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Date: 9 DECEMBER 2021
Via email: ORADevices1FirmResponse@fda.hhs.gov
U.S. Food and Drug Administration
Office of Medical and Radiological Health Operations Division 1 – East
Attention: OMDRHO Div1 Correspondence
One Montvale Avenue
Stoneham, MA 02180

Re: Response to FDA-483 received November 9, 2021
Philips Respironics, Inc.
Inspection Dates: August 26, 2021 – November 9, 2021
Facility Establishment Number: No. 2518422

To Whom It May Concern:

Enclosed are Philips Respironics, Inc.'s ("Respironics" or the "Company") responses to the FDA-483 issued after an inspection of its facility located in Murrysville, PA from August 26, 2021, to November 9, 2021. On November 29, 2021, Karen N. Archdeacon agreed to Respironics's request for an extension to submit the Company's response to FDA by close of business on December 9, 2021.

Respironics takes FDA's observations seriously. The Company has conducted investigations of the Inspectional Observations and is taking action to fully address the observations through its CAPA process, as discussed in further detail in the enclosed individual responses. In addition, Respironics is implementing several over-arching changes to further promote compliance with FDA's regulations, including changes affecting personnel and resources, as well as implementing broader actions. We discuss these changes and a brief summary of the recall that led to the FDA inspection of the Murrysville facility below.

Under separate cover, on December 10, 2021, Respironics will provide additional information on broader commitments the Company will implement to further enhance its quality management system beyond the scope of the issues described in FDA's Inspectional Observations.

Background: Recall Associated with Ventilator, CPAP, and BiPAP Devices

Respironics initiated a voluntary field action affecting certain Respironics ventilator, CPAP, and BiPAP devices, for which the Company submitted its first report under 21 C.F.R. § 806.10 on May 7, 2021 (after discussions with the agency subsequently identified by recall numbers RES 88058 and RES 88071). FDA then commenced an inspection on August 26, 2021. As explained in the May 7, 2021 and subsequent reports, Respironics became aware of two issues regarding the affected devices: (1) the polyester-based polyurethane (PE-PUR) sound abatement foam used in the affected devices may degrade and enter the air pathway; and (2) based on testing completed as of the May 7, 2021 report, the PE-PUR sound abatement foam used in these devices may emit certain chemicals.

Since submission of the May 7, 2021 report, Respironics has coordinated with FDA to ensure that Respironics executes the remediation plan for affected devices efficiently, effectively, and promptly. Specifically, Respironics initiated the following actions:

- Submitted three (3) 510(k) premarket notifications to FDA regarding a change to the sound abatement foam (change from PE-PUR foam to (b) (4) foam) for devices affected by RES 88058:
  - (b) (4) – DreamStation BiPAP S/T; DreamStation BiPAP AVAPS
  - (b) (4) – DreamStation BiPAP autoSV
  - (b) (4) – DreamStation (CPAP); DreamStation (CPAP Pro); DreamStation (Auto CPAP)

- Submitted a rework protocol to FDA regarding the remediation of returned DreamStation devices affected by RES 88058 (*Repair Process for DreamStation Devices Affected by Philips Medical Device Recall Letter issued June 14, 2021, FCO 2021-05-A, Related FSNs, Document FC: 16-700-622, Revision 03*), authorized by FDA on August 16, 2021;

- Submitted a rework protocol regarding the remediation of returned Trilogy 100/200 devices affected by RES 88071 (*Repair Process for Trilogy 100/200 Devices Affected by*

Philips Medical Device Recall Letter issued June 14, 2021, FCO 2021-6-A, Document FC: 16-700-628, Revision 00);

- Submitted a rework protocol regarding the remediation of unopened DreamStation devices affected by RES 88071 (*Rework process for Non-Opened DreamStation Finished Goods affected by Philips Medical Device Recall Letter issued June 14, 2021, FCO 2021-05-A, and Related FSNs, Revision 01*);

- Providing timely, detailed responses to FDA's written questions and feedback regarding the recall;

- Attending ad-hoc meetings with FDA when requested by the Agency concerning specific topics associated with the recall; and

- Attending bi-weekly calls with FDA to provide updates regarding the remediation plan and ongoing testing, and to ensure the Agency's follow-up questions are fully addressed.

Leadership and Resource Changes

To further promote compliance with FDA's requirements and address the issues identified by FDA in its Inspectional Observations, Respironics invested in new personnel to manage its quality management system (QMS), including changes to Respironics's top management and investment in additional resources to support the QMS and related activities. Specifically:

- On March 29, 2021, Respironics onboarded a new Business Leader, defined as Management with Executive Responsibility, Mr. David Ferguson. Mr. Ferguson has a diverse global background across a range of health tech areas, including critical care devices, diagnostic imaging, high-volume disposables, and pharmaceuticals. His most recent position was at Baxter Healthcare, where he led the (b) (4) global Medication Delivery business—for hospital and home—which included infusion pumps, infection management, antimicrobial stewardship, and analytics software products, and specialty IV solutions. Mr. Ferguson's CV is provided as **Attachment CL-1**.

- On November 16, 2021, Respironics onboarded a new Head of Quality, Thomas J. Fallon. The Head of Quality operates as Respironics's Management Representative. Mr. Fallon brings over 30 years of quality and regulatory industry experience to the role. His

experience includes 14 years with Philips serving as Head of Quality for Hospital Patient Monitoring; Senior Director, Quality Transformation Lead; Director of Quality Assurance and Regulatory Affairs for Emergency Care; and Director of Quality Assurance and Regulatory Affairs for Patient Monitoring. Before joining Respironics, Mr. Fallon held quality and regulatory roles with multi-national device and combination products companies, and he began his career in the United States Marine Corp. Mr. Fallon's CV is provided as **Attachment CL-2**.

- In March 2021, created a dedicated team of internal subject-matter experts within Respironics that focuses on biocompatibility, cleaning and disinfection, and toxicology. Through the creation of the team, Respironics has centralized oversight, accountability, and information sharing for all Company matters that concern biocompatibility, cleaning and disinfection, and toxicology. Specifically, the Company is adding full-time, subject-matter expert headcount to provide data utilized for evaluating risk:
  - (b) (4) Toxicologists who will support biocompatibility evaluations
  - (b) (4) PhD Engineers who will support biocompatibility evaluations
  - (b) (4) director of the biocompatibility, cleaning and disinfection, and toxicology team

- Adding headcount to support existing organization, including additional personnel to support the following functions: Quality, Regulatory, Design Quality, Supplier Management, Post-market, and Medical Affairs.

Broader Actions

Beyond the specific actions described in the enclosed individual responses to the Inspectional Observations, Respironics has initiated a number of broader actions to fully address FDA's feedback. Specifically:

- Enhancing the knowledge of Respironics personnel by engaging outside experts to perform in-depth, company-wide training on the Quality System Regulation (QSR) (21 C.F.R. Part 820); Medical Device Reporting (21 C.F.R. Part 803); and Reporting of Corrections/Removals (21 C.F.R. Part 806). As part of the training, the outside experts will provide guidance on FDA's current expectations related to specific regulatory requirements.

- Implementing an (b) (4) training requirement for all Respironics personnel to better

ensure they understand the function and importance of their role in helping to ensure that the Company meets its FDA regulatory obligations. In addition, the training will help make personnel aware of potential risks/failures that could result from the improper performance of their specific job.

- Engaging outside quality system experts to assist the Company with reviewing the procedural enhancements made in response to the FDA-483 to help ensure the improvements meet FDA requirements and expectations.

- Utilizing a risk-based approach to prioritize reviewing the Design History Files (DHFs) for the currently marketed products developed at Respironics against the enhanced design control procedure and process (see Respironics's response to Inspectional Observation 7 for background on the enhanced design control procedure). Based on the review, the Company will enhance the Design Documentation where required. Finally, where necessary, Respironics will take appropriate containment activities resulting from its DHF review activity.

- Assigned a project management coordinator to help ensure that commitments made in the individual responses to the FDA-483 meet the established completion dates.

- After the implementation of actions taken to address the Inspectional Observations, Respironics will engage a third-party, independent expert to confirm the effectiveness of the actions taken in resolving the Inspectional Observations.

- As further described in the enclosed individual responses to the Inspectional Observations, Respironics is further enhancing processes and procedures, including:
    - CAPA
    - Risk Management
    - Complaint Handling
    - Field Action/Health Hazard Evaluation (HHE)
    - Reportability of Corrections/Removals
    - Quality Data Trending
    - Design Controls
    - Engineering Change Control
    - Management Review (Responsibility)
    - Supplier Management

- As further described in the enclosed individual responses to the Inspectional Observations, Respironics is conducting retrospective reviews to evaluate work products generated under historical processes and procedures, including:
    - CAPAs
    - Complaints
    - HHEs where the Company determined no action was required to confirm decision-making
    - Quality data trending
    - Engineering change requests concerning changes to service manual
    - Field communications to verify the evaluation of actions per the corrections/removals process
    - Design specifications associated with the currently marketed product
    - Qualification of suppliers serving in a consulting role

Meeting Request

Respironics respectfully requests a meeting with FDA senior leadership in Q2 2022 so the Company can: (1) introduce its new senior leadership; and (2) present data demonstrating the effectiveness of the enhancements made to the Respironics QMS. Respironics will follow up under separate cover in Q1 2022 to arrange the meeting with the Agency.

Format of this Response

In the remainder of this letter, Respironics responds to each of the specific observations. To ensure clarity, FDA's observations are provided in ***bold italicized*** text, followed by Respironics's response to each item. For all Inspectional Observations, Respironics first begins with a general summary of its response followed by a discussion of background information. Respironics concludes its response with a detailed description of the actions the Company has taken, or plans to take, to fully address the Inspectional Observation. Where Respironics has completed an action, the Company has appended objective evidence of completion to this Response.

Respironics is committed to the completion of the actions described in this Response in the period prescribed and will supplement this FDA-483 response with additional information that updates the Agency on the status of the outstanding actions, including objective evidence substantiating the completion of remaining actions. The first update will be submitted by January 7, 2022, and subsequent periodic updates will be submitted thereafter.

If you have further questions or require additional information, please contact me at tom.fallon@philips.com. Please send all correspondence regarding this matter to my attention at the following address: Philips Respironics, Inc., 1001 Murry Ridge Lane, Murrysville, PA 15668-8517.

Sincerely yours,

Thomas J. Fallon
Head of Quality
Sleep and Respiratory Care
Philips Respironics, Inc.

cc:

- David Ferguson, Business Leader, Sleep and Respiratory Care, Philips Respironics, Inc.
- William Maisel, M.D., Office Director, Office of Product Evaluation and Quality, CDRH, FDA
- Malvina Eydelman, M.D., Office Director, Office of Product Evaluation and Quality, Office of Health Technology 1, CDRH, FDA
- Jan Welch, Program Director, Office of Medical Device and Radiological Health Operations, ORA, FDA
- Gina Brackett, Director of Compliance Branch, Division 1, Office of Medical Device and Radiological Health Operations, ORA, FDA
- Karen Archdeacon, Compliance Officer, Division 1, Office of Medical Device and Radiological Health Operations, ORA, FDA

Respironics considers this letter and response to contain trade secret, privileged, or confidential commercial or financial information and, accordingly, is both: (1) exempt from disclosure under exemption 4 of the Freedom of Information Act (FOIA) and pursuant to 21 C.F.R. § 20.61; and (2) prohibited from being publicly disclosed, pursuant to the affirmative restrictions in the Trade Secrets Act, 18 U.S.C. § 1905, and in section 301(j) of the Federal Food, Drug, and Cosmetic Act (FFDCA). Pursuant to 21 C.F.R. § 20.61(d), Respironics formally designates all the information in this letter and response as exempt from disclosure under exemption 4 of the

FOIA and asks that the Agency follow the procedures for pre-disclosure notification set forth in 21 C.F.R. § 20.61(e). In particular, Respironics requests that the Agency notify the Company by telephone or e-mail before sharing any information in, or related to, this letter and response with any non-Departmental entity or person, whether in response to a FOIA request or otherwise. In such instance, Respironics requests the opportunity to substantiate the privileged or confidential nature of all such information, as well as the opportunity to redact all trade secret, confidential commercial information, and other protected information from this letter and response and from any related records prior to disclosure. Respironics reserves its rights to seek a protective order if the Agency feels it necessary to share any of this information with a non-governmental entity or person.

Exhibits

1. **Philips 483 Response December 2021 – Attachment CL-1 - *David Ferguson CV***
2. **Philips 483 Response December 2021 – Attachment CL-2 - *Thomas Fallon CV***
3. **Philips 483 Response December 2021 – Attachment 1(a)-1 - QSP 16.2.9 *Manage Corrective and Preventive Action* Ver 09**
4. **Philips 483 Response December 2021 – Attachment 1(a)-2 - FRM 5278 *CAPA Review Checklist* Ver 01**
5. **Philips 483 Response December 2021 – Attachment 1(c)-1 - WI 8.4-838 *Complaint Evaluation, Investigation, and Closure* Ver 26**
6. **Philips 483 Response December 2021 – Attachment 1(c)-2 - WI 8.4-621 *Product Investigation Lab Procedure* Ver 17**
7. **Philips 483 Response December 2021 – Attachment 1(c)-3 - WI 8.4-995 *Third-Party Evaluation Process* Ver 03**
8. **Philips 483 Response December 2021 – Attachment 1(c)-4 - QSP 8.4-836 *Complaint Handling* Ver 23**
9. **Philips 483 Response December 2021 – Attachment 1(c)-5 - WI 7.3-388 *Issue Tracking Process* Ver 08**
10. **Philips 483 Response December 2021 – Attachment 1(c)-6 - QSP 7.3-286 *Risk Management* Ver 22**
11. **Philips 483 Response December 2021 – Attachment 1(c)-7 - FRM 5362 *CRB Meeting Template* Ver 02**
12. **Philips 483 Response December 2021 – Attachment 1(e)-1 - WI 8.6-840 *Complaint Trending* Ver 11**
13. **Philips 483 Response December 2021 – Attachment 1(e)-2 - FRM 1256 *Health Hazard Evaluation (HHE) Template* Ver 08**
14. **Philips 483 Response December 2021 – Attachment 1(f)-1 - FRM 1279 *Post Market Risk Assessment* Ver 05**
15. **Philips 483 Response December 2021 – Attachment 2(c)(1)-1 - QSP 8.4-836 *Complaint Handling* Ver 23**
16. **Philips 483 Response December 2021 – Attachment 2(c)(2)-1 - WI 8.6-840 *Complaint Trending* Ver 11**
17. **Philips 483 Response December 2021 – Attachment 2(c)(2)-2 - FRM 5278 *CAPA Review Checklist* Ver 01**
18. **Philips 483 Response December 2021 – Attachment 2(d)-1 - WI 8.4-838 *Complaint Evaluation, Investigation, and Closure* Ver 26**
19. **Philips 483 Response December 2021 – Attachment 2(d)-2 - WI 8.4-621 *Product***

Investigation Lab Procedure **Ver 17**

20. **Philips 483 Response December 2021 – Attachment 2(d)-3 - WI 8.4-995 *Third-Party Evaluation Process* Ver 03**
21. **Philips 483 Response December 2021 – Attachment 3(a)-1 - FRM 1256 *Health Hazard Evaluation (HHE) Template* Ver 08**
22. **Philips 483 Response December 2021 – Attachment 3(a)-2 - QSP 7.3-286 *Risk Management* Ver 22**
23. **Philips 483 Response December 2021 – Attachment 4(b)-1 - 7.3-287 *Managing Design Changes* Ver 14**
24. **Philips 483 Response December 2021 – Attachment 4(b)-2 - 4.2-1100 *Engineering Change Requests (ECRs)* Ver 09**
25. **Philips 483 Response December 2021 – Attachment 4(b)-3 - 4.2-007 *Approval Matrix* Ver 40**
26. **Philips 483 Response December 2021 – Attachment 6-1 - *David Ferguson CV***
27. **Philips 483 Response December 2021 – Attachment 6-2 - *Thomas Fallon CV***
28. **Philips 483 Response December 2021 – Attachment 6-3 - QSP 16.5.4 *Operate and Assess the MS-QMS* Ver 01**
29. **Philips 483 Response December 2021 – Attachment 7-1 - QSP 3.1.0.1 *Design Controls* Ver 01**
30. **Philips 483 Response December 2021 – Attachment 8-1 - WI 16.2.18.1.2 *Perform Supplier Classification* Ver 02**
31. **Philips 483 Response December 2021 – Attachment 8-2 - WI 16.2.18.1.3 *Perform Supplier Qualification* Ver 04**

OBSERVATION 1

Risk analysis is inadequate

Specifically,

RESPONSE TO OBSERVATION 1

The cited examples, to which Respironics provides individual responses below, concern Respironics processes and procedures for evaluating risk. Specifically, Inspectional Observation 1 cites issues related to: consideration of all data (e.g., testing, complaint data, MDRs) when evaluating risk; risk scoping decisions; evaluating risk in a timely manner; initiating risk analysis processes when becoming aware of a quality issue; and risk estimation (e.g., severity and probability determinations).

To address the cited issues, Respironics is: (1) enhancing several procedures and processes associated with its risk management program; and (2) conducting several retrospective reviews of the Company's previous work product concerning risk. See the *Actions in Response to FDA's Inspectional Observation* sections of the individual responses for details on the procedural enhancements and retrospective reviews.

More broadly, as noted in the Cover Letter, to further enhance Respironics's risk management program, the Company is doing the following:

- Enhancing the knowledge of Respironics personnel by engaging outside experts to perform in-depth, company-wide training on the Quality System Regulation (QSR) (21 C.F.R. Part 820); Medical Device Reporting (21 C.F.R. Part 803); and Reporting of Corrections/Removals (21 C.F.R. Part 806). As part of the training, the outside experts will provide guidance on FDA's current expectations related to specific regulatory requirements, such as FDA requirements and expectations for evaluating risk.

- Developing an in-depth training program for personnel involved in the risk management process.

- In March 2021, created a dedicated team of internal subject-matter experts within Respironics that focuses on biocompatibility, cleaning and disinfection, and toxicology. Through the creation of the team, Respironics has centralized oversight, accountability,

and information sharing for all Company matters that concern biocompatibility, cleaning and disinfection, and toxicology. Specifically, the Company is adding full-time, subject-matter expert headcount to provide data utilized for evaluating risk:

- (b) (4) who will support biocompatibility evaluations.
- (b) (4) who will support biocompatibility evaluations.
- (b) (4) director of the biocompatibility, cleaning and disinfection, and toxicology team.

- Further augmenting the Risk Management capabilities, including additional headcount (e.g., consultants) to assist with conducting risk management activities.

a) There is no documented investigation, risk analysis, or design failure mode effect analysis to support your firm's rationale for which polyester polyurethane foam-containing products were affected, included, or not included in your firm's ongoing recalls. Your firm is currently conducting on-going, Class 1 medical device recalls of various models of Philips Respironics ventilator, CPAP, and BiPAP devices, due to polyester polyurethane foam degradation and volatile organic compound emission, which was publicly announced on 06/14/2021.

The provided justification document titled, "REQ 310 - Rationale for Concluding which Devices are Impacted by the Recall" does not document the performance or results of an investigation, risk analysis, or design failure mode effect analysis, therefore you have not sufficiently demonstrated that other devices, also containing polyester polyurethane foam, should not be included in your ongoing recalls, as well.

RESPONSE TO OBSERVATION 1(a)

Background

At the time of the inspection, Respironics had an established corrective and/or preventive action (CAPA) procedure, QSP 16.2.9, *Manage Corrective and Preventive Action*, which included instructions on how to scope the issue under investigation, as well as any subsequent correction and containment actions.

The cited example concerns a recall Respironics initiated on May 7, 2021, in relation to its ventilator, CPAP, and BiPAP devices (RES 88058 or RES 88071). See the Cover Letter to this Response for additional information concerning this recall. The recall is included as part of

CAPA 7211. Through CAPA 7211, and in accordance with QSP 16.2.9, *Manage Corrective and Preventive Action*, Respironics evaluated and documented the scope of affected devices. The methodology used at the time to initially scope the impacted products was limited to any product that had the PE-PUR foam within the airpath. Respironics is confident that the current list of affected devices encompasses all devices that contain PE-PUR in the airpath.

In response to FDA's feedback, Respironics is confirming the scoping of the recall. In addition, Respironics is making additional improvements to QSP 16.2.9, *Manage Corrective and Preventive Action*, to help ensure scoping decisions are adequate and fully documented within the CAPA record. See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 1(a), Respironics initiated CAPA 1505260, which contains the following actions:

- With regard to the cited example, Respironics is documenting more clearly its evaluation of the affected devices included in the scope of recalls RES 88058 or RES 88071, which arose out of CAPA 7211. This documented evaluation will include an assessment of all Respironics devices to determine whether they contain any PE-PUR material in any part of the device. Respironics expects to complete the assessment of whether existing marketed devices may be impacted by RES 88058 or RES 88071 using a risk-based methodology by December 17, 2021. Additionally, Respironics is working to define a timeline for the evaluation of legacy (i.e., no longer marketed) devices. The methodology and results of this evaluation are being recorded in CAPA 7211. Based on the evaluation conducted to date, we have not identified any additional devices that would be impacted by RES 88058 or RES 88071.

- Respironics enhanced QSP 16.2.9, *Manage Corrective and Preventive Action* (Version 09; refer to **Attachment 1(a)–1**), to better clarify the requirements for:
  - Establishing a methodology and rationale (b) (4), for instance, Risk Analysis) for determining the affected devices included in the scope of the activities;
  - Ensuring that such methodology and rationale are clearly documented; and
  - Ensuring that the methodology and rationale are updated upon receipt of new information, as appropriate.

- Respironics enhanced FRM 5278, *CAPA Review Checklist* (Version 01; refer to **Attachment 1(a)–2**), to confirm that the methodology and rationale for affected devices are fully documented within the CAPA records.

- Training of affected personnel on the enhanced procedure is underway and will be completed by January 5, 2022.

- To verify the effectiveness of the actions, an audit will be conducted using FRM 5278, *CAPA Review Checklist*, on at least 35 product-related CAPAs after they move from the (b) (4) (at this point the investigation activities, root-cause investigation, and effectiveness check plans have been defined by the CAPA team and approved by the CAPA Review Board (CRB)). The actions will be deemed effective if the requirements of QSIT Table 1 are met. The FDA Inspection Guide QSIT Table 1 ((b) (4)) will be used to determine the sample size. Successful records will include methodology and rationale for determining the affected devices included in the scope of any containment and/or correction activities.
    - Note: This effectiveness check permits the use of (b) (4) sampling.

- Respironics is performing a retrospective review of all Corrections and Removals which required reporting to the Agency per 21 C.F.R. § 806.10 in the last five (5) years (December 1, 2021, to December 1, 2016) to evaluate the accuracy of the scoping of the action. Respironics expects to release a protocol to conduct the review by January 31, 2022. The review protocol will include the timeline for completion of the review.

b) No investigation, health hazard evaluation, risk analysis, or design review was performed or documented when your firm was made aware that a preventative maintenance procedure for Trilogy ventilator devices was being implemented by another Philips entity in (b) (4) due to potential foam degradation, and related complaints, on Trilogy ventilator devices in the field.

On or around 11/25/2015, your firm was aware and knowledgeable of a preventative maintenance servicing procedure implemented by another Philips entity in (b) (4) , on Trilogy ventilator products, and no further investigation, health hazard evaluation, risk analysis, or design review was performed, or documented by your firm. This preventative maintenance was implemented by Philips (b) (4) LTD., in (b) (4) only, in response to foam degradation issues and complaints in the field related to Trilogy ventilator products.

Your firm provided the email, dated 11/25/2015, sent from the other Philips entity to applicable servicing technicians/departments within their organization, detailing this new preventative maintenance procedure and timeline. This email was provided in response to an inspection request for any applicable documentation, communication, investigation, or follow-up that your firm has or did, in response to these polyester polyurethane foam degradation complaints/issues received in or prior to 2015, and this resulting preventative maintenance, implemented by another Philips entity in (b) (4) .

No further investigation, health hazard evaluation, risk analysis, or design review was performed or documented by your firm regarding potential polyester polyurethane foam degradation on any Philips Sleep and Respiratory Care products. Additionally, no further preventative maintenance servicing procedures were implemented by your firm,

Your firm is currently conducting on-going, Class 1 medical device recalls of over 15 million Philips Respironics ventilator, CPAP, and BiPAP devices, due to polyester polyurethane foam degradation and volatile organic compound emission, which was publicly announced on 06/14/2021.

RESPONSE TO OBSERVATION 1(b)

Background

At the time this change in preventive maintenance (PM) was made for Trilogy devices in (b) (4) only, Philips Respironics (b) (4) (b) (4) was the Marketing Authorization Holder for the Trilogy devices in (b) (4) The relationship between Respironics and (b) (4) which was subsequently codified in an agreement on August 29, 2017, makes clear that Philips (b) (4) ,[1] is the Marketing Authorization Holder in (b) (4) However, Respironics understands that it can enhance its contractual relationship with Philips (b) (4) . See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 1(b), Respironics initiated CAPA 1505260, which contains the following actions:

(b) (4) is now called Philips (b) (4)

- Respironics will strengthen its contract with Philips (b) (4) to further clarify the process in regard to requests for changes such as the cited example. Specifically, the contract will be revised to state that: (1) Philips (b) (4) prior authorization; and (2) if Philips (b) (4) , Philips (b) (4) Respironics will handle the change as a change request in accordance with its procedural requirements, which include conducting all requisite change control activities. Respironics expects to complete the contract revision by February 28, 2022.

    - The effectiveness of this change will be verified via an audit of Philips (b) (4) by Respironics to confirm that no design changes have been made that have not gone through the change control system.

- Respironics will conduct a review to verify that the current PM protocol and schedule in (b) (4) is consistent with Respironics's PM protocol and schedule. Respironics expects to complete the review by January 31, 2022.

- With respect to the cited example, containment is not required because the foam being used with Trilogy 100 and 200 is currently under recall and being replaced with a new material. Respironics will follow its design control process to determine the PM activities (if any) required for the new foam and that such PM activities are appropriately qualified.

c) A risk analysis is inadequate or was not performed when appropriate or within an appropriate time frame of your firm becoming aware of potential polyester polyurethane foam degradation and/or Volatile Organic Compound (VOC) emission concerns regarding various CPAP, BiPAP, and ventilator devices. Specifically, there were at least fourteen instances, assessments, and/or test reports, dated from 04/01/2016 to 01/22/2021, where your firm was aware of issues and concerns related to potential foam degradation and/or Volatile Organic Compound (VOC) emissions, with various Sleep and Respiratory care devices, including:

1. ***The "(b) (4) ", dated 04/01/2016, which is documented in and utilized Trilogy 100 field samples from consumer complaint numbers 306210645 and 306220735, both received by your firm***

in October 2015, documents base polymer cleavage and embrittlement of the returned foam material of the related field samples.

As a result, a risk analysis was not performed and no further design change, corrective action, or field correction was conducted when appropriate or within an appropriate timeframe.

2. ***Test Report A5T282T-161438, dated 08/30/2016 and titled, "Degradation (b) (4) respironics Trilogy appliance", states in part, "The chemical analysis group was requested to analyze (b) (4) from the respironics Trilogy 200 series", "The samples which were received by the chemical analysis group are (b) (4) production samples from 2016, 2 customer complaints from 2015 with sample codes 10360957 and 10360958 and (b) (4) samples from 2001. The main focus of this report will be on polyester polyurethane (PUR) analysis and degradation". It further states, "At (b) (4) of the (b) (4) test de foam became (b) (4), even after (b) (4), and at (b) (4) it was a (b) (4). Also the color changes from (b) (4) (b) (4) to a (b) (4), (b) (4) and finally a (b) (4) (b) (4) is observed during visual inspection", "All foams are polyester based urethanes except (b) (4). Polyester urethanes show bad resistance against high humidity in combination with high temperature". This test report was conducted as a result of field reports/complaints regarding foam degradation in Trilogy 200 ventilator devices in 2015.***

   As a result, a risk analysis was not performed and no further design change, corrective action, or field correction was conducted when appropriate or within an appropriate timeframe.

3. ***Test Report AST 282T-161459, dated 11/25/2016 and titled, "(b) (4) of (b) (4) foam", states in part, "Previously the degradation of polyester urethane foams, which are used in the air inlet path of the Respironics Trilogy 200 series, have been tested (see report AST 282T-161438). In this follow-up study (b) (4) different type of foams, made of (b) (4) ", "The focus of this research is on whether these foams (b) (4) ". It further states, "In contrary to polyester urethane foams, (b) (4) foams show a far better resistance against high humidity at high temperature. Some degradation is observed, as can be seen from (b) (4) , but it happens only slowly and gradually'. This test***

report was conducted as a result of field reports/complaints regarding foam degradation in Trilogy 200 ventilator devices in 2015 and as a follow-up to A5T282T-161438.

As a result, a risk analysis was not performed and no further design change, corrective action, or field correction was conducted when appropriate or within an appropriate timeframe.

4. *Test Report AST 282T-182160, dated 12/12/2018 and titled "(b) (4) ", states in part, "There was a problem of degradation of the damping foam in Trilogy Respironics appliance in 2016. Investigation had done and the problem was found as (b) (4) polyester polyurethane. (refer to AST 282T-161438 attached below) Currently the project team is considering (b) (4) . Therefore, there are no data for polyester polyurethane (b) (4) . (b) (4) also (b) (4) ". This test report was conducted as a result of field reports/complaints regarding foam degradation in Trilogy ventilator devices in 2016 and is documented in CAPA 7211.*

   As a result, a risk analysis is inadequate and no further design change, corrective action, or field correction was conducted when appropriate or within an appropriate timeframe.

5. *The test report identified as "(b) (4) ", dated 05/22/2019, states in part, "At your request the following samples were analyzed by (b) (4) (b) (4) , for investigation of degradation of a polyurethane foam". It concludes, "The most significant evidence that the (b) (4) gives is of a (b) (4) "This chemical reaction can occur if the foam is constantly wet, i.e. exposier to high heat and humidity". The test samples are described as, "Degraded Polyurethane foam", "Polyurethane Foam", and "Current Production Foam". The test report identified as "(b) (4) is documented in CAPA 7211.*

As a result, a risk analysis is inadequate and no further design change, corrective action, or field correction was conducted when appropriate or within an appropriate timeframe.

6. (b) (4) ***, dated 01/30/2020, documents that a DreamStation 1 device failed emissions testing for VOCs and Aldehydes, which was analyzed/tested from 01/18/2019 to 01/25/2019. Specifically, Table 3 documents that the tolerable limits of the Formaldehyde compound were exceeded during initial operation, as well as at the*** (b) (4) ***. This Test Report was conducted to support FDA guidance and following the guidelines of ISO 18562-3, and the test subject was a DreamStation (1) CPAP device. As a result, a risk analysis is inadequate and no further design change, corrective action, or field correction was conducted when appropriate or within an appropriate timeframe.***

7. (b) (4) ***, dated 01/30/2020, documents that a DreamStation 1 device failed emissions testing for VOCs and Aldehydes, which was analyzed/tested from 01/25/2019 to 02/01/2019. Specifically, Table 3 documents that the tolerable limits of the Formaldehyde compound were exceeded during initial operation, as well as at the*** (b) (4) ***. This Test Report was conducted to support FDA guidance and following the guidelines of ISO 18562-3, and the test subject was a DreamStation (1) CPAP device.***

As a result, a risk analysis is inadequate and no further design change, corrective action, or field correction was conducted when appropriate or within an appropriate timeframe.

8. ***ER 2241475 V00 Biological Risk Assessment, dated 07/02/2020 and titled, "EXPOSURE TO POLYESTER-POLYURETHANE FOAM PARTICULATES FROM SYSTEM ONE FOAM DEGRADATION: BIOLOGICAL RISK ASSESSMENT", states in part, "Compounds of concern were identified as analytes with Margin of Safety (MOS) values*** (b) (4) ***of these compounds had MOS values*** (b) (4) ***. Based upon the exposure to*** (b) (4) ***with potential for carcinogenicity, mutagenicity, and systemic toxicity, the biological and toxicological risks from exposure to degraded PE-PUR foam are of concern and the severity of harm is crucial with respect to both the 30 kg and 70 kg patient populations of the System***

One medical device". This Biological Risk Assessment was conducted as a result of field reports/complaints regarding degraded sound abatement foam in various CPAP and ventilator products and states in part, "Philips Respironics Inc. (PRI) was made aware in May 2019 that four CPAP units were returned to a service center with degraded sound abatement foam". This Biological Risk Assessment is documented in CAPA 7211.

As a result a risk analysis is inadequate and no further design change, corrective action, or field correction was conducted when appropriate or within an appropriate timeframe.

9. ***Biological Risk Assessment ER 2241475 Appendix C, dated 12/10/2020 and titled "DEGRADED POLYESTER-POLYURETHANE FOAM-BIOLOGICAL RISK ASSESSMENT", states in part, "The purpose of this report is to evaluate the potential biological risks posed by the degraded PE-PUR foam according to the risk management process outlined in FDA Guidance 2020 and ISO 10993-1:2018". It further states, "The cytotoxicity and positive genotoxicity results observed from degraded PE-PUR foam samples indicate a potential patient risk. Potential cytotoxicity and genotoxicity leading to carcinogenicity are possible outcomes from degraded PE-PUR foam exposure. Overall, based on an understanding of the toxicological significance of the foam degradants and the results of the ISO 10993 testing to include mutagenic responses in both a bacterial and mammalian system, the degraded PE-PUR foam is not considered biocompatible and presents a significant biological risk to those patient populations who are exposed to degraded PE-PUR foam".***

    This Biological Risk Assessment was conducted as a result of field reports/complaints regarding degraded sound abatement foam in various CPAP and ventilator products and states in part, "Philips Respironics Inc. (PRI) has received field reports of CPAP and ventilator units returned to service centers with degraded sound abatement foam", This Biological Risk Assessment is documented in CAPA 7211.

    As a result, a risk analysis is inadequate and no further design change, corrective action, or field correction was conducted when appropriate or within an appropriate timeframe.

10. ***The "Biocompatibility Risk Assessment for Degraded Sound Abatement Foam in CPAP and Ventilator Units", written by*** (b) (4), (b) (6) ***and***

dated 01/11/2021, states in part, "Based on an understanding of the toxicological significance of the foam degradants and the results of the biological testing to include mutagenic responses in both a bacterial and mammalian system, the degraded PE-PUR foam is not considered biocompatible and presents a significant biological risk to patients exposed to the degraded PE-PUR foam. Potential cytotoxicity and genotoxicity leading to carcinogenicity are possible outcomes from degraded PE-PUR foam exposure", "I have read and concur with the findings in the Biological Risk Assessment noted above and I have no further comments". This Biocompatibility Risk Assessment was conducted as a result of field reports/complaints regarding degraded sound abatement foam in various CPAP and ventilator products and is documented in CAPA 7211.

As a result, a risk analysis is inadequate and no further design change, corrective action, or field correction was conducted when appropriate or within an appropriate timeframe.

11. *The* (b) (4) *report, "FINAL GLP REPORT: 20-03961-G2", dated 01/13/2021, states in part, "The purpose of the study is to determine the potential mutagenicity of the test article or its extract on various strains of* (b) (4) *) and* (b) (4) *, via* (b) (4) *". The test article is polyester polyurethane foam (PE-PUR), and this test report concludes, "Based on the criteria of the study protocol, the test article is considered to be mutagenic". The* (b) (4) *report, "FINAL CLP REPORT: 20-03961-62" is documented in CAPA 7211.*

    As a result, a risk analysis is inadequate and no further design change, corrective action, or field correction was conducted when appropriate or within an appropriate timeframe.

12. *The* (b) (4) *report, "FINAL GLP REPORT: 20-03961-65", dated 01/13/2021, states in part, "The purpose of the study was to determine the potential mutagenicity effect on* (b) (4) *) in response to the test article extract", The test article is polyester polyurethane foam (PE-PUR), and this test report concludes, "Based on the criteria of the protocol, the test article does not meet the requirements of the test and is considered mutagenic". The test article, polyester polyurethane foam (PE-PUR) is used in various Sleep and*

Respiratory Care Products and the (b) (4) ***report, "FINAL GLP REPORT: 20-03961-G5" is documented in CAPA 7211.***

As a result, a risk analysis is inadequate and no further design change, corrective action, or field correction was conducted when appropriate or within an appropriate timeframe.

13. ***The*** (b) (4) ***report, "FINAL GLP REPORT: 20-03961-Cl", dated 01/13/2021, states in part, "The purpose of the study was to determine the potential biological reactivity of a mammalian cell culture*** (b) (4) ***in response to the test article extract". The test article is polyester polyurethane foam (PE-PUR), and this test report concludes, "Based on the criteria of the protocol and the ISO 10993-S guidelines, the test article does not meet the requirements of the test and is considered to have a cytotoxic potential". The test article, polyester polyurethane foam (PE-PUR) is used in various Sleep and Respiratory Care Products and the*** (b) (4) ***report, "FINAL GLP REPORT: 20-03961-Cl' is documented in CAPA 7211.***

    As a result a risk analysis is inadequate and no further design change, corrective action, or field correction was conducted when appropriate or within an appropriate timeframe.

14. ***ER 2241475 V00 Biological Risk Assessment, dated 01/22/2021, and titled, "DEGRADED POLYESTER POLYURETHANE SOUND ABATEMENT FOAM: BIOLOGICAL RISK ASSESSMENT", states in part, "Overall, based on an understanding of the toxicological significance of the foam degradants and the results of the ISO 10993 testing to include mutagenic responses in both a bacterial and mammalian system, the degraded PE-PUR foam is not considered biocompatible and presents a significant biological risk to those patient populations who are exposed to degraded PE-PUR foam". This Biological Risk Assessment was conducted as a result of field reports/complaints regarding degraded sound abatement foam in various CPAP and ventilator products and is documented in CAPA 7211.***

    As a result a risk analysis is inadequate and no further design change, corrective action, or field correction was conducted when appropriate or within an appropriate timeframe.

Your firm is currently conducting on-going, Class 1 medical device recalls of over 15 million Philips Respironics ventilator, CPAP, and BiPAP devices, due to polyester polyurethane foam degradation and volatile organic compound emission, which was publicly announced on 06/14/2021.

RESPONSE TO OBSERVATION 1(c)

Background

At the time of the inspection, Respironics had processes that require risk assessments be performed when the Company becomes aware of quality issues. The source of the quality issue drives the risk process utilized. For example:

- Per WI 8.4-837, *Complaint Evaluation, Investigation, and Closure*, the complaint-handling process requires an evaluation to determine whether the complaint represents a potential impact to health. Complaints identified as representing a potential impact to health help to drive the requisite complaint investigatory activities to be performed and consideration for escalation to the CAPA process.

- Per QSP 16.2.9, *Manage Corrective and Preventive Action*, the CAPA process requires that, for every initiated CAPA, a risk analysis be conducted. The results of the risk analysis are used to appropriately scope CAPA activities.

- Per QSP 7.3-388, *Issue Tracking Process*, a risk severity analysis is conducted for issues identified during design and development.

As further discussed below with respect to the fourteen (14) cited examples, Respironics understands that it can further improve its underlying processes to help ensure that quality issues receive adequate risk assessments and are addressed in a timely manner:

- *Example 1(c)(1)*: The cited testing was performed to support a complaint investigation. The results of the testing were analyzed as part of the complaint investigation and included as part of the complaint's risk analysis evaluation. Based partly on the cited testing, the complaint investigation concluded that the risk management file addressed the hazard presented by the complaint. In light of FDA's feedback, Respironics will update the risk management file to fully address the information learned through the complaint investigation. In addition, Respironics will enhance its complaint investigation

procedure to help ensure that complaints are appropriately evaluated against the risk management file.

- *Example 1(c)(2)*: The cited testing was initiated to support complaint investigations. Testing was conducted but not utilized as part of the complaint investigation analysis. In response to FDA's feedback, Respironics will enhance the complaint-handling process to help ensure that all testing initiated as part of a complaint investigation is fully evaluated within the complaint-handling process.

- *Examples (1)(c)(3)–(4), (6)–(7)*: The cited testing was performed to support product development. In response to FDA's feedback, Respironics will enhance its design control process to help ensure timely evaluation for risk analysis of information learned during product development that may impact released products.

- *Examples (1)(c)(5) and (8)–(14)*: The cited testing was conducted to support the investigation of CAPA 7211 and the risk analysis activities, which included a Health Hazard Evaluation (HHE) performed as part of the CAPA. Respironics understands that FDA is not challenging the analysis provided in the cited test reports, but that its feedback concerns completing the risk analysis portion of CAPA 7211 in a timely manner. The risk analysis is used to drive other activities within the CAPA (e.g., type and timing of implementation of action). In response to FDA's feedback, Respironics will enhance its risk analysis process to help ensure the analysis is conducted in a timely manner.

See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 1(c), Respironics initiated CAPA 1505260, which contains the following actions:

- To address *Example (1)(c)(1)*:
  - Respironics enhanced WI 8.4-838, *Complaint Evaluation, Investigation, and Closure* (Version 26), WI 8.4-621, *Product Investigation Lab Procedure* (Version 17), and WI 8.4-995, *Third-Party Evaluation Process* (Version 03), to require that when a new hazard/failure is identified during a complaint investigation, Quality Assurance (QA) is to be notified. QA is required to evaluate the new hazard/

failure in accordance with QSP 7.3-286, *Risk Management*, to determine whether additional action is required (e.g., HHE). (Refer to **Attachments 1(c)–1, 1(c)–2, and 1(c)–3**.)
    - Training of affected personnel on the enhanced procedure is underway and will be completed by January 5, 2022.

- Respironics enhanced QSP 8.4-836, *Complaint Handling* (Version 23), to clarify that when a complaint represents a new Hazard/Failure Mode or a change to an existing Hazard/Failure Mode requiring update to the Risk Management File, the complaint is escalated to the CAPA process for handling. (Refer to **Attachment 1(c)–4**.)
    - Training of affected personnel on the enhanced procedure is underway and will be completed by January 5, 2022.

- To assess effectiveness of the action, a knowledge check (in the form of a simulation) will be required subsequent to training to the new revision of the process to ensure the expectations of the updated procedures are well understood. The simulation will be conducted using a formalized protocol which will (b) (4) A passing grade of 100% must be achieved by all simulation participants to be considered effective.

- To address *Example (1)(c)(2)*:
    - Respironics enhanced WI 8.4-995, *Third-Party Evaluation Process* (Version 03), to require that when testing is ordered utilizing returned product that is the subject of a complaint, the function ordering the testing must report the test results to the complaint-handling unit for inclusion in the complaint file associated with the returned product. (Refer to **Attachment 1(c)–3**.)
        - Training of affected personnel on the enhanced procedure is underway and will be completed by January 5, 2022.

    - To assess effectiveness of the action, a knowledge check (in the form of a simulation) will be required subsequent to training to the new revision of the process to ensure the expectations of the updated procedures are well understood. The simulation will be conducted using a formalized protocol which will (b) (4)

(b) (4) A passing grade of 100% must be achieved by all simulation participants to be considered effective.

- To address *Examples (1)(c)(3)–(4), (6)–(7)*:
  - Respironics enhanced QSP 7.3-388, *Issue Tracking Process* (Version 08), to require that, (b) (4) Where the risk is determined to be High or Moderate, the issue must trigger a CAPA request. (Refer to **Attachment 1(c)–5**.)
    - Training of affected personnel on the enhanced procedure is underway and will be completed by January 5, 2022.

  - To assess effectiveness of the action, a knowledge check (in the form of a simulation) will be required subsequent to training to the new revision of the process to ensure the expectations of the updated procedures are well understood. The simulation will be conducted using a formalized protocol which will (b) (4) A passing grade of 100% must be achieved by all simulation participants to be considered effective.

- To address *Examples (1)(c)(5) and (8)–(14)*:
  - Respironics enhanced QSP 7.3-286, *Risk Management* (Version 22), to clarify the timeliness of performing risk analysis activities (under the post-market risk assessment (PMRA)/HHE process). Specifically, PMRAs are to be completed (or a justification provided and approved via a preliminary PMRA) within (b) (4)) business days of the initiation of a CAPA or of escalation of an issue to the Risk Manager per QSP 7.3-286, *Risk Management*, and HHEs within (b) (4) additional business days after the final PMRA's completion. The performance against PMRA and HHE timeliness metrics will be monitored in the monthly Quality Review Board meetings. (Refer to **Attachments 1(c)–6**.)

  - To confirm the effectiveness of the actions, a (b) (4) derivation of (b) (4) confidence and reliability will be used to pull the next 18 consecutive PMRA/HHEs to evaluate whether content (new form and MDR considerations) has been documented correctly and conforms to the timeliness requirements. If

any inadequacies are found in the documentation of the PMRA/HHE, the actions taken will be ineffective.

- Since the cited example, but prior to the inspection, Respironics enhanced on February 18, 2021, its monitoring program of CAPA activities (which includes the completion of HHEs) by improving QSP 16.2.9, *Manage Corrective and Preventive Action*, to formalize CAPA timelines (Version 09; refer to **Attachment 1(a)–1**). Figure 1-1 below explains the target metrics for CAPA timeliness performance management as explained in QSP 16.2.9, *Manage Corrective and Preventive Action*.

Figure 1-1: Visual Depiction of CAPA Target Timelines

- The CAPA Investigation Phase includes the completion of the risk assessment activities (including an HHE if indicated). The expectation is that these activities are completed within (b) (4) days.

- In order to progress manage according to the timeliness expectations, after (b) (4) days from initiation of the CAPA, incomplete Investigations are flagged as (b) (4) " for timeliness and continue to flag as "(b) (4) " (b) (4)) until (b) (4) days. After (b) (4) days, CAPA Investigations that are incomplete are reported as "(b) (4) " ((b) (4) . Table

1-1 below explains the target metrics for CAPA timeliness performance management

Table 1-1: CAPA Target Timelines

Metric Info	CAPA Requests (CR)	Investigate	Close
(b) (4)			

- The CAPA timeliness metrics are reviewed by the CRB during its periodic (b) (4) minimum) meetings. If a metric shows a CAPA record as being "(b) (4)," the CRB can direct resources to address the metric. The CRB membership includes Business/Site Leadership and Quality Leadership. The CRB is responsible for overseeing the performance and timeliness of the CAPA process. Refer to Inspectional Observation 2 for CAPA quality assurance oversight activities by the CRB.

- In June 2021, the CAPA process was further enhanced to strengthen the oversight by Respironics Leadership through the creation of a CRB meeting template that requires an evaluation of the status of each CAPA identified as being (b) (4) " or "(b) (4) " for review and handling by the CRB. See FRM 5362, *CRB Meeting Template* (Version 01; refer to **Attachment 1(c)–7**).[2]

- As discussed in the Company's response to Inspectional Observation 6, Respironics enhanced the management review process by clarifying the metrics used to communicate the status of product issues to management with executive responsibility (e.g., CAPA Investigation status which includes completion of risk management activities). If a product is identified with a "(b) (4)"

[2] During preparation of this Response, Respironics corrected a typographical error found in FRM 5362, *CRB Meeting Template* (Version 00, released in June 2021).

status, the enhanced management review process requires the initiation of an action item or action plan to resolve the issue. See the *Actions in Response to FDA's Inspectional Observation* section of Respironics's response to Inspectional Observation 6.

- To verify the effectiveness of the action, after the implementation of the action, a (b) (4) derivation of (b) (4) confidence and reliability will be used to examine the next (b) (4) consecutive full Management Review records to evaluate for proper usage of the enhanced process requirements. Specifically:
  - Presentation of Top Product Quality Issues during a Management Review, in alignment with instructions for the same provided in QSP 16.5.4, *Operate and Assess the MS-QMS* (Version 01).
  - 100% correct (b) (4) indicator usage for reporting the status of Product Issues presented during Management Review.
  - Creation of Action Items and/or Action Plans for 100% of Product Issues identified with a (b) (4) Indicator (unless Action Item or Action Plan is already open for the same).

o Respironics will assess current, open risk assessments (i.e., PMRAs and HHEs) consistent with the new requirements described above per the recently enhanced QSP 7.3-286, *Risk Management* (Version 22).

d) No risk analysis, health hazard evaluation, or design review was documented as a result of an A Series CPAP device, containing silicone foam, failing Volatile Organic Compound (VOC) testing as part of ISO 18562-2 and 18562-3 testing.

Test Report Number 600253-RP-12 (Rev A), dated 08/24/2021, documents that an A Series CPAP device failed VOC testing as part of ISO 18562-2 and 18562-3 testing. Test Report Number 600253-RP-12 (Rev A) documents that (b) (4) compounds of concern (COC5) were identified, and (b) (4) compounds were confirmed, due to their carcinogenic/mutagenic properties. Additionally, Report Number 600253-RP-12 (Rev A) documents that pediatric patients would potentially be exposed to higher concentrations of compounds of concern, if they utilized an A Series CPAP device for sustained periods of time.

No health hazard evaluation, risk analysis, or design review was documented by your firm.

The affected A Series device contains silicone foam and is not affected by the ongoing Class I recalls related to polyester polyurethane foam.

RESPONSE TO OBSERVATION 1(d)

Background

The cited example concerns testing of a foam product in the (b) (4) Series device that has *not* been released to any market (U.S. or OUS). Specifically, Respironics intends to change the foam currently found in released product (i.e., PE-PUR) to silicone foam. As of the date of this Response, Respironics is in the process of qualifying the design change in accordance with its design control process, QSP 3.1.0.1, *Design Controls*, which requires that Respironics validate or, where appropriate, verify, review, and approve design changes before their implementation.

The cited testing is part of the design qualification activities Respironics is performing to qualify the change. Specifically:

- On August 24, 2021, Respironics received notice that a single test of the (b) (4) -Series device had unacceptable results for VOCs (specifically formaldehyde and (b) (4) (b) (4)). Respironics initiated an investigation, as required per QSP 7.3-388, *Issue Tracking Process*.

- In response to this test result, Respironics escalated the investigation to a full CAPA (CAPA 1373795) per QSP 16.2.9, *Manage Corrective and Preventive Action*.

- As part of the CAPA 1373795 investigation, Respironics contracted two independent laboratories, (b) (4) . and (b) (4) , which ran additional VOC and toxicological testing on the (b) (4) Series device. These tests all showed passing test results.

- Respironics's preliminary investigation suggests the following:
    - The physical behavior of the failing formaldehyde VOC profile is inconsistent with expected ISO 18562 VOC release profiles.

- A statistical analysis on the formaldehyde VOC profile of the cited report, compared to other testing performed, revealed that the failing formaldehyde VOC profile was a statistical outlier.

- Respironics is continuing to investigate the issue. As part of its continuing investigation, Respironics will evaluate the GC-MS detection and potential sources of (b) (4) (b) (4) based on the cited report and literature information on this compound.

- As part of the CAPA 1373795 investigation, Respironics will conduct a risk analysis as required by QSP 16.2.9, *Manage Corrective and Preventive Action*.

Therefore, our change control processes were properly followed and worked as intended to stop the qualification of this change after receipt of the unacceptable ISO 18562 VOC results. The change is on hold. The change will not be implemented until the investigation is complete and all appropriate design qualification activities are successfully completed.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 1(d), Respironics initiated CAPA 1505260, which contains the following actions:

- As noted above in Respironics's response to Inspectional Observation 1(c), the Company has updated QSP 7.3-286, *Risk Management* (Version 22), and QSP 7.3-388, *Issue Tracking Process* (Version 08), to provide further clarity on the requirements to ensure timeliness of actions.

- Once the investigation is complete, Respironics will take all necessary actions to address the investigation's findings. Respironics will also assess the potential impact on other existing devices that utilize silicone foam, once the investigation is complete.

e) The Biological Risk Assessment, dated 05/22/2018, and Health Hazard Evaluation ER2227646 V06, both related to CAPA NV 0988, are inadequate because they do not accurately reflect the known data at that time. CAPA INV 0988, the Biological Risk Assessment, dated 05/22/2018, and Health Hazard Evaluation ER2227646 V06 were all initiated to investigate potential polyester polyurethane foam degradation in Trilogy ventilator devices, as alleged in various field complaints and medical device reports.

The Biological Risk Assessment, dated 05/22/2018, titled, "EXPOSURE TO POLYESTER-POLYURETHANE FOAM PARTICULATES FROM TRILOGY 100 INLET AIR PATH FOAM DEGRADATION: BIOLOGICAL RISK ASSESSMENT", states in part, "A total of 17 cases were reported pertaining to the degraded foam in the Trilogy ventilator device". The Health Hazard Evaluation ER2227646 V06, related to CAPA INV 0988, states in part, "Post market surveillance information revealed 17 instances allegedly related to degradation of air inlet path foam".

[However] [i], a query of your firm's consumer complaints from 01/01/2008 to current, for the keywords contaminants, particles, foam, debris, airway, particulate, airpath, and black, resulted in over 222,000 complaints, and over 20,000 of which occurred between 2008 to 2017 and involved Trilogy devices. Additionally, your firm performed a foam related complaint data analysis in April 2021 on complaints confirmed to be related to or involve foam degradation issues. The raw complaint data documents that 30 Trilogy related complaints were received from 2014 to 2017, and 1,254 related complaints were received across all products containing the affected foam, from 2014 to 2021. Therefore, this Biological Risk Assessment and Health Hazard Evaluation are not adequate because they do not accurately reflect the known data at that time.

Your firm is currently conducting on-going, Class 1 medical device recalls of over 15 million Philips Respironics ventilator, CPAP, and BiPAP devices, due to polyester polyurethane foam degradation and volatile organic compound emission, which was publicly announced on 06/14/2021.

RESPONSE TO OBSERVATION 1(e)

Background

At the time of the inspection, Respironics had a procedure to evaluate health hazards and determine whether the Company should take action on an issue. Specifically, QSP 7.3-286, *Risk Management*, includes a process for conducting an HHE which requires the determination of a severity and probability for scoring a hazard. One of the key inputs for determining probability is an evaluation of post-market data, including complaint information.

The cited example concerns an HHE performed in 2018 to evaluate the health hazards associated with degraded foam and Trilogy devices. As noted in Respironics's response to

Inspectional Observation 5, the Company performed a correction/removal to address the issue (which Respironics will be retrospectively reporting under Inspectional Observation 5). To help determine probability, Respironics attempted to identify the complaints alleging degraded foam with Trilogy devices.

In light of FDA's feedback, Respironics investigated how it attempted to identify the seventeen (17) complaints included within the HHE. The investigation determined that the Company performed complaint word searches of its database. Respironics understands that it can enhance its methodology and process for better identifying relevant complaints when performing an HHE. In addition, Respironics can better document within its records its rationale and methodology for performing complaint searches used to support HHEs. See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 1(e), Respironics initiated CAPA 1505260, which contains the following actions:

- To address the cited HHE:
    - Using an approved protocol and statistical methodology, Respironics is performing an assessment of the over 222,000 complaints cited by FDA based on keyword searches, including the over 20,000 involving Trilogy devices, to assess whether these complaints are related to potential foam degradation in order to determine the applicability of the dataset with respect to the Biological Risk Assessment, dated 5/22/2018, and ER 2227646 V06, *Health Hazard Evaluation*. Respironics anticipates completion by December 17, 2021.

    - Since 2018, Respironics completed on April 27, 2021, an HHE (ER 2241623, Version 00) to evaluate foam degradation and Trilogy devices based on new information. The April 2021 HHE supersedes the 2018 HHE and resulted in a new correction/removal (RES 88071) described in the Cover Letter to this Response that was reported to the Agency on May 7, 2021. Therefore, the cited HHE has already been addressed by the April 2021 HHE. Should the review of the 220,000 complaints discussed in the bullet point above change the summary of the complaint information documented in the April 2021 HHE, Respironics will update the April 2021 HHE.

- Respironics enhanced QSP 8.4-836, *Complaint Handling* (Version 23), and WI 8.6-840, *Complaint Trending* (Version 11), to clarify the requirements for complaint search criteria and documentation requirements for complaint searches, including those that are used to support CAPA Investigations (inclusive of PMRAs and HHEs). In addition, FRM 5278, *CAPA Review Checklist*, has been enhanced to require that complaint searches stored within CAPAs (such as in support of HHEs) document the methodology and rationale of the complaint search (Version 01). (Refer to **Attachments 1(c)–4, 1(e)–1, and 1(a)–2**.)

    - Training of affected personnel on these updated procedures is underway and will be completed by January 5, 2022.

    - Effectiveness of updates to QSP 8.4-836, *Complaint Handling*, and WI 8.6-840, *Complaint Trending Work Instruction*, will be determined via a (b) (4) derivation of (b) (4) confidence and reliability, which will be used to pull the next 18 consecutive complaint queries performed in support of Risk Analyses performed under 7.3-286, *Risk Management*, (e.g., PMRAs and HHEs) to evaluate for proper documentation of methodology and rationale for the query parameters.

    - After implementation of the actions (enhancement of the CAPA Review Checklist), an audit will be conducted to ensure that any complaint searches included within the sampled CAPAs have documented the complaint search methodology and rationale on at least 35 product-related CAPAs after they move from the "Investigate" to the "Implement" phase in (b) (4) (at this point the root-cause investigation and effectiveness check plans have been defined by the CAPA team and approved by the CRB). The actions will be deemed effective if the requirements of QSIT Table 1 are met. The FDA Inspection Guide QSIT Table 1 ((b) (4)) will be used to determine the sample size.
        - Note: This effectiveness check permits the use of (b) (4) sampling.

- Respironics enhanced FRM 1256, *Health Hazard Evaluation (HHE) Template* (Version 08), that includes specific instructions on how to conduct and document the various aspects of the HHE, including probability and severity determinations. (Refer to **Attachment 1(e)–2**.)
    - Training of affected personnel on the enhanced HHE form is underway and will be completed by January 5, 2022.

- Respironics is performing a retrospective review of all HHEs completed in the last five (5) years (December 1, 2021, to December 1, 2016) where the HHE did not result in a correction/removal to evaluate the following aspects:

    - Whether all post-market data (e.g., complaint and MDR data) were accurate and appropriately considered within the HHE.
    - Whether the HHE appropriately evaluated the worst-case device configuration.
    - Whether the HHE appropriately evaluated the relevant patient populations.

  Respironics expects to release a protocol to conduct the review by January 31, 2022. The review protocol will include the timeline for completion of the review.

f) Health Hazard Evaluation ER2227646 V06, approved and closed on 06/15/2018 and related to CAPA INV 0988 and foam degradation on Trilogy 100 and Trilogy 200 ventilator devices, is inadequate because it does not accurately reflect the probability and severity of harm related to such foam degradation. Health Hazard Evaluation ER2227646 V06 and CAPA INV 0988 were both initiated to investigate potential polyester polyurethane foam degradation in Trilogy ventilator devices, as alleged in various field complaints and medical device reports.

Specifically, Health Hazard Evaluation ER2227646 V06 documents a probability of harm score of (b) (4) or unlikely, which is defined as, "'Not likely' that use will cause harm*; possible but improbable". Health Hazard Evaluation ER2227646 V06 further states, *Note: If harm has already occurred as a result of the issue under review, then:", "Probability level (b) (4) and (b) (4) can only be used if the investigation shows the harm was the result of an isolated incident and no other units are likely to be affected; a detailed rationale for why harm is not likely to occur again must be provided". [However] [i], this Health Hazard Evaluation also states in part, "Post market surveillance information revealed 17 instances allegedly related to degradation of air inlet path foam". Additionally, at least fourteen of these seventeen complaints have associated medical device reports filed by either your firm or another entity. Therefore, potential foam degradation in Trilogy ventilator devices is not an isolated incident, and you also have not documented a detailed rationale for why harm is not likely to occur again, as required by your Health Hazard Evaluation's instructions.

Your firm is currently conducting on-going, Class 1 medical device recalls of over 15 million Philips Respironics ventilator, CPAP, and BiPAP devices, due to polyester polyurethane foam

degradation and volatile organic compound emission, which was publicly announced on 06/14/2021.

RESPONSE TO OBSERVATION 1(f)

Background

At the time of the inspection, Respironics had a procedure for evaluating health hazards to determine whether the Company should take action on an issue. Specifically, QSP 7.3-286, *Risk Management*, includes a process for conducting an HHE which requires the determination of a severity and probability for scoring a hazard.

The cited example concerns an HHE performed in 2018 to evaluate the health hazards associated with degraded foam and Trilogy devices. See Respironics's response to Inspectional Observation (1)(e) for additional background concerning the HHE. To help determine probability, Respironics attempted to identify the complaints alleging degraded foam with Trilogy devices (including events reported to FDA as MDRs). In light of FDA's feedback in Inspectional Observation 1(f), Respironics understands that it can enhance its process for conducting an HHE to help ensure that an HHE appropriately identifies and considers whether complaint information was reported to FDA as MDRs. See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 1(f), Respironics initiated CAPA 1505260, which contains the following actions:

- As noted in Respironics's response to Inspectional Observation 1(e) above concerning the cited HHE, since 2018, Respironics completed on April 27, 2021, an HHE (ER 2241623 Version 00) to evaluate foam degradation and Trilogy devices based on new information. The April 2021 HHE supersedes the 2018 HHE and resulted in a new correction/removal (RES 88071) described in the Cover Letter to this Response that was reported to the Agency on May 7, 2021. Accordingly, an enhancement to the cited HHE has already been addressed by the April 2021 HHE. As noted in the response to Inspectional Observation 1(e) above, Respironics is performing an assessment of post-market data which may impact the number of MDRs reported in the April 2021 HHE. Respironics will update the HHE as necessary based on the results of the review.

- Respironics enhanced FRM 1256, *Health Hazard Evaluation (HHE) Template* (Version 08), FRM 1279, *Post Market Risk Assessment* (Version 05), and QSP 7.3-286, *Risk Management* (Version 22), to clarify that, when assessing the probability of harm, it is necessary to also consider whether MDRs have been submitted for the event. (Refer to **Attachments 1(e)–2, 1(f)–1, and 1(c)–6**.)

    - Training of affected personnel on these updated documents is underway and will be completed by January 5, 2022.

    - To confirm the effectiveness of the actions, a (b) (4) derivation of (b) (4) confidence and reliability will be used to pull the next 18 consecutive PMRAs/HHEs to evaluate whether content (new form and MDR considerations) has been documented correctly.

- As noted in Respironics's response to Inspectional Observation 1(e) above, the Company is performing a retrospective review of all HHEs completed in the last five (5) years (December 1, 2021, to December 1, 2016) where the HHE did not result in a correction/removal to evaluate the following aspects:

    - Whether all post-market data (e.g., complaint and MDR data) were accurate and appropriately considered within the HHE.
    - Whether the HHE appropriately evaluated the worst-case device configuration.
    - Whether the HHE appropriately evaluated the relevant patient populations.

  Respironics expects to release a protocol to conduct the review by January 31, 2022. The review protocol will include the timeline for completion of the review.

OBSERVATION 2

Procedures for corrective and preventive action have not been adequately established.

RESPONSE TO OBSERVATION 2

The cited examples under Inspectional Observation 2, to which Respironics provides individual responses below, concern Respironics's CAPA processes and procedures, including how and when CAPAs are initiated, the requirements to verify the effectiveness of CAPA actions, (b) (4) impact assessments, and the evaluation of MDR and complaint data. As described further below, prior to the FDA inspection, Respironics had implemented several enhancements to its CAPA processes and procedures. Further, to address FDA's specific feedback, Respironics is: (1) implementing additional enhancements to its CAPA, complaint-handling and complaint-trending processes; and (2) conducting several retrospective reviews related to CAPAs. See the *Actions in Response to FDA's Inspectional Observation* sections of the individual responses for details on the procedural enhancements and retrospective reviews.

Specifically,

a) No formal CAPA was initiated or implemented, when appropriate, and no verification of effectiveness was performed. Specifically, CAPA INV 0988 was opened due to various complaints alleging foam degradation in Trilogy ventilator devices but was never made into a formal CAPA and was closed approximately (b) (4)

CAPA INV 0988 was opened on 04/12/2018, due to, "Units were returned from the field where the Trilogy Removable Air Path Foam (b) (4) ***) and the foam in the Inlet Air Path Assembly (*** (b) (4) ***) was degrading, and getting into the motor/air path, causing at least 1 Trilogy unit to fail". At the time, your firm's process was to open CAPA requests, referred to as CAPA INVs, as a precursor to formal CAPAs, but would only be made into formal CAPAs, if approved by a CAPA Review Board, or delegate(s), as documented by your written procedure in place at that time, QSP 8.5-206 v 30 titled, "Manage Corrective and Preventive Actions (CAPA)". [However][i], CAPA INV 0988 was closed on 06/20/2018 and no formal CAPA was initiated or implemented. Additionally, CAPA INV 0988 documents your firm implemented Field Communication IC 16-700-403 v 00, as a correction to the potential foam degradation in Trilogy ventilator devices. FC 16-700-403 v 00 is a preventative maintenance procedure affecting, "All Trilogy models with Air Path Assembly", specifically all***

Trilogy 100 and 200 ventilator models, which requires that "At both the (b) (4) ***(whichever comes first) and*** (b) (4) ***, the Inlet Air Path Assembly and Removable Air Path Foam are to be replaced". [However][i], no verification of effectiveness was performed for this corrective and preventive action.***

Your firm is currently conducting on-going, Class 1 medical device recalls of over 15 million Philips Respironics ventilator, CPAP, and BiPAP devices, due to polyester polyurethane foam degradation and volatile organic compound emission, which was publicly announced on 06/14/2021.

RESPONSE TO OBSERVATION 2(a)

Background

The cited example, INV 0988, concerns a "CAPA INV." A CAPA INV was a CAPA-like process for investigating issues, determining causes, and taking action to address an issue. If warranted, INVs could be escalated for handling as a CAPA which, if handled as a CAPA, includes the requirement to perform a verification of effectiveness check. The INV process was managed under then-current CAPA procedure QSP 8.5-206, *Manage Corrective and Preventive Actions (CAPA)*.

Subsequent to the processing of CAPA INV 0988 and prior to the FDA inspection, Respironics obsoleted the CAPA INV process on June 5, 2019. In addition, on June 5, 2019, Respironics enhanced its CAPA program and procedure with the release of QSP 16.2.9, *Manage Corrective and Preventive Action* (Version 00), which replaced QSP 8.5-206, *Manage Corrective and Preventive Actions (CAPA)*. QSP 16.2.9, *Manage Corrective and Preventive Action* (Version 00), required, and continues to require under the current version, that corrective and preventive action be verified as effective.

Since the release of Version 00 of QSP 16.2.9, *Manage Corrective and Preventive Action*, Respironics has further enhanced the CAPA program, with the most significant enhancements implemented through the release of Version 04 of QSP 16.2.9, *Manage Corrective and Preventive Action*, on February 18, 2021. These enhancements resulted from a self-assessment of the CAPA process conducted under CAPA 499421. Version 04 of QSP 16.2.9, *Manage Corrective and Preventive Action* (and subsequent versions), includes requirements to help ensure that CAPAs are fully complete, appropriately scoped, and managed to timeliness targets.

Since February 18, 2021, QSP 16.2.9, *Manage Corrective and Preventive Action*, has included requirements to help ensure that all aspects of a CAPA (e.g., investigation, root-cause analysis, identification and implementation of corrective/preventive action, and verification of effectiveness) are adequately completed. Specifically, an (b) (4) CAPA reviewer is required to utilize a checklist (FRM 5278, *CAPA Review Checklist*) to confirm that all CAPA activities are adequately completed. With respect to verification of effectiveness, FRM 5278, *CAPA Review Checklist*, mandates that CAPAs are evaluated based on the following criteria before closure:

- Were Verification/Validation activities performed and completed?
- Do the objective evidence of the Effectiveness Check correlate with the Effectiveness Check Plan or is rationale provided as to why not?
- Does the outcome of the Effectiveness Check clearly meet the predefined effectiveness criteria?

With respect to the cited example, INV 0988 was initiated to investigate complaints related to potential foam degradation for the Trilogy devices in Australia and to determine what actions should be taken. INV 0988 also included an assessment of whether further escalation to a full CAPA was required. Respironics determined that INV 0988 did not require escalation to the full CAPA process based on a risk assessment. See response to Inspectional Observation 1 for enhancements to Respironics's risk analysis program. As noted above, Respironics obsoleted the CAPA INV program. Under the current CAPA program QSP 16.2.9, *Manage Corrective and Preventive Action*, the cited issue would trigger a CAPA which would require that a verification of effectiveness check be performed.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 2(a), Respironics initiated CAPA 1505261, which contains the following actions:

- As described above, INV 0988 was processed under a historical procedure (QSP 8.5-206, *Manage Corrective and Preventive Actions (CAPA)*) that was made obsolete on June 5, 2019, and was replaced by QSP 16.2.9, *Manage Corrective and Preventive Action* (Version 00), which has itself been subsequently improved. The introduction of QSP 16.2.9 obsoleted the CAPA INV program. As noted above, under this enhanced CAPA process, the cited issue would trigger a CAPA which would require that a verification of effectiveness check be performed.

Prior to the inspection, Respironics initiated CAPA 499421 to further enhance its CAPA program. As part of CAPA 499421, Respironics initiated a retrospective review of CAPAs (per CAPA 499421) under a defined protocol. The scope of the review encompasses open, closed, and cancelled CAPA Requests and CAPAs with a CAPA Request Start date corresponding to the period of January 1, 2019, through December 31, 2020. The objective of the review is to assess the quality of historical CAPAs and determine the need for action. In response to Inspectional Observation 2(a), Respironics will increase its retrospective review scope back to December 1, 2016, to include the evaluation of CAPA INVs. The retrospective review is in progress to assess and correct, as needed, the identified CAPAs. The action encompasses an evaluation of the effectiveness verification of these historical CAPAs. Respironics expects to update the protocol being used for this review by Dec 17, 2021. The revised protocol will include the timeline for completion of the expanded review.

- To verify the effectiveness of the action, an audit will be conducted using FRM 5278, *CAPA Review Checklist*, on at least 35 CAPAs after they move from the "Investigate" to the "Implement" phase in (b) (4) (at this point the investigation activities, root-cause investigation, and effectiveness check plans have been defined by the CAPA team and approved by the CAPA Review Board (CRB)). The actions will be deemed effective if the requirements of the FDA Inspection Guide QSIT Table 1 (b) (4) are met.
    - Note: This effectiveness check permits the use of (b) (4) sampling.

b) CAPA INV 0988 involves Trilogy 100 and 200 ventilator devices only and does not include, investigate, or examine all of your firm's CPAP and BiPAP medical devices, which also include similar air path assemblies and/or the affected polyester polyurethane foam, which is susceptible to degradation.

CAPA INV 0988 included only Trilogy 100 and Trilogy 200 ventilators and states in part, "This issue impacts all Trilogy 100 and Trilogy 200 devices (All Trilogy Models with an Inlet Air Path Assembly). The related Biological Risk Assessment, dated 05/22/2018, also only included the Trilogy 100 and Trilogy 200 ventilator devices. [However][i], your firm manufactures various CPAP and BiPAP devices, which also include similar air path assemblies and/or the affected polyester polyurethane foam. Furthermore, per a complaint analysis conducted by your firm on April 9, 2021, your firm received approximately eighty complaints related to foam degradation, on non-Trilogy ventilator devices, from 2014 to 2017.

RESPONSE TO OBSERVATION 2(b)

As noted in Respironics's response to Inspectional Observation 2(a) above, INV 0988 was initiated in 2018 under the then-current CAPA procedure QSP 8.5-206, *Manage Corrective and Preventive Actions (CAPA)*, Version 30.

Subsequent to the processing of CAPA INV 0988 and prior to the FDA inspection, Respironics obsoleted the CAPA INV process on June 5, 2019. In addition, on June 5, 2019, Respironics enhanced its CAPA program and procedure with the release of QSP 16.2.9, *Manage Corrective and Preventive Action* (Version 00), which replaced QSP 8.5-206, *Manage Corrective and Preventive Actions (CAPA)*.

Since the release of Version 00 of QSP 16.2.9, *Manage Corrective and Preventive Action*, Respironics has further enhanced the CAPA program, with the most significant enhancements implemented through the release of Version 04 of QSP 16.2.9, *Manage Corrective and Preventive Action*, on February 18, 2021. These enhancements resulted from a self-assessment of the CAPA process conducted under CAPA 499421. Version 04 of QSP 16.2.9, *Manage Corrective and Preventive Action* (and subsequent versions), includes requirements to help ensure that CAPAs are fully complete, appropriately scoped, and managed to timeliness targets. More specifically with respect to CAPA scoping, enhancements include:

- Introduction of FRM 5278, *CAPA Review Checklist*, which requires that an (b) (4) Reviewer objectively assess the quality of CAPA records prior to their submission to the CRB.

- Section C of FRM 5278, *CAPA Review Checklist*, requires that (b) (4) risk be identified.

- Section D of FRM 5278, *CAPA Review Checklist*, includes a requirement for comprehensive scoping (b) (4)).

For each item of FRM 5278, *CAPA Review Checklist*, the independent CAPA Reviewer must make a "Yes," "No," or "N/A" assessment. Only CAPAs which have been reviewed and determined to have met the assessment criteria (unless otherwise justified) can be advanced for approval by the CRB. These enhancements to the CAPA program ensure that a horizontal impact assessment is performed within the record.

With respect to the cited example, INV 0988 was initiated to investigate complaints related to potential foam degradation for the Trilogy devices in Australia and to determine what actions should be taken. As noted above, Respironics obsoleted the CAPA INV program. Under the current CAPA program QSP 16.2.9, *Manage Corrective and Preventive Action*, the cited example would trigger a CAPA. Further, processing the issue through the current CAPA program would have result in an appropriate (b) (4) assessment.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 2(b), Respironics initiated CAPA 1505261, which contains the following actions:

- As described above, INV 0988 was processed under a historical procedure (QSP 8.5-206, *Manage Corrective and Preventive Actions (CAPA)*) that was made obsolete on June 5, 2019, and was replaced by QSP 16.2.9, *Manage Corrective and Preventive Action* (Version 00) which has itself been subsequently improved. The introduction of QSP 16.2.9, *Manage Corrective and Preventive Action*, obsoleted the CAPA INV program. Additionally, as noted above, these enhancements to the CAPA program ensure that a (b) (4) impact assessment is performed within the record.

  Prior to the inspection, Respironics initiated CAPA 499421 to further enhance its CAPA program. As part of CAPA 499421, Respironics initiated a retrospective review of CAPAs (per CAPA 499421) under a defined protocol. The scope of the review encompasses open, closed, and cancelled CAPA Requests and CAPAs with a CAPA Request Start date corresponding to the period of January 1, 2019, through December 31, 2020. The objective of the review is to assess the quality of historical CAPAs and determine the need for action. In response to Inspectional Observation 2(b), Respironics will increase its retrospective review scope back to December 1, 2016, to include the evaluation of CAPA INVs. The retrospective review is in progress to assess and correct, as needed, the identified CAPAs. The action encompasses an evaluation of the effectiveness verification of these historical CAPAs. Respironics expects to update the protocol being used for this review by December 17, 2021. The revised protocol will include the timeline for completion of the expanded review.

- To verify the effectiveness of the action, an audit will be conducted using FRM 5278, *CAPA Review Checklist*, on at least 35 product-related CAPAs after they move from the "Investigate" to the "Implement" phase in (b) (4) (at this point the investigation

activities, root-cause investigation, and effectiveness check plans have been defined by the CAPA team and approved by the CRB). The actions will be deemed effective if the requirements of the FDA Inspection Guide QSIT Table 1 (b) (4) are met.

- Note: This effectiveness check permits the use of (b) (4) sampling.

c) Analysis of quality data, such as complaints and medical device reports, was not adequately performed to identify or detect quality problems.

1. No formal investigation, risk analysis, or CAPA were initiated, performed, or documented, in response to the at least 222,000 complaints that could potentially be related to foam degradation and received from 2008 to 2017, prior to the initiation of CAPA INV 0988 in 2018.

CAPA INV 0988 was initiated on 04/12/2018 in response to field complaints alleging foam degradation on Trilogy ventilator devices, and CAPA 7211 was initiated on 06/19/2019 in response to field complaints alleging foam degradation on ventilator, CPAP, and BiPAP devices. A query of your firm's consumer complaints from 01/01/2008 to current, for the keywords contaminants, particles, foam, debris, airway, particulate, airpath, and black, resulted in over 222,000 complaints, and over 175,000 of which occurred between 2008 to 2017. [However][i], no formal investigation, risk analysis, or CAPA were initiated, performed, or documented, in response to the at least 175,000 complaints potentially related to degraded foam, prior to CAPA INV 0988, initiated on 04/12/2018.

Furthermore, your firm performed a foam degradation-related complaint analysis, dated 04/09/2021, as part of CAPA 7211, and identified 1,254 complaints confirmed to be related to foam degradation from 2014 to April 2021. Your analysis also identified 110 foam degradation related complaints were received from 2014 to 2017, before the initiation of CAPA INV 0988 on 04/12/2018.

RESPONSE TO OBSERVATION 2(c)(1)

Respironics will enhance: (1) its complaint-handling process to provide better criteria and guidance for determining when a complaint should be escalated to the CAPA process; and (2) its quality-trending process so that it can better detect product trends at a more granular failure code level. With respect to the cited example, prior to the inspection, Respironics initiated CAPA 7211 to investigate the issue and, through the CAPA, has taken action to fully resolve the issue. See *Actions in Response to FDA's Inspectional Observation* section below.

Background

At the time of the inspection, Respironics had a process for: (1) escalating a complaint issue to the CAPA process for action; and (2) trending quality data in order to determine whether a CAPA is required.

Complaint Handling Process and Escalation to CAPA

As part of each complaint investigation, Respironics is required per WI 8.4-836, *Complaint Handling*, to determine whether the complaint should be escalated to the CAPA process for initiation of action. WI 8.4-836, *Complaint Handling*, requires that complaints associated with device malfunctions that are confirmed through a complaint investigation to have caused or could cause deaths and/or serious injuries be escalated to the CAPA process.

In addition, codes are assigned to each complaint as part of the investigation process. Specifically, three (3) codes are assigned to each complaint:

- (b) (4)
-
-

Codes are established for each product family as an output of the development of the risk management file for the product family. New codes are to be added when there is an update to the risk management file or when the complaint investigator concludes that the existing codes do not adequately describe the complaint under review.

In light of FDA's feedback, Respironics will enhance its complaint-handling procedure to provide better criteria and guidance for determining when a single complaint should be escalated to the CAPA process. See *Actions in Response to FDA's Inspectional Observation* section below.

Quality Data Trending

QSP 8.6-702, *Statistical Methods and Data Analysis Techniques*, requires that quality data be analyzed utilizing (b) (4) to determine whether an issue should be escalated to

the CAPA process. Underlying WI 8.6-840, *Complaint Trending*, requires that complaints be trended (b) (4) (at a minimum) using (b) (4).

To execute the requirements of the procedures above, Respironics holds Quality Business Review (QBR) meetings on a routine basis (generally every month) to review and discuss in detail the following two trend analyses:

- For each device model/product family, a trend evaluation of shifts in complaint rates over time. Where a rate exceeds a target established on an (b) (4) basis, the issue is escalated to the CAPA process for consideration of action. In 2021, QSP 8.6-702, *Statistical Methods and Data Analysis Techniques*, was enhanced to procedurally include specific triggers to the CAPA process.

- In addition to evaluating complaint rates, Respironics's trends utilize what is referred to as a "Quality Triangle." A quality triangle is intended to measure how well a product is performing in the field over time. The calculation is performed by (b) (4). The data are then tracked over time. The data can be used to evaluate whether changes implemented within a product build require escalation for action.

In addition to the analysis above, Respironics establishes for certain products "(b) (4)" that trend certain complaint failure codes (representing safety and performance issues) over time utilizing (b) (4)

In light of FDA's feedback, Respironics will enhance its current trend program to better detect product trends at the more granular complaint code level. Accordingly, Respironics will redesign its complaint-trending process and program so that Respironics trends using a better statistical methodology at the complaint code level over time. The procedure will include (b) (4) for escalating trend signals to the CAPA process for investigation. In addition, so that complaint data are properly coded, Respironics will enhance its procedures to provide guidance and criteria for creating complaint codes/adding new codes. See *Actions in Response to FDA's Inspectional Observation* below.

Complaints Cited in Inspectional Observation 2(c)(1)

With respect to FDA's statement that since January 1, 2008, Respironics has been aware of more than 220,000 complaints that concern "contaminants, particles, foam, debris, airway, particulate, airpath, and black," for which 175,000 occurred between 2008 to 2017, see Respironics's response to Inspectional Observation 1(e).

Prior to the inspection, Respironics initiated CAPA 7211 to investigate the issue and, through the CAPA, has taken action to fully resolve the issue.

Actions in Response to FDA's Inspectional Observation

To address the cited issue, prior to the inspection, Respironics initiated CAPA 7211 to investigate the issue and, through the CAPA, is taking action to fully resolve the issue. Actions to address the issue are being tracked to closure through CAPA 7211.

Further, to address Inspectional Observation 2(c)(1), Respironics initiated CAPA 1505261, which contains the following actions:

- Respironics enhanced WI 8.4-836, *Complaint Handling* (Version 23), to provide better triggers for determining when a single complaint should be escalated to the CAPA process. (Refer to **Attachment 2(c)(1)–1**.)
    - Training of affected personnel on the enhanced procedure is underway and will be completed by January 5, 2022.

- To verify the effectiveness of the action above, an audit of investigated complaints will be conducted after implementation of the procedural update to ensure that any complaint investigations that should have been escalated to CAPA were properly escalated. A stratified sample of complaint investigations processed by members of the complaint investigation team will be reviewed. The actions will be deemed effective if the requirements of the FDA Inspection Guide QSIT Table 1 (b) (4) are met.
    - Note: This effectiveness check permits the use of (b) (4) sampling.

- Respironics will redesign its complaint-trending process and program so that Respironics trends using a better (b) (4) at the complaint code level over time. The procedure will include (b) (4) for escalating trend signals to the CAPA process for investigation. In addition, so that complaint data are properly coded, Respironics will enhance procedures to provide better guidance and criteria for creating complaint codes/adding new codes. Respironics will release a quality plan that includes

specific tasks (e.g., onboarding of additional resources, revising procedures, establishing new procedures) and timelines for completion of the tasks.

- Respironics will retrospectively trend two years of complaint data to determine whether the Company has missed any quality signals that should have been escalated to the CAPA process for consideration. In order to conduct the retrospective trending, Respironics will review the two years of complaint data in order to:

    - Apply failure codes using the enhanced coding process; and
    - Review the complaint information against the enhanced complaint-handling CAPA triggers described in the second bullet point above to evaluate whether the single complaint event should be cause for immediate escalation to the CAPA process.

  The timeline for completion of the retrospective trending will be included in the quality plan described in the bullet above.

2. Your analysis of quality data related to medical device reports conducted in or around February 2021, was not adequately performed to identify, or detect quality problems because it did not include all the known data at that time. Specifically, your firm performed a search of the Maude database, as part of CAPA 7211 activities and investigations, which resulted in three MDRs associated with your firm and potential foam degradation on Trilogy ventilator devices from 01/01/2011 to 01/31/2021. [However][i], CAPA INV 0988, opened and closed in 2018, documented seventeen complaints related to foam degradation in Trilogy 100 and Trilogy 200 Ventilator devices, and at least 14 of these 17 complaints had related medical device reports, filed by either your firm or another entity. Therefore, your analysis of quality data did not include all applicable medical device reports known at that time.

RESPONSE TO OBSERVATION 2(c)(2)

Background

The cited example concerns CAPA 7211, which is currently open. CAPA 7211 was initially handled under a historical CAPA procedure (QSP 8.5-206, *Manage Corrective and Preventive Actions (CAPA)*) that has since been obsoleted, as described in Respironics's responses to Inspectional Observations 2(a) and (b) above. CAPA 7211 is currently being managed under the current CAPA program, QSP 16.2.9, *Manage Corrective and Preventive Action*. As noted in

Respironics's response to Inspectional Observation 2(a), Respironics has further enhanced the CAPA program, with the most significant enhancements implemented through the release of Version 04 of QSP 16.2.9, *Manage Corrective and Preventive Action*, on February 18, 2021. These enhancements resulted from a self-assessment of the CAPA process conducted under CAPA 499421. Version 04 of QSP 16.2.9, *Manage Corrective and Preventive Action* (and subsequent versions), includes requirements to help ensure that CAPAs are fully complete, appropriately scoped, and managed to timeliness targets. More specifically with respect to CAPA investigation, enhancements include:

- Introduction of FRM 5278, *CAPA Review Checklist*, which requires that an independent Reviewer objectively assess the quality of CAPA records prior to their submission to the CRB.

- Section D of FRM 5278, *CAPA Review Checklist*, includes a requirement for comprehensive scoping (b) (4)) and includes as an example reviews of open/closed complaints.

For each item of FRM 5278, *CAPA Review Checklist*, the independent CAPA Reviewer must make a "Yes," "No," or "N/A" assessment. Only CAPAs which have been reviewed and determined to have met the assessment criteria (unless otherwise justified) can be advanced for approval by the CRB. These enhancements to the CAPA program help to ensure the adequacy of CAPA investigatory activities.

In light of FDA's feedback concerning the investigational activities conducted to support CAPA 7211, Respironics investigated how it attempted to identify the MDR events included within the CAPA's investigation. The investigation determined that the Company performed complaint word searches of its database as well as the MAUDE database. Respironics understands that it can enhance its methodology and process for better identifying relevant complaints when conducting a CAPA investigation. In addition, Respironics can better document within its records its rationale and methodology for performing complaint searches used to support CAPA investigations. See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 2(c)(2), Respironics initiated CAPA 1505261, which contains the following actions:

- To address the cited CAPA 7211:
  - As noted in the Company's response to Inspectional Observation 1(e), using an approved protocol and statistical methodology, Respironics is performing an assessment of the over 222,000 complaints (including any MDRs) cited by FDA based on keyword searches, including the over 20,000 involving Trilogy devices, to evaluate whether these complaints are related to potential foam degradation in order to determine the applicability of the dataset with respect to the Biological Risk Assessment, dated 5/22/2018, and ER 2227646 V06, *Health Hazard Evaluation*. Respironics anticipates completion by January 31, 2022.

  - Should the review of the 220,000 complaints (including any MDRs) discussed in the bullet point above change the summary of the complaint information documented in CAPA 7211, Respironics will update CAPA 7211.

- Respironics enhanced QSP 8.4-836, *Complaint Handling* (Version 23), and WI 8.6-840, *Complaint Trending Work Instruction* (Version 11), to clarify the requirements for complaint/MDR search criteria and documentation requirements for complaint/MDR searches, including those that are used to support CAPA Investigations (inclusive of PMRAs and HHEs). In addition, FRM 5278, *CAPA Review Checklist*, has been enhanced to require that complaint/MDR searches stored within CAPAs (such as in support of HHEs) document the methodology and rationale of the complaint search (Version 01). (Refer to **Attachments 2(c)(1)–1, 2(c)(2)–1, and 2(c)(2)–2**.)

  - Training of affected personnel on these updated procedures is underway and will be completed by January 5, 2022.

  - Effectiveness of updates to QSP 8.4-836, *Complaint Handling*, and WI 8.6-840, *Complaint Trending Work Instruction*, will be determined via a (b) (4) derivation of (b) (4) confidence and reliability to pull the next 18 consecutive complaint queries conducted in support of Risk Analyses performed under 7.3-286, *Risk Management*, (e.g., PMRAs and HHEs) to evaluate for proper documentation of methodology and rationale for the query parameters.

  - After implementation of the actions (enhancement of the CAPA Review Checklist), an audit will be conducted to ensure that any complaint searches included within the sampled CAPAs have documented the complaint search methodology and rationale on at least 35 product-related CAPAs after they move

from the "Investigate" to the "Implement" phase in (b) (4) (at this point the investigation activities, root-cause investigation, and effectiveness check plans have been defined by the CAPA team and approved by the CRB). The actions will be deemed effective if the requirements of the FDA Inspection Guide QSIT Table 1 (b) (4) are met.

- Note: This effectiveness check permits the use of (b) (4) sampling.

3. Your analysis of quality data related to complaints, was not adequately performed to identify, or detect quality problems because it did not include all the known data at that time. Specifically, your firm performed a foam degradation-related complaint analysis, dated 04/09/2021, as part of CAPA 7211, and identified 1,254 complaints confirmed to be related to foam degradation from 2014 to April 2021, across all affected product platforms.

[However][i], the raw data listing of these 1,254-foam degradation-related complaints, does not include 7 of the 17 complaints documented in CAPA INV 0988, opened and closed in 2018, and that are confirmed to be related to foam degradation in Trilogy 100 and 200 ventilator devices. Your analysis of quality data did not include all applicable complaints known at that time and therefore, was not adequately performed to identify, or detect the severity or magnitude of potential quality issues/concerns.

RESPONSE TO OBSERVATION 2(c)(3)

Background

The cited example concerns CAPA 7211, which is currently open. As noted in Respironics's response to Inspectional Observation 2(c)(2), CAPA 7211 was initially handled under a historical CAPA procedure (QSP 8.5-206, *Manage Corrective and Preventive Actions (CAPA)*) that has since been obsoleted, as described in the Company's responses to Inspectional Observations 2(a) and (b) above. CAPA 7211 is currently being managed under the current CAPA program, QSP 16.2.9, *Manage Corrective and Preventive Action*. As noted in Respironics's response to Inspectional Observation 2(c)(2), Respironics has further enhanced the CAPA program to help ensure the adequacy of CAPA investigatory activities.

In light of FDA's feedback concerning the investigational activities conducted to support CAPA 7211, Respironics has investigated how the Company attempted to identify the complaint events included within the CAPA's investigation. The investigation determined that Respironics performed complaint word searches of its database. Respironics understands that it can

enhance its methodology and process for better identifying relevant complaints when conducting a CAPA investigation. In addition, Respironics can better document within its records its rationale and methodology for performing complaint searches used to support CAPA investigations. See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

Please refer to Respironics's response to Inspectional Observation 2(c)(2) above for: (1) action taken to address the cited CAPA 7211; and (2) improvements made to clarify the requirements for complaint search criteria and documentation requirements for complaint searches, including those that are used to support Biological Risk Assessments, HHEs, and CAPAs.

The verification of effectiveness will be conducted under Inspectional Observation 2(c)(2).

d) No formal CAPA was initiated or implemented, when appropriate. Specifically, email correspondence between your firm and your raw foam supplier beginning 10/30/2015 and forward, document that your firm was made aware of polyester polyurethane foam degradation issues in/around October 2015, which was later confirmed by your foam supplier on 08/05/2016, via email. [However][i], no CAPA was initiated or implemented.

An email message from your firm to your supplier, dated 10/30/2015, implies that a customer made your firm aware of polyester polyurethane foam degradation issues. A subsequent response from your supplier to your firm, dated 08/05/2016, implies that degradation of polyester polyurethane foam is likely and could occur in as little (b) (4) ***.***

Additionally, a later email message from your firm to your supplier, dated 04/20/2018, documents that your firm has received complaints related to foam degradation in Trilogy ventilator devices, and that disintegrated foam has been pulled into ventilator and patients' air pathways. A follow-up email amongst your firm's personnel, dated 08/24/2018, states that testing confirmed that the affected foam breaks down in high heat and high humidity environments, which concurred with Trilogy ventilator related complaints received from both Florida and (b) (4) ***. It further states that your firm made the decision not to change the design, and continue to include polyester polyurethane foam, in the Trilogy ventilator platform of devices.***

RESPONSE TO OBSERVATION 2(d)

Background

Inspectional Observation 2(d) concerns two (2) quality events:

1. In 2015, Respironics received two (2) complaints alleging an issue associated with the PE-PUR foam within the Trilogy devices.

    - To investigate the complaints:
        - Respironics corresponded with the supplier of the foam material (the 2015 correspondence discussed in the Inspectional Observation).

        - In addition, as discussed in Respironics's response to Inspectional Observation 1(c)(1) above, the Company conducted testing of the foam material.

    - The results of the testing were analyzed as part of the complaint investigation and included as part of the complaint's risk analysis evaluation. Based partly on the cited testing, the complaint investigation concluded that the risk management file addressed the hazard presented by the complaint and thus the issue did not require escalation to the CAPA process. See Respironics's response to Inspectional Observation 1(c) above for action to help ensure that complaints are appropriately evaluated against the risk management file.

2. In 2018, Respironics received complaints from Australia alleging an issue associated with the PE-PUR foam within the Trilogy devices. The complaints were escalated to the CAPA process that was in place at the time, resulting in the initiation of INV 0988. Through INV 0988, Respironics corresponded with the supplier of the foam (the 2018 correspondence discussed in Inspectional Observation 2(d)). See Respironics's response to Inspectional Observations 2(a) and 2(b) above for background information on INV 0988 and the historical CAPA process. As noted in the responses, the CAPA INV process has since been obsoleted and the CAPA program at Respironics has been enhanced.

Since processing of the events above, Respironics initiated CAPA 7211 which addresses issues that led to the above-cited complaints.

In light of FDA's feedback in Inspectional Observation 2(d), Respironics will enhance its complaint investigation process to help ensure that all information learned through its

investigatory activities is evaluated for purposes of determining whether a complaint should be escalated to the CAPA process. In addition, as discussed above in response to Inspectional Observation 2(c)(1), Respironics has enhanced the triggers for when a single complaint should be escalated to the CAPA process. See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

Prior to the inspection, Respironics initiated CAPA 7211 which addresses issues that led to the above-cited complaints.

To address Inspectional Observation 2(c)(2), Respironics initiated CAPA 1505261, which contains the following actions:

- Respironics enhanced WI 8.4-838, *Complaint Investigation* (Version 26), WI 8.4-621, *Product Investigation Lab Procedure* (Version 17), and WI 8.4-995, *Third-Party Evaluation Process* (Version 03), to clarify how information learned during the course of complaint investigation (e.g., feedback from suppliers) is captured back into the complaint record. (Refer to **Attachments 2(d)–1, 2(d)–2, and 2(d)–3]**.)

- To verify the effectiveness of the action above, an audit of investigated complaints will be conducted after implementing the procedural update to ensure that all information learned through the investigatory activities are captured in the complaint record. A sampling of 35 complaint investigations processed by each member of the Product Investigation Lab will be reviewed. The actions will be deemed effective if the requirements of FDA Inspection Guide QSIT Table 1 (b) (4) are met.
    - Note: This effectiveness check permits the use of (b) (4) sampling.

- As described in Respironics's response to Inspectional Observation 2(c)(1), the Company enhanced WI 8.4-836, *Complaint Handling* (Version 23), to provide better triggers for determining when a single complaint should be escalated to the CAPA process. (Refer to **Attachment 2(c)(1)–1**.)
    - Training of affected personnel on the enhanced procedure is underway and will be completed by January 5, 2022.

- As described in Respironics's response to Inspectional Observation 2(c)(1), to verify the effectiveness of the action above, an audit of investigated complaints will be conducted

after implementing the procedural update to ensure that any complaint investigations that should have been escalated to CAPA were properly escalated. A stratified sample of complaint investigations processed by members of the Complaint Investigation team will be reviewed. The actions will be deemed effective if the requirements of the FDA Inspection Guide QSIT Table 1 (b) (4) are met.

- Note: This effectiveness check permits the use of (b) (4) sampling.

- As described in Respironics's response to Inspectional Observation 2(c)(1), the Company is retrospectively trending two years of complaint data to determine whether it has missed any quality signals that should have been escalated to the CAPA process for consideration. As part of this activity, Respironics is reviewing the two years of complaints. In the course of this review, Respironics will verify that, where investigational activities were initiated, the complaint investigation record is complete.

The timeline for completion of this review will be described in the quality plan being initiated to enhance Respironics's quality-trending program, as described in the Company's response to Observation 2(c)(1).

OBSERVATION 3

Design validation did not ensure the device conforms to defined user needs and intended uses.

RESPONSE TO OBSERVATION 3

Although the Inspectional Observation suggests the cited examples as being associated with Design Validation, FDA's feedback concerns an HHE Respironics conducted to assess a quality issue. As noted in the responses to the individual cited examples, Respironics is enhancing its process for preparing HHEs. In addition, Respironics is retrospectively reviewing existing HHEs. See *Actions in Response to FDA's Inspectional Observation* for each of the cited examples.

Specifically,

a) Health Hazard Evaluation ER2227646 V06, approved and closed on 06/15/2018, related to CAPA INV 0988, and concerning Trilogy 100 and 200 ventilator devices, documents typical and healthy lung and bodily functions, and does not conform to or address the user needs of the intended patient population of these ventilatory medical devices. The intended patient population of Trilogy 100 and 200 ventilator devices are individuals requiring mechanical ventilation, that potentially lack typical and healthy lung and bodily functions considered in your HHE. Furthermore, Health Hazard Evaluation ER2227646 V06 does not consider patients with a tracheostomy, which are also part of the intended patient population of these Trilogy ventilator devices.

Health Hazard Evaluation ER2227646 V06 states in part, "If particulate was to reach the patient, the patient's upper airway filtering mechanisms would remove the particulate from the airway. The large particulate (greater than 5 microns) would be removed from the airway by the cilia and mucosal lining through inertial impaction. Impacted particles would then be expectorated by the patient. The increased velocity of the particulate due to the flow generated by the device would increase the probability of impacting in the upper airway. Medium particulate (1-5 microns) would be removed from the airway by the cilia and mucosal lining through sedimentation. Sedimentation occurs as particulates deposit into the mucosal layer of the airway as flow decreases. Small particles (less than 1 micron) not removed through impaction and sedimentation would be subjected to Alveolar Macrophages. Alveolar Macrophages, a type of white blood cell on the surface of alveoli, are another defense mechanism for the lungs. Alveolar Macrophages seek out deposited particles, bind to them,

ingest them, kill any that are living, and digest them. When the lungs are exposed to serious threats, additional white blood cells in the circulation, especially neutrophils, can be recruited to help ingest and kill pathogens. For example, when the person inhales a great deal of dust, more macrophages are produced and neutrophils are recruited."

The intended use for both the Trilogy 100 and 200 ventilator devices is for "continuous or intermittent ventilatory support for the care of individuals who require mechanical ventilation", which also includes patients with a tracheostomy. [However][i], this Health Hazard Evaluation ER2227646, documents typical and healthy lung and bodily functions, and does not conform to or address the user needs of the intended patient population of these ventilatory medical devices, including patients with a tracheostomy or that lack typical and healthy lung and bodily functions.

RESPONSE TO OBSERVATION 3(a)

Although the Inspectional Observation suggests the cited example as being associated with Design Validation, Respironics understands this Inspectional Observation to be tied more specifically to an HHE the Company conducted to assess a quality issue.

Background

At the time of the inspection, Respironics had a procedure for evaluating health hazards to determine whether the Company should take action on an issue. Specifically, QSP 7.3-286, *Risk Management*, includes a process for conducting an HHE. As part of the HHE, the impacted patient population must be identified.

The cited example concerns an HHE performed in 2018 to evaluate the health hazards associated with degraded foam and Trilogy devices. As noted in Respironics's response to Inspectional Observation 5, the Company performed a correction/removal to address the issue (which Respironics will be retrospectively reporting under Inspectional Observation 5).

In light of FDA's feedback, Respironics understands that it can enhance its process to help ensure that appropriate patient populations are considered in performing HHEs. See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 3(a), Respironics initiated CAPA 1505262, which contains the following actions:

- Since 2018, Respironics completed on April 27, 2021, an HHE (ER 2241623, Version 00) to evaluate foam degradation and Trilogy devices based on new information. The April 2021 HHE supersedes the 2018 HHE and resulted in a new correction/removal (RES 88071) described in the Cover Letter to this Response that was reported to the Agency on May 7, 2021. Therefore, the cited HHE has already been addressed by the April 2021 HHE. During preparation of this Response, Respironics confirmed that the appropriate patient population was evaluated in the April 2021 HHE.

- Respironics enhanced FRM 1256, *Health Hazard Evaluation (HHE) Template* (Version 08), that includes specific instructions on how to conduct and document the various aspects of the HHE, including determining the impacted patient population. (Refer to **Attachment 3(a)–1**.)
    - Training of affected personnel on the enhanced HHE form is underway and will be completed by January 5, 2022.

- Respironics enhanced QSP 7.3-286, *Risk Management* (Version 22), to clarify:

    - The requisite clinical expertise level required for the HHE approver representing the Medical Affairs function. The Medical Affairs function provides input on identifying the impacted patient population within the HHE; and
    - That the HHE should consider the intended vulnerable patient populations in addition to general populations.

    (Refer to **Attachment 3(a)–2**.) Training of affected personnel on the enhanced procedure is underway and will be completed by January 5, 2022.

- To confirm the effectiveness of the actions, a (b) (4) derivation of (b) (4) confidence and reliability will be used to pull the next 18 consecutive HHEs to evaluate whether appropriate patient populations were considered and the appropriate Medical professional provided input to the HHE.

- As noted in Respironics's response to Inspectional Observations 1(e) and 1(f), the Company is performing a retrospective review of all HHEs completed in the last five (5)

years (December 1, 2021, to December 1, 2016) where the HHE did not result in a correction/removal to evaluate the following aspects:

- Whether all post-market data (e.g., complaint and MDR data) were accurate and appropriately considered within the HHE.
- Whether the HHE appropriately evaluated the worst-case device configuration.
- Whether the HHE appropriately evaluated the relevant patient populations.

Respironics expects to release a protocol to conduct the review by January 31, 2022. The review protocol will include the timeline for completion of the review.

b) Health Hazard Evaluation ER2227646 V06, approved and closed on 06/15/2018 and related to CAPA INV 0988, and the Biological Risk Assessment, dated 05/22/2018 and also related to CAPA INV 0988, titled, "EXPOSURE TO POLYESTER-POLYURETHANE FOAM PARTICULATES FROM TRILOGY 100 INLET AIR PATH FOAM DEGRADATION: BIOLOGICAL RISK ASSESSMENT", do not ensure Trilogy 100 and 200 ventilator devices conform to defined user needs and intended uses. They document the risk and hazard evaluation based on the use of a humidifier and/or bacterial filter with the use of Trilogy 100 and 200 ventilator devices, but neither component nor attachment is required for proper use of these ventilators.

Health Hazard Evaluation ER2227646 V06, states in part, "To reach the patient, particulate would have to pass through the device, through the humidifier and through the patient circuit. If a bacteria filter was in place, the particulate would not reach the patient". Furthermore, the Biological Risk Assessment, dated 05/22/2018, states in part, "The Trilogy user manual recommends the use of a bacterial filter for invasively ventilated patients or if the device will be used on multiple patients. This filter would catch any particulates released into the Trilogy airpath". [However][i], neither the humidifier or bacterial filter are required for use of the Trilogy ventilator devices, and both the Trilogy 100 and Trilogy 200 ventilator devices will function properly without the use of the humidifier and/or bacterial filter accessories. Therefore, the design validation, Health Hazard Evaluation ER2227646 V06, and the Biological Risk Assessment, dated 05/22/2018, do not ensure Trilogy 100 and 200 devices conform to defined user needs and intended uses.

Your firm is currently conducting on-going, Class 1 medical device recalls of over 15 million Philips Respironics ventilator, CPAP, and BiPAP devices, due to polyester polyurethane foam degradation and volatile organic compound emission, which was publicly announced on 06/14/2021.

RESPONSE TO OBSERVATION 3(b)

Although the Inspectional Observation suggests the cited example as being associated with Design Validation, FDA's feedback concerns an HHE Respironics conducted to assess a quality issue.

Background

As noted above in response to Inspectional Observation 3(a), at the time of the inspection, Respironics had a procedure for evaluating health hazards to determine whether the Company should take action on an issue. Specifically, QSP 7.3-286, *Risk Management*, includes a process for conducting an HHE. As part of the HHE, the device configuration must be identified.

The cited example concerns an HHE performed in 2018 to evaluate the health hazards associated with degraded foam and Trilogy devices. As noted in Respironics's response to Inspectional Observation 5, the Company performed a correction/removal to address the issue (which Respironics will be retrospectively reporting under Inspectional Observation 5). Although the cited HHE could potentially be interpreted to suggest that the bacteria filter and the humidifier (which are both optional accessories) were primary mitigations, that was not Respironics's intent.

In light of FDA's feedback, Respironics understands that it can enhance its process to help ensure that appropriate device configurations are utilized in performing HHEs. See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 3(b), Respironics initiated CAPA 1505262, which contains the following actions:

- Since 2018, Respironics completed on April 27, 2021, an HHE (ER 2241623, Version 00) to evaluate foam degradation and Trilogy devices based on new information. The April 2021 HHE supersedes the 2018 HHE and resulted in a new correction/removal (RES 88071) described in the Cover Letter to this Response that was reported to the Agency on May 7, 2021. Therefore, the cited HHE has already been addressed by the April 2021

HHE. During preparation of this Response, Respironics confirmed that the appropriate device configuration was evaluated in the April 2021 HHE.

- Respironics enhanced FRM 1256, *Health Hazard Evaluation (HHE) Template* (Version 08), that includes specific instructions on how to conduct and document the various aspects of the HHE, including determining the device configuration. (Refer to **Attachment 3(a)–1**.)
    - Training of affected personnel on the enhanced HHE form is underway and will be completed by January 5, 2022.

- Respironics enhanced QSP 7.3-286, *Risk Management* (Version 22), to make it clear that device configurations included in HHEs are representative of worst-case configurations and conform to defined user needs and intended uses. (Refer to **Attachment 3(a)–2**.)
    - Training of affected personnel on the enhanced procedure is underway and will be completed by January 5, 2022.

- To confirm the effectiveness of the actions, a (b) (4) derivation of (b) (4) confidence and reliability will be used to pull the next 18 consecutive HHEs to evaluate whether the correct device configuration (including worst-case configurations) was considered.

- As noted in Respironics's response to Inspectional Observations 1(e) and 1(f), the Company is performing a retrospective review of all HHEs completed in the last five (5) years (December 1, 2021, to December 1, 2016) where the HHE did not result in a correction/removal to evaluate the following aspects:

    - Whether all post-market data (e.g., complaint and MDR data) were accurate and appropriately considered within the HHE.
    - Whether the HHE appropriately evaluated the worst-case device configuration.
    - Whether the HHE appropriately evaluated the relevant patient populations.

Respironics expects to release a protocol to conduct the review by January 31, 2022. The review protocol will include the timeline for completion of the review.

OBSERVATION 4

Procedures for design change have not been adequately established.

Specifically, design changes, including changes and updates to preventative maintenance schedules and servicing procedures, were not adequately verified, reviewed, or validated before implementation.

a) A preventative maintenance procedure for Trilogy ventilator devices, the intended replacement component, or the (b) (4) time frame for this preventive maintenance were not verified, reviewed, or validated before implementation.

On or around 11/25/2015, your firm was aware and knowledgeable of a preventative maintenance servicing procedure implemented by another Philips entity in (b) (4), on Trilogy ventilator products, which was implemented in (b) (4) only, in response to issues/complaints in the field related to polyester polyurethane foam degradation. This preventative maintenance servicing procedure instructed service personnel of the other Philips entity in (b) (4) to "exchange the air inlet assembly at (b) (4)", which is a requirement to replace the air intake assembly component of Trilogy ventilator devices (b) (4). This preventative maintenance procedure, the intended replacement component, or the (b) (4) time frame were not verified, reviewed, or validated before implementation.

RESPONSE TO OBSERVATION 4(a)

Background

At the time (b) (4) implemented the above-referenced changes to the PM servicing procedure for the Trilogy ventilator products in Japan only, (b) (4) was the Marketing Authorization Holder for the Trilogy devices in (b) (4). As the Marketing Authorization Holder, (b) (4) implemented the change and, at that time, was responsible for implementing the change per the relevant (b) (4) laws and regulations. The relationship between Respironics and (b) (4) that was subsequently codified in an agreement on August 29, 2017, makes clear that (b) (4) is the Marketing Authorization Holder in (b) (4). However, Respironics understands that it can enhance its contractual relationship with (b) (4). See *Actions in Response to FDA's*

[3] PRJ is now called Philips Japan.

Inspectional Observation section below.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 4(a), Respironics initiated CAPA 1505295, which contains the following actions:

- With respect to the cited example, containment is not required because the foam being used with Trilogy 100 and 200 is currently under recall and being replaced with a new material. Respironics will follow its design control process to determine what PM activities (if any) are required for the new foam and that such PM activities are appropriately qualified.

- Respironics will strengthen its contract with (b) (4) to further clarify the process in regard to requests for changes such as the cited example. Specifically, the contract will be revised to state that: (1) (b) (4) shall not make changes without Respironics's prior authorization; and (2) if (b) (4) has a request for change, (b) (4) will submit the request to Respironics for evaluation. Respironics will handle the change as a change request in accordance with its procedural requirements, which include conducting all requisite change control activities. Respironics expects to complete the contract revision by February 28, 2022.

    - The effectiveness of this change will be verified via an audit of (b) (4) by Respironics to confirm that no design changes were made that did not go through the change control system.

- Respironics will conduct a review to verify that the current PM protocol and schedule in (b) (4) is consistent with Respironics's PM protocol and schedule. Respironics expects to complete the review by January 31, 2022.

b) A preventative maintenance procedure for Trilogy 100 and 200 devices, the intended replacement components, or the (b) (4) and time frame were not verified, reviewed, or validated before implementation.

As part of CAPA INV 0988 and in response to polyester polyurethane foam degradation complaints in the field, your firm implemented Field Communication 16-700-403, on/around 06/12/2018, which states in part, "At (b) (4)

(b) (4) and (b) (4), the Inlet Air Path Assembly and Removable Air Path Foam are to be replaced". This preventative maintenance procedure, the intended replacement components, or (b) (4) and time frame were not verified, reviewed, or validated before implementation.

Your firm is currently conducting on-going, Class 1 medical device recalls of over 15 million Philips Respironics ventilator, CPAP, and BiPAP devices, due to polyester polyurethane foam degradation and volatile organic compound emission, which was publicly announced on 06/14/2021.

RESPONSE TO OBSERVATION 4(b)

Respironics will enhance its change control process to add clarity to procedures and controls to help ensure that changes to Service Manuals/PM Schedules (processed at Respironics as Service Engineering Change Requests (ECRs)) are appropriately qualified. See *Actions in Response to FDA's Inspectional Observation* section below.

Background

At the time of the inspection, Respironics had a procedure for controlling and qualifying design changes, which as discussed below include changes to Service Manuals/PM Schedules. Specifically:

- In accordance with WI 7.3-287, *Managing Design Changes*, design changes are defined to include "any change to a controlled design input or design specification. This includes changes to the Product Requirements Document, sub-system requirements documents, design documents, drawings, and, in some cases, component or material specifications, packaging and labeling."

- When a design change is requested, per QSP 4.2-1100, *Engineering Change Requests (ECRs)*, the originator of the design change request issues an ECR within Respironics's electronic (b) (4) system and creates a Change Notice Outline (CNO) (FRM 1006). For more complicated design changes, a Design Change Plan (FRM 2369) may be created in addition to a CNO.

- Per QSP 4.2-1100, *Engineering Change Requests (ECRs)*, the originator is required to classify the design change into one (1) of the following five (5) categories (listed in Table

1 of QSP 4.2-1100). A change request can be classified as more than one ECR type, with the more conservative classification controlling the requisite qualification activities for the request.[4]

Table 4-1: Types of Engineering Change Requests

	Change Type	Description
1.	(b) (4)	
2.		
3.		
4.		
5.		

- The CNO (FRM 1006) outlines the qualification activities that need to be performed in order to qualify the change. With respect to qualification from a design perspective, Section B of the CNO provides guidance and outlines the requisite design control activities that may need to be performed in order to qualify the change (e.g., design verification testing, design transfer activities).

[4] For example, (b) (4)
(b) (4)

- Per WI 7.3-287, *Managing Design Changes*, the CNO must be reviewed by the originator with representatives from Engineering, Product Management, Regulatory Affairs, Design V&V, and Design Quality Assurance. Other relevant stakeholders may also be asked to review the planning document.

- The CNO must be approved by the author and any other members contributing to the CNO's content. In practice, because ECRs that concern design changes require design engineering expertise, a Design Quality Engineer will be an approver of the CNO.

- After completion of the qualification activities provided in the CNO, the ECR proceeds to approval in order to release the change. Approval of the ECR is dependent upon the classification of the ECR provided in **Table 4-1**. Specifically, the ECR classification directs who from within the quality organization is required to approve the request. For example, changes classified as "Design" are approved by a Design Quality Engineer, whereas changes classified as "Service" are approved by a Supplier Quality.

The cited change made in 2018 to the Service Manual/PM Schedule for Trilogy 100 and 200 devices was made under the immediate *prior* version of QSP 4.2-1100, *Engineering Change Requests (ECRs)*, Version 07 (obsoleted in 2020). Under Version 07, ECRs classified as "Service" were explicitly defined to not include any "Design or Process Control Impacts." As a result, ECRs classified as only "Service" would not have Section B of the CNO outline completed (Section B requires the author to outline the requisite design control activities that may need to be performed in order to qualify the change). The cited PM Schedule change to Trilogy 100/200 units was processed as an ECR classified as "Service."

In response to FDA's feedback, Respironics will enhance its change control process to add clarity to procedures and controls to help ensure that Service change requests are appropriately qualified. See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 4(b), Respironics initiated CAPA 1505295, which contains the following actions:

- With respect to the cited example, containment is not required because the foam being used with Trilogy 100 and 200 is currently under recall and being replaced with a new material. Respironics will follow its design control process to determine what PM activities (if any) are required for the new foam and that such PM activities are appropriately qualified.

- Respironics enhanced the definition of "Design Changes" included in WI 7.3-287, *Managing Design Changes* (Version 14), to make it clearer that changes to PM and/or service requirements are design changes. (Refer to **Attachment 4(b)–1**.)

- Respironics enhanced Table 1 of QSP 4.2-1100, *Engineering Change Requests (ECRs)* (Version 09), as follows:

  - (b) (4)

  - (b) (4)

  Refer to **Attachment 4(b)–2**.

- Although in practice CNOs are reviewed and approved by subject-matter experts within Quality, Respironics enhanced WI 4.2-007*, Approval Matrix* (Version 40), to procedurally require that CNOs be reviewed and approved by subject-matter experts within Quality. (Refer to **Attachment 4(b)–3**.)

- Training of affected personnel on the above-listed enhanced procedures is underway and will be completed by January 5, 2022.

- Respironics will retrospectively review the current Service Manuals of currently marketed products to confirm that all service requirements, including PM requirements, since the initial release have been verified and validated. Respironics expects to formalize a review protocol for this activity and provide an estimated completion timeline by January 31, 2022. Based on the results of the review, Respironics will develop a remediation plan as required.

- After implementation of the actions specified in this Response, an audit will be conducted on at least 35 completed ECRs (comprising the Design, Process, and Design and Process types) for changes related to Service to confirm that they were correctly processed per the revised process instructions. Design type changes will have the correct information in Sections B and C of the CNO. The actions will be deemed effective if the requirements of the FDA Inspection Guide QSIT Table 1 (b) (4) are met.
    - Note: This effectiveness check permits the use of (b) (4) sampling.

OBSERVATION 5

A correction or removal, conducted to reduce a risk to health posed by a device, was not reported in writing to FDA.

Specifically, the corrective actions implemented as a result of CAPA INV 0988 included a field correction of Trilogy 100 and 200 ventilator devices to reduce a risk to health and was not reported to the FDA. The field correction is documented in Field Communication 16-700-403 v 00, dated 06/12/2018, which affected (b) (4) ***Trilogy 100 ventilators and*** (b) (4) ***Trilogy 200 ventilators.***

Field Communication 16-700-403 v 00 states in part, "At (b) (4) ***, the Inlet Air Path Assembly and removal Air Path Foam are to be replaced". This field correction was implemented as a corrective action in response to CAPA INV 0988, which was initiated due to multiple field complaints and at least 1 Trilogy unit failure, caused by polyester polyurethane foam degradation. This affected foam was later found to be mutagenic, cytotoxic, carcinogenic, and non-biocompatible.***

Additionally, per a complaint analysis performed by this firm on 04/09/2021, this firm received approximately 30 complaints related to foam degradation of Trilogy devices from 2014 to 2017, and approximately 80 complaints related to degraded foam on other CPAP and BiPAP devices from 2014 to 2017.

Your firm is currently conducting on-going, Class 1 medical device recalls of over 15 million Philips Respironics ventilator, CPAP, and BiPAP devices, due to polyester polyurethane foam degradation and volatile organic compound emission, which was announced on 06/14/2021.

RESPONSE TO OBSERVATION 5

Respironics will retrospectively report the cited Field Communication (FC), FC 16-700-403, to FDA in accordance with 21 C.F.R. § 806.10. In addition, Respironics will enhance its corrections/ removals process to provide additional guidance and criteria for identifying and evaluating corrections/removals for reportability to FDA. See *Actions in Response to FDA's Inspectional Observation* section below.

Background

At the time of the inspection, Respironics had a procedure for evaluating the reportability of corrections/removals in accordance with 21 C.F.R. Part 806. Specifically, QSP 16.2.10, *Correction and Removal Process*, requires in Section 5.1.3 that corrections and removals be evaluated for reportability to the respective jurisdictions impacted by the correction/removal. The definitions for "Correction" and "Removal" are pulled directly from 21 C.F.R. Part 806 and are defined in the underlying work instruction, WI 8.5-095, *Corrections and Removals*:

- Correction: "Repair, modification, adjustment, relabeling, destruction, or inspection (including patient monitoring) of a product without its physician removal to some other location."

- Removal: "The physical removal of a device from its points of use to some other location for repair, modification, adjustment, relabeling, destruction, or inspection."

Section 5.1.3 of QSP 16.2.10, *Correction and Removal Process*, states that corrections/removals which address situations that present a risk to health be reported to government authorities. The decision as to whether a correction or removal requires reporting is made by the Head of Business Quality in collaboration with International Market Quality, and it is documented on FRM 5292, *Correction and Removal Strategy*. Per WI 8.5-095, *Corrections and Removals*, Section 3.12 requires that the rationale for not reporting a correction/removal be documented on FRM 5292, *Correction and Removal Strategy*.

In response to FDA's feedback, Respironics is enhancing its corrections/removals process and procedures to provide additional guidance and criteria for determining: (1) what is a correction/removal; (2) whether a correction/removal requires reporting to FDA; and (3) for actions not reported to FDA, that documentation is created in accordance with 21 C.F.R. § 806.20. See *Actions in Response to FDA's Inspectional Observation* section below.

Cited Example

The cited example concerns a change to the PM schedule to the Trilogy 100 and 200 ventilator devices that was deployed to field units through the FC process via FC 16-700-403 (see Respironics's response to Inspectional Observation 4(b) which discusses implementation of the change to the service manual for Trilogy 100/200 through the change control process).

- Per QSP 7.8-083, *Service Operations Process Development & Equipment Qualification*, corrections and/or changes to a service process must be evaluated for deployment to units in the field.

- Where it is determined that a change needs to be deployed to the field, the change is communicated to the field through an FC that is reviewed and approved in accordance with underlying WI 7.8-770, *Creating and Revising Service Technical Documentation*.

- Because FCs may meet the definition of a correction/removal, the author of the FC and Quality Assurance are required per the approval matrix provided in WI 7.8-770, *Creating and Revising Service Technical Documentation*, to evaluate the change in accordance with WI 8.5-095, *Corrections and Removals*.

With respect to the cited example, Respironics evaluated whether FC 16-700-403 represented a correction/removal per WI 8.5-095, *Corrections and Removals*, at the time it issued the FC. Respironics concluded that the action did not meet the definition of a correction/removal. As noted above and described below, Respironics is enhancing its corrections/removals process to provide additional guidance and criteria. See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 5, Respironics initiated CAPA 1505301, which contains the following actions:

- With respect to the cited example concerning FC 16-700-403, Respironics will retrospectively report the action in accordance with 21 C.F.R. § 806.10. Respironics expects to complete the action by January 31, 2022.

- As noted in the Cover Letter to this Response, Respironics is enhancing the knowledge of Respironics personnel by engaging outside experts to perform company-wide training, which will include understanding what actions meet the definition of a correction/ removal per 21 C.F.R. Part 806.

- Respironics will enhance its corrections/removals process and procedures to provide additional guidance and criteria for determining: (1) what is a correction/removal; (2) whether a correction/removal requires reporting to FDA; and (3) for actions not

reported to FDA, that documentation is created in accordance with 21 C.F.R. § 806.20. Respironics expects to complete this action by January 31, 2022 (including the completion of training).

- Respironics will define the criteria for verification of effectiveness of the actions by January 31, 2022.

- After release of the enhanced procedure, Respironics will evaluate FCs issued in the last five (5) years (from December 1, 2021, to December 1, 2016)[5] to determine whether the FCs meet the definition of a correction/removal but were not evaluated per WI 8.5-095, *Corrections and Removals*. If an FC meets the definition of a correction/removal, Respironics will evaluate whether the action requires reporting to FDA per 21 C.F.R. § 806.10 or internal record-keeping per 21 C.F.R. § 806.20. Respironics expects to complete the review by January 31, 2022. Based on the results of the review, Respironics will implement a remediation plan and take appropriate action, as required.

[5] This retrospective review period aligns with the HHE retrospective review being performed in response to Inspectional Observation numbers (1)(e); (1)(f); 3(a); and 3(b).

OBSERVATION 6

Management with executive responsibility has not ensured that the quality policy is understood, implemented and maintained at all levels of the organization.

Specifically, firm management, including management with executive responsibility, were aware of potential foam degradation issues concerning CPAPs, BiPAPs, and Trilogy ventilators since at least 01/31/2020, or earlier, and implemented no further corrective actions until April 2021. Polyester polyurethane foam degradation issues concerning CPAPs, BiPAPs, and Trilogy Ventilators were discussed at all (b) (4) management review meetings, since the 2019 (b) (4) dated 01/31/2020. [However][i], firm management implemented no further corrective actions until April 2021. Additionally, your firm became aware of this issue and related field complaints in at least 2015 or earlier.

Your Quality Manual QMS-0031 defines Sleep and Respiratory Care's (SRC) Management with Executive Responsibility as, "Top Management for the overall SRC Organization is the Business Leader/General Manager (Management with Executive Responsibility)", and both your Quality Manual and Management Review 5.1-079 written procedure document that your Business Leader (Management with Executive Responsibility) and Head of Quality (Management Representative) are required attendees of management review meetings. Both your Sleep and Respiratory Care Business Leader and Head of Quality, that held the position at the time, attended all seven management review meetings since the 2019 (b) (4) (b) (4) which were on the following dates: (b) (4) (b) (4)

Your firm is currently conducting on-going, Class 1 medical device recalls of over 15 million Philips Respironics ventilator, CPAP, and BiPAP devices, due to polyester polyurethane foam degradation and volatile organic compound emission, which was publicly announced on 06/14/2021.

RESPONSE TO OBSERVATION 6

Since initiation of the cited example, in 2021 Respironics onboarded new management with executive responsibility (MWER) and a Management Representative. In addition, prior to the inspection, but after the first cited Management Review meeting in (b) (4) 2019, Respironics enhanced its Management Review process to help ensure that issues are properly evaluated and that appropriate action is taken. In response to FDA's feedback, Respironics further

enhanced its Management Review process to help ensure that issues are better tracked to resolution and that the Respironics management takes timely action where appropriate. Finally, as more described in the Cover Letter to this Response, the Respironics management has directed resources to fully address the issue concerning the PE-PUR foam utilized in CPAPs, BiPAPs, and Trilogy ventilators. See *Actions in Response to FDA's Inspectional Observation* section below.

Background

At the time of the FDA inspection, Respironics had a process that allows management to review the suitability and effectiveness of the Quality Management System and take action where required. Specifically, QSP 5.1-079, *Management Review*, requires on a (b) (4) basis that MWER review a number of data points to evaluate the quality system. These inputs include, but are not limited to:

- Complaints
- Product Recalls/Field actions
- Product Trending
- Corrective Action
- Preventive Action
- Changes that could affect the Quality Management System, including changes in external and internal issues that are relevant to the Quality Management System
- Adequacy of Resources

Where appropriate, MWER establishes a KPI/metric that is used to assess the adequacy of the input (e.g., CAPA timeliness).

Respironics's Management Representative (defined per the Quality Manual to be Respironics Head of Quality) labels each Management Review process input and KPI/metric (where applicable) to provide MWER an indication of the underlying inputs in accordance with the color code scheme in Table 1.

Table 1: QMS Data Input Indicators

Indicator	Definition
(b) (4)	(b) (4)

In addition, the Management Representative in practice compiles a list of "Top Product Quality Issues" to present to MWER. The product issues were also scored with a "(b) (4) " status to indicate "Reliability" and "Investigation Status." The Reliability color code is intended to communicate the urgency of resolution and for the prioritization of the issue.

Based on its evaluation of the data inputs, QSP 5.1-079, *Management Review*, requires that MWER issue specific tasks to resolve the Management Review inputs that were "less than the defined target" by issuing an "Action Item" or an "Action Plan." Action Items are one-off tasks intended to address a discrete issue noted by MWER, whereas Action Plans are intended to group action items that concern the same/similar issue. Until determined to be closed, Action Items and Plans are required to be followed up at the next scheduled (b) (4) Management Review meeting.

Prior to the inspection, but after the first cited Management Review meeting in Q4 2019, Respironics enhanced its Management Review process. Specifically, QSP 5.1-079, *Management Review* (Version 20), was enhanced in Q2 2021 as follows:

- Required that a binary "(b) (4) " color that is more appropriate for KPIs be utilized to indicate status.

- Better defined what is an Action Plan and how it is executed. Specifically, a template was released within the Management Review report template (FRM 4797, Version 02) to document Action Plans. Action Plans are now required to include:

    - A defined problem statement;
    - A plan of action;
    - Owners of the action plan;
    - Estimated dates for completion of the actions; and
    - Reference to CAPAs (if applicable).

- Clarified that Action Plans are required for any KPI labeled with a red color code.

- For product issues reviewed during Management Review, required citation of the associated quality record driving the product issue (e.g., CAPA #, SCAR #, ECR #). By referencing the quality record, MWER has additional visibility to better track the resolution of the product issue.

In response to FDA's feedback, Respironics can further enhance its Management Review process to help ensure that product issues are presented with greater clarity and that management takes timely action where appropriate. With respect to the cited issue concerning the PE-PUR foam utilized in CPAPs, BiPAPs, and Trilogy ventilators, as noted in the Cover Letter to this Response, the Respironics management has committed to and provided resources to help drive the issue to resolution in a timely manner. See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 6, Respironics initiated CAPA 1505302, which contains the following actions:

- To enhance oversight and culture of the Quality Management System, Respironics onboarded new senior management. Specifically:

    - On March 29, 2021, Respironics onboarded a new Business Leader who is defined as MWER, David Ferguson. Mr. Ferguson has a diverse global background across a range of health tech areas, including critical care devices, diagnostic imaging, high-volume disposables, and pharmaceuticals. His most recent position was at Baxter Healthcare, where he led the €2.5 billion global Medication Delivery business—for hospital and home—which included infusion pumps, infection management, antimicrobial stewardship and analytics software products, and specialty IV solutions. Mr. Ferguson's CV is provided as **Attachment 6–1**.

    - On November 16, 2021, Respironics onboarded a new Head of Quality, Thomas J. Fallon. The Head of Quality operates as Respironics's Management Representative. Mr. Fallon brings over 30 years of quality and regulatory

industry experience to the role, including 14 years with Philips where he served as Head of Quality for Hospital Patient Monitoring; Senior Director, Quality Transformation Lead; Director of Quality Assurance and Regulatory Affairs for Emergency Care; and Director of Quality Assurance and Regulatory Affairs for Patient Monitoring. Prior to joining Respironics, Mr. Fallon held quality and regulatory roles with large multi-national pharmaceutical corporations, and he began his career in the United States Marine Corps. Mr. Fallon's CV is provided as **Attachment 6–2**.

- With respect to the cited issue concerning the PE-PUR foam utilized in CPAPs, BiPAPs, and Trilogy ventilators, the Respironics management dedicated in Q1 2021 support and resources to help drive completion of the investigation and identification of corrective actions. The project team frequently meets to drive actions to closure and reports on its status to management on a regular basis. Actions to address the issue are being tracked to closure through CAPA 7211.

- Respironics enhanced the Management Review process with the release of a new management review procedure, QSP 16.5.4, *Operate and Assess the MS-QMS* (Version 01; refer to **Attachment 6–3**) (replacing QSP 5.1-079, *Management Review*). When compared to the legacy Management Review procedure, QSP 16.5.4, *Operate and Assess the MS-QMS*, includes the following enhancements:

    - Codifies and provides direction on the presentation of Top Product Quality Issues during a Management Review.
    - Defines (b) (4) indicators with additional specificity that is more appropriate for reporting the status of Product Issues presented during Management Review.
    - Defines that Action Items and/or Action Plans are required when a Product Issue is identified with a (b) (4) Indicator.

  Training of affected personnel on the enhanced procedure is underway and will be completed by January 5, 2022.

- Respironics has undertaken a review of all product issues within the cited Management Reviews (Q4 2019 to date), as well as the most recent Management Review, and is applying the newly clarified (b) (4) indicators to these prior issues for review at its next scheduled full Management Review planned for January 2022. The agenda

from January's Management Review, will show completion of this review. Where required, Respironics will initiate Action Items and/or Action Plans to address product issues that have not previously been assigned a formal action but are required to under the enhanced QSP 16.5.4, *Operate and Assess the MS-QMS* (Version 01).

- To verify the effectiveness of the actions, after the implementation of the action, a (b) (4) derivation of (b) (4) confidence and reliability will be used to examine the next three (3) consecutive full Management Review records to evaluate for proper usage of the enhanced process requirements. Specifically:
    - Presentation of Top Product Quality Issues during a Management Review, in alignment with instructions for the same provided in QSP 16.5.4, *Operate and Assess the MS-QMS* (Version 01).
    - 100% correct (b) (4) indicator usage for reporting the status of Product Issues presented during Management Review.
    - Creation of Action Items and/or Action Plans for 100% of Product Issues identified with a (b) (4) Indicator (unless Action Item or Action Plan is already open for the same).

To further ensure that the Quality Policy is understood, implemented, and maintained at all levels of the organization, MWER will:

- Confirm that the Quality Policy is prominently posted at all Respironics facilities (by January 31, 2022).
- Host employee dialogues concerning the Quality Policy, including personalized examples of how the Quality Policy applies to employees (by March 31, 2022).
- Make available printed cards of the Quality Policy for employees to add as inserts to their employee badges. In this way, employees will have the Quality Policy at hand and accessible for reference (by March 31, 2022).

OBSERVATION 7

Procedures to ensure that all purchased or otherwise received product and services conform to specified requirements have not been adequately established.

Specifically, you have no established data, documentation, or written agreement that clearly describes or references the quality requirements of your raw foam supplier, or the specified requirements of the raw material components they supply, including raw foam components/materials.

Furthermore, SCAR 1052449, initiated 06/28/2021, and HHE ER2227930 V16, approved and closed on 09/23/2021, document that an incorrect and non-specified polyester polyurethane, raw foam product, sourced from your raw foam supplier resulted in (b) (4) ***non-conforming Trilogy Evo ventilatory finished devices being approved, released, and distributed, which further resulted in the ongoing correction and removal, identified with if 2021-CC-SRC-018 and approved on 09/15/2021. SCAR 1052449 documents that the suspect lot of raw foam was moved to your production line for use on 04/15/2021. SCAR 1052449, F-HE ER2227930 V16, and correction and removal U 2021-CC-SRC-018 were established as part of this firm's response to failed VOC and ISO 18562 testing of related Trilogy EVO ventilatory medical devices, documented in PSN Report Number 700018-RP-02 (Rev B), dated 08/09/2021, which resulted from the presence of the non-specified polyester polyurethane foam component, incorrectly supplied by your raw foam supplier. [However][i], this firm's supplier performance monitoring of this supplier documents no issues or concerns were observed, which was documented on*** (b) (4)

Your firm is currently conducting on-going, Class 1 medical device recalls of over 15 million Philips Respironics ventilator, CPAP, and BiPAP devices, due to polyester polyurethane foam degradation and volatile organic compound emission, which was publicly announced on 06/14/2021.

RESPONSE TO OBSERVATION 7

Respironics believes there are two issues noted in Inspectional Observation 7: (1) Development of the Foam Specification; and (2) Supplier Monitoring.

The Inspectional Observation suggests a connection between the two issues. Specifically, the suggestion is that specifications/requirements for the muffler foam—defined in mechanical

drawing 1126746, *Muffler Foam Base,* (b) (4) (hereinafter "(b) (4) Foam")—utilized in the Trilogy EVO Ventilator may not have been sufficiently detailed. As a result, the supplier that makes the (b) (4) Foam purchased incorrect foam material from its sub-supplier (resulting in a product recall).

As further discussed below, Respironics will provide additional clarity on the specification of the foam material within its design drawings. However, the recall was due to a mix-up at the sub-supplier due to incorrectly labeled foam material supplied to Respironics's supplier to make the (b) (4) Foam. A SCAR was issued to the supplier to address the issue and was considered at the (b) (4) Supplier Performance Monitoring meeting held on August 13, 2021 (reviewing Q2 2021 supplier performance data). Nonetheless, Respironics can further enhance its monitoring program as discussed below. See *Actions in Response to FDA's Inspectional Observation* section below.

Background

Development of the Foam Specification

The cited product Trilogy EVO was designed in accordance with a legacy design control process that has since been replaced with an enhanced design control process.

- The legacy process used to design Trilogy EVO (QSP 7.3-276, *Product Development Process*) required the creation of design outputs, which were defined to include mechanical design/drawings. The design outputs were created based on design inputs established at the product level (not at the part level).

- The current design control process, QSP 3.1.0.1, *Design Controls* (Version 01, released January 28, 2020), better drives the development of more robust part specifications (i.e., design outputs) because the enhanced process requires the development of requirements (i.e., design inputs) at the part level (refer to **Attachment 7–1**). Specifically:

    - An underlying work instruction WI 3.1.3, *Detail Designs [Prod&Sys]*, requires in Task 12 that requirements be documented in FRM 4847, *Requirements*, for the parts in the device.

    - FRM 4847, *Requirements*, provides guidance on how to draft requirements.

Specifically, the requirements musty be unambiguous, correct, clear, singular, and verifiable. In addition, the requirements must be in quantifiable terms so that they can be verified against the design output (e.g., drawing) created to satisfy the requirement.

With respect to the cited polyether polyurethane[6] material utilized to make the (b) (4) Foam, the foam material is defined under "Note 1" as "Material: (b) (4) ." A visual image of the (b) (4) Foam is provided below:

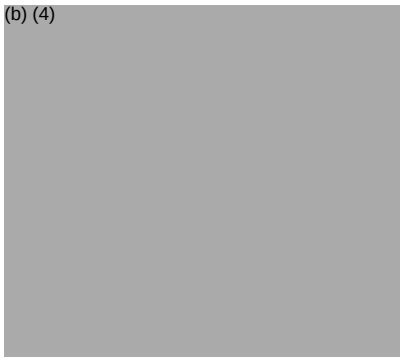

Figure 7-1: Visual Depiction of Foam

The (b) (4) Foam is manufactured for Respironics as follows:

Table 7-1: Supplier Flow Diagram for Manufacturing (b) (4) Foam

Raw Material Supplier		Sub-Supplier		Respironics Supplier
(b) (4)	→	(b) (4)	→	(b) (4)

[6] Note that the cited example incorrectly refers to the foam as polyester polyurethane; it is polyether polyurethane.

- "Note 1" identified in the Respironics drawing refers to a specification controlled by sub-supplier (b) (4) .

- Foam material identified as (b) (4) was utilized in Respironics's design verification and validation testing of Trilogy EVO and was thus codified within Respironics's product drawing for making the (b) (4) Foam.

- To help ensure that suppliers do not change their specifications, per WI 16.2.18.1.3, *Perform Supplier Qualification*, Respironics requires that suppliers enter agreements (either Quality or Change Notice) with terms that require the suppliers to obtain approval from Respironics before changing specifications.

Note that in addition to the (b) (4) Foam, there are three (3) other foam components that make up the Trilogy EVO muffler. The three (3) other foam components contain the same "(b) (4) " to define the foam material.

Under the current design control process released in January 2020, the foam components would have been better specified because documented specifications for the foam components would have been developed using FRM 4847, *Requirements*. In light of FDA's feedback, Respironics can further enhance its design control process to provide additional guidance on helping to ensure that part requirements are fully established by incorporating part risk into requirement development (e.g., parts that are Critical to Quality/Safety have more detailed requirements when compared to lower risk parts).

Therefore, to address the cited example, Respironics will:

- Better define the foam material specification for all (b) (4) foam muffler components, which include the cited (b) (4) Foam, in accordance with QSP 3.1.0.1, Design Controls, after the process has been further enhanced.

- In connection with CAPA 7211 (see response to Inspectional Observations 1(c)(1)), Respironics is revising the risk management file for Trilogy EVO. Because of the potential hazards associated with air pathway components learned through post-market data, the severity and probability rankings for air pathway components (inclusive of sound abatement foam) will be increased in the revised risk management file, thus resulting in all components and materials found in the air pathway (which will include the (b) (4) foam muffler components) being identified as critical components. As a

result of this change, per WI 16.2.18.1.3, *Perform Supplier Qualification*, Respironics will be required to conduct an onsite audit and enter into a quality agreement with its suppliers of air pathway components/materials.

See *Actions in Response to FDA's Inspectional Observation* section below.

Supplier Monitoring and SCAR 1052449

Supplier Corrective Action Request (SCAR) 1052449 was initiated because Respironics's supplier (b) (4) received foam material from its supplier (b) (4) that was incorrectly labeled as *polyether* polyurethane, whereas, in fact, it was *polyester* polyurethane (see **Table 7-1** above for a description of the relationships between the parties). SCAR 1052449 was *not* issued because the foam material specification was not sufficiently specified. Specifically:

- (b) (4) provides (b) (4) a number of foam materials including both *polyether* polyurethane and *polyester* polyurethane. (b) (4) uses the following prefixes on its material labels to identify material type:
    - Foam skived from *polyether* polyurethane is identified with prefix "(b) (4)."
    - Foam skived from *polyester* polyurethane is identified with prefix "(b) (4)."
- Prior to receipt of the cited (b) (4) test report, in late May 2021, Respironics manufacturing issued a Quality Notification (QN 202535059) (i.e., nonconformance report) because there was a suspicion that the (b) (4) Foam supplied by (b) (4) may have been nonconforming. Specifically, the color of the (b) (4) foam component did not appear to be the same color as that in prior received lots.
    - As a result of QN 202535059, Respironics issued in June 2021 SCAR 1052449 to (b) (4) to investigate the potentially nonconforming (b) (4) Foam component.
    - (b) (4) investigation identified that its supplier (b) (4) incorrectly labeled foam skived from *polyester* polyurethane with prefix code "(b) (4);" the material should have been labeled with prefix code "(b) (4)"
        - By the time Respironics became aware of the mix-up, Respironics had

manufactured and released Trilogy EVO product with the *polyester* polyurethane foam.

- In early May 2021 (prior to issuance of QN 202535059), Respironics sent Trilogy EVO units to (b) (4) to perform ISO 18562 testing to support a response to a request for additional information concerning a 510(k) premarket notification to cover changes to Trilogy EVO made since the product's launch in 2019.
    - After initiation of the testing by (b) (4) but prior to completion, Respironics determined that the Trilogy EVO units sent to (b) (4) may have contained the *polyester* polyurethane foam. Respironics proceeded with completing the testing because the test results were used as an input to the Health Hazard Evaluation (HHE) conducted to evaluate the issue.

- In the Q2 2021 Supplier Performance Monitoring report, Respironics did factor SCAR 1052449 into its evaluation of (b) (4). Specifically, (b) (4) performance rating did change from the previous (b) (4) review in part due to the cited SCAR 1052449.

Respironics believes FDA's feedback regarding supplier scoring concerns the Company's evaluation of (b) (4) (not (b) (4)) in the Q2 2021 Supplier Performance Monitoring report, which is performed in accordance with WI 16.2.18.5, *Monitor and Report Quality Performance of Suppliers* (Version 03). As noted above, (b) (4) is a sub-supplier of Respironics's supplier (b) (4) for the (b) (4) Foam. Therefore, manufacturing issues associated with the (b) (4) Foam (e.g., SCARs) were used to evaluate the performance of (b) (4). As noted in the last bullet point above, Respironics did consider the cited SCAR 1052449 in evaluating (b) (4) at its recent Supplier Performance Monitoring meeting.

(b) (4) is a Respironics supplier but not for the purposes of making the (b) (4) Foam (this relationship is managed by (b) (4) as (b) (4) supplies the foam material to (b) (4)). (b) (4) directly supplies Respironics with other foam components, and thus Respironics monitors (b) (4) in its (b) (4) Supplier Performance Monitoring for the provision of these items.

In response to FDA's feedback, Respironics will enhance its (b) (4) Supplier Performance Monitoring program to require that if a sub-supplier is also a Respironics supplier, any metrics

impacted by the supplier when it acts in the sub-supplier role will be considered in the supplier's (b) (4) evaluation. See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 7, Respironics initiated CAPA 1505303, which contains the following actions:

Enhancements Related to the Foam Specification

- Respironics will enhance its design control process to provide additional guidance on helping to ensure that part requirements are fully established by incorporating part risk into requirement development (e.g., parts that are Critical to Quality/Safety have more detailed requirements when compared to lower risk parts). Respironics expects to complete this action (including the completion of training) by February 28, 2022.

- With respect to the cited example, Respironics will better define the foam material specification for all (b) (4)) foam muffler components, which include the cited (b) (4) Foam, after release of the enhancements to the design control process described in the bullet point above. Respironics expects to complete this action by March 31, 2022.

- After the (b) (4) foam muffler component specifications are better defined as noted in the bullet point above, Respironics will evaluate the previously manufactured (b) (4)) foam muffler components (including the (b) (4) Foam) to confirm that the foam material utilized in the foam muffler components meets specification. Respironics expects to complete the review by April 29, 2022, and it will take appropriate action based on the results of the review (if required).

- As part of CAPA 7211 (see response to Inspectional Observations 1(c)), Respironics is revising the risk management file for Trilogy EVO. Because of the potential hazards associated with the foam components learned through post-market data, the severity and probability rankings for foam will be increased in the revised risk management file, thus resulting in all components and materials found in the air pathway (which will include the (b) (4) foam muffler components) being identified as critical components. As a result of this change, per WI 16.2.18.1.3, *Perform Supplier Qualification*, Respironics will be required to conduct an onsite audit (if not already complete) and enter into a

quality agreement (if not already in place) with the suppliers of air pathway components/materials. Respironics expects to complete this action by June 30, 2022.

  - The same analysis process described above will be applied to other applicable components /materials managed under the Respironics quality system and will be tracked to completion through CAPA 7211.

- Using a risk-based approach, beginning with (b) (4) foam, Respironics will review its drawings associated with its currently marketed products against the enhanced design control process described in the first bullet point in this section to confirm that the specifications are adequately established. Respironics expects to formalize a review protocol for this activity and provide an estimated completion timeline by January 31, 2022. Based on the results of the review, Respironics will define a plan for performing appropriate remediation where required.

- To verify the effectiveness of the actions, after implementation of the corrective actions, Respironics will evaluate a sample of 35 part requirement documents (FRM 4847) generated for new or revised parts to confirm that: (1) confirm that the requirements are adequately robust and detailed; and (2) design outputs have been created that address the part requirements. The actions will be deemed effective if the requirements of the FDA Inspection Guide QSIT Table 1 (b) (4) are met.
  - Note: This effectiveness check permits the use of (b) (4) sampling.

Enhancements to Supplier Monitoring Program

- Respironics will enhance WI 16.2.18.5, *Monitor and Report Quality Performance* (Version 02), to require that if a sub-supplier is also a Respironics supplier, any metrics impacted by the supplier when it acts in the sub-supplier role will be considered in the supplier's (b) (4) evaluation. Respironics expects to release the enhanced procedure (including the completion of training) by December 31, 2021.

- At the next (b) (4) Supplier Performance Monitoring meeting taking place by January 31, 2022, Respironics will re-evaluate all suppliers in accordance with the enhanced procedure described in the previous bullet. Based on the results of the re-evaluation, Respironics will take appropriate action where required.

- To verify the effectiveness of the actions, after implementation of the actions, a

(b) (4) Estimator sample with (b) (4) confidence and reliability will be used to evaluate the minutes from the next three (3) consecutive (b) (4) Supplier Performance Monitoring meetings conducted in 2022 (three (3) meetings) to confirm that if a sub-supplier is also a Respironics supplier, any metrics impacted by the supplier when it acted in the sub-supplier role were properly considered in the supplier's (b) (4) evaluation.

- Note: If there are no opportunities to evaluate the effectiveness of this action (as there are very few sub-tier suppliers who are also upper-tier suppliers), a simulation using a pre-approved protocol can be used in place as a verification of effectiveness. The participants of the simulation will be those personnel responsible for performing the process. Minimum passing grade is 100%

OBSERVATION 8

Potential consultants were not evaluated and selected based on their ability to meet specified requirements.

Specifically, (b) (4) ***consultants were not evaluated and selected based on their ability to meet specified requirements, including quality requirements. Additionally, this firm did not evaluate, select, and approve these consultants, as approved suppliers before utilizing their consulting services on the quality issue of polyester polyurethane foam degradation and CAPA 7211.***

The Work Instruction titled, Perform Supplier Qualification" with document number 16.2.18.1.2, states in part, Service Supplier: A third party is contracted to deliver agreed services. Examples may include, but are not limited to; (b) (4) ***." Additionally, no Supplier Qualification Forms, Form 5077, were completed for the*** (b) (4) ***consultants, as required per your supplier quality procedures and work instructions.***

Your firm is currently conducting on-going, Class 1 medical device recalls of over 15 million Philips Respironics ventilator, CPAP, and BiPAP devices, due to polyester polyurethane foam degradation and volatile organic compound emission, which was publicly announced on 06/14/2021.

RESPONSE TO OBSERVATION 8

Respironics is retrospectively qualifying the two cited consultants in accordance with its supplier management process. Respironics expects to complete this action by January 31, 2022. In response to FDA's feedback, Respironics has enhanced its qualification process to help ensure that consultants are appropriately qualified and is performing a review activity to help ensure that it has qualified all consultants impacting a quality function. See *Actions in Response to FDA's Inspectional Observation* section below.

Background

At the time of the inspection, Respironics had a process for qualifying suppliers, including consultants that provide services that impact the quality management system. Specifically:

- Per WI 7.4-813, *Procurement*, any Respironics employee that intends to purchase non-production goods and services must evaluate whether the service requires qualification per Respironics's supplier qualification program.
    - If the employee determines that the service affects product quality, patient safety, or the overall quality system, the supplier is identified as a "Service Supplier" and must be qualified in accordance with the supplier approval process.

- Supplier types and categories are further defined in WI 16.2.18.1.2, *Perform Supplier Classification*[7]. As noted in the cited example, the WI defines that Service Suppliers include consultants performing functions which impact the quality management system.
    - WI 16.2.18.1.3, *Perform Supplier Qualification*, provides further clarity in that Service Suppliers include individuals providing regulatory or clinical services. In addition, WI 16.2.18.1.3, *Perform Supplier Qualification*, provides that when the Regulatory and Clinical Departments engage regulatory or clinical services in accordance with their internal processes, Regulatory and Clinical are responsible for providing the Supplier Approval Form (FRM 5077, *Supplier Qualification Form (ACD Form)*).

- Per WI 16.2.18.1.3, *Perform Supplier Qualification*, the specific qualification requirements for Service Suppliers are based on the risk of the service that the supplier is performing (higher-risk suppliers require additional qualification activities when compared to lower-risk suppliers).
    - Supplier approval is documented on FRM 5077, *Supplier Qualification Form (ACD Form)*, and qualified suppliers are listed on the Respironics Approved Supplier List (ASL).

- Suppliers approved and listed on the ASL are then populated in Respironics's Purchase Order (PO) software management tool (b) (4). To help ensure that suppliers utilized by Respironics are approved and included on the ASL, Respironics will release a procedure that requires Respironics to (b) (4) See *Actions in Response to FDA's Inspectional Observation* section below.

[7] Note that the cited example incorrectly refers to the title of this procedure as "*Perform Supplier Qualification*."

During the preparation of this Response, Respironics initiated retrospective qualification of the two (2) suppliers cited in Inspectional Observational 8. In light of the cited example and FDA's feedback, Respironics understands that it can further enhance its supplier qualification program to help ensure that Service Suppliers providing a quality function are reviewed/approved in accordance with Respironics's supplier qualification program. Specifically, Respironics can provide additional clarity and instruction as to what constitutes a Service Supplier (e.g., consultants providing medical advice utilized in evaluating product risk). See *Actions in Response to FDA's Inspectional Observation* section below.

Actions in Response to FDA's Inspectional Observation

To address Inspectional Observation 8, Respironics initiated CAPA 1505304, which contains the following actions:

- Respironics is retrospectively qualifying the (b) (4) cited consultants in accordance with its supplier management process. Respironics expects to complete this action by January 31, 2022.

- Respironics enhanced WI 16.2.18.1.2, *Perform Supplier Classification* (Version 02), to provide additional clarity and instruction as to what constitutes a "Service Supplier" (Refer to **Attachment 8–1**.). The enhanced procedure clarifies that service suppliers include consultants.
    - Training of affected personnel on the enhanced procedure is underway and will be completed by January 5, 2022.
    -
- Respironics enhanced WI 16.2.18.1.3, *Perform Supplier Qualification* (Version 04), to better establish qualifications tailored to Service Suppliers performing consulting services. (Refer to **Attachment 8–2**.) The enhanced procedure outlines tailored qualification activities for consultants.

    - Training of affected personnel on the enhanced procedure is underway and will be completed by January 5, 2022.

- Respironics will establish a procedure that codifies its PO process. The procedure will require that a check be performed to confirm that suppliers that can impact the quality management system have been qualified and included on the ASL. Respironics expects

to complete this action (including the completion of appropriate training) by February 28, 2022.

- Utilizing its PO database, Respironics will identify and confirm that it has appropriately qualified all current Consultants providing services that can impact the quality management system, as defined in the enhanced WI 16.2.18.1.2, *Perform Supplier Classification* (Version 02), and WI 16.2.18.1.3, *Perform Supplier Qualification* (Version 04). (Refer to **Attachments 8–1** and **8–2**.) Respironics expects to complete its review by December 31, 2021. Based on the results of the review, Respironics will release a remediation plan to address the review's findings if required.

- To verify the effectiveness of the actions, Respironics will evaluate a sample of new Service Suppliers providing consulting services, who are onboarded after implementation of the actions, to confirm that the new Service Suppliers were appropriately qualified in accordance with the procedural requirements and added to the ASL. The actions will be deemed effective if the requirements of the FDA Inspection Guide QSIT Table 1(b) (4) are met.
    - Note: This effectiveness check permits the use of (b) (4) sampling.

[i] Please note the Form FDA 483 states "Alternatively" here, but the Company interpreted this to mean "However".