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Via Electronic Submission (http://www.regulations.gov)

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, RM. 1061
Rockville, Maryland 20852

Re: Request for Comments for Industry Proposal for "Tobacco Product Manufacturing Practices for Electronic Nicotine Delivery Systems"; FDA Docket No.: FDA-2013-N-0227

The American E-Liquid Manufacturing Standards Association (AEMSA) appreciates this opportunity to respond to the Food and Drug Administration (FDA or Agency) request for comments on the updated recommendations for regulations on Tobacco Product Manufacturing Practices (TPMPs) for Electronic Nicotine Delivery Systems (ENDS) that were submitted to FDA by a group of industry stakeholders (FDA Docket No. FDA-2013-N-0227). This comment provides background on AEMSA's voluntary standards and feedback on the proposed TPMPs. As described herein, AEMSA supports responsible, science-based and appropriate tailored regulations for ENDS, including good manufacturing practices.

I. Background on AEMSA

AEMSA is the first and only manufacturers' trade association completely dedicated to creating responsible and sustainable standards for the manufacturing of E-liquids used in ENDS devices, also known as ENDS, e-liquid components, ENDS hardware devices, and distribution and retail standards and best practices. AEMSA is an all-volunteer 501(c)(6) organization, formed by U.S. manufacturers of e-liquids, to promote safety and responsibility through self-regulation. One of AEMSA's primary goals is to provide consumers and government regulators with confidence that our Members' products are manufactured in a professionally responsible and safe manner until FDA promulgates TPMPs for ENDS. In this regard, AEMSA has developed manufacturing standards for e-liquids, attached hereto as **Exhibit A**, and which may be downloaded from our website at: http://www.aemsa.org/standards/.

The purpose of AEMSA's e-liquid manufacturing standards is to create a responsible and sustainable practices and processes for the safe manufacturing of e-liquids used in ENDS. Our Members believe it is the industry's responsibility to self-regulate the e-liquid manufacturing process based on professional criteria and in the absence of FDA guidance or good manufacturing practices (GMPs). One of AEMSA's primary goals is to provide consumers with more confidence that our Members' products are manufactured with professionalism, accuracy

and safety. AEMSA standards are established based on the following core beliefs that e-liquid manufacturers must:

- verify the accuracy of nicotine content in their products;
- ensure the quality of all ingredients in their product;
- prepare their products in a clean, sanitary and safe environment;
- ensure their products are packaged and delivered in a safe manner; and
- provide a level of transparency into the monitoring and verification process.

AEMSA supports reasonable, responsible and science-based regulation of ENDS (e-liquids and ENDS devices), and is also now developing good manufacturing practices and products standards for e-liquid components (flavors), ENDS hardware devices and distribution and retail standards and best practices.

II. 2012 Proposed TPMPs

To date, FDA has not yet proposed TPMPs for any tobacco product categories. But, in January 2012, several large tobacco manufacturers ("Big Tobacco") proposed TPMPs for FDA to consider (the "2012 Proposed TPMPs"); that proposal was recently supplemented to consider differences between ENDS (i.e., ENDS) and traditional tobacco products (e.g., cigarettes and smokeless). Because of inherent safety concerns with these traditional tobacco products, unlike the established current GMPs for drugs and medical devices, for example, the 2012 Proposed TPMPs are not meant to ensure the safety and effectiveness of a tobacco product.

Rather, because of the inherent risks associated with the use of *tobacco*, the Big Tobacco TPMPs were aimed at ensuring that (1) tobacco products are not contaminated (*e.g.*, by prohibiting introduction of a substance in a tobacco product if the substance is not ordinarily contained in tobacco products and the presence of the substance presents a risk of injury beyond that generally posed by the same category of tobacco product); (2) the manufacturing of tobacco products does not result in such products being adulterated or misbranded; and (3) tobacco product manufacturers have flexibility to manufacture, label, pack, and store tobacco products in a manner which accounts for different product categories, different manufacturing processes, and the inherent variability of tobacco, while assuring all such activities are conducted in a controlled manner.

On March 19, 2013, FDA published a notice in the *Federal Register* requesting any interested parties to comment on the tobacco industry proposal.[1] The comment period closed in May 2013 and no further announcements were made until November 21, 2017, when FDA published a new letter from a group of tobacco and ENDS industry stakeholders seeking to amend the 2012 Proposed TPMPs to include ENDS specific manufacturing standards (the "Supplemental Proposal"). More specifically, the Supplemental Proposal argued that differences between ENDS and combusted tobacco products needed to be recognized in any TPMPs.

To assure that that the public health is protected and that ENDS are manufactured in compliance with science-based manufacturing practices, AEMSA, by in large, agrees with the Supplemental Proposal's call for TPMP regulations that allow ENDS manufacturers to establish and maintain procedures for specification changes, process qualification, controlling and verifying the acceptability of process capability and product characteristics, validating and approving test methods to establish specifications and batch conformance, sample testing, product stability testing and batch sample retention. Below we summarize our main concerns with the Supplemental Proposal.

III. FDA Should Consider that ENDS Do Not Contain Tobacco When Promulgating TPMPs for these Products

The Supplemental Proposal notes that when promulgating TPMPs, FDA should consider that ENDS are not typically subject to the same agricultural variability as traditional tobacco products because they use USP grade (or equivalent) nicotine. AEMSA agrees that TPMPs for ENDS should consider the fact that these products are dramatically different from tobacco-leaf products.

E-liquids used in ENDS may contain nicotine, which is often derived from tobacco, but they also may not (zero nicotine e-liquids also have a substantial and growing segment of the market). On the contrary, traditional tobacco products contain leaves of the tobacco plant (*Nicotiana tabacum or Nicotiana rustica*), an agricultural product, along with hundreds of added chemicals and additives. For example, traditional cigarettes involve tobacco leaf, tobacco processing byproducts, and additives wrapped in paper that is sealed with glue and contains a cellulose filter, which is combusted by ignition at one end of the product and inhalation by the consumer at the other end. Such combusted products are the most harmful and dangerous tobacco products on the "continuum of risk" and should be treated as such. It is well established, for example, that the more pyrolyzed tobacco constituents a user inhales from a combustible tobacco product, such as a cigarette, the greater the risk of tobacco-related disease that product

[1] *See* 78 Fed. Reg. 16,824 (Mar. 19, 2013).

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poses.[2] Of the approximately 5,300 chemicals identified in tobacco smoke, at least 60 are known human carcinogens, including polycyclic aromatic hydrocarbons (PAHs) and tobacco-specific nitrosamines (TSNAs).[3] ENDS are far less risky to individual users than tobacco/combusted products because they do not result in the inhalation of pyrolyzed chemicals.

Furthermore, ENDS involve a completely different manufacturing process, ingredients, evaluations and considerations compared to combustible tobacco cigarettes, cigars or pipes.

TPMPs for ENDS should focus on establishing product, manufacturing, and testing standards that consider the rapidly evolving technology and the need to improve quality and safety. The primary areas of concern for these products is the safety profile of the aerosol inhaled by the consumer, *i.e.*, its chemical composition and toxicity, and the device design features that are being developed to enhance safety, *i.e.*, power control, temperature control and volumetric air flow rate measurement. In order to be able to predict the safety profile of ENDS, regulatory agencies must understand the chemical composition and potential toxicity of the inhaled aerosol, which will depend on a number of factors, including the manufacturing process, ingredients and impurity profile of the e-liquid, the materials and manufacturing methods used for the hardware components, the amount of wattage applied to power the devices and, importantly, the maximum temperature the device and its component parts (*e.g.*, coil) can reach during use. Identifying and establishing TPMPs, product and testing standards for each of these elements, while allowing manufacturers to modify their products to improve safety as scientific and regulatory requirements dictate, should be FDA's goal

The safety profile of traditional tobacco products, on the other hand, can vary greatly simply because they are agricultural products, dependent on factors such as growing conditions and other uncontrollable natural variations. Because ENDS are *technology* products, however, the various processes and chemical reactions that occur during use can be identified and, ultimately, controlled.

IV. FDA Should Consider the Relative Harm of ENDS Compared to Combustible Tobacco When Developing TPMPs

The Supplemental Proposal notes that FDA should consider that ENDS may reduce the risk of tobacco-related disease relative to combusted tobacco products, *i.e.*, they are lower on the continuum of risk, when promulgating TPMPs. AEMSA agrees.

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[2] *See* R.R. Baker, *et al.*, *The pyrolysis of tobacco ingredients*, 71 J. Anal. Appl. Pyrolysis 223-311 (2004).

[3] *See* Rodgman, A. and Perfetti, T.A., *The Chemical Components of Tobacco and Tobacco Smoke*, Boca Raton, FL: CRC Press (2009).

By way of background, the Food, Drug and Cosmetic Act (FDCA), as amended by the Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act) authorizes FDA to use its rulemaking authority to promulgate good manufacturing practices, also called TPMPs, for tobacco products, including ENDS, that have now been deemed to be *regulated* tobacco products by FDA. More specifically, Section 906(e) of the Tobacco Control Act directs FDA to issue regulations requiring that the methods used in, and the facilities and controls used for, the manufacture, pre-production design validation (including a process to assess the performance of a tobacco product), packing, and storage of tobacco products conform to (1) current GMPs or (2) hazard analysis and critical control point (HACCP) methodology. We further note that Section 902 of the Tobacco Control Act states that "[a] tobacco product shall be deemed to be adulterated if the methods used in, or the facilities or controls used for, its manufacture, packing, or storage are not in conformity with applicable requirements under section 906(e)(1) or an applicable condition prescribed by an order under section 906(e)(2)." In other words, even if a finished tobacco product meets all prescribed specifications, if it was manufactured in a non-compliant manner or if the facility where it was produced is found to be in violation of cGMPs, the product will be considered adulterated. This distribution of an adulterated tobacco product is a prohibited act. **Critically for ENDS, Section 906(e) explicitly authorizes FDA to promulgate cGMP regulations that "differ based on the type of tobacco product involved."**

When developing TPMPs for ENDS, FDA should consider the wealth of information available supporting the relative safety of ENDS compared to combustible tobacco, and particularly cigarettes. FDA already acknowledges that ENDS are significantly less harmful than cigarettes. Indeed, in the Deeming Rule itself, and more recently in Commissioner Gottlieb's announcement[4], FDA recognizes that using ENDS likely presents far less risk than smoking cigarettes, and that individuals switching from combustible tobacco products to ENDS may significantly reduce their harm.[5] The Agency also recognizes that the availability of ENDS

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[4] *See* Protecting American Families: Comprehensive Approach to Nicotine and Tobacco, available at: https://www.fda.gov/NewsEvents/Speeches/ucm569024.htm.

[5] *See* FDA Response to Comment 118 in the preamble to the Deeming Rule, 81 Fed Reg. at 29030 ("FDA recognizes that completely switching from combusted cigarettes to ENDS may reduce the risk of tobacco-related disease for individuals currently using combusted tobacco products, given the products' comparative placement on the continuum of nicotine-delivering products.").

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could potentially lead to increased smoking cessation rates in this country and ultimately reduce tobacco-related disease and death.[6]

These conclusions are consistent with a growing body of scientific research, both in the United States and abroad, finding that ENDS are substantially less harmful than combustible tobacco products. Indeed, a number of public health experts agree that vaping is significantly less harmful than smoking cigarettes and "could be among the most significant health innovations of the twenty-first century—perhaps saving hundreds of millions of lives".[7] In 2016, the Royal College of Physicians issued a report lauding the benefits of ENDS as safer alternatives to combustible tobacco. The report estimates that ENDS are only 5 percent as harmful as traditional cigarettes and that the long-term effects of nicotine use from ENDS are likely to be minimal. This estimate corresponds with the conclusions of Public Health England, an executive agency sponsored by Britain's Department of Health, which calculated the level of harm caused by different nicotine delivery systems, including from cigarettes, cigars, pipes, nicotine patches, and ENDS, and took into account a wide range of risks, from the effect of addiction on people's incomes to fatal lung damage to accidental poisoning, and ultimately found that ENDS are 95 percent less harmful than traditional cigarettes.[8]

V. FDA Should Consider the Low-Risk for Microbial Contamination of ENDS When Promulgating TPMPs

The Supplemental Proposal notes that HACCP analysis should be performed for e-liquid manufacturing operations to allow manufacturers to address, among other things, the potential for microbial contamination. HACCP is a systematic preventive approach to food safety from biological, chemical, and physical hazards in production processes that can cause the finished product to be unsafe, and designs measurements to reduce these risks to a safe level. As noted above, one of AEMSA's core beliefs is that e-liquid manufacturers are responsible for ensuring that the products are prepared in a clean, sanitary and safe environment. However, FDA should

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[6] *See* FDA Response to Comment 144 in preamble to the Deeming Rule. 81 Fed. Reg. at 29037 ("We recognize that there is emerging data that some individual smokers may potentially use ENDS to transition away from combustible tobacco products").

[7] *See* Abrams, D., Axéll, T., Bartsch, P., et al. (2014). Statement from specialists in nicotine science and public health policy. World Health Organisation, Geneva. http://www.nicotinepolicy.net/documents/letters/MargaretChan.pdf.

[8] *See* McNeil, B.A., Calder, R., Hitchman, S.C., Hajek, McRobbie, H. (2015). E-cigarettes: an evidence update, Public Health England. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/457102/Ecigarettes_an_evidence_update_A_report_commissioned_by_Public_Health_England_FINAL.pdf.

consider the unique characteristics and manufacturing processes of e-liquids when determining whether to mandate HACCP, Hazard Analysis and Risk-based Preventive Controls (HARPC) or similar controls for these products.

Specifically, both HACCP and HARPC were developed for the food industry, where microbiological contamination is a major public health concern. With respect to e-liquids, however, the risk of such contamination is exceedingly low, as demonstrated by the:

- lack of illness-outbreak data;
- lack of historical data identifying the ingredients (e.g., vegetable glycerol (or vegetable glycerin), propylene glycol, flavorings, nicotine, and water) as containing microbiological hazards;
- lack of scientific, technical or published data indicating the ingredients are sources of microbiological hazards (a recent publication reported that the examination of 42 e-liquids for microbiological criteria found no evidence of high microbial counts indicative of contamination or microbiological hazards[9]);
- use of the antimicrobials, e.g., propylene glycol, as a base ingredient/carrier for flavoring components and nicotine;
- antimicrobial impact of the manufacturing processes (e.g., evaporation, distillation, solvent extraction, acid treatment, condensing, enzymatic processing) used in the production of the ingredients; and
- fact that microorganisms require a growth matrix that is substantially more nutritionally-rich than e-liquids, many of which contain over 90% propylene glycol and glycerol (or glycerin), which is not conducive to survival or growth of microbial hazards.

Additionally, in comments submitted in response to FDA Docket No. FDA-2014-N-0053, *Designation of High-Risk Foods for Tracing: Request for Comments for Scientific Data and Information*, the Flavor and Extract Manufacturers Association (FEMA) indicated that

[9] *See* Varlet, V., Farsalinos, K., Augsburger, M., Thomas, A. and Etter, J; 2015, *Toxicity Assessment of Refill Liquids for Electronic Cigarettes, Int. J. Environ. Res. Public Health* 12: 4796-4815.

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flavorings, many of which are used in e-liquids, have not been associated with foodborne outbreaks and are not high-risk ingredients.[10]

With respect to the antimicrobial effect of propylene glycol, numerous studies have demonstrated that the carrier is an effective antimicrobial against both Gram-negative (e.g., e. coli) and Gram-positive (e.g., Staphylococcus aureus, S. epidermidis, Streptococcus pyogenes A, S. mitis) bacteria, as well as viruses and yeasts (e.g., Candida albicans).[11] The antimicrobial effect (that can occur as quickly as within 20 hours[12]) reportedly is caused by interference with the normal functions of the cell membrane and a reduction in the water activity (i.e., decreasing the availability of free water).

Finally, unlike foods, e-liquids are not ingested but vaporized and inhaled. The vaporizing of e-liquids in typical open-system ENDS devices requires the heating coil to reach temperatures above the boiling point of the e-liquid, approximately 320°F. Generally, operational coil temperatures are set near 390°F to 460°F. In studies of several thousand actual users, the actual coil temperatures have a mean value of about 390°F with a range of 200°F to 600°F (both are extremes in the distribution with few users reporting these temperatures).[13] At 200°F, vaporization does not occur, signaling the user to increase the temperature to at least 320°F. Vegetative microbiological hazards and viruses (including norovirus, the number one known cause of foodborne illness) that may be introduced by humans during manufacturing generally are killed at temperatures of 165°F in low-fat matrices such as e-liquids. Accordingly,

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[10] *See* https://www.regulations.gov/document?D=FDA-2014-N-0053-0033.

[11] *See e.g.*, De Spiegeleer, B., Wattyn, E., Siegers, G., Van der Meeren, P., Vlaminck, K. and Van Vooren, L., 2006, The importance of the cosolvent propylene glycol on the antimicrobial preservative efficacy of a pharmaceutical formulation by DOE-ruggedness testing. *Pharm Dev Technol*, 11(3): 275-284; Herman, E.B., Haas, G.J., Crosby, W.H. and Cante, C.J., 2008, Antimicrobial Action of Short Chain Alcohols and Glycols, *J. Food Safety*, 2(3): 131-139; and Nalawade, T.M., Bhat, K. and Sogi, S.H.P., 2015, Bactericidal activity of propylene glycol, glycerin, polyethylene glycol 400, and polyethylene glycol 1000 against selected microorganisms, *J. Int. Soc. Prev. Community Dent.*, 5(2): 114-119.

[12] *See* Kinnunen, T. and Koskela, M. 1991, Antibacterial and antifungal properties of propylene glycol, hexylene glycol, and 1,3-butylene glycol in vitro. *Acta Derm Venereol*, 71(2): 148-140.

[13] *See* www.ecigstats.org.

the heating and vaporization of e-liquids is an additional control point for destruction of vegetative microbial hazards, including viruses.

Although microbial contamination from humans or equipment during manufacturing is possible, extensive HACCP or HARPC-type controls may not be necessary considering the unique characteristics and manufacturing processes of e-liquids described above. FDA should also recognize the potential burdensome cost, particularly for small businesses, of preparing manufacturing environments to pass USP specification if the HACCP microbial requirements are enforced. This would require labs to operate at USP 797 classification (which is more rigorous than ISO 14644:1 Class 6), a classification that is nearly impossible for manufacturers that do not currently have dedicated cleanrooms, and an extremely difficult level to reach even for larger labs (even if they are currently operating in a pressurized environment). Accordingly, basic GMPs and Standard Operating Procedures (SOPs) (such as described in AEMSA's Standards) may be sufficient to protect from potential microbial hazards.

VI. FDA Should Exempt from the Premarket Review Requirements Changes Made to ENDS Pursuant to TPMP Established Procedures

The Supplemental Proposal notes that FDA should allow ENDS manufacturers to establish and maintain procedures for changes to a specification, process or procedure that may impact the original specified design requirements. AEMSA agrees, and further requests that any such changes made within a TPMP compliant procedure be exempt from FDA premarket review.

In the Deeming Rule FDA chose not to amend the February 15, 2007 "grandfather date" for deemed products. Any tobacco product that was commercialized before the grandfather date may remain on the market without obtaining FDA pre-market authorization. However, manufacturers of "new tobacco products" must obtain such authorization. Moreover, because there are no known grandfathered ENDS, the only viable pre-market pathway is the Premarket Tobacco Product Application (PMTA), which is significantly more onerous than the Substantial Equivalence (SE) and SE Exemption pathways, and is estimated to cost millions of dollars.[14]

[14] The PMTA requires manufacturers to submit, inter alia, substantial amounts of information for each new tobacco product showing that marketing the product is "appropriate for the protection of public health." This "population effects" standard requires FDA to take into account the product's impact on the population as a whole, including the likelihood that people will stop using tobacco products (i.e., cessation), as well as start using them (i.e., initiation). FDCA § 910(c).

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Pursuant to the Deeming Rule's compliance policy, which was recently extended by FDA guidance[15], the deadline to submit PMTAs for non-combustible tobacco products (like ENDS) that were on the market as of August 8, 2016 is now August 8, 2022. While this extension is welcome, the compliance policy only effects products on the market prior to the effective date of the rule; new ENDS intended to be introduced *after* August 8, 2016 must *first* obtain PMTA authorization. The effect of this is that even minor changes made to a product specification, process or procedure that results in a design change would require a full-blown PMTA, even if that change was made pursuant to a TPMP-compliant procedure or purely for safety purposes. Accordingly, FDA should exempt such changes from the premarket review requirements.

VII. Rapidly Evolving ENDS Technology Demonstrate the Need for Science-Based TPMPs and Product Standards

The original, modern e-cigarette was developed in the early 2000s in China and entered the U.S. market between 2007 and 2008. Those early products known as cigarette look-alikes, or "cigalikes," are very different from the vast majority of products on the market today. Compared to today's advanced open-system vaporizers, early disposable cigalikes are rudimentary. ENDS technology has improved immensely since those first products entered the U.S. A few examples of the types of safety and engineering advancements that have now become common – thanks to the many innovative and entrepreneurial technology companies that make up the ENDS industry – include improved battery and charger technology, variable power levels, auto-shut off capabilities, short-circuit and over/under-charge protections, temperature limitations, and e-liquid wicking and quality improvements. Moreover, e-liquids are also much less harmful (*i.e.*, they contain fewer unintended impurities, etc.) today because many manufacturers now use better quality ingredients and manufacturing processes have improved.

As the ENDS industry continues to grow, regulatory agencies, such as FDA, should work with industry and standards-setting bodies, like International Organization for Standardization/American National Standards Institute (ISO/ANSI), United States Pharmacopeia (USP) and Underwriters Laboratories (UL), as well as industry knowledgeable and experienced standards professionals with subject matter experts (SMEs) like AEMSA, when developing TPMPs and product standards.

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[15] *See* FDA Guidance for Industry, Extension of Certain Tobacco Product Compliance Deadlines Related to the Final Deeming Rule, available at: https://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM557716.pdf.

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Many other industries have benefitted from this approach, and FDA has worked with standards setting bodies in the past in this very way. For example, in 2006 FDA issued an updated list of consensus standards recognized by the Agency for use in evaluating medical devices prior to receiving premarket approval for entry. The Food and Drug Administration Modernization Act (FDAMA) of 1997 authorized the Agency to recognize standards developed in an open and transparent process, such as those developed by ANSI-accredited standards developing organizations, as well as ISO and the International Electrotechnical Commission (IEC).[16]

Ultimately, with respect to e-liquids, TPMPs and product standards should be designed to ensure that the ingredients used are USP grade (where applicable) and are suitably pure for their intended use (*i.e.*, the amount of impurities/contaminants do not exceed specified levels), that well-known impurities such as diethylene glycol and diacetyl, among others, are not detectable at appropriately sensitive analytical detection limits using standard test procedures, and that the concentrations of nicotine and other baseline ingredients are verifiable and accurate. Specific manufacturing environments, labeling, child-resistant and tamper-evident packaging and traceability should also be mandated for all (nicotine and non-nicotine containing) e-liquids sold to consumers. Furthermore, as detailed below, TPMPs for e-liquids should be established based on AEMSA's manufacturing standards to ensure these products are manufactured in a safe manner.

Regarding ENDS hardware (e.g., devices and components and parts), manufacturing practices and standards should focus on the following core principles:

- FDA should strive to harmonize its TPMPs for ENDS with existing standards, such as those being developed by UL for Electrical Systems for Electronic Cigarettes.[17]

- Products should incorporate standard safety features including, but not limited to, auto-shut off capabilities, short-circuit protections, and "smart charging" ability,[18] over/under-

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[16] *See* ANSI, *FDA Issues List of Recognized Consensus Standards for Medical Devices*, available online at: http://www.ansi.org/news_publications/news_story.aspx?menuid=7&articleid=1190.

[17] *See* UL 8139, available at: https://standardscatalog.ul.com/standards/en/outline_8139_1?_ga=2.69361232.1171397039.1513811852-1364145921.1495045189.

[18] Smart charging ability refers to technology typically found in smart phones that stops charging current flow to the battery when fully charged.

charge protections, and consumer safety features to prevent abuse/misuse (*i.e.*, child-proof packaging).

- All e-cigarette devices and components should incorporate electronic protections designed and constructed so that a short-circuit in the atomizer, improperly installed battery, incorrect battery, or any reasonably foreseeable error by the consumer (*i.e.*, using an unauthorized car charger) will not cause unacceptably elevated temperatures, charring, smoke, or fire.

- Batteries and chargers appropriate for use with ENDS devices should be identified; the use of "smart chargers" designed to ensure devices/batteries will not over-heat or cause electrical damage to the device should be emphasized.

- ENDS devices and components should be required to meet standards similar to the European Union's Restriction of Hazardous Substances Directive 2002/95/EC (RoHS or RoHS2), which restricts the use of certain hazardous substances (*e.g.*, lead, mercury, cadmium, hexavalent chromium, polybrominated biphenyls, polybrominated diphenyl ether) in electrical and electronic equipment.

- Standards should be developed to ensure that the aerosol contains no more than determined maximum levels of identified impurities and/or toxicants.

- Guidelines should be developed for the safe handling of nicotine when mixing e-liquids in the home. Maximum nicotine content levels (*e.g.*, 10% or 100mg/ml) should be considered for direct to consumer Do-It-Yourself (DIY) nicotine sales.

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AEMSA appreciates the opportunity to submit these comments, and would be glad to discuss with FDA at its earliest convenience.

Sincerely,

Scott Eley
President
American E-Liquid Manufacturing Standards Association
(AEMSA) on behalf of AEMSA and its Members