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

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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 platforms by their air path design, as set forth in **Tables 1 and 2**, 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 System One foam (See **Section II** for a description of Used and Lab-Aged conditions).

The results were subsequently extrapolated across all device platforms, 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 VOCs. 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. Summaries of the testing results and third-party confirmed conclusions available for the five device platforms are provided in **Tables 1 and 2** below, as grouped by devices containing only Type A PE-PUR foam (**Table 1**: first-generation DreamStation, DreamStation Go, and System One) or devices containing Type B PE-PUR foam (**Table 2**: Trilogy 100/200, A-Series).

Table 1. Summary of Testing Results for Devices Containing Only Type A Foam.

Devices grouped by device air path design	PE-PUR Foam Type	Percentage of Registered Recalled Devices	Device Level Evaluation		Foam Level Evaluation	Third-Party Risk Conclusions	Underlying Results
			VOC risks: # of Devices/Foams	Particulate exposure risks: # of Devices/Foams	Particulate Hazard Analysis		
DreamStation (DS1) DreamStation CPAP, BiPAP, Auto CPAP DreamStation ASV DreamStation ST, AVAPS E30	A*	68%	New – 20 devices Used – 21 devices Lab-Aged – 33 devices Ozone Treated – 9 devices	New – 63 devices Used – 96 devices Lab-Aged – 24 devices Ozone treated – 28 devices	Foam Level Testing is applicable to all devices containing Type A foam and was considered in the overall Risk Assessments for each of the three device platforms containing only Type A foam. Chemical Characterization and Toxicological Risk Assessment per ISO 10993-18 and ISO 10993-17 New, Used (foam from 7 devices)#, Lab-Aged Genotoxicity, Cytotoxicity, Sensitization, and Irritation per ISO 10993-3, ISO 10993-5, and ISO 10993-10 New, Lab-Aged	**Potential patient exposure to foam particulates and VOCs from Type A foam within the breathing gas pathway of first-generation DreamStation, DreamStation Go, and System One is unlikely to result in an appreciable harm to health in patients.**	**Section V.A.; Table 5**
DreamStation Go (DS Go) DreamStation Go CPAP, APAP, Auto CPAP	A*	1%	New – 4 devices Lab-Aged – 3 devices	New – 8 devices Lab-Aged – 6 devices			**Section V.B.; Table 6**
System One System One 60-Series System One 50-series System One ASV4 C-Series ASV C-series S/T, AVAPS System One (Q-series) REMstar SE Auto Dorma 400, 500 CPAP, Auto CPAP (not marketed in US)	A*	26%	New – 7 devices Used – 7 devices Lab-Aged – 20 devices Ozone Treated – 5 devices	New – 7 devices Used – 7 devices Lab-Aged – 20 devices Ozone Treated – 5 devices			**Section V.C.; Table 7**

*The total amount of foam in the devices varies from approximately 1 g to 10 g, depending on the device airpath design and configuration. Devices within each platform share the same airpath design and configuration, including the amount of foam present.
#The foam from 7 different Used DS1 devices was chemically characterized per ISO 10993-18 and -17 and included foam representative of a range of visual degradation states.

Table 2. Summary of Testing Results for Devices Containing Type B Foam.^

Devices grouped by device air path design	PE-PUR Foam Type	Percentage of Registered Recalled Devices	Device Level Evaluation		Foam Level Evaluation	Third-Party Risk Conclusions	Underlying Results
			VOC risks: # of Devices/Foams	Particulate exposure risks: # of Devices/Foams	Particulate Hazard Analysis		
Trilogy 100/200 **Trilogy 100** **Trilogy 200** Garbin Plus, Aeris, LifeVent Ventilator (not marketed in US)	B*	3%	New – 6 devices	New – 9 devices Lab-Aged – 12 devices	Foam Level Testing is applicable to all devices containing Type B foam and will be considered in the overall Risk Assessments for each device platform containing Type B foam. Genotoxicity, Cytotoxicity, Sensitization, and Irritation per ISO 10993-3, ISO 10993-5, and ISO 10993-10 New, Lab-Aged	**No overall risk conclusion is available at this time.**	**Section VI.A.; Table 8**
A-Series A-Series BiPAP V30 Auto Ventilator A-Series BiPAP Hybrid OmniLab Advanced Plus A30 (not marketed in US) A-Series BiPAP A30 (not marketed in US) A-Series BiPAP A40 (not marketed in US)	A* and B*	2%	New – 2 devices Used – 3 devices	New – 7 devices Lab-Aged – 21 devices		**No overall risk conclusion is available at this time.**	**Section VI.B.; Table 9**

^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.

*The total amount of foam in the devices varies from approximately 3 g to 7 g, depending on the device airpath design and configuration. Devices within each platform share the same airpath design and configuration, including the amount of foam present.

As described in **Table 1** above and referenced in the testing results hereafter, comprehensive third-party risk assessments have concluded that potential patient exposure to foam particulates and VOCs from Type A foam within the breathing gas pathway of first-generation DreamStation, DreamStation Go, and System One device platforms is unlikely to result in an appreciable harm to health in patients. These risk assessments characterized the chemicals present in degraded foam and included conservative exposure assumptions, including that all Type A foam in a device (i.e., 100% of the foam in the device) could become severely degraded, emitted from the device, and reach a patient. These assumptions are conservative and protective as visual inspection data has indicated the prevalence of significant visual foam degradation/volume reduction to be limited (See **Section V.A. and V.C.**).

Regarding device platforms that contain Type B PE-PUR foam (Trilogy 100/200 and A-Series), testing is ongoing and comprehensive third-party risk assessments are not yet available.

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 into five device platforms (see **Tables 5-9**). Within each device platform, 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 quantitative risk assessment calculations described for first-generation DreamStation (**Table 5**, **Row 24**), DreamStation Go (**Table 6**, **Row 11**), or System One (**Table 7**, **Row 13**) platforms.

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.

Risk assessments on devices containing only Type A foam (first-generation DreamStation, DreamStation Go, and System One device platforms) are complete. Risk assessments on devices containing Type B foam remain ongoing. Like the assessments completed on devices containing Type A foam, the results of testing on devices containing Type B Foam 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.

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 are 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 US 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 ISO 10993-17. 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. These assessments are complete for device platforms containing only Type A PE-PUR foam (i.e., first-generation DreamStation, DreamStation Go, and System One), but additional assessments are ongoing for device platforms containing Type B PE-PUR foam (i.e., Trilogy 100/200 and A-Series).

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), risk assessments are based on custom testing and application of conservative assumptions. 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 5, Rows**

16 and 17). For conservative assumptions, a risk assessment completed on Type A foam included the assumption that all 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 Used 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.**). Similarly, an inspection of 2,923 Used System One devices identified significant visual foam degradation/volume reduction in a limited number of devices (8%), with the majority of foam present even in those devices with significant visual foam degradation/volume reduction (See **Section V.C.**).

II.B. Foam Level and Additional Device Level Testing

Additional testing was/is being performed in accordance with ISO 10993 (Biological evaluation of medical devices) to facilitate a toxicological risk assessment. This testing includes: *in vitro* assessment (i.e., tests performed in a test tube, dish, etc. outside the body), *in vivo* assessment (i.e., animal testing), and chemical characterization (i.e., what chemicals may potentially extract or leach from the foam and have direct contact with body tissues and/or fluids) 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. While risk assessments are complete for Type A PE-PUR foam, additional testing is still ongoing or planned for Type B foam, including testing on New, Lab-Aged, and Used foam; and device level testing for Trilogy 100/200, and OmniLab/A-Series devices.

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. Per ISO 10993, a non-passing test triggers a required follow-up evaluation including identification of potential confounding factors, and chemical characterization and toxicological risk assessement per ISO 10993 Part 17: Establishment of allowable limits for leachable substances, and Part 18: Chemical characterization of medical device materials within a risk management process.

This chemical evaluation of New, Used, and Lab-Aged Type A PE-PUR foam was conducted by identifying and quantifying chemicals that may be extracted or leached from the Type A PE-PUR foam. The worst-case estimate of daily exposure was informed by experiments to assess the amount of Type A 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 was then 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 Type A PE-PUR foam, the worst-case estimate of daily exposure was 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 was presented as a Margin of Safety (MOS) factor with an MOS value greater than 1.0, indicating the compound's worst-case estimate was below the compound's tolerable intake, and therefore suggests no appreciable harm to health. A third-party chemical evaluation and toxicological risk assessment is complete for Type A foam in first-generation DreamStation (DS1) devices (see **Table 5, Row 24**), DreamStation Go devices (see **Table 6**, **Row 11**), and System One devices (see **Table 7**, **Row 13**), but ongoing for Type B foam.

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 Type A and B foam.

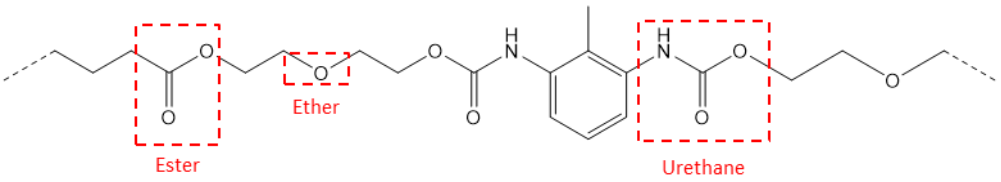

Figure 1: Chemical structure of the main building block of the PE-PUR foam (Types A and B).

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) 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.

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 5, Row 23**) 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 7 Used devices, including devices with

severe foam degradation, did not detect TDA in the Used foam extract (See **Table 5, Row 22**).
- 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.

Note that for Type A foam, these chemicals have not been detected in Used devices at levels exceeding toxicological thresholds as determined by the ISO 18562 and ISO 10993 standards, and risk assessments have been completed for first-generation DreamStation devices (see **Table 5, Row 24**), DreamStation Go devices (see **Table 6**, **Row 11**), and System One devices (see **Table 7**, **Row 13**). For Type B foam, testing of Used devices according to ISO 18562 and ISO 10993 standards is ongoing.

IV. General Testing Limitations Considered During Risk Assessments

Healthcare providers and patients are advised that certain limitations exist regarding the current results presented and described in more detail below. These limitations were considered for Type A foam toxicological risk assessments and are still being considered with ongoing and planned testing and evaluations for Type B foam.

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 considered 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 VOCs and/or 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 has addressed it through further testing and analyses per ISO 10993-1: 2018 and US FDA guidance (2020). 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 consultation with third-party subject matter experts, custom testing, and application of conservative assumptions, including the assumption for third-party risk assessments completed on devices containing only Type A foam that all foam in the device could become degraded and contact the patient. This assumption is known to be conservative and protective since visual inspection 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.**). Similarly, an inspection of 2,923 Used System One devices identified significant visual foam degradation/volume reduction in a limited number of devices (8%), with the majority of foam present even in those devices with significant visual foam degradation/volume reduction (See **Section V.C.**).

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.**). 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 considered in the third-party risk assessments include the number of Used devices that have finished testing. For example, 21 Used first-generation DreamStation devices were selected for testing (refer to **Table 5**) based on the devices exhibiting varying degrees of visibly degraded PE-PUR foam, and based on visual inspection to date (see **Section V.A.**), 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. The VOCs measured in these devices suggested no appreciable harm to health, and based on the varying degrees of degradation and usage of the devices selected for testing, amongst other factors, a third-party risk assessment determined that potential exposure to VOCs from Type A foam in first-generation DreamStation devices is unlikely to result in an appreciable harm to health in patients (**Table 5**, **Row 24**). Additional data collected for DreamStation Go (**Table 6**, **Row 11**) and System One (**Table 7**, **Row 13**) similarly supported a third-party risk assessment that exposure to VOCs from Type A foam in these device platforms are unlikely to result in an

appreciable harm to health in patients. Additional testing of Used devices and Lab-Aged devices for device platforms containing Type B foam is ongoing.

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.

Regarding cytotoxicity, sensitization, irritation, and genotoxicity testing, these tests are evaluated against *a priori* acceptance criteria to determine if the PE-PUR foam has "Passed" the test, but the results of an individual test are not reflective of the overall patient risk. For example, as presented below in **Section V.A.** and **VI.A.**, 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 were assessed through additional testing (including the amount of foam that may contact a patient based upon the level of degradation) for Type A foam, while testing on Type B is ongoing. 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. For Type A foam, this evaluation determined that TDA was being produced in measurable quantities as a consequence of Lab-Aging, which lead to a positive Ames result; however, degraded foam from Used devices did not contain measurable quantities of TDA, even when severe degradation was observed in the foam. 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 were conducted for devices containing only Type A foam, and are ongoing for devices containing 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, except where indicated in overall third-party toxicological risk assessments for Type A foam in first-generation

DreamStation (see **Table 5, Row 24**), DreamStation Go (see **Table 6**, **Row 11**), and System One (see **Table 7**, **Row 13)** device platforms.

V. Devices Containing Only Type A Foam - Testing Status and Results by Platform

Specific conclusions regarding available testing results and third-party confirmed conclusions reported to date for devices containing only Type A foam are contained in **Tables 5-7**, which are organized by device platform. **Table 10** lists all acronyms and abbreviations.

Type A foam is used in multiple device platforms as indicated in **Table 1 and 2**. 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

As described 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 5, 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.

Volatile Organic Compounds (VOCs) Risk Assessment

Concerning risks related to VOCs, testing in **Table 5** shows that for all tested devices, there were no identified toxicological risks. 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, 6 of the 21 Used devices had significant visual foam degradation/volume reduction, 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 devices from the US and Canada included a data set of 60,847 devices and an additional analysis of 100,000 devices (See **Table 3 and Table 4**), which identified visual foam degradation/volume reduction in a limited number of devices (2%). Based on the collective data, a third-party risk assessment concluded that potential patient exposure to VOCs from Type A foam within the breathing gas pathway of first-generation DreamStation is unlikely to result in an appreciable harm to health in patients.

Particulate Risk Analysis

Concerning risks related to respirable particulate exposure to patients, testing in **Table 5 (Row 2, 5, 14-17, 20, 21**) shows that all tested devices were below the allowable respirable particulate limits specified in ISO 18562-2. 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.

Concerning risks related to larger particulates (> 10 µm), a third-party analysis of the chemicals present in degraded foam from 7 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 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 5, Row 24**).

Ozone Exposure

As discussed above, data to date for first-generation DreamStation indicates that devices with user-reported ozone cleaning are approximately 14 (**Table 5, Row 18**) to 17 (**Table 5, Row 19**) 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, when comparing testing results of first-generation DreamStation devices undergoing simulated use with exposure to increasing cycles of ozone cleaning, and those without exposure to ozone cleaning. The devices with ozone cleaning had increasingly more severe foam visual degradation, and degradation was also detectable by changes in pH and conductivity, direct chemical measurement (FTIR), and degradation-related VOC emission of diethylene glycol (DEG), a foam degradation product (**Table 5, Row 21**). By comparison, devices exposed to simulated use cycles without ozone cleaning did not have visual degradation, did not have appreciable changes in pH, conductivity, or direct chemical measurement (FTIR), and did not have degradation-related VOC emission of DEG. After 200 ozone cleaning cycles (each cycle simulating one night of use and then ozone cleaning), DEG became detectable as a VOC in ISO 18562-3 testing, with the highest concentration of DEG detected after the highest number of ozone cleaning cycles tested (1300 cycles). By comparison, no DEG was detected in devices exposed to 1300 simulated use cycles without ozone cleaning. A VOC toxicological risk of this ozone-induced degradation determined that exposure to VOCs emissions from the assessed DS1 devices treated with ozone suggests no appreciable risk to health for patients (**Table 5, Row 21)**.

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 5, Row 22**) 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.

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, Ames (genotoxicity), and mouse lymphoma assay (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 seven 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 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 5, Rows 1, 2, 5, 14-17, 20, 21**) and larger (greater than 10 µm, see **Table 5, 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 5, Row 24**).

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 visual inspection, 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 3**).

Table 3: 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 3** 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 14 times 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.

An additional analysis using an algorithm to assess collected images of foam within a representative random sample of 100,000 Used devices (devices were selected to represent different manufacture dates, and approximately 10% of the devices were from the original 60,847 device dataset) showed that 2,011 devices (~2%) were identified as having significant visual degradation/volume reduction (see **Table 4** below). A comparison of ozone use among these devices found that devices for which the user self-reported ozone use were approximately 17 times more likely to have significant visual foam degradation/volume reduction (1,368 out of 14,971 or 9.1%) than those where the user reported no ozone use (357 out of 68,702 or 0.5%).

Table 4: Additional analysis of degradation prevalence of first-generation DreamStation devices from the US and Canada

	# Assessed devices	# Devices with significant visual foam degradation/ volume reduction
No use of ozone cleaning*	68,702	357
Use of ozone cleaning*	14,971	1,368
Unknown*	16,327	286
Total	**100,000**	**2,011**

* Self-reported by the user

Thus, the analysis of both data sets from the US and Canada (i.e., 60,847 Used devices assessed as part of the repair process, and images from a representative random sample of 100,000 Used devices assessed by an algorithm) supports the conclusion that ozone use is associated with greater prevalence of foam degradation/volume reduction, at a rate of approximately 14-17 times more likely than devices self-reported without ozone use.

Type A PE-PUR foam, such as that used in the first-generation DreamStation devices, 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.

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. An additional analysis of images from a representative random sample of 152,000 devices from Europe and 241,000 devices from Japan were analyzed by an algorithm to identify significant visual degradation/volume reduction. A subset of devices from Europe and Japan were identified by the algorithm as potentially having significant visual degradation/volume reduction, and this subset was manually inspected. It was observed that 17 devices of the 152,000 devices (~0.01 %) from Europe and 3 devices of the 241,000 devices (0.001%) from Japan had significant visual 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 previously.

As previously noted, the low rates of visual degradation observed in Used/returned first-generation DreamStation devices was not a factor used in the previously described risk assessment.

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).

All tested devices (4 New and 3 Lab-Aged) passed VOC and PM testing (See **Table 6**). A third-party review concluded that the testing results on DS1 and System One devices are applicable to DS Go devices to determine health risks for patients from ozone treatment and Type A foam degradation, based on multiple lines of evidence including, but not limited to, the same intended use, the same operating parameters, the same type of foam, the same foam degradation products, less foam contained within DS Go, and the conservative, protective nature of the testing and risk assessments performed.

A third-party risk assessment concluded that potential patient exposure to foam particulates and VOCs from Type A foam within the breathing gas pathway of DreamStation Go is unlikely to result in an appreciable harm to health in patients (See **Table 6**, **Row 11**).

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).

All tested devices (7 New, 20 Lab-Aged, 7 Used, 5 Ozone Treated) passed VOC and PM testing (See **Table 7**). Similar to testing of first-generation DreamStation devices, DEG was detected in devices treated with ozone (**Table 7, Row 12**). A VOC toxicological risk assessment of System One devices exposed to up to 500 cycles of ozone cleaning determined that exposure to VOCs emissions, including DEG, from the assessed System One devices suggests no appreciable risk to health for patients (**Table 7, Row 12)**.

An inspection of 2,923 Used System One devices from Japan, India, and Brazil identified significant visual foam degradation/volume reduction in a limited number of devices (8%), with the majority of foam present even in those devices with significant visual foam degradation/volume reduction (See **Table 7**).

A third-party risk assessment concluded that potential patient exposure to foam particulates and VOCs from Type A foam within the breathing gas pathway of System One is unlikely to result in an appreciable harm to health in patients (See **Table 7, Row 13**).

VI. <u>Devices containing Type B Foam – Testing Status and Results by Platform</u>

VI.A. 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.

Three New Trilogy devices tested according to standards available prior to the acceptance of ISO 18562 passed VOC and PM testing (**Table 8, Row 1**). Additionally, six New Trilogy devices passed ISO 18562-2 and three passed ISO 18562-3 testing (**Table 8, Row 3**). Devices containing foam previously Lab-Aged for 1 week (3 devices), 2 weeks (3 devices), 3 weeks (3 devices), or 4 weeks (3 devices) at 80°C and 75% RH passed ISO 18562-2 PM testing (**Table 8, Row 8**). Further testing of Trilogy is ongoing.

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.

VI.B. 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).

One New A-series device passed VOC and PM testing, and six additional A-series passed PM testing (**Table 9, Row 1**). One New OmniLab device (**Table 9, Row 6**) and three Used OmniLab devices (**Table 9, Row 15**) passed ISO 18562-3 testing with all detected VOCs having MOSs > 1.0. A-series devices containing foam previously Lab-Aged for 11 days (3 devices), 3 weeks (3 devices), 4 weeks (3 devices), 5 weeks (3 devices), 6 weeks (3 devices), 7 weeks (3 devices) or 8 weeks (3 devices) at 80°C and 75% RH passed ISO 18562-2 PM testing (**Table 9, Row 14**). Further testing is ongoing.

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.

VII. 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 that evaluated whether use of Continuous or Bilevel Positive Airway Pressure (PAP) devices were associated with an increased risk of cancer in obstructive sleep apnea (OSA) patients.

It is important to note that OSA itself may increase the risk of cancer, as do risk factors for OSA such as increased age, tobacco smoking, and obesity. Therefore, to minimize confounding by indication, studies were limited to those which cancer risk was compared between OSA patients with and without use of PAP devices. Additionally, studies were evaluated for scientific rigor including adjustment 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 January 25, 2023, 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;60:2200551.

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 5. List of Testing Results for First-generation DreamStation platforms (Foam Type A)

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[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

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
	New [Foam A]	2 tests	Genotoxicity test ISO 10993-3: MLA	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.
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 24**)
			Lab-Aged		
10	Lab-Aged [Entire Device]	9 devices (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 24**).
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.

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
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 24**).
14	Lab-Aged [Entire Device]	12 12	PM (ISO 18562-2)[e] and VOCs (ISO 18562-3)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds. PM testing included devices with foam previously aged for 4, 15, 28, 35, 40, or 46 days at 80°C and 75% relative humidity. Targeted VOC assessment on foam degradation products had MOSs > 1.0. VOC testing included devices with foam previously aged for 10, 19, 27, 34, 39, or 45 days at 80°C and 75% relative humidity.
15	Lab-Aged [Entire Device]	12 12	PM (ISO 18562-2) and VOCs (ISO 18562-3)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds. Targeted VOC assessment on foam degradation products had MOSs > 1.0. 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) and VOCs (ISO 18562-3)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds for 16 devices.[f] All detected VOCs had MOSs > 1.0.[j] 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.

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
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 14 times more likely to have degradation than those without self-reported ozone use. • 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.

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
19	Used [Entire Device]	100,000 (US and Canada) 152,000 (Europe) 241,000 (Japan)	Visual Inspection[g]	N/A	• Images of a representative random sample of 100,000 devices from the US & Canada were analyzed by an algorithm to identify significant visual degradation/volume reduction. A subset of 3,700 devices were identified as potentially having significant visual degradation/volume reduction. This subset was manually inspected and it was observed that 2,011 devices of the 100,000 devices (~2.0 %) had significant visual degradation/volume reduction. • Of the 2,011 devices with significant visual degradation/volume reduction, 1,368 devices had self-reported ozone use, while 357 had degradation without self-reported ozone use (286 devices had unknown ozone use). Thus, in this data set, devices inspected for which the user self-reported ozone use were 17 times more likely to have degradation than those without self-reported ozone use. • Images of a representative random sample of 152,000 devices from Europe were analyzed by an algorithm to identify significant visual degradation/volume reduction. A subset of 500 devices from Europe was identified by the algorithm as potentially having significant visual degradation/volume reduction, and this subset was manually inspected. It was observed that 17 devices of the 152,000 devices (~0.01 %) from Europe had significant visual degradation/volume reduction. • Images of the 241,000 devices available from Japan were analyzed by an algorithm to identify significant visual degradation/volume reduction. A subset of 101 devices was identified as potentially having significant visual degradation/volume reduction. This subset was manually assessed and it was observed that 3 devices of the 241,000 devices (~0.001 %) had significant visual degradation/volume reduction.
Combined New, Lab-Aged and Used Device Experiments					

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
20	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 to Used devices with and without degradation did not show a statistically significant difference in probability distribution.
21	New; Ozone Exposed [Entire Device]	115 total 3 New 86 with simulated use and ozone exposure 29 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 1300 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	Ozone induces degradation and DEG production Pass	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 emissions observed above the ISO 18562-2 limits for all samples tested (28 devices with simulated use and ozone exposure, and 13 devices with simulated use and without ozone exposure, and 1 new device). 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. For the conditions tested by ISO 18562-2 (up to 500 cycles of ozone): $PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds For the conditions tested by ISO 18562-3 (up to 1300 cycles of ozone):

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
			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)		All detected VOCs had MOSs > 1.0
22	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.

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
23	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.
Overall Third-Party Risk Assessment					
24	See testing above	See testing above	See conclusions and additional information column to the right	Pass	A toxicological risk assessment was conducted of potential patient exposure to polyester-polyurethane (PE-PUR) "Type A" sound abatement foam or its degradation products within the breathing gas pathway of first-generation DreamStation. **Potential patient exposure to foam particulates and VOCs from Type A foam within the breathing gas pathway of first-generation DreamStation is unlikely to result in an appreciable harm to health in patients.**

[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 24**).

[e] While the ISO 18652-2 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.

[j] Two VOCs had MOS < 1.0 but were identified as unique environmental contaminants (each one detected in a single device) and unrelated to Type A foam.

Table 6. List of Testing Results for DreamStation Go platforms (Foam Type A)

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[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]	7 3	PM (ISO 18562-2) and VOCs (ISO 18562-3)		$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds. All detected VOCs had MOSs > 1.0
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
		2 tests	Genotoxicity test ISO 10993-3: MLA	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

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
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					
6	Lab-Aged [Entire Device]	6 3	PM (ISO 18562-2) and VOCs (ISO 18562-3)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds Targeted VOC assessment on foam degradation products had MOSs > 1.0.
7	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 completed (see **Row 11**).[f]
8	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.

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
9	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 completed (see **Row 11**).[g]
Ozone Treated					
10	Ozone Treated [Entire Device]	N/A	See conclusions and additional information to the right	Pass	A third-party review concluded that multiple lines of evidence support that the testing results on DS1 and System One devices are sufficient to bridge to DS Go devices to determine health risks for patients from ozone treatment and Type A foam degradation. Exposure to VOC emissions related to potential Type A foam degradation in DS Go devices treated with ozone indicates no appreciable harm to health for patients.
Overall Third-Party Risk Assessment					
11	See testing above	See testing above	See conclusions and additional information column to the right	Pass	A toxicological risk assessment was conducted of potential patient exposure to polyester-polyurethane (PE-PUR) "Type A" sound abatement foam or its degradation products within the breathing gas pathway of DreamStation Go. **Potential patient exposure to foam particulates and VOCs from Type A foam within the breathing gas pathway of first-DreamStation Go is unlikely to result in an appreciable harm to health in patients.**

[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 was conducted with a chemical characterization and risk assessment, see **Row 11**.

[e] Foam Type A testing reported in this table is also reported in Table 5.

[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 complete, see **Row 11**.

[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, a toxicological risk assessment was completed, see **Row 11**.

Table 7. List of Testing Results for System One platforms

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[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]	6 and 6	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
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
		2 tests	Genotoxicity test ISO 10993-3: MLA	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					

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 complete (See **Row 13**).[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 complete (See **Row 13**).[g]
9	Lab-Aged [Entire Device]	20 devices (7 aging timepoints) 20 devices (7 aging timepoints)	PM (ISO 18562-2) and VOCs (ISO 18562-3)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds Targeted VOC assessment on foam degradation products had MOSs > 1.0. 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) and VOCs (ISO 18562-3)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds. All detected VOCs had MOSs > 1.0
11	Used	2,923 devices	Visual Inspection [h]	N/A	• Devices returned from patients were inspected and imaged to determine visual degradation rates.

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
	[Entire Device]				• Images of device foam from US and Canada were not available. • Of 1,189 inspected devices from Japan, 0 devices (0%) showed foam volume reduction/deformed foam at the cm scale. • Of 880 inspected devices from India, 137 devices (~16%) showed foam volume reduction/deformed foam at the cm scale. • Of 854 inspected devices from Brazil, 105 devices (~12%) showed foam volume reduction/deformed foam at the cm scale. • Foam was imaged after physical removal from the device and handling may have contributed to further foam visual degradation.
Ozone Treated					
12	Ozone Treated [Entire Device]	16 total 13 with simulated use and ozone exposure 3 with simulated use but no ozone exposure	Simulated use and ozone treatment was performed for up to 500 ozone cycles consistent with the method description in **Table 5**, **Row 21**. Testing included Visual inspection, pH, conductivity, FTIR, PM testing (ISO 18562-2; 5 devices), and VOC testing (ISO 18562-3; 5 devices)	Pass	For the conditions tested (up to 500 cycles of ozone): DEG was detected in devices treated with ozone. $PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds All detected VOCs had MOSs > 1.0
Overall Third-Party Risk Assessment					

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
13	See testing above	See testing above	See conclusions and additional information column to the right	Pass	A toxicological risk assessment was conducted of potential patient exposure to polyester-polyurethane (PE-PUR) "Type A" sound abatement foam or its degradation products within the breathing gas pathway of System One. **Potential patient exposure to foam particulates and VOCs from Type A foam within the breathing gas pathway of System One is unlikely to result in an appreciable harm to health in patients.**

[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 was conducted with a chemical characterization and risk assessment, see **Row 13**.

[e] Foam Type A testing reported in this table is also reported in Table 5.

[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 complete, see **Row 13**.

[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, a toxicological risk assessment was completed, see **Row 13**.

[h] Visual inspection performed internally.

Table 8. List of Testing Results for Trilogy 100/200

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information
			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.
		3	PM (ISO 18562-2)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds.
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	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.

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information
				Skin irritation: Pass	Negative for skin irritation under laboratory conditions for all aging timepoints. Associated toxicological risk assessment **ongoing**.[e]
8	Lab-Aged [Entire Device]	12	PM (ISO 18562-2)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds. Testing included devices containing foam previously aged for 1 week, 2 weeks, 3 weeks, or 4 weeks at 80°C and 75% RH.
Combined New, Lab-Aged and Used Device Experiments					
9	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 9. List of Testing Results for BiPAP A30/A40/V30 and OmniLab

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[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]	6	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 Skin irritation: Pass	Positive for cytotoxicity under laboratory conditions.[c] Negative for skin sensitization under laboratory conditions. Negative for skin irritation under laboratory conditions.

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
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.

Row	Device Category	# of Tests/Devices Tested	Testing Description	Result	Conclusion(s) and Additional Information[a]
				Skin irritation: Pass	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**.[g]
14	Lab-Aged [Entire Device] [f]	21 devices (7 aging timepoints)	PM (ISO 18562-2)	Pass	$PM_{2.5}$ and PM_{10} below ISO 18562-2 thresholds. Testing included devices containing foam previously aged for 11 days, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, and 8 weeks at 80°C and 75% RH.
Used					
15	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					
16	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 5 and 8 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 10. Acronyms and Abbreviations

AI	Additional Information
°C	Celsius
CFR	Code of Federal Regulations
DD	Dimethyl diazene
DS1	First-generation DreamStation
DS Go	DreamStation Go
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