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Philips Respironics
Update on PE-PUR Testing Results and Conclusions Available to Date

Updated: December 21, 2022

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Update on the test and research program in connection with the June 2021 recall notification/field safety notice* for specific CPAP, BiPAP and mechanical ventilator devices

I. Introduction

On June 14, 2021, Philips Respironics, initiated a voluntary recall notification/field safety notice* for certain sleep and respiratory care products to address potential health risks related to the polyester-based polyurethane (PE-PUR) sound abatement foam in these devices. The affected 18 CPAP, BiPAP and mechanical ventilator products can be grouped in five device categories by their air path design, as set forth in **Table 7**, which also identifies the foam type (Type A or Type B foam) for each device.

At the time the recall notification/field safety notice* was issued, Philips Respironics relied on an initial, limited data set and toxicological risk assessment, that comprised:

- Complaints alleging foam degradation and particulates;
- Initial and limited lab experiments on Type A foam;
- Volatile organic compounds (VOC) measurements on New DreamStation CPAP devices;
- Limited ISO 10993 assessment of Used and Lab-aged SystemOne foam (See **Section II** for a description of Used and Lab-aged conditions).

The results were subsequently extrapolated across all device types and, out of an abundance of caution, a **reasonable worst-case scenario** was considered. At the time, Philips Respironics could not exclude possible carcinogenic effects with the limited dataset that was available. Philips Respironics did not have conclusive data indicating that exposure to the particulates or emitted chemicals would lead to cancer.

Since then, together with five independent, certified testing laboratories in the US and Europe and other qualified third-party experts, Philips Respironics has been conducting a comprehensive test and research program on the PE-PUR foam to better assess and scope the potential patient health risks related to possible emission of particulates from degraded foam and volatile organic compounds. This also includes an in-depth review and re-assessment of data and toxicological risk-assessments prior to June 2021.

This Philips Respironics update is intended to provide healthcare providers, patients, and other stakeholders with updated information on the testing results and third party confirmed conclusions to date on results and findings from testing PE-PUR foam used in recalled devices for VOCs, particulate matter (PM), and other testing such that healthcare providers have additional information to make informed decisions regarding the risk of continued use of recalled products.

Philips Respironics has provided these data to FDA and other competent authorities. **The FDA is still considering the data and analyses Philips Respironics has provided and may reach a different conclusion.**

Philips Respironics remains fully committed to addressing all devices affected by the recall notification/field safety notice* and continues to work with the relevant competent authorities to further optimize the remediation plan.

Philips Respironics continues to advise patients using affected CPAP/BiPAP devices to contact their physician or care provider to decide on a suitable treatment for their condition, which may include stopping use of their device, continuing to use their affected device, using another similar device that is not part of the recall, or using alternative treatments for sleep apnea. Moreover, patients are advised to follow Philips Respironics' instructions and recommended cleaning and replacement guidelines for their CPAP machine and accessories. Ozone and UV light cleaning products are not currently approved cleaning methods for sleep apnea devices or masks and should not be used.

Philips Respironics also continues to advise users of mechanical ventilator devices to contact their healthcare providers before making any changes to their therapy.

For more information on the recall notification/field safety notice*, as well as instructions for customers, patients and physicians, affected parties may contact their local Philips representative or visit https://www.usa.philips.com/healthcare/e/sleep/communications/src-update.

* *Voluntary recall notification in the U.S. / field safety notice outside the U.S.*

II. Testing Methods

Testing results and conclusions to date are grouped by device air path design (see **Tables 2-6**). An overview of the five device types and the two types of foam (Type A and Type B) can be found in **Table 7**. Within each device type, testing was performed on one of three categories of devices/PE-PUR foam.

- **New:** pristine devices/foam tested after manufacturing, prior to use by patients;
- **Used:** devices/foam tested after patient use; years of use, environmental factors, and conditions of devices vary: Used devices with varying levels of degradation were tested;
- **Lab-Aged:** devices/foam tested after exposure to significantly elevated temperature and humidity (e.g. 90 °C and 95% relative humidity) to intentionally induce hydrolytic degradation of PE-PUR foam.

Visual assessments are performed on Used and Lab-aged devices to assess the presence of visual degradation in the foam. Visual inspections are qualitative in nature and did not contribute to the risk assessment calculation described in **Section V.A.2**.

In addition to visual assessment, three categories of testing can generally be described in assessing potential patient risk: (A) VOC testing to identify and quantify organic compounds that may be inhaled during device use, (B) Particulate Matter (PM) testing to determine concentrations of airborne particles as it relates to inhalation risks and established health thresholds, and (C) additional physical, chemical and biological testing related to patient risks

if patients were in contact with PE-PUR foam material. These categories are described in more detail below.

Testing remains ongoing. The results of this testing will be evaluated to assess potential acute and chronic toxicological risks related to patient health. As new finalized testing results/analyses become available, Philips Respironics will update this summary, including **Tables 2-6**.

II.A. Volatile Organic Compound (VOC) and Particulate Matter (PM) Testing at Device Level

VOC testing according to ISO 18562-3:2017 (Biocompatibility evaluation of breathing gas pathways in healthcare applications – Part 3: Tests for emissions of volatile organic compounds) was performed on the devices containing PE-PUR foam to (1) quantify VOC emissions from devices, and (2) assess the toxicological risk associated with exposure to the quantified concentrations of those VOCs. This testing is performed on the entire device, not just the PE-PUR foam component. The purpose of this test is to determine if a detected and quantified VOC is likely to be associated with a toxicological risk based upon exposure during use of the device. For each detected and quantified compound, a worst-case estimate of daily exposure is determined and compared to a tolerable intake, which is the total amount of a compound that is considered to be without appreciable harm to health. This comparison is presented as a Margin of Safety (MOS) factor with an MOS value greater than 1.0, indicating the compound's worst-case estimate is below the compound's tolerable intake, and therefore suggests no appreciable harm to health.

PM testing according to ISO 18562-2:2017 (Biocompatibility evaluation of breathing gas pathways in healthcare applications – Part 2: Tests for emissions of particulate matter) was performed on the devices containing PE-PUR foam to (1) quantify the particulate matter emitted from devices, and (2) assess whether the concentration detected is less than thresholds provided in the standard. This testing is performed on the entire device, not just the PE-PUR foam component. Specifically, ISO 18562-2 defines limits for airborne particles of sizes less than or equal to 2.5 µm in diameter (referred to as $PM_{2.5}$ with a limit of 12 $\mu g/m^3$) and those less than or equal to 10 µm in diameter (referred to as PM_{10} with a limit of 150 $\mu g/m^3$). As described in ISO 18562-2, these limits are taken from the US EPA National Ambient Air Quality Standards (40 § CFR Part 50). Particles greater than 10 µm in diameter are not evaluated in ISO 18562-2 testing (see **Section IV, General Testing Limitations** for more details).

The ISO 18562 standard was established in 2017 and accepted by the FDA in 2018 to assess VOCs and respirable PM of breathing gas pathways in healthcare applications. However, the ISO 18562 assessments on New devices is not protective of potential degradation processes that can result in latent product-lifestage VOC and respirable PM emissions. Therefore, in addition to ISO 18562 protocols, Philips Respironics also engaged third-party labs to perform further testing and analyses using conservative assumptions on Used and Lab-aged foam per ISO 10993-1: 2018 and FDA guidance (2020) to address degradation processes and risk.

To evaluate health risk of degradation product(s) that may result from different extents of degradation (i.e. VOC and PM emissions during the degradation process), testing was performed on Used devices with differing amounts of patient usage and observed visual foam degradation/volume reduction, and on Lab-aged foam that has been intentionally degraded to different degrees. By conducting these tests and analyses, multiple data points of potential patient exposure can be captured as a function of device degradation to estimate whether a patient health risk may exist during the degradation process.

ISO 18562-2 does not characterize the chemicals potentially present in degraded particles, and therefore the thresholds for this standard may not necessarily correlate with the toxicity of particulate matter from degraded PE-PUR. As such, chemical characterization and toxicological risk characterization of degraded Type A PE-PUR foam was performed in accordance with ISO 10993-18 and -17 (see **Section V.A.2**). These assessments can provide data on unique degradation products of interest as well as determine the toxicological risk of those products at the levels present in degraded foam. Additional assessments are ongoing for other device platforms as well as Type B PE-PUR foam.

Finally, ISO 18562-2 testing of devices quantifies the concentration of respirable particulates, i.e., for the specific size range 0.2 to 10 µm in diameter, at a discrete point in time. For the analysis of larger non-respirable particles that may be emitted from the device (i.e., >10 µm PE-PUR foam particles), a risk assessment was performed based on custom testing and application of conservative assumptions. For a risk assessment completed on Type A foam, conservative assumptions included that all the foam in the device could become degraded and contact the patient. This assumption is known to be conservative since based upon visual inspection of 60,847 first-generation DreamStation devices, only a limited amount (2%) had significant visual foam degradation/volume reduction, and foam was still present in all of those devices (See **Section V.A.1**). Custom testing included collection of particulates on a filter during ISO 18562-2 testing to identify if any particulates of PE-PUR were present (see **Table 2, Rows 16 and 17**).

II.B. Foam Level and Additional Device Level Testing

Additional testing is being performed in accordance with ISO 10993 (Biological evaluation of medical devices) to facilitate a toxicological risk assessment. This testing includes: chemical characterization (i.e. what chemicals may potentially extract or leach from the foam and have direct contact with body tissues and/or fluids), *in vitro* assessment (i.e. tests performed in a test tube, dish, etc. outside the body), and *in vivo* assessment (i.e. animal testing) of New, Lab-aged and/or Used PE-PUR foam. In these tests, PE-PUR foam material is directly tested according to the ISO 10993 standards, unlike testing according to the ISO 18562 standards, which is performed on the entire device. The results available to date are reported in the Tables below**.** As described in **Section IV**, General Testing Limitations, differences may exist in how the Lab-aged PE-PUR foam degrades compared to the Used foam over the lifetime use of the device, and these differences were considered in the toxicological risk assessments performed to date. Additional testing is still ongoing or planned, including:

- For Type A foam: Additional VOC testing for Used DreamStation devices, testing of New DreamStation devices intentionally exposed to ozone, and device level testing for System One and DreamStation Go devices.
- For Type B foam: Testing on New, Lab-aged, Used Type B foam; and device level testing for Trilogy 100/200, and OmniLab/A-Series devices.

A chemical evaluation of New, Used, and Lab-aged PE-PUR foam is being conducted by identifying and quantifying chemicals that may be extracted or leached from the PE-PUR foam. The worst-case estimate of daily exposure will be informed by experiments to assess the amount of PE-PUR foam that can potentially be emitted from the device and contact the patient. A toxicological risk assessment on the extracted or leached chemicals will then be conducted in general accordance with ISO 10993 Biological evaluation of medical devices Part 17: Establishment of allowable limits for leachable substances, and Part 18: Chemical characterization of medical device materials within a risk management process. For each quantified compound extracted or leached from the PE-PUR foam, the worst-case estimate of daily exposure is determined and compared to a tolerable intake, which is the total amount of a compound that is considered to be without appreciable harm to health. This comparison is presented as a Margin of Safety (MOS) factor with an MOS value greater than 1.0, indicating the compound's worst-case estimate is below the compound's tolerable intake, and therefore suggests no appreciable harm to health. A third-party chemical evaluation and toxicological risk assessment is currently complete for Type A foam in first-generation DreamStation (DS1) devices (see **Table 2, Row 21**) and is ongoing for Type A foam used in other platforms and for Type B foam.

In vitro and *in vivo* assessments are conducted according to ISO 10993 Biological evaluation of medical devices Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity, Part 5: Tests for *in vitro* cytotoxicity, and Part 10: Tests for irritation and skin sensitization. These tests are evaluated against *a priori* acceptance criteria to determine if the PE-PUR foam has "Passed" the test.

III. Background – PE-PUR VOCs and Foam Degradation

Origins of VOCs and Particulates

Like most plastic materials, PE-PUR foams can emit volatile organic compounds (VOCs) with characteristic emission profiles. The three possible sources are [1-3]:

- VOCs associated with the production process of the PE-PUR foam; VOC emission typically decays as a function of time;
- Absorption of VOCs by the foam from its environment and subsequent emission; VOC emission from absorption typically decays as a function of time if absorption is not persistent;
- VOCs as a result of foam degradation; VOC emission may be persistent.

Foam degradation may also result in foam volume reduction and the formation of particulates.

Foam Degradation

The polyester polyurethane (PE-PUR) sound abatement foam is an open-cell foam with a polyester-polyol building block based on diethylene glycol (DEG) and adipic acid (AA) and a polyurethane building block based on toluene di-isocyanate (TDI).

Literature [4] and experimental data to date suggest that the degradation mechanism for PE-PUR foam within the affected devices – when the devices are used according to the instructions for use – is hydrolysis, primarily of the ester groups within the foam.

The hydrolytic degradation product of an ester bond, such as that present in PE-PUR foam (see Figure 1), produces an alcohol-containing oligomer and an acid-containing oligomer. Further hydrolytic degradation of PE-PUR foam can then produce a di-alcohol (specifically DEG) and a di-acid (specifically adipic acid (AA)). Literature demonstrates that this reaction is autocatalytic, in that the acidic byproduct of an ester bond can increase the rate of hydrolysis, generating more degradation of ester bonds [4]. Moreover, the hydrolytic degradation products DEG and AA are hygroscopic (i.e., attract water).

The hydrolytic degradation product of the urethane bond produces a toluene diamine containing oligomer and further hydrolytic degradation can produce toluene diamine (TDA).

Ozone is a strong oxidant. PE-PUR foams are also susceptible to oxidation especially if they contain ether-groups [5], which is the case for foam types A and B.

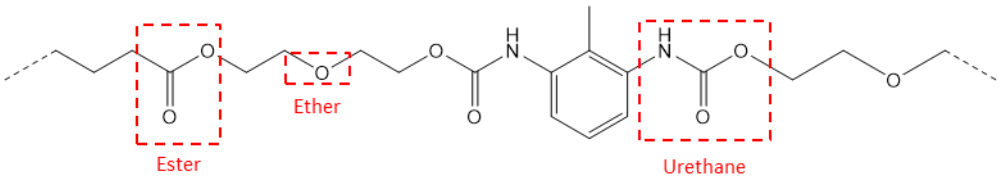

Figure 1: Chemical structure of the main building block of the PE-PUR foam (types A and B).

References:

[1] Lattuati-Derieux, A., Thao-Heu, S. & Lavédrine, B.; Assessment of the degradation of polyurethane foams after artificial and natural ageing by using pyrolysis-gas chromatography/mass spectrometry and headspace-solid phase microextraction-gas chromatography/mass spectrometry; J. Chromatogr. A 1218, 4498–4508 (2011).
[2] Characterizing Polyurethane Foam as a Sink for or Source of Volatile Organic Compounds in Indoor Air; Zhao, D.; Little J.C.; and Cox, S.S.; Journal of Environmental Engineering. Volume 130 Issue 9 - September 2004 (983 - 989).
[3] Aldehyde Emissions from Flexible Molded Foam; Al-Rashid, J., Panitzch T., Su, J., Lal, G., and Adamczyk, A.; October 2015; American Chemistry Council Center for the Polyurethanes Industry (CPI) Technical Conference.
[4] Szycher's handbook of Polyurethanes; Second edition; 2013 CRC Press; International Standard Book Number-13: 978-1-4398-6313-8.
[5] Ozone Reactions with Aliphatic Ethers in CCl4. Kinetics and Mechanism; Rakovsky, S.; Cherneva, D.; Deneva, M.; International Journal of Chemical Kinetics, 1995 (27); 153-165, 1995.

Degradation and Changes in Volume

The density of the PE-PUR foam (0.06 g/mL for foam Type A and 0.03 g/mL for foam Type B, see **Table 7**) is low, based on the open cell structure of the foam. For comparison, solid PE-PUR has a density of approximately 1 g/mL. Degradation of the foam is expected to result in collapsing of the open cell structure and a significant reduction of the material volume. For example, the total volume of foam type A in first-generation DreamStations of approximately 80 mL, theoretically can reduce to approximately 5 mL (a teaspoon) if the open cell structure collapses.

Degradation and Changes in Mass

Philips Respironics has assessed the correlation between degradation and changes in foam mass for the first-generation DreamStation devices. In the presence of humidity (such as patient use conditions), Type A PE-PUR foam becomes hygroscopic (i.e. absorbs moisture) with degradation and thus the mass is expected to increase. This is consistent with observations that negligible mass loss was measured in degraded foam and more so, even small mass increases were observed due to absorption of water. Moreover, the first-generation DreamStation particulate risk assessment by a third party is protective of a theoretical upper boundary patient exposure scenario in which there is 100% intake of all the Type A foam from a single device (see **Section V.A.2**). For these reasons, it has been concluded that mass measurements are not a reliable indicator of foam degradation.

Foam Degradation Products

As discussed above, TDI, TDA, DEG, and AA are potential degradation products of PE-PUR material, depending on the degradation mechanism (e.g., due to high temperature) and the extent of degradation.

- TDI has not been detected as a VOC, but was detected as an extractable/leachable chemical in Type A foam. Follow-up analysis (see **Table 2, Row 22**) determined that the detection of TDI as an extractable/leachable chemical was an artifact of the detection method (Gas Chromatography-Mass Spectrometry, GC-MS), which requires high heat to separate and identify chemicals. TDI is a known degradation product at high temperatures, such as those used in GC-MS (e.g. 210 °C and above), and these temperatures are well above the anticipated use conditions of the recalled devices. Based on this, TDI is not expected to be a degradation product under normal use (consistent with the instructions for use) for the recalled devices.
- TDA has not been detected as a VOC but was detected as an extractable/leachable chemical in Lab-aged foam extract. Testing of 6 Used devices, including devices with severe foam degradation, did not detect TDA in the Used foam extract (See **Table 2, Row 21**).
- DEG was detected as a VOC in multiple tests and as an extractable/leachable chemical in Lab-aged and Used foam.
- AA has not been detected as a VOC but was detected as an extractable/leachable chemical in Lab-aged and Used foam.

If present above toxicological thresholds as determined by the ISO 18562 and ISO 10993 standards, key risks related to inhalation or ingestion of TDI, TDA, DEG, or AA include:

- TDI – respiratory sensitization and irritation, asthma, and carcinogenicity;

- TDA – skin sensitization, liver toxicity, reproductive toxicity, genotoxicity, and carcinogenicity;
- DEG – kidney toxicity and liver toxicity;
- AA – respiratory irritation.

IV. General Testing Limitations

Healthcare providers and patients are advised that certain limitations exist regarding the current results presented herein, as described in more detail below, and that these limitations are still being addressed with ongoing and planned testing and evaluations. The ongoing and planned testing and evaluations include:

- For Type A foam: Additional VOC testing for Used DreamStation devices, testing of New DreamStation devices intentionally exposed to ozone, and device level testing for System One and DreamStation Go devices.
- For Type B foam: Testing on New, Lab-aged, Used Type B foam; and device level testing for Trilogy 100/200, and OmniLab/A-Series devices.

For example, ISO 18562 provides guidance for VOC (ISO 18562-3) and PM (ISO 18562-2) testing of sleep and respiratory care devices, however limitations being addressed include:

1. Default ISO 18562 testing on devices may not capture all degradation processes. Once degradation occurs, it is an ongoing process over the remaining lifetime of the device that could generate PE-PUR foam PM. Testing of a device per ISO 18562 only captures a "snapshot" of device performance during degradation, and it may not be known whether there will be maxima in concentration of hazards (i.e. VOCs or particulates) over time or whether the degradation reaction will behave asymptotically.
    a. As discussed above in **Section II.A.**, Respironics has considered this limitation and is addressing it through further testing and analyses per ISO 10993-1: 2018 and US FDA (2020) guidance. Testing was performed on Used devices with differing amounts of patient usage and observed visual foam degradation/volume reduction, and on Lab-aged foam that has been intentionally degraded to different degrees. Therefore, multiple "snapshots" of potential patient exposure can be captured as a function of device degradation to determine if a patient health risk may exist during the degradation process. Differences may exist in how the Lab-aged PE-PUR foam degrades compared to the Used foam over the lifetime use of the device, and these differences were considered in the toxicological risk assessments performed to date.

2. ISO 18562-2 testing of devices quantifies the concentration of respirable particulate based only on their size range (0.2 to 10 µm in diameter) but does not measure non-respirable particles greater than 10 µm.
    a. As discussed above in **Section II.A.**, Respironics has considered this limitation and is addressing it through custom testing and application of conservative assumptions, including an assumption that all of the foam in the device could

become degraded and contact the patient. This assumption is known to be conservative since visual inspection to date of 60,847 first-generation DreamStation devices has identified a limited amount (2%) of significant visual foam degradation/volume reduction, and foam was still present in all of those devices (See **Section V.A.1**).

3. ISO 18562-2 does not characterize the chemicals present in particles detected and therefore the thresholds for this standard (based only on particle size) may not necessarily protect against the toxicity of degraded PE-PUR particulate and its associated compounds. As such, passing an ISO 18562-2 test may not indicate 'no health risk' of PE-PUR foam particulates being emitted from the device.
    a. As discussed above in **Section II.A.**, Respironics has considered this limitation and is addressing it through chemical characterization and toxicological risk characterization of PE-PUR foam in accordance with ISO 10993-18 and -17 (for example, see **Section V.A.2**). This approach allows for protective toxicological thresholds to be applied for risk assessment of identified degradant PE-PUR products and PE-PUR foam formulation components.

Other limitations in the presented results include the number of Used devices that have finished testing. For example, 5 Used first-generation DreamStation devices were selected for testing (refer to **Table 2**) based on the devices exhibiting varying degrees of visibly degraded PE-PUR foam, and based on visual inspection to date (see **Section V.A.1**), devices with this level of degradation represent a small percentage of devices in the market. As previously described, these tests provide a snapshot of VOC detection at the time of testing and may not capture how all devices behave in the field over the lifetime of use, information which was considered during the associated risk assessment. While the VOCs measured in these devices suggested no appreciable harm to health, additional testing of Used devices and Lab-aged devices is being performed to more comprehensively evaluate "worst-case" degradation.

Visual inspections of devices include the removal of the cover of the device to view the foam, and these inspections can only identify visible particulate and cannot measure VOC generation or quantify particulate loss. Consequently, ISO 18562-2 and -3 testing was/is conducted on devices with and without visible degradation to obtain testing data across a range of potential degradation states of foam. Testing of devices that have a range of visible degradation states provides multiple snapshots but again, may not capture all potential degrees of degradation in the field over the lifetime of use. Therefore, toxicological risk assessments included conservative assumptions to be protective of all potential degrees of Used foam degradation.

Lab-aging (elevated temperature and humidity) of foam is being used to induce various levels of foam degradation and compared to levels of degradation in Used devices. The purpose and advantage of Lab-aging are to generate devices with different levels of degradation in controlled conditions without contamination from the environment. Each Lab-aged device is then used for testing to determine the overall health risk associated with that level of degradation. Lab-aging conditions are not intended to be predictive of rate of foam

degradation observed in Used devices, but it is informative for toxicological risk assessment including hazard characterizations and exposure. Notably, visual inspection of Used first-generation DreamStation devices has not identified a direct correlation with increased device use and increased foam degradation.

As presented below in **Section V.A.2** and **V.D.2**, Lab-aged foam (foam Type A and foam Type B) failed genotoxicity testing under the laboratory conditions of the Ames assay, but the implications of this result on overall patient health risk are still being assessed through additional testing (including the amount of foam that may contact a patient based upon the level of degradation). Per ISO 10993, a positive Ames result triggers a required follow-up evaluation including identification of potential confounding factors, and a weight of evidence assessment to determine a confirmed conclusion on potential risks for patients under expected usage of the device. Similarly, Lab-aged foam also failed cytotoxicity (Type A and B) and skin irritation (Type A) testing, but again like Ames testing and per the ISO 10993 standard, these results cannot standalone and require further analysis. To support the assessment of genotoxicity, cytotoxicity, and irritation risks, chemical characterization of PE-PUR foam as well as experiments to assess the amount of PE-PUR foam that can potentially contact the patient are being conducted. A third-party chemical characterization and toxicological risk assessment is currently complete for Type A foam in first-generation DreamStation (see **Table 2, Row 21**), and is ongoing for Type A foam used in other platforms and for Type B foam.

Based on these collective limitations, Philips Respironics advises caution in interpretation of any one test result (pass or fail) as reflective of the overall patient risk.

V. Summary Overview of Testing Status and Results by Platform

Specific conclusions regarding available testing results and third party confirmed conclusions reported to date for the three described categories listed above are contained in **Tables 2-6**, which are organized by device family. **Table 7** lists the type of PE-PUR foam used in each device (Type A or Type B). **Table 8** lists all acronyms and abbreviations.

- Current Status of VOC testing: Philips provided an update on December 23, 2021 that exposure to the level of VOCs identified to date for the first-generation DreamStation devices is not typically anticipated to result in long-term health consequences for patients; however, some additional VOC testing for DreamStation is ongoing (e.g., for devices exposed to ozone) and final conclusions will be provided after that testing is complete. Additional VOC testing for other devices affected by the recall is ongoing, and conclusions regarding exposure risks related to VOCs for those other devices will be provided when complete.

- Current Status of PM testing and additional testing (ISO 10993): **Tables 2-6** provide available testing results and third party confirmed conclusions reported to date for all affected devices. Comprehensive risk assessments of testing is ongoing for each device

affected by the recall, and Philips Respironics will continue to provide updates on findings from these assessments.

Further, devices may be made with one or more types of PE-PUR foam and certain foam types are used in multiple device platforms as indicated in **Table 7**. Therefore, foam testing may be applicable to multiple device platforms and is indicated as such in the tables below. Unless otherwise noted in the tables, all testing and conclusions were performed at one or more certified third-party laboratories and/or confirmed by third-party qualified experts.

V.A. First-generation DreamStation devices
Summary of Tests to Date

As described in **Section V.A.1.** and **V.A.2.** below, significant third-party testing and data analysis have been performed since Philips Respironics initiated the recall notification/field safety notice on June 14, 2021. This includes a third-party review of the data from the initial recall notification/field safety notice which found that the analytical characterization misidentified one chemical (acetone was misidentified as dimethyl diazene) and mischaracterized another [(phenol, 2,6-bis (1,1-dimethylethyl)-4-(1-methylpropyl)] as a mutagen and carcinogen. Through re-evaluation of the data, the third-party toxicological risk assessment found no risk concern for adverse health effects in patients (**Table 2, Row 4**). Lastly, expanding testing and toxicological risk assessments on multiple devices with New, Used, and Lab-aged foam have shown no detection of dimethyl diazene and no appreciable harm to health for all VOCs detected.

Concerning risks related to VOCs, testing in **Table 2** shows that ISO 18562-3 testing of 15 New devices, 5 Used devices, and 9 Lab-aged devices did not identify a toxicological risk for patients. As noted in **Section IV**, an individual ISO 18562-3 test may not account for all degradation processes. Therefore, testing selection included Used devices with different years of use and varying degrees of visible degradation. Specifically, four of the five devices had significant visual foam degradation/volume reduction (See **Section V.A.1**), and levels of diethylene glycol (DEG), a known degradation product, measured during testing were generally greater in devices with higher degrees of visual foam degradation/volume reduction, consistent with the degradation mechanism of PE-PUR. The measured levels of VOCs in these devices and all devices tested to date, including DEG and all other measured VOCs, were not at levels that present a toxicological risk for patients. Lastly, visual inspection to date of 60,847 devices (See **Table 1**), has identified visual foam degradation/volume reduction in a limited number of devices (2%).

Concerning risks related to respirable particulate exposure to patients, testing in **Table 2 (Row 2, 5, 14-17, 19, 20**) shows that ISO 18562-2 testing of 61 New devices, 96 Used devices, 28 simulated-ozone use, and 24 Lab-aged devices were all below the allowable respirable particulate limits specified in ISO 18562-2.

Concerning risks related to larger particulates (> 10 µm), a third-party analysis of the chemicals present in degraded foam from 6 different Used devices, including those with significant visual foam degradation/volume reduction was completed, and a risk assessment

was performed that conservatively assumed that all of the foam present in a device could contact the patient. That third-party risk assessment concluded that there was no appreciable harm to health in patients (See **Table 2, Row 21**).

V.A.1. Device Level Testing
Visual Inspection of Used/Returned Devices

A visual assessment was performed for Used/returned first-generation DreamStation devices as part of the repair process to determine the prevalence of visible degradation in the PE-PUR sound abatement foam and foam particles, as well as other findings (e.g., discoloration and other debris). For this assessment, the device is disassembled to permit access to the blower box (where the PE-PUR foam is located) and other parts of the device air path. The blower was also removed from the blower box to allow for full visual inspection. In addition, photographs were taken of the blower box with and without the blower for use in further assessing whether any visible degradation occurred and, if so, where any foam particles accumulated within the blower box.

This visual inspection process was performed for 60,847 returned devices to date from the US and Canada. These devices included devices where the user reported no use of ozone cleaning, the user reported use of ozone cleaning, and devices for which it was unknown whether ozone cleaning was used (see **Table 1**).

Table 1: Visual inspection of first-generation DreamStation devices from the US and Canada

	# inspected devices	**# devices with significant visual foam degradation/ volume reduction**
No use of ozone cleaning*	36,341	164
Use of ozone cleaning*	11,309	777
Unknown*	13,197	164
Total	**60,847**	**1,105**

* Self-reported by the user

As shown in **Table 1** above, 1,105 of the devices showed significant visual foam degradation/volume reduction, which corresponds to approximately 2% of the inspected devices. Devices for which the user self-reported ozone use were 14x more likely to have significant visual foam degradation/volume reduction (777 out of 11,309 or 7%) than those where the user reported no ozone use (164 out of 36,341 or 0.5%).

422 devices of the inspected 60,847 devices were linked to a foam degradation complaint, however only 18 out of the 422 (4%) showed significant visual foam degradation/volume reduction.

Type A PE-PUR foam, such as that used in the first-generation DreamStation devices (refer to **Table 7**), becomes hygroscopic (i.e. absorbs moisture) and sticky with degradation, loses significant volume and increases density as the structure changes from a foam to a viscous liquid material, and can accumulate within the airpath inside the device: in the blower cavity prior to entering the blower, and within the blower itself.

Additionally, an analysis of 2,469 DreamStation devices from Europe found one device with significant visual foam degradation/volume reduction (1 out of 2,469, or 0.04%), and an analysis of 1,964 DreamStation devices from Japan found no devices with significant visual foam degradation/volume reduction.

The observed accumulation of degraded foam within the airpath inside the device suggests that, even when Type A PE-PUR particulates are formed by degradation, they are likely to accumulate and may not be directly emitted by the device. This is also supported by the PM measurement results to date, as discussed below.

Volatile Organic Compounds (VOCs)

As previously provided in an update on December 23, 2021, exposure to the level of VOCs identified to date for the first-generation DreamStation devices is not anticipated to result in long-term health consequences for patients based on ISO 18562-3 testing and evaluation of New, Lab-aged, and Used devices (**Table 2**). It is important to note that these tested New and Lab-aged DreamStation devices were not exposed to ozone cleaning, in accordance with the instructions for use.

Particulate Matter (PM)

61 New devices, 96 Used devices, 28 simulated-ozone devices, and 24 Lab-aged devices were all compliant with ISO 18562-2 allowable limits for PM emissions. Tested PM emissions of Used devices with degradation (8 devices) were not statistically different than PM emissions from Used devices without degradation (67 devices), suggesting that degradation did not contribute to appreciable elevated levels of respirable particles in the devices tested.

Used/returned devices were evaluated for cleanliness based on a visual inspection of the exterior of the device. For these devices, average particulate matter counts in devices classified as 'dirty' were significantly greater than those classified as 'clean'. Please note that cleanliness does not refer to foam degradation. This is a visual assessment based on the presence of environmental materials on the external surface of the device, such as the inlet filter location.

Ozone Exposure

As discussed above, data to date for first-generation DreamStation indicates that devices with user-reported ozone cleaning are 14 times more likely to have significant visible foam degradation/volume reduction compared to devices with no user-reported ozone exposure. This observation is consistent with laboratory testing, where first-generation DreamStation

devices exposed to increasing cycles of ozone cleaning had increasingly more severe visual degradation (**Table 2, Row 20**). Regarding VOCs, this testing also showed that after 200 ozone cleaning cycles (each cycle simulating one night of use and then ozone cleaning), diethylene glycol (DEG) became detectable as a VOC in ISO 18562-3 testing. The VOC toxicological risk of this ozone-induced degradation is still being assessed, and this summary will be updated after results and conclusions are available.

Regarding risks associated with respirable and non-respirable particulates, testing to date has been performed on devices with known ozone exposure. For example, two Used first-generation DreamStation devices with user-reported ozone exposure and three additional Used devices with unknown ozone use (see **Table 2, Row 21**) were included in extractables and leachables testing, which formed the foundation for a toxicological risk assessment of Type A foam particulate. That third-party collective analysis concluded that exposure to particulate from degraded Type A foam in first-generation DreamStation devices is unlikely to result in an appreciable harm to health in patients.

V.A.2. Foam Level Testing

Biocompatibility testing of (degraded) PE-PUR foam according to ISO 10993 is relevant if (degraded) foam particulates can potentially reach the patient.

New foam (Type A) passed ISO 10993 irritation, sensitization, and Ames (genotoxicity) testing. For cytotoxicity, New foam passed the Agar diffusion test, and failed the MEM elution test. The difference in these cytotoxicity results is likely due to the different procedural aspects of both tests. For Agar diffusion the intact foam sample is applied directly to the surface of the agar with the cell culture, whereas for MEM elution, the foam sample is extracted in MEM solution, and then only the foam extract is tested on the cell culture. Per the ISO 10993 cytotoxicity standard, a further evaluation was conducted as discussed below in the chemical characterization and risk assessment section.

Lab-aged foam (Type A) failed ISO 10993 genotoxicity testing, and therefore a weight of evidence assessment was conducted to provide a confirmed conclusion on potential risks for patient under the expected usage. A preliminary non-exhaustive chemical characterization and toxicological risk assessment on Lab-aged foam indicated all detected compounds had MOSs > 1.0. To support the full toxicological risk assessment, additional chemical characterization as well as experiments to assess the probability and amount of degraded PE-PUR foam that can potentially reach the patient were conducted. Lab-aged foam passed ISO 10993 skin sensitization testing, and failed ISO 10993 skin irritation testing. Per the ISO 10993 irritation standard, a further toxicological analysis based on chemical was conducted as described below in the chemical characterization and risk assessment section.

Used foam was characterized with New foam and Lab-aged foam as described below in the chemical characterization and risk assessment section. ISO 10993-3 bioassays were not conducted on Used foam as each foam sample would contain uncontrolled environmental contamination such that the bioassay results would not be able to discriminate from PE-PUR foam associated degradation. Lastly, chemical characterization of Used foam does allow for

discrimination of PE-PUR foam degradation associated compounds for quantitative toxicological risk assessment.

Chemical Characterization and Risk Assessment

Further chemical characterization and risk assessment was performed per the ISO 10993 standard, based on the results described above. An extractables and leachables chemical characterization per ISO 10993-18: *Chemical characterization of medical device materials within a risk management process* was performed by a third-party laboratory to identify and quantify the chemicals that may be extracted from the PE-PUR foam (Type A) if contacted by patients. Specifically, foam was analyzed from six Used first generation DreamStation devices with visible foam degradation, including two devices with self-reported ozone use. New and Lab-aged foam (2 weeks or 4 weeks exposure to 90 °C and 95% RH) were also evaluated. A risk assessment per ISO 10993-17: *Establishment of allowable limits for leachable substances* was performed by a qualified third-party and included consideration of potential degradation products like TDI, TDA, DEG, and/or AA detected within the foam, and the associated potential risks including but not limited to sensitization, irritation, asthma, genotoxicity, carcinogenicity, liver toxicity, kidney toxicity, and reproductive toxicity.

As degraded Type A PE-PUR foam was considered as potentially genotoxic (by ISO 10933-3 bioassay testing of Lab-aged foam), a follow-up stepwise weight-of-evidence assessment per the ISO 10993-3 standard, was required including a chemical characterization and quantitative carcinogenicity risk assessment of Used and Lab-aged foam. Therefore, a third-party expert evaluated the carcinogenicity risk for each compound or groups of structurally similar compounds associated with foam degradation detected in both Used and Lab-aged foam samples per ISO 10993-17, -18 and US FDA (2018), including considerations on compounds unique to clinical conditions of use versus lab aging. The third-party expert concluded there was no appreciable carcinogenicity risk under clinical conditions of use.

The risk assessment conservatively assumed patient exposure to all of the degraded Type A PE-PUR foam within the device; however, it should be noted that the assumption of patient exposure to all of the degraded PE-PUR foam is not supported by testing to date on first-generation DreamStation devices. The results from that testing indicate that both small (less than 10 µm, see **Table 2, Rows 1, 2, 5, 14-17, 19, 20**) and larger (greater than 10 µm, see **Table 2, Rows 16, 17)** PE-PUR particle emission is observed to be minimal. Even with the conservative assumption of exposure to all degraded Type A PE-PUR foam within the device, the third-party risk assessment concluded that exposure to particulate from degraded Type A foam in DreamStation devices is unlikely to result in an appreciable harm to health in patients (**Table 2, Row 21**).

V.B. DreamStation Go

Testing includes VOC and PM testing on the entire device containing PE-PUR sound abatement foam, and the foam type is the same as first-generation DreamStation (Type A).

V.B.1. Device Level Testing
One New device passed VOC and PM testing. Further testing of DreamStation Go is ongoing.

V.B.2. Foam Level Testing
Please refer to the foam testing of first-generation DreamStation.

V.C. System One

Testing includes VOC and PM testing on the entire device containing PE-PUR sound abatement foam, and the foam type is the same as first-generation DreamStation (Type A).

V.C.1. Device Level Testing
One New device passed VOC testing. Four New, twenty Lab-aged, and seven Used devices passed PM testing. Further testing is ongoing.

V.C.2. Foam Level Testing
Please refer to the foam testing of first-generation DreamStation.

V.D. Trilogy 100/200
Testing includes VOC and PM testing on the entire device containing PE-PUR sound abatement foam, and investigational materials characterization of the foam. Trilogy 100/200 contains Type B PE-PUR foam.

V.D.1. Device Level Testing
Three New Trilogy devices tested according to standards available prior to the acceptance of ISO 18562 passed VOC and PM testing. Additionally, three New Trilogy devices passed ISO 18562-2 and ISO 18562-3 testing. Further testing of Trilogy is ongoing.

V.D.2. Foam Level Testing
Biocompatibility testing of (degraded) PE-PUR foam according to ISO 10993 is relevant if (degraded) foam particulates can potentially reach the patient. This testing is ongoing.

New foam (Type B) passed ISO 10993 cytotoxicity, irritation and sensitization testing. Preliminary foam material testing suggested that PE-PUR shows measurable degradation with exposure to high temperature and high humidity. New foam failed ISO 10993 genotoxicity testing, and therefore a weight of evidence assessment is ongoing to provide a confirmed conclusion on potential risks for patient under the expected usage. Similar to the analyses performed for Type A foam, additional chemical characterization as well as experiments to assess the probability and amount of degraded PE-PUR foam that can potentially reach the patient are being conducted to support the full toxicological risk assessment.

Lab-aged foam (Type B) failed ISO 10993 genotoxicity testing, and therefore a weight of evidence assessment is ongoing to provide a confirmed conclusion on potential risks for patient under the expected usage. Similar to the analyses performed for Type A foam, additional chemical characterization as well as experiments to assess the probability and amount of degraded PE-PUR foam that can potentially reach the patient are being conducted

to support the full toxicological risk assessment. Lab-aged foam passed ISO 10993 skin sensitization testing, and ISO 10993 skin irritation testing. Lab-aged foam failed ISO 10993 cytotoxicity testing. Per the ISO 10993 cytotoxicity standard, further evaluation is being conducted with an ongoing chemical characterization and risk assessment.

V.E. BiPAP A-Series and OmniLab

Testing includes VOC and PM testing on the entire device containing PE-PUR sound abatement foams. Each device contains foam Types A and B, one is the same as the PE-PUR foam in first-generation DreamStation (Type A) and another one is the same as PE-PUR foam in Trilogy (Type B).

V.E.1. Device Level Testing

One New A-series device passed VOC and three passed PM testing. One New OmniLab device and three Used OmniLab devices passed ISO 18562-3 testing with all detected VOCs having MOSs > 1.0. Further testing is ongoing.

V.E.2. Foam Level Testing

Please refer to the foam testing (Type A and Type B) described above for first-generation DreamStation and Trilogy 100/200. Further testing on Lab-aged and Used foam is still ongoing.

VI. Independent clinical analysis: Philips Respironics CPAP devices not associated with increased cancer risk

Philips Respironics engaged external scientific experts to perform an independent systematic literature review of epidemiological studies to evaluate whether use of Continuous or Bilevel Positive Airway Pressure (PAP) devices was associated with an increased risk of cancer in obstructive sleep apnea (OSA) patients. When investigating this question, it is important to note that OSA itself may increase the risk of cancer, as do risk factors for OSA such as aging, tobacco smoking, and obesity. Therefore, cancer risk would be compared between OSA patients with and without use of PAP devices, adjusting for relevant risk factors that differ between these groups.

In accordance with standard guidelines for systematic literature reviews, a search was conducted in PubMed, the U.S. National Library of Medicine's biomedical literature database, to identify studies of humans, published up to July 14, 2022, that compared the risk of overall and site-specific cancers between OSA patients using or not using PAP devices. After excluding non-human studies, studies of OSA patients not treated with PAP therapy, studies lacking a comparison group without PAP device use, and articles without original research data (e.g., reviews, commentaries, and letters), 13 relevant epidemiological studies were identified. The design, methods, and results of each study were evaluated for scientific rigor and risk of bias according to standard epidemiological considerations, as well as for their relevance to the topic of interest.

Based on these 13 epidemiological studies, no statistical increase in cancer risk due to use of PAP devices has been established, including the Philips Respironics PAP devices. Two rigorous, third-party studies showed no statistical difference in cancer risk between OSA patients who used Philips Respironics PAP devices versus other brands of PAP devices.[#] A third rigorous study showed no statistically significant difference in overall or site-specific cancer risk (prostate, colon, breast, lung, or other sites) between OSA patients with or without adherence to PAP therapy in general. The ten remaining epidemiological studies provided little additional insight into this question, but their results did not suggest an elevated risk of cancer associated with PAP use for OSA. Philips Respironics and external experts will continue to monitor newly published studies on this topic.

[#]*References:*

Philips Respironics PAP devices versus other brands of PAP devices

Kendzerska T, Leung RS, Boulos MI, et al. An association between positive airway pressure device manufacturer and incident cancer? a secondary data analysis. Am J Respir Crit Care Med 2021;204:1484-1488.

Justeau G, Gerves-Pinquie C, Jouvenot M, et al. Cancer risk in adherent users of polyurethane foam-containing CPAP devices for sleep apnoea. Eur Respir J 2022.

OSA patients with or without adherence to PAP therapy in general.

Justeau G, Bailly S, Gervès-Pinquié C, et al. Cancer risk in patients with sleep apnoea following adherent 5-year CPAP therapy. Eur Respir J 2022.

Table 2. List of Testing Results for First-generation DreamStation

Device	Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
First-generation DreamStation (Foam Type A)	**New Devices**					
	1	New [Entire Device]	4	Indoor Air Quality Evaluation for VOC and PM	Pass	All VOC emissions and particulates were below established limits. Testing conducted on standards available prior to ISO 18562.
	2	New [Entire Device]	16	PM (ISO 18562-2)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds.
	3	New [Entire Device]	14	VOCs (ISO 18562-3)	Pass	All detected VOCs had MOSs > 1.0.
	4	New [Entire Device]	1	VOCs (ISO 18562-3)	Pass	DD and phenol stabilizer were identified initially as compounds of potential concern; Follow up toxicological risk assessment on phenol stabilizer suggests no risk concern for adverse health effects in patients. Additional analysis on DD indicates DD was misidentified during initial characterization.
	5	New [Entire Device]	1	PM (ISO 18562-2) and VOCs (ISO 18562-3)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds. All detected VOCs had MOSs > 1.0.
	6	New [Foam A]	3 tests	ISO 10993-5: Agar diffusion ISO 10993-10: GPMT, skin irritation	Pass	Negative for cytotoxicity, sensitization, and skin irritation under laboratory conditions
	7	New [Foam A]	6 tests (3 pre-treatment conditions[c], 2 labs)	Genotoxicity test ISO 10993-3: Ames	Pass	Negative for genotoxicity under laboratory conditions
	8	New [Foam A]	1	Preliminary chemical characterization by ISO 18562-4/ISO 10993-18 (non-exhaustive)[b]	Pass	All detected compounds had MOSs > 1.0.

Device	Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
	9	New [Foam A]	3 tests	ISO 10993-5: MEM elution ISO 10993-10: GPMT, skin irritation	MEM Elution: Fail/AI GPMT: Pass Skin irritation: Pass	Positive for cytotoxicity under laboratory conditions.[d] Negative for skin sensitization under laboratory conditions. Negative for skin irritation under laboratory conditions. Associated toxicological risk assessment completed (see **Row 21**)
					Lab-Aged	
	10	Lab-Aged [Entire Device]	3 aging timepoints	VOCs (ISO 18562-3)[b]	Pass	All detected VOCs had MOSs > 1.0. Testing included devices with foam previously aged for 1 week, 2 weeks, or 3 weeks at 90°C and 95% relative humidity.
	11	Lab-Aged [Foam A]	24 tests (4 aging timepoints, 3 pre-treatment conditions[c], 2 labs)	Genotoxicity test ISO 10993-3: Ames	Fail/AI	Positive for genotoxicity under laboratory conditions for all foam aged at 90°C 95% RH for ≥2 weeks, and 1/6 foam samples aged at 90°C and 95% RH for 1 week. Associated toxicological risk assessment completed (see **Row 21**).
	12	Lab-Aged [Foam A]	3 aging timepoints	Preliminary chemical characterization by ISO 18562-4/ISO 10993-18 (non-exhaustive)[b]	Pass	All detected compounds had MOSs > 1.0 Testing included devices with blower box containing foam previously aged for 1 week, 2 weeks, or 3 weeks at 90°C and 95% RH.
	13	Lab-Aged [Foam A]	3 tests (2 aging timepoints)	ISO 10993-5: MEM elution ISO 10993-10: GPMT, skin irritation	MEM Elution: Fail/AI GPMT: Pass Skin irritation: Fail/AI	Positive for cytotoxicity under laboratory conditions for foam aged at 90°C 95% RH for 4 weeks. Foam aged at 2 weeks was negative for cytotoxicity under laboratory conditions. Negative for skin sensitization under laboratory conditions for all aging timepoints. Positive for skin irritation under laboratory conditions for all aging timepoints (2 and 4 weeks at 90°C 95% RH). Associated toxicological risk assessment completed (see **Row 21**).

Device	Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
	14	Lab-Aged [Entire Device]	12	PM (ISO 18562-2)[e]	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds. Testing included devices with foam previously aged for 4, 15, 28, 35, 40, or 46 days at 80°C and 75% relative humidity.
	15	Lab-Aged [Entire Device]	12	PM (ISO 18562-2)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds. Testing included devices with foam previously aged for 1, 2, 3, or 4 weeks at 90°C and 95% relative humidity.
				Used		
	16	Used [Entire Device]	5	PM (ISO 18562-2) and VOCs (ISO 18562-3)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds. All detected VOCs had MOSs > 1.0. Used devices were selected based on varying levels of degradation with four devices having visible degradation. Particulates emitted were also collected on a filter, and particulates greater than 20 µm were analyzed by FTIR. No particulates were found to be consistent with the Type A PE-PUR foam.
	17	Used [Entire Device]	16	PM (ISO 18562-2)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds for 16 devices.[f] Particulates emitted were also collected on a filter, and particulates greater than 20 µm were analyzed by FTIR. No particulates were found to be consistent with the Type A PE-PUR foam.
	18	Used [Entire Device]	60,847	Visual Inspection[g]	N/A	• Devices returned from patients were inspected for visual degradation. • Of 60,847 inspected devices from US & Canada, 1,105 devices showed significant visual degradation/volume reduction (~2%). • For devices not linked to a complaint that were inspected (60,425), approximately 2% (1,087) showed significant visual degradation/volume reduction. • For devices linked to a complaint that were inspected (422), approximately 4% (18) showed significant visual degradation/volume reduction. • Devices inspected for which the user self-reported ozone use were 14x more likely to have degradation than those without self-reported ozone use.

Device	Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
						• For 659 devices inspected at random, 13 showed significant visual degradation/volume reduction. Of the 13 devices, 11 had self-reported ozone use, and 2 had unknown ozone use. • An analysis of 2,469 first-generation DreamStation devices from Europe found one device with significant visual foam degradation/volume reduction (1 out of 2,469, or 0.04%), and an analysis of 1,964 first-generation DreamStation devices from Japan found no devices with significant visual foam degradation/volume reduction. • With degradation, the foam becomes hygroscopic (absorbs moisture) and sticky, loses significant volume and increases density as the structure becomes more like a liquid material, and can accumulate within the airpath inside the device (in the blower cavity prior to entering the blower, and within the blower itself). • Higher degradation risk exists with devices that have increased use; however, data to date suggests that there is not a direct correlation that would indicate degradation occurs after a certain amount of device use.
		Combined New, Lab-Aged and Used Device Experiments				
	19	Used [Entire Device] w/ New [Entire Device] for comparison	75 (Used) 41 (New)	Particulate matter (PM) testing in general accordance with ISO 18562-2[h]	Pass	PM_3 and PM_{10} below ISO 18562-2 thresholds for all 116 tested devices (41x New and 75x Used). PM_3 and PM_{10} of Used devices with degradation (8 total devices) were not statistically different than measured PM_3 and PM_{10} of Used devices without degradation (67 devices), suggesting that degradation did not contribute to appreciable elevated levels of respirable particles in the devices tested. When devices were classified based on cleanliness, average particulate counts in devices classified as 'dirty' were significantly greater than those classified as 'clean'.[i] Comparing the PM_3 and PM_{10} levels from New DS1 devices

Device	Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
						to Used devices with and without degradation did not show a statistically significant difference in probability distribution.
	20	New; Ozone Exposed [Entire Device]	115 total 3 New 84 with simulated use and ozone exposure 28 with simulated use but no ozone exposure	Simulated use was performed by turning a DS1 on for 1 hour, turning off, and then exposing to ozone per the manufacturer's instructions. This was considered one cycle, and the process was repeated (turning a DS1 device on, turning off, and exposing to ozone) for up to 500 cycles. For a control, DS1 devices were turned on for 1 hour, turned off, and then were kept off for the duration that the other devices were exposed to ozone. This was considered one cycle for the control devices. Testing included Visual inspection, pH, conductivity, FTIR, PM testing (ISO 18562-2), and VOC testing (ISO 18562-3)	Ozone induces degradation and DEG production	Differences in foam between devices exposed to ozone and those not exposed to ozone were detectable by pH, conductivity, and FTIR testing. There was no PM observed above the ISO 18562-2 limits for all samples tested (28 devices with simulated use and ozone exposure, and 14 devices with simulated use and without ozone exposure). Visual degradation occurred in ozone exposed devices between 150-300 cycles of simulated use/ozone exposure. By 200 cycles of simulated use and ozone exposure, DEG levels were first measurable by ISO 18562-3 testing. For all control samples (i.e., no ozone exposure): no visual degradation was observed. Additional analysis on these samples is ongoing.

Device	Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
	21	Used; New; Lab-Aged [Foam A]	6 Used devices [2 with user-reported ozone use, 3 with unknown ozone use, and 1 with user-reported no ozone use] New Lab-Aged [Condition 1: 2 weeks at 90°C 95% RH]; [Condition 2: 4 weeks at 90°C 95% RH]	Chemical Characterization by Extractables and Leachables and Toxicological Risk Assessment: ISO 10993-18 and ISO 10993-17	Pass	There was no detection of unbound 2,4-TDA in the Used foam (6 different devices) up to the limit of detection (<0.2 µg/g). **Primary conclusion** Overall, the various lines of scientific evidence collectively demonstrate that exposure to particulate from degraded Type A foam in DS1 devices is unlikely to result in an appreciable harm to health in patients.
	22	Used; New; Lab-Aged; [Foam A]	Multiple	The potential for TDI formation as an artifact of Gas Chromatography-Mass Spectrometry (GC-MS) was investigated. A calibration curve of an authentic 2,4-TDI reference standard was generated. Detection of TDI from foam extracts was detected as a function of GC-MS inlet temperature (180 °C, 210 °C, and 275 °C).	See conclusions	In the presence of isopropyl alcohol (IPA) or water, TDI reacts with IPA or water and is not observed as free TDI. TDI was confirmed as an artifact in Lab-Aged Type A PE-PUR extracts, resulting from GC-MS inlet temperatures of 210 °C and above. TDI is not expected to be free and present within a PE-PUR foam sample extract.

[a] For reports that did not directly calculate a MOS, if the detected concentration or calculated dose was acknowledged as below the associated tolerable limit that is considered equivalent to MOS > 1.0.

[b] Analytical data collection, chemical characterization, and/or VOC identification of 3 devices per aging timepoint (9 devices total) performed internally; toxicological risk assessment using averaged value of triplicate measurement provided by a qualified third party.

[c] Each aging condition tested one of three samples that were treated prior to aging as follows: (1) production equivalent foam/untreated, or (2) exposed to ozone, or (3) place in ventilated oven set at 60°C for a period of 24 hours prior to aging.

[d] For cytotoxicity, New foam passed the Agar diffusion test, and failed the MEM elution test. The difference in these cytotoxicity results is likely due to the different procedural aspects of both tests. For Agar diffusion the intact foam sample is applied directly to the surface of the agar with the cell culture, whereas for MEM elution, the foam sample is extracted in MEM solution, and then only the foam extract is tested on the cell culture. Per the ISO 10993 cytotoxicity standard, further evaluation was conducted with a chemical characterization and risk assessment (see **Row 21**).

[e] While the ISO18652-2 standard uses $PM_{2.5}$, the fixed size bin definition of the OPC was such that PM_3 is reported instead: Bin sizes of OPC: 0.3 – 0.5 – 1.0 – 3.0 – 5.0 – 10.0µm. For this analysis, PM_3 is considered to be comparable to $PM_{2.5}$.

[f] For one device, $PM_{2.5}$ was detected at 14 µg/m^3 for 0 -1 h and then detected <5 µg/m^3 for 1 – 4 h. Further analysis indicated the emission profile in its entirety would be compliant with US EPA 40 § CFR Part 50 (basis for ISO 18562-2:2017 allowable limits). ISO 18562-2:2017 allowable limits are based on the US EPA National Ambient Air Quality Standards (NAAQS; 40 CFR § 50.18). The ISO 18562-2:2017 $PM_{2.5}$ allowable limit for $PM_{2.5}$ is 12 µg/m^3 is based on a three-year annual average limit. The NAAQS also provide a 24-hr average limit for $PM_{2.5}$ of 35 µg/m^3.

[g] Visual inspection performed internally.

[h] Testing was performed at 75 LPM, however the optical particle counter (OPC) sampled at 28.3 LPM, such that a correction factor was applied for the non-isokinetic flow and for the funneling effect based on the sampling nozzle shape of the OPC. While the ISO18652-2 standard uses $PM_{2.5}$, the fixed size bin definition of the OPC was such that PM_3 is reported instead: Bin sizes of OPC: 0.3 – 0.5 – 1.0 – 3.0 – 5.0 – 10.0µm. For this analysis, PM_3 is considered to be comparable to $PM_{2.5}$. The device was positioned vertically with the output flow of the DS1 above the optical particle counter funnel-shaped nozzle. Testing was performed internally.

[i] Cleanliness does not refer to foam degradation. This is a general observation based in part on the presence of environmental materials on the external surface of the device, such as the inlet filter location.

Table 3. List of Testing Results for DreamStation Go

Device	Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
DreamStation Go (Foam Type A)				**New**		
	1	New [Entire Device]	1	Indoor Air Quality Evaluation for VOC and PM	Pass	All VOC emissions and particulates were below established limits. Testing conducted on standards available prior to ISO 18562.
	2	New [Foam A][e]	3 tests	ISO 10993-5: Agar diffusion ISO 10993-10: GPMT, skin irritation	Pass	Negative for cytotoxicity, sensitization, and skin irritation under laboratory conditions
	3	New [Foam A] [e]	6 tests (3 pre-treatment conditions[b], 2 labs)	Genotoxicity test ISO 10993-3: Ames	Pass	Negative for genotoxicity under laboratory conditions
	4	New [Foam A] [e]	1	Preliminary chemical characterization by ISO 18562-4/ISO 10993-18 (non-exhaustive)[c]	Pass	All detected compounds had MOSs > 1.0
	5	New [Foam A] [e]	3 tests	ISO 10993-5: MEM elution ISO 10993-10: GPMT, skin irritation	MEM Elution: Fail/AI GPMT: Pass Skin irritation: Pass	Positive for cytotoxicity under laboratory conditions.[d] Negative for skin sensitization under laboratory conditions. Negative for skin irritation under laboratory conditions.
				Lab-Aged		

Device	Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
	6	Lab-Aged [Foam A] [e]	24 tests (4 aging timepoints, 3 pre-treatment conditions[b], 2 labs)	Genotoxicity test ISO 10993-3: Ames	Fail/AI	Positive for genotoxicity under laboratory conditions for all foam aged at 90°C and 95% RH for ≥2 weeks, and 1/6 foam samples aged at 90°C and 95% RH for 1 week. Associated toxicological risk assessment **ongoing**[f]
	7	Lab-Aged [Foam A] [e]	3 aging timepoints	Preliminary chemical characterization by ISO 18562-4/ISO 10993-18 (non-exhaustive)[d]	Pass	All detected compounds had MOSs > 1.0 Testing included devices with blower box containing foam previously aged for 1 week, 2 weeks, or 3 weeks at 90°C and 95% RH.
	8	Lab-Aged [Foam A] [e]	3 tests (2 aging timepoints)	ISO 10993-5: MEM elution ISO 10993-10: GPMT, skin irritation	MEM Elution: Fail/AI GPMT: Pass Skin irritation: Fail/AI	Positive for cytotoxicity under laboratory conditions for foam aged at 90°C 95% RH for 4 weeks. Foam aged at 2 weeks was negative for cytotoxicity under laboratory conditions. Negative for skin sensitization under laboratory conditions for all aging timepoints. Positive for skin irritation under laboratory conditions for all aging timepoints (2 and 4 weeks at 90°C 95% RH). Associated toxicological risk assessment **ongoing**.[g]

[a] For reports that did not directly calculate a MOS, if the detected concentration or calculated dose was acknowledged as below the associated tolerable limit that is considered equivalent to MOS > 1.0.

[b] Each aging condition tested one of three samples that were treated prior to aging as follows: (1) production equivalent foam untreated, or (2) exposed to ozone, or (3) place in ventilated oven set at 60°C for a period of 24 hours prior to aging.

[c] Analytical data collection, chemical characterization, and/or VOC identification performed internally; toxicological risk assessment provided by a qualified third party.

[d] For cytotoxicity, New foam passed the Agar diffusion test, and failed the MEM elution test. The difference in these cytotoxicity results is likely due to the different procedural aspects of both tests. For Agar diffusion the intact foam sample is applied directly to the surface of the agar with the cell culture, whereas for MEM elution, the foam sample is extracted in MEM solution, and then only the foam extract is tested on the cell culture. Per the ISO 10993 cytotoxicity standard, further evaluation is being conducted with an ongoing chemical characterization and risk assessment.

[e] Foam Type A testing reported in this table is also reported in Table 2.
[f] Per the ISO 10993-3 standard, a positive result triggers a follow-up evaluation including identification of potential confounding factors, and a weight of evidence assessment to provide a confirmed conclusion on potential risks for patient under the expected usage. This is currently ongoing.
[g] The ISO 10993 MEM elution, skin sensitization, and skin irritation tests only provide an indication of potential toxicity and cannot necessarily be determined to assess biocompatibility for a given clinical application. As these test results cannot standalone per the ISO 10993 standard, there is an ongoing toxicological risk assessment to determine if there is an appreciable health risk to patients.

Table 4. List of Testing Results for Trilogy

Device	Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information
Trilogy 100/200 (Foam Type B)				**New**		
	1	New [Entire Device]	3	Indoor Air Quality Evaluation for VOC and PM	Pass	All VOC emissions and particulates were below established limits. Testing conducted on standards available prior to ISO 18562.
	2	New [Foam B][c]	3 tests	ISO 10993-5: Elution test ISO 10993-10: GPMT, skin irritation	Pass	Negative for cytotoxicity, sensitization, and skin irritation under laboratory conditions
	3	New [Entire Device]	3	PM (ISO 18562-2) and VOCs (ISO 18562-3)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds. All detected VOCs had MOSs > 1.0.
	4	New [Foam B][b]	1 test	Genotoxicity test ISO 10993-3: Ames	Fail/AI	Positive for genotoxicity under laboratory conditions. Associated toxicological risk assessment **ongoing.**[d]
	5	New [Foam B]	3 tests	ISO 10993-5: Elution test ISO 10993-10: GPMT, skin irritation	Pass	Negative for cytotoxicity,[b,c] sensitization, [b] and skin irritation[b,c] under laboratory conditions.
				Lab-Aged		
	6	Lab-Aged [Foam B][b]	4 tests (4 aging conditions)	Genotoxicity test ISO 10993-3: Ames	Fail/AI	Positive for genotoxicity under laboratory conditions for foam aged at 80°C and 75% RH for 1, 2, 3, and 4- weeks. Associated toxicological risk assessment **ongoing.**[d]
	7	Lab-Aged [Foam B][b]	4 tests (4 aging timepoints)	ISO 10993-5: MEM elution ISO 10993-10: GPMT, skin irritation	MEM Elution: Fail/AI GPMT: Pass Skin irritation: Pass	Positive for cytotoxicity under laboratory conditions for foam aged at 80°C 75% RH for 1- and 3- weeks. Foam aged at 2 and 4 weeks was negative for cytotoxicity under laboratory conditions. Negative for skin sensitization under laboratory conditions for all aging timepoints. Negative for skin irritation under laboratory conditions for all aging timepoints. Associated toxicological risk assessment **ongoing**.[e]

Combined New, Lab-Aged and Used Device Experiments					
8	New, Lab-Aged and Used [Foam B]	4 tests/various conditions	pH, conductivity, FTIR, DSC[a]	N/A	PE-PUR foam shows measurable degradation with exposure to high temperature and high humidity. Testing included foam previously aged for 1, 4, 7, 11 or 14 days at 90°C and 100% RH, as well as 2 Used/returned customer complaint foams

[a] Analytical data collection performed internally.
[b] Foam Type B without adhesive
[c] Foam Type B with adhesive
[d] Per the ISO 10993-3 standard, a positive result triggers a follow-up evaluation including identification of potential confounding factors, and a weight of evidence assessment to provide a confirmed conclusion on potential risks for patient under the expected usage. This is currently ongoing.
[e] The ISO 10993 MEM elution, skin sensitization, and skin irritation tests only provide an indication of potential toxicity and cannot necessarily be determined to assess biocompatibility for a given clinical application. As these test results cannot standalone per the ISO 10993 standard, there is an ongoing toxicological risk assessment to determine if there is an appreciable health risk to patients.

Table 5. List of Testing Results for BiPAP A30/A40/V30 and OmniLab

Device	Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
BiPAP A30/A40/V30; OmniLab (Foam Types A and B)				**New**		
	1	New [Entire Device]	1	Indoor Air Quality Evaluation for VOC and PM	Pass	All VOC emissions and particulates were below established limits. Testing conducted on standards available prior to ISO 18562.
		New [Entire Device]	3	PM (ISO 18562-2)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds.
	2	New [Foam A] [f]	3 tests	ISO 10993-5: Agar diffusion ISO 10993-10: GPMT, skin irritation	Pass	Negative for cytotoxicity, sensitization, and skin irritation under laboratory conditions
	3	New [Foam B] [f]	3 tests	ISO 10993-5: Elution test ISO 10993-10: GPMT, skin irritation	Pass	Negative for cytotoxicity, sensitization, and skin irritation under laboratory conditions
	4	New [Foam A] [f]	6 tests (3 pre-treatment conditions[b], 2 labs)	Genotoxicity test ISO 10993-3: Ames	Pass	Negative for genotoxicity under laboratory conditions
	5	New [Foam A] [f]	1	Preliminary chemical characterization by ISO 18562-4/ISO 10993-18 (non-exhaustive)[e]	Pass	All detected compounds had MOSs > 1.0
	6	New [Entire Device]	1	VOCs (ISO 18562-3)	Pass	All detected VOCs had MOSs > 1.0[h]
	7	New [Foam A] [f]	3 tests	ISO 10993-5: MEM elution ISO 10993-10: GPMT, skin irritation	MEM Elution: Fail/AI GPMT: Pass	Positive for cytotoxicity under laboratory conditions.[c] Negative for skin sensitization under laboratory conditions. Negative for skin irritation under laboratory conditions.

Device	Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
					Skin irritation: Pass	
	8	New [Foam B][f]	1 test	Genotoxicity test ISO 10993-3: Ames	Fail/AI	Positive for genotoxicity under laboratory conditions. Associated toxicological risk assessment **ongoing**[d]
					Lab-Aged	
	9	Lab-Aged [Foam A][f]	24 tests (4 aging timepoints, 3 pre-treatment conditions[b], 2 labs)	Genotoxicity test ISO 10993-3: Ames	Fail/AI	Positive for genotoxicity under laboratory conditions for all foam aged at 90°C and 95% RH for ≥2 weeks, and 1/6 foam samples aged at 90°C and 95% RH for 1 week. Associated toxicological risk assessment **ongoing**[d]
	10	Lab-Aged [Foam A][f]	3 aging timepoints	Preliminary chemical characterization by ISO 18562-4/ISO 10993-18 (non-exhaustive)[e]	Pass	All detected compounds had MOSs > 1.0 Testing included devices with blower box containing foam previously aged for 1 week, 2 weeks, or 3 weeks at 90°C and 95% RH.
	11	Lab-Aged [Foam A][f]	3 tests (2 aging timepoints)	ISO 10993-5: MEM elution ISO 10993-10: GPMT, skin irritation	MEM Elution: Fail/AI GPMT: Pass Skin irritation: Fail/AI	Positive for cytotoxicity under laboratory conditions for foam aged at 90°C 95% RH for 4 weeks. Foam aged at 2 weeks was negative for cytotoxicity under laboratory conditions. Negative for skin sensitization under laboratory conditions for all aging timepoints. Positive for skin irritation under laboratory conditions for all aging timepoints (2 and 4 weeks at 90°C 95% RH). Associated toxicological risk assessment **ongoing**.[g]
	12	Lab-Aged [Foam B][f]	4 tests (4 aging conditions)	Genotoxicity test ISO 10993-3: Ames	Fail/AI	Positive for genotoxicity under laboratory conditions for foam aged at 80°C and 75% RH for 1, 2, 3, and 4- weeks. Associated toxicological risk assessment **ongoing.**[d]
	13	Lab-Aged [Foam B][f]	4 tests (4 aging timepoints)	ISO 10993-5: MEM elution ISO 10993-10: GPMT, skin irritation	MEM Elution: Fail/AI GPMT: Pass	Positive for cytotoxicity under laboratory conditions for foam aged at 80°C 75% RH for 1- and 3- weeks. Foam aged at 2 weeks was negative for cytotoxicity under laboratory conditions. Negative for skin sensitization under laboratory conditions for all aging timepoints.

Device	Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
					Skin irritation: Pass	Negative for skin irritation under laboratory conditions for all aging timepoints. Associated toxicological risk assessment **ongoing**.[g]
				Used		
	14	Used [Entire Device]	3	VOCs (ISO 18562-3)	Pass	All detected VOCs had MOSs > 1.0[h]
				Combined New, Lab-Aged and Used Device Experiments		
	15	New, Lab-Aged and Used [Foam B] [f]	4 tests/various conditions	pH, conductivity, FTIR, DSC[i]	N/A	PE-PUR foam shows measurable degradation with exposure to high temperature and high humidity. Testing included foam previously aged for 1, 4, 7, 11 or 14 days at 90°C and 100% RH, as well as 2 used/returned customer complaint foams

[a] For reports that did not directly calculate a MOS, if the detected concentration or calculated dose was acknowledged as below the associated tolerable limit that is considered equivalent to MOS > 1.0

[b] Each aging condition tested one of three samples that were treated prior to aging as follows: (1) production equivalent foam untreated, or (2) exposed to ozone, or (3) place in ventilated oven set at 60°C for a period of 24 hours prior to aging.

[c] For cytotoxicity, New foam passed the Agar diffusion test, and failed the MEM elution test. The difference in these cytotoxicity results is likely due to the different procedural aspects of both tests. For Agar diffusion the intact foam sample is applied directly to the surface of the agar with the cell culture, whereas for MEM elution, the foam sample is extracted in MEM solution, and then only the foam extract is tested on the cell culture. Per the ISO 10993 cytotoxicity standard, further evaluation is being conducted with an ongoing chemical characterization and risk assessment.

[d] Per the ISO 10993-3 standard, a positive result triggers a follow-up evaluation including identification of potential confounding factors, and a weight of evidence assessment to provide a confirmed conclusion on potential risks for patient under the expected usage. This is currently ongoing.

[e] Analytical data collection, chemical characterization, and/or VOC identification performed internally; toxicological risk assessment provided by a qualified third party.

[f] Foam Type A and B testing reported in this table is also reported in Tables 2 and 4 respectively.

[g] The ISO 10993 MEM elution, skin sensitization, and skin irritation tests only provide an indication of potential toxicity and cannot necessarily be determined to assess biocompatibility for a given clinical application. As these test results cannot standalone per the ISO 10993 standard, there is an ongoing toxicological risk assessment to determine if there is an appreciable health risk to patients.

[h] Devices were OmniLab with a selected test duration of 16 hours based on device use duration.

[i] Analytical data collection performed internally.

Table 6. List of Testing Results for SystemOne, Dorma, REMstar, C-series BiPAP

Device	Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
SystemOne; Dorma; REMstar; C-series BiPAP (Foam Type A)				**New**		
	1	New [Entire Device]	1	Indoor Air Quality Evaluation for VOC and PM	Pass	All VOC emissions and particulates were below established limits. Testing conducted on standards available prior to ISO 18562.
		New [Entire Device]	3	PM (ISO 18562-2)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds.
	2	New [Foam A][e]	3 tests	ISO 10993-5: Agar diffusion ISO 10993-10: GPMT, skin irritation	Pass	Negative for cytotoxicity, sensitization, and skin irritation under laboratory conditions
	3	New [Foam A][e]	6 tests (3 pre-treatment conditions[b], 2 labs)	Genotoxicity test ISO 10993-3: Ames	Pass	Negative for genotoxicity under laboratory conditions
	4	New [Foam A][e]	1	Preliminary chemical characterization by ISO 18562-4/ISO 10993-18 (non-exhaustive)[c]	Pass	All detected compounds had MOSs > 1.0
	5	New [Foam A][e]	3 tests	ISO 10993-5: MEM elution ISO 10993-10: GPMT, skin irritation	MEM Elution: Fail/AI GPMT: Pass Skin irritation: Pass	Positive for cytotoxicity under laboratory conditions.[d] Negative for skin sensitization under laboratory conditions. Negative for skin irritation under laboratory conditions.
				Lab-Aged		

Device	Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
	6	Lab-Aged [Foam A] [e]	24 tests (4 aging timepoints, 3 pre-treatment conditions[b], 2 labs)	Genotoxicity test ISO 10993-3: Ames	Fail/AI	Positive for genotoxicity under laboratory conditions for all foam aged at 90°C and 95% RH for ≥2 weeks, and 1/6 foam samples aged at 90°C and 95% RH for 1 week. Associated toxicological risk assessment **ongoing**[f]
	7	Lab-Aged [Foam A] [e]	3 aging timepoints	Preliminary chemical characterization by ISO 18562-4/ISO 10993-18 (non-exhaustive)[d]	Pass	All detected compounds had MOSs > 1.0 Testing included devices with blower box containing foam previously aged for 1 week, 2 weeks, or 3 weeks at 90°C and 95% RH.
	8	Lab-Aged [Foam A] [e]	3 tests (2 aging timepoints)	ISO 10993-5: MEM elution ISO 10993-10: GPMT, skin irritation	MEM Elution: Fail/AI GPMT: Pass Skin irritation: Fail/AI	Positive for cytotoxicity under laboratory conditions for foam aged at 90°C 95% RH for 4 weeks. Foam aged at 2 weeks was negative for cytotoxicity under laboratory conditions. Negative for skin sensitization under laboratory conditions for all aging timepoints. Positive for skin irritation under laboratory conditions for all aging timepoints (2 and 4 weeks at 90°C 95% RH). Associated toxicological risk assessment **ongoing**.[g]
	9	Lab-Aged [Entire Device]	20 devices (7 aging timepoints)	PM (ISO 18562-2)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds Testing included devices with foam previously aged for 11 (2 devices), 21 (3 devices), 28 (3 devices), 35 (3 devices), 42 (3 devices), 49 (3 devices), and 56 days (3 devices) at 80°C and 75% relative humidity.
		Used				
	10	Used [Entire Device]	7 devices	PM (ISO 18562-2)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds.

[a] For reports that did not directly calculate a MOS, if the detected concentration or calculated dose was acknowledged as below the associated tolerable limit that is considered equivalent to MOS > 1.0

[b] Each aging condition tested one of three samples that were treated prior to aging as follows: (1) production equivalent foam untreated, or (2) exposed to ozone, or (3) place in ventilated oven set at 60°C for a period of 24 hours prior to aging.

[c] Analytical data collection, chemical characterization, and/or VOC identification performed internally; toxicological risk assessment provided by a qualified third party.

[d] For cytotoxicity, New foam passed the Agar diffusion test, and failed the MEM elution test. The difference in these cytotoxicity results is likely due to the different procedural aspects of both tests. For Agar diffusion the intact foam sample is applied directly to the surface of the agar with the cell culture, whereas for MEM elution, the foam sample is extracted in MEM solution, and then only the foam extract is tested on the cell culture. Per the ISO 10993 cytotoxicity standard, further evaluation is being conducted with an ongoing chemical characterization and risk assessment.

[e] Foam Type A testing reported in this table is also reported in Table 2.

[f] Per the ISO 10993-3 standard, a positive result triggers a follow-up evaluation including identification of potential confounding factors, and a weight of evidence assessment to provide a confirmed conclusion on potential risks for patient under the expected usage. This is currently ongoing.

[g] The ISO 10993 MEM elution, skin sensitization, and skin irritation tests are for screening hazard identification, and do not determine the risk of that hazard occurring in a patient via the relevant route(s) of exposure. An ongoing toxicological risk assessment is being conducted to determine if there is an appreciable health risk to patients.

Table 7. Sound abatement foam type per device

Devices grouped by device air path design	Foam Type	Foam Material	Foam Density (g/mL)	Percentage of Registered Devices
Dreamstation CPAP, BiPAP, AutoPAP Dreamstation ASV Dreamstation ST, AVAPS E30	**A**	PE-PUR	0.06	68%
DreamStation Go CPAP, AutoPAP	**A**	PE-PUR	0.06	1%
SystemOne 60-Series SystemOne 50-series SystemOne ASV4 C-series S/T, AVAPS Dorma 400, 500 CPAP, Auto CPAP (not marketed in US)	**A**	PE-PUR	0.06	26%
Trilogy 100 Trilogy 200 Garbin Plus, Aeris, LifeVent Ventilator (not marketed in US)	**B**	PE-PUR	0.03	3%
A-Series BiPAP V30 Auto Ventilator A-Series BiPAP Hybrid A30 (not marketed in US) A-Series BiPAP A30 (not marketed in US) A-Series BiPAP A40 (not marketed in US) OmniLab Advanced Plus	**A and B**	PE-PUR for both	0.06 0.03	2%

The total amount of foam in the devices varies from 1 g to 10 g, depending on the device airpath design and configuration. As indicated in **Table 7** above, there are two main types of PE-PUR foam used in the recalled devices – referred to as "Type A" and "Type B." The known differences

between the Type A and Type B foams are that Type B foam can be used with an acrylic pressure sensitive adhesive, has a lower density, has a different thickness, and also contains an additive to reduce potential flammability.

Table 8. Acronyms and Abbreviations

AI	Additional Information
°C	Celsius
CFR	Code of Federal Regulations
DD	Dimethyl diazene
DSC	Differential Scanning Calorimetry
EPA	U.S. Environmental Protection Agency
FDA	U.S. Food and Drug Administration
FTIR	Fourier Transform Infrared Spectroscopy
GC-MS	Gas Chromatography-Mass Spectrometry
GPMT	Guinea Pig Maximization Test
HHE	Health Hazard Evaluation
In vitro	Experimental studies conducted in biological material, e.g. cells in a test tube, outside the body
In vivo	Experimental studies conducted in animal model
ISO	International Organization for Standardization
MOS	Margin of Safety
PE-PUR	Polyester-Polyurethane
Phenol Stabilizer	Phenol, 2,6-bis(1,1-dimethylethyl)-4-(1-methylpropyl)
PM	Particulate Matter
$PM_{2.5}$	Particulate Matter with a diameter of 2.5 micrometers or less
PM_{10}	Particulate Matter with a diameter of 10 micrometers or less
RH	Relative Humidity
VOC	Volatile Organic Compounds
Wks	Weeks
MEM	Minimum essential medium
GPMT	Guinea pig maximization test
$\mu g/m^3$	Micrograms per cubic meter
LPM	Liters per minute