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EPA-HQ-OPP-2013-0244

FRL-10818-01-OCSPP

Ethylene Oxid Case Number 2275

Attn: Jessica Bailey

U.S. Environmental Protection Agency

**RE: Docket ID No. EPA-HQ-OPP-2013-0244; U.S. Environmental Protection Agency  
Proposed Interim Registration Review Decision Applicable to Ethylene Oxide**

Dear Ms. Bailey:

The Advanced Medical Technology Association (“AdvaMed”), on behalf of itself and its membership, submits the following comments in response to the U.S. Environmental Protection Agency’s (“EPA’s”) Proposed Interim Registration Review Decision (“PID”) for Ethylene Oxide pursuant to the Federal Insecticide Fungicide Rodenticide Act (“FIFRA”) released on April 13, 2023.

AdvaMed is the largest association representing the companies that develop lifesaving, life-enhancing medical technology innovations for patients nationwide and around the world. We represent more than 450 companies supplying the sterile devices upon which Americans depend. Our members create and manufacture IV tubing, blood sample kits, surgical tools, heart valves, pacemakers, syringes, catheters, and much more, serving patients in every healthcare setting. Many of AdvaMed’s members use, or rely on commercial sterilizers who use, ethylene oxide (or “EtO”) to sterilize medical devices they develop and manufacture.

Use of ethylene oxide for the sterilization of medical equipment has been and will continue to be safe, and the sterilization process, including with respect to EtO, continues to be subject to existing



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and stringent regulations, which have applied for decades.<sup>1</sup> EtO sterilization is crucial for preventing infection in patients undergoing surgical procedures and other medical treatments. The process is used to sterilize half of all medical devices in the United States each year. As EPA notes, EtO sterilizes an estimated 95 percent of all surgical kits. Additionally, it is the only effective, viable sterilization method for many medical devices.

Community and worker safety are a priority for the medtech industry whose ongoing production of life-saving, life-enhancing devices medical devices is vital in every healthcare setting across the U.S. and abroad—including hospital operating room, emergency room, doctors’ offices, vaccine clinic, neonatal unit, nursing home, and post-treatment care or condition management at home. While protecting our communities and workers, EPA and its federal partners must also consider the critical benefits of medical technologies and the impacts to this sector from any proposals that would force dangerous capacity reductions or shutdowns.

AdvaMed member companies vary in many ways, including with respect to products and packing, cycle design, equipment, facility design and configurations, process, and geographies. These are not uniform operations—there is no “one-size-fits-all” approach to the medical technology industry. Therefore, as a starting point, any final determination must allow for flexibility to meet the needs of the diverse facilities, products and processes to ensure innovation and technological advancements can continue without interruption to prevent any delays in lifesaving, life-enhancing, and timely patient care.

Further, it is of paramount importance that EPA takes into consideration the importance of EtO in our healthcare system and for individual patients. Amid tremendous demand in the U.S. healthcare system for sterile medical technologies, EtO sterilization is already at capacity. AdvaMed is gravely concerned that the final PID, if not reasonable and feasible (both economically and technically), will force significant capacity reduction on EtO sterilizers and manufacturers of critical medical technologies (with no ability to shift that capacity across the market).

**Based on site-by-site analysis across the industry, the proposed PID as drafted will result in an estimated total capacity reduction at U.S. sterilization facilities of 30 to 50% per site and even upwards of 70% or more for some facilities.<sup>2</sup>**

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<sup>1</sup> Most relevant here, EPA also regulates EtO under the Clean Air Act and has proposed significantly more burdensome emissions limits in tandem with this PID. FDA regulates EtO’s use in sterility assurance under the Food, Drug, and Cosmetic Act. OSHA regulates EtO under the Hazard Communication Standard and as a chemical hazard in laboratories.

<sup>2</sup> Based on industry estimates, **the cycle validation/re-validation length will be further increased by 70 to 800%** by imposition alone of all-in-one sterilization cycles with substantial impact to US capacity with increased dwell time necessary with all-in-one processing, understanding that a number of products



A capacity reduction of this magnitude will result in supply chain shortages of critical medical devices that patients need.

Importantly, the proposal also does not appropriately take into account the time and cost of cycle revalidation that would be necessitated for changes in manufacturers' FDA-regulated sterility assurance processes. Millions of products would require revalidation, which includes extensive product testing and change management with U.S. and worldwide regulatory submissions and approvals taking even longer. This validation work will also cut capacity sharply amidst sterilization capacity constraints, and it jeopardizes U.S. supply chain resiliency and overall critical infrastructure of sterile medical devices.

**All of this, in turn, will likely result in a significant disruption and risk a public healthcare crisis because AdvaMed's members will be constrained in their ability to serve patients with the timely and steady supply of safe, effective, and sterile medical technology that our healthcare system requires.**

AdvaMed appreciates EPA's efforts in development of the PID. AdvaMed requested EPA conduct an impact and risk assessment of the PID, prior to development and publication of the PID. Unfortunately, EPA did not take this important step, and the PID suffers significantly as a result. AdvaMed has a long-standing record of being a collaborative and cooperative stakeholder with EPA (and other agencies) in a variety of regulations and initiatives that help supply the American people with the most innovative medical technology in the world, while protecting community members and employees. In fact, the medical technology industry has been proactive—well before publication of the PID—in researching and developing improved sterilization cycles, equipment, and facility design. This knowledge and experience are invaluable to the rulemaking process.

With this in mind, AdvaMed asks that EPA seriously consider the following comments, inclusive of Appendices I and II in the course of this registration review and work together with us to meaningfully address these concerns prior to issuance of a final decision that must ensure uninterrupted supply of vital sterile medical technologies for U.S. patients and the overall public health.

**Our membership places the highest priority on the safety of our communities, employees, and millions of patients we serve, and we support reasonable and balanced rules and regulations.**

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cannot be sterilized with this type of processing, which EPA itself acknowledges. These capacity constraints are further compounded if gas concentrations are reduced, which will also permanently reduce industry capacity due to longer required sterilization cycle times to maintain FDA regulated sterility assurance.



**TABLE OF CONTENTS**

Executive Summary .....6  
Comments .....8  
I. The PID ignores or trivializes significant costs and vastly overestimates the stated risk of EtO. ....10  
    A. EPA failed to undertake the required assessment of the “economic, social, and environmental costs and benefits of the use of” EtO. ....10  
    B. EPA drastically overstates the risk of EtO exposure by relying on a unit risk factor derived from flawed modeling and inconsistent with the scientific literature. ....10  
II. EPA does not have authority to limit EtO concentrations used in sterilization cycles, nor may EPA mandate infeasible and onerous engineering controls in sterilization facilities. ....13  
III. EPA should not adopt the proposed rate reduction.....17  
    A. The proposed rate limit would not necessarily reduce EtO exposure.....18  
    B. EPA should extend compliance timelines if EPA adopts a use rate limit. ....19  
IV. Commercial Sterilization Facilities Engineering Controls (Medical Device) .....21  
    A. EPA Should Not Mandate All-In-One Systems.....21  
    B. Significant time needed to implement all-in-one systems, where feasible. ....23  
    C. Requiring a covered conveyor to transport materials from treatment to aeration to storage is infeasible, unnecessary, and should not be required. ....24  
    D. EPA should not mandate a fixed level of ventilation for product storage and packaging areas. ....27  
    E. Given the requisite domestic and international regulatory approvals, significant costs and time for implementing engineering controls, product re-design cycle, and product supply chain disruption, the implementation process for engineering controls should be staggered and begin at least five years after EPA publishes the final registration decision. ....28  
    F. The final decision should allow facilities to select the type of engineering controls or safety processes to reduce EtO exposure. ....30  
V. Personal Protective Equipment (Medical Device).....30  
    A. EPA should not require respirator use at an entire facility, including processing and non-processing areas, when EtO concentrations exceed 10 ppb.....32  
    B. The proposed 10 ppb ambient air concentration threshold for requiring respirators to reduce worker exposure is technologically infeasible.....35  
VI. Comments on factual information EPA requested.....35  
    A. There are currently no viable alternative sterilization methods for many medical devices. ....35  
    B. The technology and methodology to reliably measure EtO concentrations in ambient air at or below 0.11 ppt does not currently exist. ....37  
    C. Facilities set limits based on OSHA’s PEL and guidelines. ....38

VII.	EPA must carefully analyze the interplay between the proposed NESHAP for EtO and the PID. ....	39
VIII.	Conclusion .....	40



## EXECUTIVE SUMMARY

The PID proposes fundamental changes that would have profound negative effects on commercial sterilizers like AdvaMed's members and, therefore, on the critical medical device supply chain.

**No two sterilization facilities are identical.** The overarching problem with the PID is that it fails to account for the wide variation in the commercial sterilization industry. Facilities sterilize a broad range of products in varying configurations and use many different types of equipment (both for sterilization and pollution control) at every stage of the process. Even facilities with similar equipment may process different products, have entirely different layouts and entirely different operations. With tens of thousands of medical device designs, and millions of individual products, the permutations of sterilization methods are nearly infinite.

Designing and implementing sterility assurance protocols is time- and resource-intensive under the best of circumstances. Validating even one of these protocols with FDA and foreign regulators can take months or years. Placing an arbitrary cap on the concentration level—just one of many elements that must be fine-tuned—makes the already difficult task impossible. **There is no feasible timeline for implementing a use-rate limit with respect to existing, already validated cycles for millions of devices currently available in the U.S. and worldwide for patient care.**

**EPA's proposed engineering controls to address perceived occupational risk are also far too generalized and would require at least five years to implement (where even possible).** The PID's very specific and prescriptive facility design requirements would require extensive reconstruction or renovation in many existing facilities. Some existing facilities' layouts are so incompatible with the proposed requirements that it may be more cost-effective to simply abandon the facility altogether. And the proposal would, at best, minimize occasional very short-duration exposure, with little to no impact on EPA's purported concern with chronic health effects from long-term exposure.

**EPA's proposed 10 ppb action limit is far too low.** It is *100 times* lower than the current OSHA permissible exposure limit (PEL), and far lower than any regulatory limit in any other jurisdiction. AdvaMed shares the concerns of EPA and of OSHA with the potentially outdated PEL and proposes using the NIOSH Recommended Exposure Level (REL) of 0.1 ppm.

Despite these extensive and worrying proposals, **EPA did not allow sufficient time for AdvaMed and other citizen stakeholders** "to meaningfully review the proposed rule and provide informed comment,"<sup>3</sup> especially given the agency is currently "engage[d] in a slew of interrelated rulemaking activity."<sup>4</sup> Further, EPA provided this insufficient comment period after not

<sup>3</sup> *Centro Legal de la Raza v. Executive Office for Immigration Review*, 524 F. Supp. 3d 919, 936, 955 (N.D. Cal. 2021).

<sup>4</sup> *Catholic Legal Immigration Network, Inc. v. Executive Office for Immigration Review*, No. CV 21-00094 (RJL), 2021 WL 3609986, at \*3 (D.D.C. Apr. 4, 2021).

conducting a proper inter-agency review as AdvaMed requested. EPA's failure to properly consider the profound effects on the regulatory jurisdictions of FDA and OSHA is reflected in the current proposals in the published PID.

Finally, **constraints on the critical medical device supply chain will be inevitable.** If EPA moves forward with the PID as written, critical supply shortages will be devastating. As noted in the PID, "EtO is used on approximately 50% of all sterilized medical devices, annually, including an estimated 95% of all surgical kits."<sup>5</sup> "[T]here are no viable alternatives to EtO for the sterilization of certain medical devices and equipment."<sup>5</sup> In addition, "EtO sterilization facilities operate continuously at near full capacity with few breaks and most manufacturers cannot use any alternative methods to substitute for EtO."<sup>6</sup> **As a result, "[t]he absence of EtO for use on medical devices and equipment would cause widespread disruption to the availability of sterile medical devices."**<sup>7</sup> FDA has emphasized that EtO sterilization is a critical component in providing safe medical devices in the U.S. and abroad.<sup>8</sup>

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<sup>5</sup> PID, at 3, 12, 28.

<sup>6</sup> EPA, *Regulatory Impact Analysis for the Proposed National Emission Standards for Hazardous Air Pollutants: Ethylene Oxide Commercial Sterilization and Fumigation Operations* (March 2023) at 2-8 (hereinafter "RIA").

<sup>7</sup> PID at 3, 28.

<sup>8</sup> See FDA Center for Devices and Radiological Health Medical Device Benefits (March 15, 2023), <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0244-0049%20> (noting the critical role EtO plays in sterilizing medical devices and the shortages that resulted when Sterigenics Willowbrook closed in 2019).

## COMMENTS

The PID suffers from several critical legal and practical flaws that, if not corrected, would render a final registration decision invalid.

*First*, several of EPA’s proposals are based on arbitrary and capricious agency analysis and do not have the support of substantial evidence. An agency decision is arbitrary and capricious if it fails to “examine the relevant data and articulate a rational connection between the facts found and the choice made.”<sup>9</sup> A registration review decision must also be supported by “substantial evidence when considered on the record as a whole” that identifies “such relevant evidence as a reasonable mind might accept as adequate to support a conclusion.”<sup>10</sup> In the FIFRA context, courts have held that an agency acts arbitrarily and capriciously when it adopts a one-size-fits-all approach that is not tailored to address the problem at hand and where the agency does not consider economic feasibility of implementing that approach.<sup>11</sup>

EPA’s approach assumes that because the agency has studied the specific factors of one facility, it has in essence studied and understood the fundamentals of all sterilization facilities. But the fact that a requirement may be effective or reasonable for one facility, or one product, or one cycle, says nothing about how that same requirement applies to another facility or product or cycle. EPA does not take into account a large number of variables such as facility size, facility layout, material use, products sterilized, capacity, monitoring, equipment, testing outcomes, manufacturing capabilities and location-based variables (such as ambient temperature and humidity). If EPA has examined the specific factors of one facility, that simply means that EPA understands these various factors as they apply to that one specific facility. There was a significant amount of information available for review from the Section 114 Information Requests that appears to have been ignored by EPA in development of this approach.

A one-size-fits all approach, therefore, could never be reasonable. Absent substantial evidence that EPA thoroughly considered all the potentially relevant factors that differ from one facility to the next, EPA’s proposed rules would be arbitrary and capricious if implemented.

EtO sterilization facilities also differ in terms of available resources, financial or otherwise, that they can dedicate to EPA’s proposals. Even otherwise reasonable requirements for some facilities may be infeasible for all facilities once costs, resources, and equipment availability are taken into

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<sup>9</sup> See *Motor Vehicle Mfrs. Ass’n v. State Farm Mut. Auto Ins.*, 463 U.S. 29, 52 (agency “must offer a ‘rational connection between the facts found and the choice made’” (quoting *Burlington Truck Lines, Inc. v. United States*, 371 U.S. 156, 168 (1962))).

<sup>10</sup> *NRDC v. EPA*, 38 F.4th 34, 44 (9th Cir. 2022) (quoting *NRDC v. EPA*, 857 F.3d 1030, 1035–36 (9th Cir. 2017)).

<sup>11</sup> See, e.g., *Dow AgroSciences LLC v. Nat’l Marine Fisheries Serv.*, 707 F.3d 462, 474–75 (2013) (holding that the agency’s requirement for pesticide buffer zones was overbroad and not tailored to the location of the protected species, especially where the agency did not address the economic feasibility of the requirement).



consideration. FIFRA PID's requirement and resulting burdens must be proportionate to a facility's size and capabilities. EPA is otherwise simply implementing requirements where compliance by facilities is not feasible.

EPA's decision to proceed with a one-size-fits all approach irrespective of facilities' variations can be further seen in its approach to healthcare facilities. Despite the inherent and obvious differences between hospitals, dental offices, and veterinary facilities, EPA is proposing the same set of requirements for all such healthcare facilities. Hospital facilities alone vary vastly in size and capabilities depending on factors such as location, specialties, associations with medical schools, decisions to undertake research, etc. None of this seems to have impacted EPA's proposal.

*Second*, the PID does not satisfy the FIFRA requirement to take into account economic, social, environmental, and public health costs and benefits. FIFRA § 2(bb) requires EPA to determine whether a pesticide poses “any unreasonable risk to man or the environment, taking into account the economic, social, and environmental **costs and benefits of the use** of [the] pesticide,” and specifically requires EPA to “weigh any risks of the pesticide against the health risks such as the diseases transmitted by the vector to be controlled by the pesticide.”<sup>12</sup> Consistent with this statutory instruction, EPA “specifically request[s] public comment on *the cost of the proposed mitigation measures*” so that the agency can “meet[] the FIFRA section 2(bb) mandate by taking into account the ‘economic, social, and environmental costs and benefits of the use of any pesticide.’”<sup>13</sup>

But EPA failed to adequately account for either side of this balancing exercise. The agency undervalues EtO's role in preventing fatal infections in healthcare settings, consistently ignores or understates the costs required to implement the PID's proposed mitigation measures,<sup>14</sup> and unreasonably overstates the purported risk of EtO exposure.

*Finally*, the PID attempts to prescribe sterility and workplace safety standards, which is beyond EPA's authority and recklessly interferes with the jurisdictions of other agencies. Nothing in FIFRA grants EPA power to prescribe engineering controls, dictate a maximum EtO concentration to use in sterilization cycles, or promulgate occupational safety rules—let alone to countermand the duly enacted regulations of FDA and OSHA.

In addition to these serious legal infirmities, the PID proposes mandates that would be extremely difficult, and in some cases impossible, to implement, especially on EPA's unreasonable compliance timeline.

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<sup>12</sup> 7 U.S.C. § 136(bb).

<sup>13</sup> PID at 68 (quoting FIFRA § 2(bb)).

<sup>14</sup> Based on industry assessment, implementation of all-in-one sterilization will cost more than \$1 million per site, not including the cost of product revalidations.

AdvaMed provides the following comments against the backdrop of these standards.

**I. The PID ignores or trivializes significant costs and vastly overestimates the stated risk of EtO.**

**A. EPA failed to undertake the required assessment of the “economic, social, and environmental costs and benefits of the use of” EtO.**

Despite the requirement to consider economic, social, and environmental cost and benefits, the PID states: “As is typical of the Registration Review process under FIFRA, OPP did not conduct a cost analysis for the proposed mitigation in this PID.”<sup>15</sup> Thus, EPA has not yet performed an appropriate analysis of economic, social, and environmental costs and benefits. As discussed below in Sections IV and V, the PID’s proposals would have drastic consequences for the supply chain of critical medical devices—resulting in economic, social, and public health costs—and would be extremely expensive or infeasible to implement. As explained in the Supply Chain and Capacity Considerations report by economists at the National Economics Research Associates (or NERA), the inelasticity of demand for medical devices “means that even modest sized shifts or disruptions in supply will cause medical device shortages that will affect patients.”<sup>16</sup>

These factors fall into economic, social, and public health costs and benefits that EPA is to consider as part of the “unreasonable adverse effects” standard, meaning EPA must consider them, as is consistent with EPA’s own solicitation of information on costs.

Additionally, under FIFRA, EPA must also “take into account the difference in concept and usage between various classes of pesticides” when promulgating regulations.<sup>17</sup> Although the registration process is not a rulemaking, this statutory provision nevertheless demonstrates Congress’s special consideration that the usage and concept of different pesticides be taken into account. This further underscores the need for EPA to fully consider costs and downstream impacts to society resulting from the proposed changes to EtO labelling and use.

**B. EPA drastically overstates the risk of EtO exposure by relying on a unit risk factor derived from flawed modeling and inconsistent with the scientific literature.**

EPA’s risk assessment is fatally flawed because it is based on an IRIS risk value that is scientifically unsound.

The PID states that the “concentration at which the cancer risk is . . . not considered by OPP to be of concern” is “0.00011 ppb (0.11 ppt).”<sup>18</sup> But EPA’s own ambient air measurements show EtO

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<sup>15</sup> PID at 53–54.

<sup>16</sup> See Appendix I (NERA Report) at 7.

<sup>17</sup> 7 U.S.C. § 136w(a)(1).

<sup>18</sup> PID at 17, 22, 69.

concentrations as high as 0.22 ppb or 220 ppt—two thousand times higher than the level EPA purports to use as its risk threshold.<sup>19</sup> EtO in much higher concentrations is produced by lawnmowers (up to 18,000 ppbv) and backyard barbecue grills (5,000 ppbv).<sup>20</sup>

Exposure from natural human biological processes is even higher, up to 27,000 times EPA’s risk threshold. A recent study examined eight EtO-emitting facilities and found that average “concentrations were not substantially elevated above the related background mean concentrations” and exposure from the facilities “composed a small fraction of the endogenous” exposure.<sup>21</sup> The 2016 EtO IRIS value creates “a serious gap in confidence in interpreting the health significance of general population E[t]O exposure,” in large part because it is not “consistent with clinical metrics for which the risk of disease does not increase significantly until the values are above the healthy population normal range defined by individual variability within the population.”<sup>22</sup>

EPA’s risk assessment arrives at an unjustifiably low IRIS value by adopting a flawed model and statistically significant over-predictions that are unsupported by epidemiological, toxicological and biological studies. Based on EPA’s risk assessment, “the background levels of [EtO] in the population would be predicted to cause more lymphoid cancer than is actually observed in the general population (and ignoring any other potential cause of lymphoid cancer).”<sup>23</sup> In short, EPA’s risk assessment is, on its face, indefensible and scientifically unsound. Our view is shared by regulatory agencies, industry experts, and the scientific community.

The Texas Commission on Environmental Quality (TCEQ) Toxicology, Risk Assessment, and Research Division identified “several substantial scientific issues with U.S. EPA’s [risk] assessment,” including EPA’s model fit criteria calculations, visual misrepresentation of model fit, and statistically significant model over-predictions.<sup>24</sup> TCEQ found, inter alia, that the linear two-piece spline model used in EPA’s assessment overpredicted key NIOSH data and the “consistent with the statistically significant over-predictions by USEPA’s preferred model (i.e., the linear two-piece spline model) . . . for the key and supporting cohorts, the reality checks above based on endogenous/background levels of EtO alone suggest that USEPA’s lymphoid cancer [unit risk

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<sup>19</sup> See EPA, *National Air Toxics Trends and Urban Air Toxics Monitoring Sites Oct.1 2018 – March 31, 2019*.

<sup>20</sup> See Montrose Air Quality Services Emerging Technologies Test Report: Proton Transfer Reaction/Time of Flight Mass Spectrometry (PTR-TOF-MS) Measurements of “Everyday Sources” for Ethylene Oxide (Oct. 16, 2019).

<sup>21</sup> Patrick J. Sheehan et al., *Ethylene Oxide Exposure in U.S. Populations Residing Near Sterilization and Other Industrial Facilities: Context Based on Endogenous and Total Equivalent Concentration Exposures*, 18 INT’L J. ENV’T’L RES. & PUBLIC HEALTH 607 (Jan. 12, 2021).

<sup>22</sup> *Id.*

<sup>23</sup> Texas Commission on Environmental Quality, Ethylene Oxide Development Support Document website, <https://www.tceq.texas.gov/toxicology/ethylene-oxide>.

<sup>24</sup> Texas Commission on Environmental Quality, *Ethylene Oxide Carcinogenic Dose-Response Assessment Development Support Document* (May 15, 2020) at 135.

factor] is scientifically unreasonable (i.e., leaving no room in the background rate for other causes of lymphoid cancer).”<sup>25</sup>

The TCEQ’s critiques were echoed in a thorough and scholarly report prepared by eight experienced scientists. This scientific report explained that “a steep supralinear model . . . should not be used because it is not consistent with the epidemiological and biological evidence” and that “both USEPA (2005) cancer risk assessment guidelines and Crump (2005) strongly caution against the use of steep slopes because they can lead to low-dose extrapolations that distort the true exposure-response relationship.”<sup>26</sup> The report also noted that EPA’s model selection was based almost exclusively on a fundamentally flawed statistical analysis and a flawed assessment of visual fit in relation to categorical data without considering biological plausibility.<sup>27</sup>

A 2019 scientific study on cancer evidence integration and dose-response implication regarding EtO concluded that the inhalation unit risk (IUR) derived by EPA using the two-piece spline model grossly overestimates risk.<sup>28</sup> The study states that “the IUR derived by EPA using the two-piece spline model is approximately 1000-fold more potent than the IURs derived from animal data and the TCEQ unit risk estimate based on the same epidemiological evidence.”<sup>29</sup>

Many other parties have raised issues with both the IRIS process itself and the 2016 EtO IRIS analysis in particular,<sup>30</sup> including perhaps most notably repeated reports by the National Academy of the Sciences and the Government Accountability Office (which at one point added the IRIS program to its “High-Risk List” of programs vulnerable to fraud, waste, abuse, and mismanagement).

A full discussion of the problems with the 2016 EtO IRIS would take up considerably more space and potentially distract from comments on other important aspects of the Proposed Rule. To avoid that result, the attached report of toxicologist Dr. Lucy Frasier summarizes the most significant of those issues.<sup>31</sup>

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<sup>25</sup> *Id.* at 160.

<sup>26</sup> *Cancer Risk Estimates for Ethylene Oxide Based on Epidemiological and Biological Weight-of-Evidence*, EXPONENT (March 11, 2020) at 4.

<sup>27</sup> *Id.* at 6–18.

<sup>28</sup> Melissa J. Vincent *et al.*, *Ethylene Oxide: Cancer Evidence Integration and Dose-Response Implications*, DOSE-RESPONSE (Dec. 11, 2019).

<sup>29</sup> *Id.*

<sup>30</sup> The ranking member of the House Committee on Science, Space, and Technology referred to the IRIS program’s “lack of transparency” and “improper scientific processes” that led to “an absurd risk value that is 19,000 lower than the levels . . . that naturally occur in the human body.” Opening Statement of Ranking Member Frank Lucas at Joint Subcommittee Hearing on EPA’s IRIS Program (March 27, 2019); *see also* Angela Logomasini, Ph.D., *EPA’s Flawed Iris Program Is Far from Gold Standard* (Feb. 12, 2019) (“IRIS has a long history of sloppy research and lack of transparency that has advanced faulty and often counterproductive regulations that impose needless burdens on the public.”).

<sup>31</sup> *See* Appendix II.

EPA’s risk-assessment “model bears no rational relationship to the characteristics of the data to which it is applied”<sup>32</sup> and there is no “rational connection between the factual inputs, modeling assumptions, modeling results and conclusions drawn from these results.”<sup>33</sup> These pervasive flaws undermine EPA’s entire premise for regulation and render the PID arbitrary and capricious.

**II. EPA does not have authority to limit EtO concentrations used in sterilization cycles, nor may EPA mandate infeasible and onerous engineering controls in sterilization facilities.**

EPA is not authorized to regulate how sterilization facilities conduct sterilization cycles; that authority belongs to the FDA. EPA is not authorized to dictate worker exposure levels; that authority belongs to OSHA. Any final determination must take into account the areas where FDA and OSHA have expertise and authority.

**The PID states that FDA and OSHA are too constrained by their authorizing statutes, and therefore, EPA should step in to fix the perceived problem. That is no basis for EPA’s asserted authority, especially given that FIFRA does not clearly authorize EPA to step into these other agencies’ regulatory lanes and require such onerous requirements of an entire industry.**

“Regardless of how serious the problem an administrative agency seeks to address, . . . it may not exercise its authority ‘in a manner that is inconsistent with the administrative structure that Congress enacted into law.’”<sup>34</sup> And in determining that administrative structure, federal courts recognize that “Congress . . . does not alter the fundamental details of a regulatory scheme in vague terms or ancillary provisions.”<sup>35</sup> **FIFRA does not permit EPA to reach into other agencies’ domains and prescribe expensive and onerous regulatory requirements across the entire sterilization industry.**

In assessing whether a particular agency has the authority to regulate specific activities, courts scrutinize whether Congress intended for the agency to do so, and as part of that analysis courts look at which agency is the best placed to act, considering its expertise and experience. Indeed, “[w]hen an agency has no comparative expertise’ in making certain policy judgments, . . . Congress presumably would not task it with doing so.”<sup>36</sup>

EPA’s PID would exercise control over an entire sector of the American economy by dictating highly prescriptive and expensive measures applicable to all commercial sterilization facilities.

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<sup>32</sup> *EME Homer City LLP v. EPA*, 795 F.3d 118, 137 (D.C. Cir. 2015) (quoting *Appalachian Power Co. v. EPA*, 135 F.3d 791, 802 (D.C. Cir. 1998)).

<sup>33</sup> *Id.*

<sup>34</sup> *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 125 (2000).

<sup>35</sup> *Whitman v. Am. Trucking Ass’ns*, 531 U.S. 457, 468 (2001).

<sup>36</sup> *West Virginia v. EPA*, 142 S. Ct. 25987, 2612 (2022) (quoting *Kisor v. Wilkie*, 139 S. Ct. 2400, 2417 (2019)).

These measures would create significant downstream effects on the medical device supply chain and medical care to patients in hospitals, surgical centers, and other healthcare facilities around the nation. The PID’s proposal to limit the exact concentrations EtO sterilizers use “hijacks” FDA’s authority—and undermines the Congressional allocation of regulatory oversight.<sup>37</sup> Additionally, the PID’s proposal to dictate expensive, often infeasible, and costly facility overhauls hijacks OSHA’s authority to regulate safe workspaces. In each instance, FDA and OSHA regulate under much more particularized (and in some ways more confined and limited) delegations of authority, but EPA seeks to disrupt Congress’s well-tailed statutory schemes, based merely on a general grant of authority in FIFRA to specify labeling requirements pursuant to the no-unreasonable-adverse-effects standard. This is improper.

***First, EPA oversteps into FDA’s regulatory lane.*** The PID proposes establishing a concentration limit of EtO of 500 mg/L for sterilization cycles.<sup>38</sup> In regulating different classes of medical devices, FDA must:

1. “[P]rovide reasonable assurance of the safety and effectiveness of [a medical] device”<sup>39</sup> and
2. “[W]eigh any probable benefit to health from the use of the device against any probable risk of injury or illness from such use.”<sup>40</sup>

Importantly, and also recognized by EPA, in 1997 Congress passed the Food and Drug Administration Modernization Act, which directed FDA to take the least burdensome approach to medical device premarket evaluation to eliminate unnecessary burdens and delay marketing of beneficial new products.<sup>41</sup> EPA recent action clearly fails to develop requirements that are the least burdensome to achieve its goals.

**In short, Congress has tasked FDA with assuring the safety and effectiveness of medical devices—not EPA. And with respect to new beneficial medical devices, Congress has directed that FDA take a least-burdensome approach to premarket evaluation.**

EPA, recognizing FDA’s authority for approving the safety and effectiveness of medical devices, nevertheless deems there to be “limitations” in FDA’s review.<sup>42</sup> These include, according to EPA: (1) FDA not being authorized to require device makers to justify “why a certain sterilization

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<sup>37</sup> *See id.*

<sup>38</sup> PID at 72–73.

<sup>39</sup> 21 U.S.C. § 360c.

<sup>40</sup> *Id.* § 360c(a)(2)(C).

<sup>41</sup> *See* FDA, Guidance, The Least Burdensome Provisions: Concept and Principles (Feb. 2019), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/least-burdensome-provisions-concept-and-principles> (discussing the statute and how FDA has interpreted least burdensome).

<sup>42</sup> PID at 32.

modality is used to support marketing authorization rather than another”;<sup>43</sup> (2) “FDA does not request” “information [that] was not provided in a premarket submission [if] that information is not needed to support a determination that the device meets the applicable statutory and regulatory standards”;<sup>44</sup> and (3) FDA’s role in reviewing sterilization procedures “is to evaluate whether the sterilization data (irrespective of method) submitted for premarket review is adequate to support a claim that a subject device is sterile as part of the overall benefit/risk assessment carried out on all FDA-regulated devices.”<sup>45</sup> EPA justifies the PID’s wide-ranging requirements on EPA’s perceived limitations in FDA’s role for ensuring safe and effective medical devices. These limitations were an intentional decision of Congress and put in place to ensure appropriate governing of medical devices. EPA cannot just ignore those restraints.

Not only does EPA propose acting in FDA’s place, but EPA has proposed requirements that may well interfere and conflict with FDA’s role. For example, if EtO concentrations above 500 mg/L are required for sterilization assurance, so that FDA can approve a method as safe and effective, then EPA’s proposal to limit EtO concentrations at that level would conflict with FDA’s role in assuring safe and effective medical devices. Moreover, for the development of new products that would require concentrations above 500 mg/L, the PID’s proposed limit undermines the Food and Drug Administration Modernization Act’s instruction to FDA to take the least burdensome approach to medical device premarket evaluation to eliminate unnecessary burdens and delay marketing of beneficial new products. EPA’s approach would outright bar any new products that require concentrations above 500 mg/L for sterilization.

These potentials for conflict illustrate in part why the federal courts are increasingly suspicious of agencies stepping outside of their traditional lanes and areas of expertise.<sup>46</sup> Furthermore, when the potential for interagency conflict results from an agency stepping outside its traditional lane to impose new restrictions on an entire sector of the American economy that “alter[s] the fundamental details of a regulatory scheme,”<sup>47</sup> then “clear congressional authorization” is required.<sup>48</sup> For this reason, the PID’s proposed concentration limit exceeds EPA’s congressionally delegated authority.

***Second, EPA oversteps OSHA’s responsibility to set “occupational safety and health standards.”***<sup>49</sup> The PID acknowledges this when it explains that “OSHA has numerous standards that could apply to pesticidal uses of chemicals” and that “OSHA sets legally enforceable limits

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<sup>43</sup> *Id.* at 30.

<sup>44</sup> *Id.* at 31–32.

<sup>45</sup> *Id.* at 32 (emphasis added).

<sup>46</sup> See *Wyoming*, 493 F. Supp. 3d at 1065–66 (noting conflict between Interior rule and state, tribal, and local standards approved by EPA).

<sup>47</sup> *Whitman*, 531 U.S. at 468.

<sup>48</sup> *West Virginia v. EPA*, 142 S. Ct. 2587, 2614 (2022) (quoting *Utility Air Regulatory Group v. EPA*, 573 U.S. 302, 324 (2014)).

<sup>49</sup> *Nat’l Fed. Of Independent Business v. Dep’t of Labor*, 142 S. Ct. 661, 665 (2022) (emphasis in original).

on the concentrations of hazardous chemicals in the air in a workplace.”<sup>50</sup> But EPA then notes that “OSHA’s legal requirement to demonstrate that its [Occupational Safety and Health (“OSH”) Act Section] 6(b)(5) standards are technologically and economically feasible often precludes OSHA from imposing exposure control requirements sufficient to ensure that the chemical substance no longer presents a significant risk to workers.”<sup>51</sup> The PID is correct that OSHA’s authority is limited in this way.<sup>52</sup> OSHA is also limited in another important way because OSHA must establish that a standard is “reasonably necessary or appropriate to provide safe or healthful employment” under Section 3(8) of the OSH Act.<sup>53</sup> In contrast with the OSH Act’s limitations, FIFRA provides a generalized grant of authority for EPA to include label conditions that does not expressly limit workplace regulations to a feasibility standard.

Rather than take the OSH Act’s instructions to OSHA as a lesson that regulating exposure to harmful physical agents in the workplace requires technical and economic feasibility or that EPA is reaching beyond Congress’s intended delegation, EPA views Congress’s policy decision as an impediment to be skirted. **With healthcare in the balance, the PID seeks to capitalize on the generalized grant of authority in FIFRA by proposing highly prescriptive, onerous and often-infeasible requirements for all facilities, including requiring the use of all-in-one systems and enclosed conveyors for transporting sterilized products.**<sup>54</sup>

These proposals’ infeasibility, excessive cost, and compliance timeline challenges are discussed below, and they demonstrate the importance of the feasibility limitation included in the OSH Act. Through the OSH Act, Congress clearly balanced the need to provide for workplace safety against the importance of not shutting down workplaces with infeasible requirements, as reflected in the OSH Act’s more specific statutory instructions for avoiding workplace exposures.<sup>55</sup>

EPA exceeds its statutory authority here by sidestepping the statutory constraints placed on OSHA and imposing infeasible workplace requirements.<sup>56</sup> To be sure, EPA is authorized to specify

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<sup>50</sup> PID at 35.

<sup>51</sup> *Id.* (emphasis added).

<sup>52</sup> *See, e.g.*, 29 U.S.C. § 655(b)(5) (instructing the secretary to “set the standard which most adequately assures, *to the extent feasible*, on the basis of the best available evidence, that no employee will suffer material impairment of health or functional capacity even if such employee has regular exposure to the hazard dealt with by such standard for the period of his working life” (emphasis added)).

<sup>53</sup> *See AFL-CIO v. Am. Petroleum Inst.*, 448 U.S. 607, 614 & n.3 (1980) (“The Act imposes on OSHA the obligation to enact only standards that are reasonably necessary or appropriate to provide safe or healthful workplaces. If a standard does not fit in this definition, it is not one that OSHA is authorized to enact.”).

<sup>54</sup> PID at 57–59. Notably, these requirements are specifically tied to occupation risk rather than bystander risk.

<sup>55</sup> *See Am. Textile Mfrs. Inst., Inc. v. Donovan*, 452 U.S. 490, 509 (1981) (“Congress itself defined the basic relationship between costs and benefits, by placing the ‘benefit’ of worker health above all other considerations *save those making attainment of this ‘benefit’ unachievable.*” (emphasis added)). *Cf. RadLAX Gateway Hotel, LLC v. Amalgamated Bank*, 566 U.S. 639, 645–46 (2012) (more specific statute controls over more general statute.).

<sup>56</sup> *See Wyoming*, 493 F.3d at 1065.



labelling requirements and attendant conditions on use of pesticides under its generalized grant of authority in FIFRA. However, that generalized grant of authority in FIFRA must yield when its exercise would “alter the fundamental details of [the] regulatory scheme” for protection to exposure in the workplace by allowing EPA to mandate infeasible facility retrofits.<sup>57</sup> Moreover, an agency “may not exercise its authority in a manner that is inconsistent with the administrative structure that Congress enacted into law.”<sup>58</sup> Without a clearer statement from Congress, EPA does not have authority to require excessively costly and infeasible workplace EtO requirements like all-in-one processing and closed conveyors.<sup>59</sup>

### **III. EPA should not adopt the proposed rate reduction.**

The PID proposes that the EtO concentration for new and existing cycles be reduced to 500 mg/L, with a 2-year compliance timeline for new cycles and a 5-year compliance timeline for existing cycles.<sup>60</sup> EPA seeks comment on the feasibility of these two compliance timelines.<sup>61</sup>

As an initial matter, as previously stated EPA lacks authority to set concentration levels. Further, EPA’s assumptions are not correct. The PID does not explain the connection between EtO concentrations and EtO exposure, nor what evidence EPA relies on in concluding that reducing the former will reduce the latter. EPA also fails to adequately assess the potential benefits or the feasibility of implementation.

**If EPA insists on imposing concentration limits, those limits should only apply prospectively—and not to existing, already validated sterility assurance measures. Even this somewhat more reasonable application only to new cycles would require at least five years to implement, considering the time and expense required. Redesigning and revalidating**

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<sup>57</sup> *Whitman*, 531 U.S. at 468.

<sup>58</sup> *Brown & Williamson*, 529 U.S. at 125 (internal quotations omitted); *see also id.* at 133 (“[T]he meaning of one statute may be affected by other Acts, particularly where Congress has spoken . . . more specifically to the topic at hand.”).

<sup>59</sup> Alternatively, Congress has impermissibly delegated its lawmaking authority to EPA. Congress must “make[] the policy decisions when regulating private conduct” and can only “authorize another branch to ‘fill up the details’” or “make the application of [a] rule depend on executive fact-finding.”<sup>59</sup> FIFRA’s open-ended delegation to EPA would violate this principle. Congress has impermissibly delegated its policymaking function to EPA to decide what constitutes “unreasonable adverse effects on the environment,” considering “the economic, social, and environmental costs and benefits of the use of any pesticide.” Rather than providing a gap-filling role or fact-finding role, the no-unreasonable-adverse-effects standard—instructing EPA to consider, for example, “social” costs and benefits—is a delegation of Congress’s policymaking powers, contravening fundamental principles of separation of powers. In recognition of the impermissibly broad delegation here, EPA should not proceed with the PID’s proposals.

<sup>60</sup> PID at 48.

<sup>61</sup> *Id.* at 48, 73.

**existing cycles would take decades and bring the industry to a standstill in their ability to provide critical medical technologies to patients.**

**A. The proposed rate limit would not necessarily reduce EtO exposure.**

It is not true as a general matter that “[r]educing the application rate of EtO would result in less EtO exposure.”<sup>62</sup> EtO concentration is just one of the variables that impact sterility, absorption, and levels of residual EtO from sterilized devices. Temperature, time, humidity, product and packaging design, application method, equipment design—these are just some of the many factors that influence the effectiveness of a sterilization process as well as residual EtO.

To be sure, reducing EtO concentration *can* result in less residual EtO. But it may also have no effect. Some commercial sterilizers have tested cycles using 50% less EtO and discovered that this rate reduction had precisely no impact on post-sterilization residual EtO and attendant potential for exposure. EtO remaining after sterilization is a function of cycle construction (i.e., temperature, phase time, vacuum depth, number of pulses, and other factors), not just the amount of EtO used.

Sterilizers, as well as industry, are already incentivized to keep the level of EtO used as low as possible. Sterilization cycles are optimized as a matter of good business practices.

Depending on product and cycle design, in some instances the proposed limit may actually increase total residual exposures—if facilities are required to increase the number of cycles they undertake as a result of reduced concentrations because of the extensive validation testing that will be required, then total exposure may well increase.

Moreover, a concentration limit is a blunt and ineffective tool for reducing EtO exposure. A concentration limit would not be feasible for some products or require additional exposure time during gas dwell phase and may require additional gas “top ups” to maintain phase conditions actually resulting in more use of EtO. Products that are pressure sensitive—such as devices with sensitive components or so called “complex geometries”—are often sterilized using a shallow vacuum cycle, which require a higher concentration of EtO to assure sterility. Validation is more complex and difficult in these sterilization settings. Likewise, a minimum concentration of 550 mg/L is often required to ensure penetration to the device for products sterilized in the final packaging, and changing this would increase the supply time to the customer and requires more employees to handle, potentially increasing exposure pathways.<sup>63</sup>

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<sup>62</sup> PID at 51.

<sup>63</sup> Additionally, commercial sterilizers often establish a “set point” for EtO concentration as part of their cycle, but in implementing that cycle there can be a range of EtO concentrations either above or below that set point. It is unclear if the proposed 500 mg/L limit is proposed as a “maximum” range, which could potentially require sterilizers to use an even lower concentration “set point.”

EPA's unsupported and incorrect conclusion that lower concentrations result in less exposure is arbitrary and capricious.<sup>64</sup> EPA did not consider important aspects of the problem, failed to examine relevant data and articulate a rational connection between the facts found and the choice made, and made a decision not based on substantial evidence.

Although reducing the concentration of EtO would not likely affect the level of EtO residuals, it would affect the supply chain for medical devices even if it is feasible for some products and cycles. First, cycle time and sterilization capacity are scarce, not unlimited resources. Reducing concentrations will require additional cycle time in many circumstances, which in turn will result in a lower production capacity for critical medical equipment and pharmaceutical product availability. Reduced capacity is one of AdvaMed's chief concerns, and EPA must consider this factor.

Second, extended dwell times (and attendant longer exposure to high temperatures) may damage products or reduce their shelf lives due to prolonged periods at elevated temperatures used in EtO processing. Third, a use limit would place undue constraints on the development of new life saving technologies where a higher gas concentration may be required to ensure product sterility. EPA should not foreclose the ability to innovate by requiring a fixed concentration limit that does not reflect the individual requirements of the products and cycles.

#### **B. EPA should extend compliance timelines if EPA adopts a use rate limit.**

EPA should provide sufficient time for implementing the proposed 500 mg/L limit or any maximum EtO usage limit in the final rule.

**For new cycles, EPA should adopt a compliance timeframe of at least five years**—i.e., new cycles would adhere to the limit if they begin commercial use at least five years after any label amendments require limiting concentrations below 500 mg/L.

AdvaMed cannot support any compliance timeline for existing sterilization cycles. There are simply too many technical and regulatory hurdles for re-validation to determine a timeline for existing cycles. **Therefore, there is no feasible timeline for implementing a use-rate limit with respect to existing, already validated cycles for millions of devices currently available in the U.S. and worldwide for patient care.**

As EPA acknowledges, “[s]terilization facilities conduct extensive testing to identify the correct levels of the key parameters that determine a cycle’s efficacy, including temperature, humidity, pressure, exposure time, and EtO gas concentration.”<sup>65</sup> Using a lower EtO gas concentration may impact device functionality or performance for drug coated products. Accordingly, a change in

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<sup>64</sup> See also *Tex. Tin Corp. v. EPA*, 992 F.2d 353, 355 (D.C. Cir. 1993) (holding EPA’s conclusion to be arbitrary and capricious where its analysis was relied on “nothing more than unsupported assumptions”).

<sup>65</sup> RIA at 2-6.

EtO concentration would require changes to product design or specification and in some cases could trigger a repetition of clinical trials. And EPA is aware that “completing the revalidation for a single product can potentially take months.”<sup>66</sup> This will lead to a much longer timeframe than the proposed two years for new cycles and five years for existing cycles. The complexities that require ample compliance timeframes are discussed in further detail in Section IV.E., including approximate timelines for each step needed to re-design products, re-validate cycles, and seek regulatory approval domestically and abroad.

Any change in cycles to implement reduced concentrations would require re-validating the sterilization cycles for millions of products and cost upwards of \$200,000 per cycle,<sup>67</sup> apart from the time and costs of U.S. and worldwide regulatory approvals.

Indeed, the European Union’s current medical device certification backlog crisis illustrates precisely this point. In May 2017, the European Union enacted the Medical Devices Regulations (MDR) which imposed new certification requirements for new and existing (legacy) medical devices consistent with harmonized standards.<sup>68</sup> Despite multiple compliance deadline extensions, however, the E.U. continues to experience a significant backlog in recertifications for legacy medical devices. Due to the volume of recertification requests and time needed to issue such requests, European regulators have been unable to timely recertify lifesaving medical equipment, resulting in a bottleneck and looming medical device shortage crisis. As a result, the European Union Health Commissioner proposed delaying enforcement of the MDR for legacy products by an additional three to four years to prevent product shortages.<sup>69</sup> Just last month, the Council of Europe officially extended the compliance timeframe until December 31, 2028—*more than 11 years after the original MDR regulation*.<sup>70</sup> EPA can expect a similar crisis if the current PID is finalized.

**In short, cycle validation is a time-intensive process regulated by FDA (and in the case of exports, other regulators), and EPA must leave sufficient time for this to play out completely to maintain the integrity of the medical devices supply chain. AdvaMed therefore urges EPA, if EPA moves forward with the proposed concentration limit, to adopt at least a five-year compliance timeframe for new cycles. Based on the technical, regulatory, and product-design complexity in re-validating existing cycles, EPA should not mandate a specific**

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<sup>66</sup> *Id.* at 2-7.

<sup>67</sup> This does not include the costs of product for testing nor additional testing costs such as biocompatibility testing.

<sup>68</sup> See Regulation (Eu) 2017/ 745 of The European Parliament and Of The Council - of 5 April 2017 - on medical devices, amending Directive 2001/ 83/ EC, Regulation (EC) No 178/ 2002 and Regulation (EC) No 1223/ 2009 and repealing Council Directives 90/ 385/ EEC and 93/ 42/ EEC.

<sup>69</sup> See Nick Paul Taylor, *EU Health Commissioner proposes MDR delay to prevent medical device shortages*, MEDTECH DRIVE (Dec. 12, 2022).

<sup>70</sup> See Press Release, *Council takes action to mitigate risk of medical devices shortage*, COUNCIL OF THE EUROPEAN UNION (March 7, 2023)

**timeframe for existing cycle compliance.** AdvaMed notes that commercial sterilizers regularly develop new sterilization cycles in this dynamic industry. This means that over time, new cycles would phase in to replace existing cycles, and any concerns that sterilizers would stop developing new cycles to avoid the proposed 500 mg/L limit are unfounded.

#### **IV. Commercial Sterilization Facilities Engineering Controls (Medical Device)**

##### **A. EPA Should Not Mandate All-In-One Systems.**

The PID discusses “all-in-one” processing at commercial sterilization facilities, stating “it is the Agency’s understanding that there are instances where an all-in-one sterilization chamber could be utilized, rather than the traditional sterilization configuration wherein sterilization and aeration are performed in two separate chambers.”<sup>71</sup> The PID further notes, however, that “there are certain pressure-sensitive devices that cannot be sterilized in all-in-one systems. Further, EPA acknowledges that there could be capacity constraints on the volume of medical devices that could be sterilized in all-in-one systems, which typically have a longer processing time within the chamber.”<sup>72</sup> Despite this concern, the PID proposes to require all-in-one sterilization systems in commercial sterilization facilities that do not sterilize pressure sensitive devices.<sup>73</sup>

The PID requests comment on “additional information on the feasibility of all-in-one processing (combination sterilizers) for the treatment of medical devices by commercial sterilization facilities.”<sup>74</sup> EPA also seeks comment on the “feasibility of upgrading facilities to use all-in-one systems, and the potential impacts on the medical device supply chain.”<sup>75</sup>

**AdvaMed urges EPA not to adopt this approach because—as EPA itself “acknowledges”—it is not feasible in many circumstances and would raise significant supply chain challenges by introducing unnecessary capacity constraints.**

*First*, and most fundamentally, this proposal is arbitrary and capricious because EPA fails to articulate a rational connection between the facts found and the choice made.<sup>76</sup> The PID does not even attempt to identify how or why all-in-one processing will reduce exposure to EtO. EPA acknowledges that “there *are instances* where an all-in-one sterilization chamber could be utilized, rather than the traditional sterilization configuration wherein sterilization and aeration are performed in two separate chambers.”<sup>77</sup> But the only “instances” EPA considers in making this

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<sup>71</sup> PID at 57.

<sup>72</sup> *Id.*

<sup>73</sup> *Id.*

<sup>74</sup> *Id.* at 73.

<sup>75</sup> *Id.*

<sup>76</sup> See *State Farm*, 463 U.S. at 52 (“[T]he agency . . . must offer a rational connection between the facts found and the choice made.” (internal quotations omitted) (quoting *Burlington Truck Lines, Inc. v. U.S.*, 371 U.S. 156, 168 (1962))).

<sup>77</sup> PID, at 57 (emphasis added).

proposal are pressure-sensitive devices and the fact “that there could be capacity constraints on the volume of medical devices that could be sterilized in all-in-one systems, which typically have a longer processing time within the chamber.”<sup>78</sup> Nevertheless, EPA then proposes an across-the-board mandate for the whole industry, except for pressure-sensitive devices. EPA does not explain why it is reasonable to make the unfounded leap that “*instances* where an all-in-one sterilization could be utilized” supports a mandate that an all-in-one chamber be used in *almost all instances*.

Beyond being arbitrary and capricious, EPA should not require all-in-one-systems for three reasons:

1. **All-in-one-systems are infeasible for many companies;**
2. **All-in-one-systems would result in supply chain shortages; and**
3. **All-in-one-systems would conflict with medical device manufacturer compliance with ISO 10993-7.**

**Technically infeasible.** Implementing all-in-one processing is infeasible in many circumstances, and even where feasible, it may still disrupt the entire production process. **To comply, many of AdvaMed’s members would be required to entirely redesign the layouts of their existing facilities to accommodate all-in-one processing.** This is because many sites have been designed with separate preconditioning and aeration areas, and so all-in-one processing would require adding additional rooms to maintain the same level of production. The cycles for these products would not allow for modification without significant product testing and regulatory approvals. Similarly, some AdvaMed members have sterilization facilities within a larger production facility, where sterilization is simply one step in the process. At such facilities, the costs to convert to all-in-one processing, if feasible, would be even more dramatic than at facilities with only sterilization processes because the rest of the assembly lines at such facilities are reliant on the current timing required for sterilization cycles.

**Supply-Chain Shortfalls.** EPA must consider the extent of the supply chain shortfalls that would result from the longer times required in sterilization chambers from mandating all-in-one processing, or else EPA “entirely fail[s] to consider [this] important aspect of the problem.”<sup>79</sup> **All-in-one processing would require significantly longer cycle times:**

AdvaMed members report that the average sterilization chamber time ranges from 8 to 16 hours, but all-in-one processing for these members would require approximately twice that time (16 to 32 hours).

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<sup>78</sup> *Id.*

<sup>79</sup> *State Farm*, 463 U.S. at 43.

Similarly, a number of AdvaMed members note that cycle times would increase even more dramatically, and would result in a *decrease in capacity of up to 78%* based on chamber times increasing by a factor of 1.5x or higher.

**Slowing down total processing times within sterilization chambers will dramatically reduce sterilization capacity across the industry, and this capacity cannot be readily replaced as the industry, as a whole, is already at capacity.** These downstream effects will be devastating to the supply chain for critical medical devices and the healthcare system as a whole. EPA must consider these factors, and not move forward with the all-in-one proposal as a result.

The length of aeration time required for different products varies widely. For example, different device materials, configurations, densities, packaging materials and sizes all drive different aeration times. The material used in individual devices also matters. Certain medical polymers such as polycarbonate or other resins absorb more EtO and require longer aeration times. **Because the aeration times vary so widely, all-in-one processing makes it very difficult to combine different types of devices into the same cycle; all devices must remain in the same process until the device with the longest aeration time is complete.** This would compound with the increased cycle lengths to further risk significant disruption to the medical device supply chain.

**ISO Conflict.** Use of all-in-one cycles would conflict with medical device manufacturer compliance with ISO 10993-7. This is because all-in-one cycles only on a limited basis can be validated using the “dissipation curve” within this standard. All-in-one chambers are not compatible with pulling product for testing at various stages of the aeration process per the ISO standard. **EPA cannot and should not mandate an approach that would conflict with an ISO standard.** Similarly, cycles cannot be validated using the lot-by-lot release approach without wasting three devices during each cycle, and some of AdvaMed’s members run cycles as low as 10 units. Moreover, the additional cycle chamber time will expose products to elevated heat for a longer period of time that has not been tested.<sup>80</sup> Sterilization companies would need to test product/packaging functionality issues that may result from this prolonged exposure.

#### **B. Significant time needed to implement all-in-one systems, where feasible.**

The amount of time to implement an all-in-one processing requirement, where feasible, would be significant. Few of AdvaMed’s members have all-in-one systems. All-in-one cycles will require significant cycle development to determine in-chamber aeration time, and products will be exposed to higher temperatures than traditional aeration, which may require assessment of impacts to product, packaging, shelf life, and biocompatibility. If there are potential impacts to products or packaging, resubmission for regulatory approvals would be required. Furthermore, time-sensitive EtO residuals testing would need to be conducted on products sterilized in all-in-one cycles. Because cycles may be used for sterilization of dozens of distinct products, such an endeavor would likely require years to fully complete. EPA must consider these timeline issues before

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<sup>80</sup> See PID at 47-48.

requiring all-in-one processing. **Even where the nature of a facility allows for all-in-one processing, the medical device industry would need to re-test and revalidate existing cycles to incorporate all-in-one processing, and a sufficient timeline is required for this, even if a requirement only applies to new cycles.**

If EPA moves forward with this proposal—and it should not—EPA must evaluate feasibility and capacity impacts in more detail so that EPA considers these important aspects of the problem. EPA may not rely on the unfounded assumption that what is feasible in some instances can be feasibly mandated across the entire industry.<sup>81</sup>

### **C. Requiring a covered conveyor to transport materials from treatment to aeration to storage is infeasible, unnecessary, and should not be required.**

The PID states that in “traditional EtO configurations, sterilization and aeration are performed in two separate chambers. In these systems, employees may transfer post-treatment materials from the sterilization chamber to the aeration chamber via forklift.”<sup>82</sup> However, EPA is also aware “that in some sterilization facilities, post-treatment materials are instead transferred via enclosed conveyor system, to reduce employee exposure.”<sup>83</sup> EPA therefore proposes “that all EtO commercial sterilization facilities with a traditional sterilization configuration implement an enclosed conveyor to transport sterilized materials from the sterilization chamber to the aeration chamber.”<sup>84</sup> “EPA is seeking public comment on the feasibility of reconfiguring existing EtO commercial sterilization facilities to use an enclosed conveyor system from the aeration area to the storage/shipping area.”<sup>85</sup> EPA further notes that for facilities that have all-in-one systems, “EPA is proposing automation via covered conveyor from the aeration area to the shipping and storage area.”<sup>86</sup>

EPA’s proposed automated conveyor requirement is arbitrary and capricious. As with other aspects of the PID, EPA does not take into account more cost-effective and feasible approaches that would provide the same—and even greater—exposure reductions, including the use of a self-contained breathing apparatus (“SCBA”) as PPE for short periods of time during tasks with higher potential for exposure. Indeed, the use of PPE for such tasks obviates the benefits of requiring such systems, and EPA has not purported to propose a closed conveyor systems to reduce exposure for bystanders.<sup>87</sup> For this reason, the PID’s closed conveyor proposal is not supported by substantial evidence that it is even needed. The proposal also displays a profound lack of

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<sup>81</sup> See *Tex Tin Corp.*, 992 F.2d at 355 (holding EPA’s conclusion to be arbitrary and capricious where its analysis was relied on “nothing more than unsupported assumptions”).

<sup>82</sup> PID at 57.

<sup>83</sup> *Id.*

<sup>84</sup> *Id.*

<sup>85</sup> *Id.* at 73.

<sup>86</sup> *Id.*

<sup>87</sup> See PID at 57 (“EPA is aware that in some sterilization facilities, post-treatment materials are instead transferred via enclosed conveyor system, *to reduce employee exposure.*” (emphasis added)).



understanding of traditional sterilization facilities' layouts, and EPA has failed to consider this important aspect of the problem.

Enclosed conveyors are not feasible for many facilities. EPA seems to have concluded that simply because *some* sterilization facilities have enclosed conveyors then it must be feasible for *all* sterilization facilities to have enclosed conveyors.<sup>88</sup> By making this generalization, EPA fails to account for the vast differences that exist between facilities, which make enclosed conveyors not feasible for many in the industry.

EPA does not even consider what circumstances may make enclosed conveyors feasible at some facilities.<sup>89</sup> Nor does EPA discuss the actual number of facilities that use an enclosed conveyor system as compared with those that do not.<sup>90</sup> **Notably, we are only aware of limited application of enclosed conveyor systems in specific situations.** By failing to consider these types of facilities and the important circumstances that make enclosed conveyors infeasible, EPA “entirely fail[s] fails to consider an important aspect of the problem” and also fails to “articulate a . . . rational connection between the facts found and the choice made.”<sup>91</sup>

Transporting sterilized materials from the aeration area to the shipping and storage area with an enclosed conveyor would require significant re-design or even expansion of the facility's footprint, as there are no existing spaces to locate conveyors with current facility layouts while still maintaining compliance with safety codes for adequate egress. The vast majority of existing traditional sterilization facilities (i.e., facilities where sterilization and aeration occur separately) would need to undergo significant redesign to accommodate such systems and would be limited by existing footprint and product mix. Moreover, because existing facilities have widely varying products, layouts, and packaging, it is not possible for a vendor to design one automation system and then apply a cookie-cutter approach to a wide number of facilities; bespoke designs are necessary. Accordingly, many facilities would be forced to close for significant redesign if an automated conveyor were required.

Even if modification of facilities were feasible, the extent of the modifications would be so large that the facility would require significant downtime during the retrofit. Such **downtime would last at least six months for AdvaMed's members**, and during that time the facility would have a partial or total loss of operational capacity. Downtimes spread out across many facilities would lead to medical device supply shortages. Such shortages are not a hypothetical, as FDA has

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<sup>88</sup> *Id.*

<sup>89</sup> The PID states that EPA “is aware that in some sterilization facilities, post-treatment materials are instead transferred via enclosed conveyor system, to reduce employee exposure,” but does not further specify, analyze, or consider any details about those particular facilities' operations.

<sup>90</sup> *See id.*

<sup>91</sup> *State Farm*, 463 U.S. at 43.

explained.<sup>92</sup> Further, the conveyor would take up space in the sterilization chamber, which would require full revalidation of the sterilization process and would reduce long-term capacity.

The feasibility problem is potentially even more acute for facilities where sterilization is only as one step in a longer production chain, as with the all-in-one systems discussed above. Requiring automated conveyors has the potential to disrupt those processes even more dramatically.

It is also unclear what value a conveyor system would have. Transport by forklift or other non-enclosed method typically takes a matter of minutes. Many employees already use SCBA respiratory PPE as a preventative measure when transporting products—which EPA proposed to also require in any event. In addition, automated conveyors would not eliminate the need for workers to be present. Personnel are still required to maintain and troubleshoot the conveyor system. This would necessarily be in a confined space, while wearing SCBA, and this itself presents risk. Indeed, the PID devotes only two paragraphs to the topic, neither of which assesses the expected reduction in exposure or why an enclosed conveyor would be necessary if employees use respirators for transporting materials.

As for new facilities, conveyor systems can work for custom-designed operations with standardized and smaller scale (shipping case level) product flows. However, enclosed conveyor systems for large pallet-quantity volumes or variable weights and dimensions are much more difficult and complicated to operate. The necessary maintenance and troubleshooting that would be necessary for such a system would be very difficult to accomplish and would also present risks to workers operating in confined spaces. For this reason, EPA should only require automated conveyor systems in limited circumstances—if at all. At a more fundamental level, requiring a prescriptive technology like a conveyor should be avoided, and *instead EPA could simply set an exposure level while leaving facilities the flexibility to achieve that limit (emphasis added)*.

Finally, if EPA moves forward with the requirement to retrofit existing traditional facilities with a conveyor system, EPA should at least provide an exemption for biological indicator evaluation resistometer vessels and small research chambers of less than 1 pallet in size. Automation may not be feasible for small sterilization chambers used in industry, but these chambers are essential for manufacturing biological indicators, which are a critical tool for validating and monitoring EtO sterilization processes.

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<sup>92</sup> See FDA Center for Devices and Radiological Health Medical Device Benefits (Mar. 15, 2023), <https://www.regulations.gov/document/EPA-HQ-OPP-2013-0244-0049> (noting the device shortages that resulted when Sterigenics Willowbrook closed in 2019).

**D. EPA should not mandate a fixed level of ventilation for product storage and packaging areas.**

The PID also “proposes to require that commercial sterilization facilities that use EtO have adequate ventilation in spaces where EtO-sterilized product is stored.”<sup>93</sup> Accordingly, EPA is also soliciting public comment on the number of air exchanges per hour that would adequately ventilate product storage areas.<sup>94</sup> EPA further requests comment on the use of netting rather than plastic surrounding pallets of treated medical devices to increase aeration and prevent EtO from becoming trapped in plastic wrap or other packaging.<sup>95</sup> AdvaMed responds to each issue in turn.

With regard to ventilation, EPA should not adopt any specific standard. The number of air exchanges per hour is product-, facility-, and cycle-dependent. This is because the amount of ventilation required depends on a variety of factors like the percentage of the space that is occupied by products, the amount of off-gassing that is present, the off-gassing rate, and the temperature of the space, among others. Additionally, specific amounts of EtO are also affected by room design and airflow characteristics. Imposing a standard in already effective room designs would result in unnecessary expense and loss of productivity. Moreover, a fixed number of air exchanges would have widely varying results depending on the circumstances.

AdvaMed’s members also observe that specifying a fixed number of air exchanges per hour may result in air imbalances between parts of the building and result in an inability to comply with other requirements of the PID or NESHAP. For one example, the equipment needed to implement a permanent total enclosure, as proposed for the NESHAP, would be profoundly impacted by an air exchange requirement.

Turning to netting, AdvaMed opposes a blanket requirement to use netting. Netting is only appropriate if manufacturers account for pallet load stability, and in some cases netting cannot meet the required strength to support certain loads of products. Accordingly, netting is not feasible in all circumstances, and a mandate would compromise worker safety. The use of netting may also require cardboard corner boards on pallets, which would increase the likelihood of residuals.

Sterilization facilities should be able to select the approach that works for their operational needs, subject to applicable standards for ambient air EtO concentrations.

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<sup>93</sup> PID at 56.

<sup>94</sup> *Id.* at 56, 73.

<sup>95</sup> *Id.* at 56, 73.

**E. Given the requisite domestic and international regulatory approvals, significant costs and time for implementing engineering controls, product re-design cycle, and product supply chain disruption, the implementation process for engineering controls should be staggered and begin at least five years after EPA publishes the final registration decision.**

The PID requests “comment on a reasonable timeframe for registrants to submit label amendments to implement the proposed engineering controls, as well as cost information.”<sup>96</sup> In doing so, “EPA recognizes implementation of the proposed engineering controls would require a longer timeframe than typically provided by the Agency for the implementation of risk mitigation measures, given the limited availability of new equipment, increased demand, and the potential for disrupting the supply chain if facilities need to close to make these upgrades.”<sup>97</sup> AdvaMed appreciates the opportunity to comment on this important matter. However, as discussed in the preceding sections, AdvaMed stresses that EPA should not proceed with the proposed engineering controls, given the infeasibility, exorbitant costs, and supply chain shortages the proposals would cause. Nevertheless, if EPA moves forward with the proposals, AdvaMed respectfully requests that the timeframe EPA establishes should reflect the complications identified above with implementing the engineering controls, but only for new products. AdvaMed further recommends that rather than setting “a reasonable timeframe,” EPA should establish staggered timeframes that reflect the complexity of the medical device product supply chain serviced by the facility, the sterilization processes involved, and potentially other relevant factors.

Implementation should begin no sooner than five years from the date the rule is final in order to (1) allow the regulated community sufficient time to obtain the necessary domestic and international regulatory approvals, (2) provide stakeholders and the regulated community the opportunity to plan and prepare for implementation (and costs), and (3) allow for coordination between registrants, manufacturers, sterilization facilities, contract sterilizers, vendors, distributors and retailers so as to mitigate and plan for disruption to the medical device supply chain.

To the first issue, five years is insufficient time to obtain regulatory approvals from all domestic and international regulatory agencies, particularly if all medical device companies are applying for such approval within the same five-year window. Validation alone takes up to one year per product, assuming no design changes are necessary. Depending on the number of product lines, it may take several years to validate. Products are sold both in the United States and internationally. Completing the regulatory submissions to domestic and international government agencies and regulatory bodies will take well beyond 18 months, and likely longer with the expected influx of submissions. Importantly, however, the 18-month timeline assumes no re-design. If the product must be redesigned to fit the new sterilization method, this could introduce additional delays of one to two years beyond the 18-months, at a minimum.

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<sup>96</sup> PID at 74.

<sup>97</sup> *Id.*

To the second issue, the prevalence and long history of using EtO for sterilization makes its impact on medical devices very predictable. Implementing an alternative process or control, or a new sterilization method, will require significant engineering characterization, regulatory evaluations, and efficacy studies. Even with thorough characterization and regulatory approvals, there may be undesired effects or outcomes that are not evident until the medical devices are used by customers. Given the mission critical, life-saving nature of the medical devices sterilized with EtO, these kind of changes should be implemented in a deliberate, iterative, and stepwise process. Additionally, with respect to costs, some stakeholders estimate it will cost approximately \$30-\$35 million per facility to implement controls and process changes, excluding automation. This estimate does not take into account the increase in supply costs due to industry-wide demand resulting from this PID's proposed requirements. A staggered and phased compliance timetable may help alleviate some of these costs by reducing demand and easing supply constraints and shortages.

To the third issue, the bottom line is that the engineering controls contemplated by the PID will severely disrupt the medical device supply chain. This will strain the medical supply device chain, leading to significant increases in cost and potentially supply shortages. For this reason, changes to existing cycles are not feasible and should not be required on any timeline. As noted in the PID's introduction:

EtO is used on approximately 50% of all sterilized medical devices, annually, including an estimated 95% of all surgical kits. Presently, there are no viable alternatives to EtO for the sterilization of certain medical devices and equipment. The absence of EtO for use on medical devices and equipment would cause widespread disruption to the availability of sterile medical devices.<sup>98</sup>

Reconfiguration of the magnitude proposed, and where feasible, would shut down an entire facility for many months at a time, significantly disrupting the supply of the medical devices serviced by the facility. During this time, the facility cannot sterilize any products until its new cycles and automated process/engineering controls, if applicable, are validated. The process from architecture and design to installation and then validation would likely take two to three years, at best. Importantly, however, this timeline does not include obtaining regulatory approvals (e.g., building permits) discussed above or facility air permits, meaning significant additional time would be required at minimum. AdvaMed's staggered timeline starting in no less than five years would help to minimize supply chain disruptions by giving facilities the time required and by allowing facilities to coordinate down time to maintain the integrity of the supply chain at all times.

**In conclusion, if EPA moves forward with engineering control requirements, AdvaMed supports a staggered approach to timeline for implementation, with the first required changes to take effect in no less than five years. However, this timeline should *only apply to***

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<sup>98</sup> *Id.* at 3.

***future new facilities given the infeasibility of undertaking the engineering proposals for existing facilities discussed above.***

**F. The final decision should allow facilities to select the type of engineering controls or safety processes to reduce EtO exposure.**

The PID states that “EPA is seeking public comment on whether to implement the engineering controls proposed in this PID for all existing facilities, a subset of existing facilities, or for only new facilities.” This is not a meaningful distinction as it has no direct bearing on whether a facility can or should, from a technological and economic feasibility standpoint, implement an engineering control or other safety process improvement.

AdvaMed members recognize that a new, to be planned, facility not yet constructed or in the design stages would be in the best position to implement new engineering controls. Even in this instance, however, introducing new controls may significantly increase building and design costs which could in turn delay or cause the parties to cancel the project. A new facility may be smaller and designed for specific medical device product group and therefore unable to implement certain engineering controls (e.g., automation, emissions controls) or processes. Conversely, an old facility may be larger and designed for a variety of products and therefore capable of implementing some engineering controls in certain areas of the facility, but not universally. It is also likely that a facility’s age may impact the number and type of regulatory approvals required.

As stated above, AdvaMed member companies develop different products, apply different packaging, implement different engineering design and processes, all at varying scales. Some facilities may be relatively newer operations, while others have been in operation for some time. There is no one answer on engineering and design option for all facilities because each facility is unique. At a minimum, the magnitude of controls required should correspond to the relative risks from an operation. Applying the same requirements to all facilities is overly simplistic. The commonsense solution is to allow facilities to choose the engineering controls and safety process improvements that will result in a demonstrable reduction in EtO exposure. If the goal is to reduce EtO exposure, the manner of obtaining the goal should be left up to each facility based on its specific processes, structures (i.e., buildings), and medical device products serviced. EPA should not prescribe specific engineering controls.

**V. Personal Protective Equipment (Medical Device)**

The PID requests comment on the logistical limitations of SCBA. The PID states that the “typical maximum wear time for a SCBA respirator is 45 minutes before the cylinder must be changed” and that “[s]upplied air systems are affixed to walls with a hose running to the supplied air respirator worn by the sterilization worker” and “the hose can limit worker mobility.”<sup>99</sup>

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<sup>99</sup> PID at 74.

Accordingly, “EPA seeks public comment on facility layout and typical employee work shifts, as it relates to the proposed personal protective equipment requirement in Section V.A.”<sup>100</sup>

AdvaMed has significant concerns about the ability to use either SCBA or supplied air across an entire facility rather than for discrete tasks. The amount of time that a SCBA system will last depends directly on the level of an employee’s physical exertion. More demanding activities may allow for significantly less than 45 minutes of respirator use. Members report expecting that in practice SCBA may need to be replaced up to 20 times during an 8-hour shift, or every 24 minutes. This would obviously be extraordinarily disruptive.

SCBA also presents its own set of hazards for employees: it risks snagging, bumping, or catching on fixed objects, which may cause injury. As for supplied air lines, they are not practical in many instances, given the layout and large size of facilities, and they may likewise introduce other hazards, including tripping and reduced mobility. Many employees have duties throughout a facility, making it difficult or impossible to provide a hose of the required length. Additionally, if many employees are required to use respiratory protection, facilities would need large-scale retrofitting to accommodate the number of air bottles, filling stations, compressors, filter and connection stations, piping, and storage areas for equipment.

Another logistical concern is the qualification training required for SCBA use. SCBA users must have an annual medical evaluation, fit test, and appropriate training, in accordance with OSHA’s Respiratory Protection Standard. Significantly, pre-existing medical conditions may outright disqualify a worker from being able to use SCBA and supplied airline respirators safely. These requirements could disqualify many workers from the workplace. Because of the number of people that may be required to wear a respirator under the PID’s 10 ppb proposal, this is a significant issue, and it would be difficult for sterilizers to maintain adequate staffing and hire new personnel who meet these requirements. Beyond that, the proposal to require respiratory protection when concentrations exceed 10 ppb (discussed below) may require third-party contractors, auditors, customers, and other workers to be in respirator protection. But it is infeasible for sterilization facilities to ensure that their third-party contractors, customers, or other entrants have the requisite certifications for use of respiratory protection. This is another logistical challenge that would be difficult to overcome, and it is also unnecessary because the 10 ppb level is meant to represent an entire decades-long career of exposure, not incidental minor exposures by personnel who only occasionally enter a facility.

More broadly, both SCBA and supplied air respirators place physical strain on the wearer, and the inability of workers to wear this type of respiratory protection for long periods of time is a known limitation. Industrial hygiene practices generally balance this concern and specify that respirator selection should be based on the airborne concentration of a contaminant, the respirator’s assigned protection factor, and other environmental conditions. SCBAs are also heavy—they typically

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<sup>100</sup> *Id.*

weigh 30 pounds or more, their prolonged use can lead to dehydration due to inability to drink fluids, and air delivery via SCBA is colder than ambient air, which may cause bronchoconstriction in asthmatics.<sup>101</sup> Because of these problems from prolonged respirator use, sterilizers may need to shorten shift times and hire additional personnel to reduce time spent in respiratory protection, and this approach would affect the supply chain if facilities are not able to hire and retain additional personnel.

For these many reasons, the requirement to use a respirator should be balanced against the type of exposure involved. Respirators should only be required in circumstances where there is a higher risk of exposure over a long period of time. As discussed below, 10 ppb does not meet that threshold.

**A. EPA should not require respirator use at an entire facility, including processing and non-processing areas, when EtO concentrations exceed 10 ppb.**

EPA also proposes that all employees at an entire facility use SCBA or supplied air if EtO concentrations exceed 10 ppb.<sup>102</sup> Notably, this requirement would apply to all workers, not just those that perform tasks closer to EtO processes, as opposed to the proposal on page 60 of the PID identifying tasks with more likelihood of exposure.<sup>103</sup> Additionally, EPA proposes that all employees would have the option to vacate the premises when levels exceed 10 ppb, in recognition of the fact that respirators for all employees may not be feasible.<sup>104</sup> EPA solicits comment on “the feasibility of continuous, real-time monitoring to a 10 ppb level inside of commercial sterilization facilities and the possible impacts of the daily operations of commercial sterilization facilities,” and on “the cost and how long is necessary for registrants to implement label amendments requiring compliance with this respirator requirement and the corresponding monitoring and recordkeeping requirements.”<sup>105</sup> EPA proposes two years.

AdvaMed opposes the proposal for requiring respiratory protection within an entire sterilization facility at an action level of 10 ppb. **We instead propose that the appropriate level at which to require respiratory protection is no lower than 0.1 ppm, with a reasonable duration threshold, and monitoring requirements should only apply within the sterilization area.** This

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<sup>101</sup> David Miedinger et al., *Evaluation of Fitness to Utilize Self-Contained Breathing Apparatus (SCBA)*, 47 JOURNAL OF ASTHMA 178 (Feb. 19, 2010), <https://doi.org/10.3109/02770900903483782>.

<sup>102</sup> PID at 59 (“EPA proposes that [SCBA] or supplied airline respirators be required when EtO concentrations in a sterilization facility exceed 10 ppb and proposes adding any associated fit test, training, and medical evaluation requirements.”).

<sup>103</sup> These are: (1) connecting and disconnecting EtO containers from sterilization process equipment, (2) unloading processed products from the sterilization chamber, (3) loading and unloading from the aeration area, (4) removing validation test materials from processed product at any time prior to completion of aeration, and (5) opening process lines or equipment that may contain EtO.

<sup>104</sup> *Id.*

<sup>105</sup> *Id.* at 74–75. Notably, EPA does not define “continuous, real-time monitoring,” but AdvaMed understands it to mean monitoring that can identify exceedances within 10 minutes.



level is feasible to detect on a shorter-time basis, and better balances benefits of PPE against SCBA's and supplied air's own workplace hazards. Further, it reflects the NIOSH recommended exposure limit (REL) that is 0.1 ppm (time-weighted that would trigger PPE requirements) and based on expert technical evaluation for industrial and occupational exposure threshold.

AdvaMed first reiterates and incorporates its comments above on the feasibility of SCBA and supply line air within a facility and across the facility's workforce. These logistical concerns, combined with the very low 10 ppb threshold make the proposal extremely complicated and infeasible to implement, and the constant stoppages required would likely reduce sterilization capacity.

As discussed in more detail in section VII, the 10-ppb action level is also too low for reliable measurement. Current monitoring equipment installed at facilities are not even able to reliably and practically measure below 100 ppb. EPA's NESHAP proposal even suggests inconsistency on what EPA believes is practicable to monitor in real time; EPA states, "we apply a multiplication factor of three to the [representative detection level] of 10 ppb, which yields a *workable-in-practice lower measurable value of 30 ppbv.*"<sup>106</sup> Further, setting action levels that are at the limit of current technology can lead to issues with interference in readings, resulting in frequent interruptions and supply-chain impacts because ubiquitous background levels of EtO from combustion or other sources already exceed this level.<sup>107</sup> AdvaMed's members are not collectively aware of proven, real time measuring devices for EtO that can measure concentrations at 10 ppb.<sup>108</sup> Although the PID does not say so, presumably many monitors would also need to be installed at each facility.

Additionally, EPA's proposal does not meaningfully address the problem that EPA aims to solve. Area monitoring is not easily correlated to individual worker exposure. Location and temporal differences in concentrations require monitoring within the worker's breathing zone, as reflected by OSHA's regulations for exposure monitoring.<sup>109</sup> Accordingly, any monitoring of EtO levels should be closely connected with individual worker exposure, consistent with standard industrial hygiene practices. Currently, employee exposure is typically monitored via badges worn by the employee in the breathing zone for 15 minutes and 8 hours, depending on whether short-term or full-day exposure data are needed. In order to achieve the level proposed, workers would need to wear 6L canisters for 8 hours. Continuous monitoring technologies that can measure to such low concentrations are not currently available for individual workers, and real-time monitoring is not required to determine employee exposure where exposure has historically been well below the action level. Next, the purpose of EPA's proposal is to reduce a *career-length* (i.e., 35-year) risk

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<sup>106</sup> 88 Fed. Reg. at 22,815 (emphasis added).

<sup>107</sup> ToxFAQs™ for Ethylene Oxide, AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY (August 15, 2022).

<sup>108</sup> We are aware of one vendor that advertises a continuous monitor that may be able to read at such levels. The system costs more than \$250,000 and has a lead time of 6 months.

<sup>109</sup> See 29 C.F.R. § 1910.1047(d)(1)(i) (requiring use of "breathing zone air samples").

of cancer incidence. Accordingly, it does not make sense to require respiratory protection based on a short-term exceedance of 10 ppb.

Rather, EPA should include a duration-based exposure limit (e.g., hourly, daily, weekly, or monthly) if it moves forward with this set of proposals. If EPA adopts AdvaMed's 0.1 ppm recommendation, then AdvaMed would support a shorter duration timeframe (i.e., hourly or even in real-time). This approach is also more likely than real-time monitoring to allow for feasible and cost-effective monitoring devices on or near workers. Additionally, EPA does not explain why real-time reading of above 10 ppb at only one location in a sterilization facility should trigger a response by all employees at the entire facility, regardless of facility size or layout. As discussed above, because of the substantial problems in using respirators for long periods of time or across many staff members, EPA should not move forward with such a broad-brush approach.

AdvaMed also opposes EPA's proposal that employees would be permitted to vacate the entire premises if EtO concentrations exceed 10 ppb in the facility, in both processing and non-processing areas. This presents a safety and process concern if employees are not available to staff critical systems. Also, as noted above, the purpose of EPA's proposal is to reduce long-term risk. Short-term exceedances of a 10-ppb threshold has little impact on such risk, and so workers should not be required to vacate the premises based on short-term exceedances of any threshold EPA selects. EPA should instead consider an approach that looks to longer-term exposures, especially for instances where employees are permitted to vacate facilities.

Regarding the compliance timeline, if EPA moves forward with the proposal to require respiratory protection above an "instantaneous" exposure level of 10 ppb despite significant overall feasibility concerns, then EPA should leave ample time for compliance and coordination with OSHA as the agency authorized to "set mandatory occupational safety and health standards applicable to businesses."<sup>110</sup> If EPA moves forward with the requirement, EPA should provide more than five years across the industry. See Section V.E., above, for a more detailed discussion regarding implementation timeline. This will hopefully allow time for real-time measurement technology to be developed that would reliably and cost-effectively detect EtO at the proposed 10 ppb level. It is also important that the technologies be able to monitor within the worker's breathing zone. And even if monitoring technology does not improve in 5+ years, this time will also be necessary to work through any vendors' bottlenecks as the entire sterilization industry works to implement the rule.

In conclusion, AdvaMed urges EPA to adopt a 0.1 ppm level for when PPE would be required. This approach would better balance the benefit of using PPE against the workplace hazards inherent with SCBA and supplied air. Further, a 0.1 ppm level does not suffer from the same detection limitations that the 10 ppb threshold raises. If EPA adopts a 0.1 ppm action level, a real-time action level may be supported of a time weighted average of 0.1 ppm would trigger PPE

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<sup>110</sup> 29 U.S.C. § 651(b)(3).

requirements (i.e., any real-time exceedance of a time weighted average of 0.1 ppm would trigger PPE requirements). EPA should also clarify that the monitoring requirements only apply in the portion of the facility where sterilization occurs.

**B. The proposed 10 ppb ambient air concentration threshold for requiring respirators to reduce worker exposure is technologically infeasible.**

The PID states that “it is EPA’s understanding that certain sterilization facilities in the U.S. may utilize a lower exposure limit than what is required by OSHA to set company-specific risk policies.” EPA requested public comment on facilities that utilize lower exposure limits than the OSHA PEL, and what practices these facilities use to achieve and measure these lower limits.

As noted above, some of our members’ facilities voluntarily utilize lower exposure limits than the OSHA PEL. However, EPA’s proposed 10 ppb threshold is not feasible due to technological and methodological limitations. Specifically, there is only one fixed monitoring system that may accurately measure at or below 10 ppb, and even if such systems were more widely available, there is no reliable method to differentiate how much of the measured EtO is attributable to the sterilization process versus background or other sources. A facility must be able to determine whether it is contributing to any exceedance of a regulatory limit in order to implement the appropriate corrective action. In short, a regulatory limit is not feasible if the regulated community does not have access to the technology and methods required to determine compliance.

Important to this conversation, the PID does not address background interference or the technological infeasibility of measuring the proposed EtO concentrations. Instead, EPA is putting the proverbial cart before the horse by proposing a compliance limit without determining whether it is workable or measurable.

In conclusion, although some facilities utilize lower exposure limits than the OSHA PEL, none of our members’ facilities utilize a limit resembling that proposed by EPA because the limit is fundamentally unworkable due to interference issues and limits in both existing ambient air monitoring technology and analytical laboratory methods.

**VI. Comments on factual information EPA requested**

**A. There are currently no viable alternative sterilization methods for many medical devices.**

The PID identifies potential alternative sterilization methods including gamma irradiation, x-ray sterilization, electron beam sterilization, and steam, as well as sterilization methods in development (e.g., vaporized hydrogen peroxide, nitrogen dioxide, chlorine dioxide, and vaporized peracetic acid). EPA acknowledges that there are “no viable alternatives to EtO for the sterilization of certain medical devices and equipment” and limitations of sterilization methods comparable to EtO “due to compatibility with materials and/or packaging, scalability or capacity,

and lack of validation measures or efficacy data.”<sup>111</sup> EPA seeks public comment to obtain more information about existing limitations of available alternatives, including comments on “existing and emerging alternative methods for medical device sterilization that are scalable and could most effectively replace EtO.”<sup>112</sup>

The appropriate sterilization method is specific to each device and considers the design specifications, patient safety, scale and function all while ensuring effective sterilization that does not degrade the device or impact performance. And as FDA and EPA note, EtO is the only viable modality for many devices for sterility assurance

First, there are no commercially available alternatives to EtO with similar material compatibility, and penetrating capabilities at low temperatures. Gamma radiation, x-ray, electron beam and steam sterilization methods are not compatible with devices containing electronics or manufactured with polymeric materials. This constitutes the vast majority of medical devices. The radiation energy from the gamma, x-ray and electron beams or temperature (i.e., from steam sterilization) discolors, embrittles, damages and polymerizes the materials they are sterilizing. For example, expanded polytetrafluoroethylene (ePTFE) and polytetrafluoroethylene (PTFE) are widely used in the manufacturing of medical devices and are a major component of critical-use aortic stent technology. These materials cannot withstand even low doses of radiation and would be damaged by steam or dry heat sterilization methods. In order to withstand these alternative sterilization methods, these critical devices would have to be redesigned, which may reduce or negatively impact the clinical outcomes. A redesign of this magnitude would take at least ten (10) years to complete, effectively removing a critical medical device from the market, which would cause significant harm to the patients and healthcare providers that rely on it.

Second, the alternative fumigation methods available or in development – i.e., vaporized hydrogen peroxide, nitrogen dioxide, chlorine dioxide, and vaporized peracetic acid – are largely ineffective at penetrating devices to sterilize matted surfaces and long lumens. These fumigation methods are also oxidative and damaging to many medical device material and packaging. Lastly, there are currently no recognized standard validation methods to demonstrate reproducible and predictable sterilization using these alternative fumigation methods. In addition, large or long medical devices do not currently fit within an electronic beam cell or alternative gas chamber. The devices and/or alternative methods would need to be redesigned and co-configured. The devices and methods would then need to pass a labyrinth of international and domestic regulatory hurdles.

Third, some alternative sterilization methods are not commercially available and require significant capital investment and further research and development to ensure the methods will be compatible or efficacious. The effects of these methods on medical devices are not yet well understood. Further, the available of research and development chambers are outside of the U.S,

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<sup>111</sup> PID at 3, 75.

<sup>112</sup> *Id.* at 75.

adding to complexities in both transport and time for product studies and importing and exporting of product samples.

Fourth, there are regulatory approval limitations associated with alternative sterilization modalities worldwide. Vaporized hydrogen peroxide is the only alternative sterilization method listed with an approved ISO standard for cycle validation. Many notified bodies outside of the U.S. require an ISO standard prior to adoption of sterilization modalities.

Moreover, these alternative sterilization methods, whether based on radiation or vaporized chemicals (i.e., fumigation gases), will trigger different health and safety risks for workers. These alternatives can pose a greater risk to workers, the environment and any exposed populations because they are not widely used or studied on a commercial-use scale. Sterilization, by definition, is not a harmless process. The reality of medical device sterilization is that all sterilization methods are designed to inactivate microorganisms and thus will also have similar negative impacts to other organisms. Nonetheless, sterilization is critical to successful healthcare outcomes and patient care. As acknowledged in the PID, “the absence of EtO for use on medical devices and equipment would cause widespread disruption to the availability of sterile medical devices.” The unavailability of sterile medical devices would, in turn, cause significant and irreversible harm to healthcare patients and individuals with a critical need for these devices.

The reality is that replacing a sterilization method, used for more than thirty years across the domestic and international medical device industry, cannot be reasonably accomplished in a 3- to 5-year time frame. EtO is not readily substitutable. Substituting EtO or requiring significant changes to the existing EtO sterilization processes requires deliberative, stepwise, and iterative process. We agree that alternatives should be pursued, but given the current status of the pipeline, to ensure safety and efficacy it would take at least 10 years of development and testing to ensure a commercially available alternative is effective and safe for use. Otherwise, there is a significant risk of harm to patients and individuals that rely on sterile medical devices, especially at-risk, elderly, and disadvantaged populations.

**B. The technology and methodology to reliably measure EtO concentrations in ambient air at or below 0.11 ppt does not currently exist.**

AdvaMed is not aware of any devices or methodology that can reliably measure EtO concentrations in ambient air at or below the residential population cancer risk limit identified in the PID of 0.11 parts per trillion (ppt). In addition, we are not aware of any commercially available industrial hygiene laboratories with analytical method capabilities that can achieve a 20-90 ppt level of quantitation (LOQ).<sup>113</sup>

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<sup>113</sup> The LOQ is the lowest concentration at which the analyte can not only be reliably detected but at which some predefined goals for bias and imprecision are met. David A. Armbruster *et al.*, *Limit*

As this is at the low end of existing measurement capabilities, equipment sensitivity must be evaluated and taken into consideration when establishing a realistic and measurable ambient air limit for EtO. The limit must be set above the equipment signal to noise threshold.

Equipment calibration standards do not exist for these concentration levels. A standardized/defined test method should be established to ensure consistency in the measurement (including calibration and establishing precision and accuracy estimates) and analysis methodology for these concentrations.

It is also important to recognize the ubiquity of EtO in the environment, when setting action levels and any corresponding technological and methodological analytical sampling requirements. EtO is present in the environment from the combustion of fossil fuels, manufacturing processes, as naturally created in the human body during the breakdown of ethylene, and as a naturally occurring by-product of the decay of organic matter.<sup>114</sup>

In summary, the technology and methodology required to reliably measure EtO concentration at these low concentrations does not yet exist. EPA should be mindful of setting any action levels based on these concentrations and the issues with interference readings, including background concentrations unrelated to sterilization processes and chemical interference.

### **C. Facilities set limits based on OSHA's PEL and guidelines.**

The PID states that EPA has identified risks for workers at levels below the OSHA PEL and thus does not consider the current OSHA PEL to be protective of workers. EPA is seeking public comment “to determine if facilities have voluntarily set lower exposure limits to better protect workers.”

Divergence from the OSHA PEL is not comprehensive across industry, and it cannot be universally assumed that every facility can achieve exposure limits below the OSHA PEL. As stated above, every facility is different and EPA should recognize such in determining achievable regulatory limits and prescribing appropriate methods to attain such limits. Additionally, establishing a significantly lower occupational exposure limit that is specific to commercial sterilization places the industry at odds with the majority of other industries who currently use EtO and will continue to be regulated by the OSHA PEL.

Sterilization facilities generally set exposure limits based on OSHA guidelines and the PEL for EtO. Some facilities may follow internal company occupational exposure limits for all chemicals derived from the American Conference of Governmental Industrial Hygienists (ACGIH)

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*of blank, limit of detection and limit of quantitation*, 29 THE CLINICAL BIOCHEMIST. REVIEWS Suppl 1, (2008): S49-52.

<sup>114</sup> ToxFAQs™ for Ethylene Oxide, Agency for Toxic Substances and Disease Registry (August 15, 2022).

Threshold Limit Values (TLVs). The current NIOSH REL is 0.1 ppm and ACGIH TLV for EtO is 1 ppm, based on an 8-hr time weighted average (TWA). Other facilities may set internal action levels that are 50% of the recommended exposure levels.

The mission of the ACGIH TLV®-Chemical Substances Committee is to recommend airborne concentrations of agents and exposure conditions for use in the practice of industrial hygiene and by other qualified professionals to protect worker health. The Committee's charge is to develop and disseminate occupational exposure guidelines (i.e., TLV). TLVs are based on the best available data and, whenever possible, peer-reviewed literature on human health effects resulting from industrial, occupational or other exposure situations from experimental human and animal studies with support from *in vitro* studies, human epidemiological studies; and when possible, from a combination of all these sources. TLVs are based on ACGIH®'s review of peer-reviewed scientific literature and robust data summaries.

NIOSH has the mandate to assure "every man and woman in the Nation safe and healthful working conditions and to preserve our human resources." The Occupational Safety and Health Act of 1970 established the National Institute for Occupational Safety and Health (NIOSH) as a research agency focused on the study of worker safety and health, and empowering employers and workers to create safe and healthy workplaces. NIOSH is part of the Centers for Disease Control and Prevention, in the Department of Health and Human Services. It has more than 1,300 employees spread across the United States, from a diverse set of fields including epidemiology, medicine, nursing, industrial hygiene, and safety.

Either of these organizations have the requisite expertise and mandate to determine safe exposure levels.

**VII. EPA must carefully analyze the interplay between the proposed NESHAP for EtO and the PID.**

EPA also published, pursuant to the federal Clean Air Act, proposed "National Emission Standards for Hazardous Air Pollutants: Ethylene Oxide Emissions Standards for Sterilization Facilities Residual Risk and Technology Review" published in the Federal Register on April 13, 2023 ("NESHAP Proposed Rule"). It is absolutely paramount that EPA carefully consider the interplay between the NESHAP Proposed Rule, and the Proposed EtO PID, at least to ensure the two proposals do not contradict. To date, this analysis is lacking from both administrative records, and AdvaMed is concerned that the proposals will contradict or conflict. For example, requiring specific processes under FIFRA will impact technologies deployed to reduce emissions and could contradict the NESHAP proposal, and limit the opportunity for innovative emissions reductions technologies.

## VIII. Conclusion

AdvaMed is committed to continuing to work with EPA, community members, other industry stakeholders, and other regulatory agencies to further reduce EtO use and occupational exposure without triggering a severe shortfall of critical medical device infrastructure—a result that is unfortunately all but assured if the PID is not significantly revised. We are confident that working collaboratively we can allow for progress in reducing EtO exposure through flexible standards adapted to the unique technical challenges for this source category. The standards in any final registration review decision must be achievable with existing technology across the many different facility and cycle configurations employed by nearly 100 commercial sterilizers subject to the label. AdvaMed and its members look forward to working together to achieve these shared goals.

Sincerely,

*Khaterah Calleja*

Khaterah Calleja  
Vice President  
Technology and Regulatory Affairs

(Enclosures)

Attachment I: NERA Economic Consulting, *Supply Chain, Capacity Considerations and Other Key Issues: “Ethylene Oxide Emissions Standards for Sterilization Facilities: National Emission Standards for Hazardous Air Pollutants (NESHAP)” and “Pesticide Registration Review; Proposed Interim Decision and Draft Risk Assessment Addendum for Ethylene Oxide”* (June 26, 2023)

Attachment II: Dr. Lucy Frasier, Ph.D., DABT, Comments on the U.S. Environmental Protection Agency’s Clean Air Act Rulemaking for the Commercial Sterilizer Source Category and Proposed Interim Registration Review Decision for Ethylene Oxide (June 26, 2023)