs. It is not used on safety notice and safety instruction signs."

Medical device manufacturers typically label their products uniformly in order to be sold in most all markets. Labeling our products with the same pictogram that ANSI defines will give consumers who don't live in California an inconsistent message and the universal impression of immediate hazard. OEHHA must recognize this and think more broadly on what the proposed pictogram means to consumers outside of California. No other state or country recognizes California's Proposition 65 law or list of chemicals, and as such, OEHHA should not require manufacturers to label their products with a pictogram that says the chemical is "known to the State of California to cause cancer" where elsewhere in the U.S., and throughout the world, the pictogram means something completely different.

Appendix E of FDA's Guidance on Medical Device Patient Labeling[5] provides specific information on what warnings are, their purpose and the appropriate content of a warning.

Again, medical device labels and labeling are specifically regulated by the FDA as outlined in Title 21- Part 801 Labeling and other parts of the FD&C Act. Symbols without the use of accompanying English text are not permitted by the FDA. To do so clearly invokes a requirement that is different than, and in addition to, that governed by the Federal regulatory scheme.

Closing
In closing, these comments reflect specific medical device industry concerns with the proposed regulations, however, we also echo the broader concerns voiced by the CA Chamber of Commerce in their formal comments, dated January 25, 2016.

Thank you for your consideration of our comments. Please don't hesitate to contact me if additional information or clarification is needed.

Sincerely,

Carrie A. Hartgen

5 http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070782.htm#e