DE NOVO CLASSIFICATION REQUEST FOR TRISTEL DUO ULT HIGH LEVEL DISINFECTANT

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Foam or gel chemical sterilant/high level disinfectant.** A foam or gel chemical sterilant/high level disinfectant is a germicide in the form of a foam or gel that is intended for use as the terminal step in high level disinfection of medical devices prior to patient use.

NEW REGULATION NUMBER: 21 CFR 880.6886

CLASSIFICATION: Class II

PRODUCT CODE: QWS

BACKGROUND

DEVICE NAME: TRISTEL DUO ULT

SUBMISSION NUMBER: DEN220041

DATE DE NOVO RECEIVED: July 13, 2022

SPONSOR INFORMATION:

Hyman, Phelps, & McNamara, P.C.
700 13th St NW, Suite 1200, Washington, DC 20005 USA
On behalf of:
Tristel Solutions Limited, Lynx Business Park,
Fordham Road, Snailwell, CB8 7NY, United Kingdom

INDICATIONS FOR USE

The Tristel Duo ULT high level disinfectant is indicated as follows:

> Tristel Duo ULT is a high level disinfect foam for reprocessing ultrasound probes. It can be used to high level disinfect endocavity transvaginal and transrectal probes, and skin surface transducers that may contact non-intact skin during use.
>
> Tristel Duo ULT is a high level disinfectant when used in accordance with the directions for use, including a disinfection contact time of 2 minutes, at room temperature and a concentration at or above Minimum Recommended Concentration (MRC).
>
> Tristel Duo ULT must be applied on the surface of an ultrasound probe using Duo Wipes.

Duo Wipes are intended to apply Tristel Duo ULT foam on the surface of ultrasound probes and to remove residue of the foam after high level disinfection.

Each dose of Tristel Duo ULT foam and each Duo Wipe are single use.

The semi-critical ultrasound probes reprocessed by Tristel Duo ULT must first be cleaned according to a validated cleaning protocol or standard and following the device manufacturers' instructions.

Tristel Duo ULT foam bottle is designed in a way that ensures measured dose delivery with each application generating active ingredient above the MRC.

MRC: ~90% v/v (~280ppm) at point of use. MRC of Tristel Duo ULT may be verified using Duo Test Strips.

LIMITATIONS

Tristel Duo ULT is intended to be marketed for prescription use.

PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

Tristel Duo ULT is a high level disinfectant foam intended to disinfect cleaned, reusable, non-lumened ultrasound probes. Tristel Duo ULT is intended to be used by qualified healthcare personnel. Tristel Duo ULT does not sterilize.

Tristel Duo ULT generates chlorine dioxide foam from two "precursor" solutions (Base Solution and Activator Solution), which are packaged separately within two individual containers and secured together within a single dispenser apparatus known as the "pump" shown in Figure 2. When depressed, the pump dispenses these solutions at equal volumes.

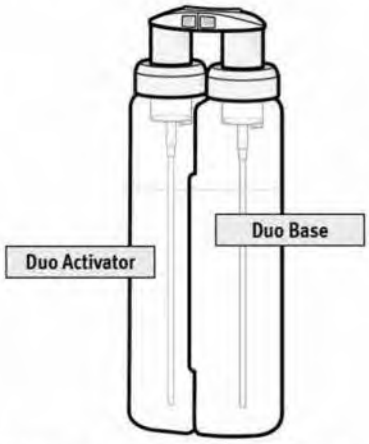

Figure 2 - Schematic Representation of Duo Bottle

The components of the Base and Activator solutions chemically react. This reaction generates chlorine dioxide in liquid solution, which is the active germicidal ingredient. A mesher present in the applicator pump causes the formulation to be dispensed as a ready-to-use foam.

The active ingredient in Tristel Duo ULT high level disinfectant is chlorine dioxide, which is generated in situ from the Activator and Base solutions. Tristel Duo ULT also contains other ingredients, such as sodium chlorite, (b)(4), (b)(4), citric acid monohydrate, (b)(4) (b)(4)

The Duo bottle configuration consists of the two bottles (containers), a single pump head with two thread neck closures and a cap. Each Duo bottle contains 125 milliliters (mL)/4.40 fl oz of Base Solution and 125 mL/4.40 fl oz of Activator Solution. The left and right containers are made to the same specification, with the difference in the orientation of the neck thread. The bottle is handheld. Shown in Figures 3 and 4.

Figure 3 - Tristel Duo Handheld Dispenser

Figure 4 - Tristel Duo in Use

An 80% V/V dilution of Duo was determined as the Minimum Effective Concentration (MEC) for Duo.

Duo Wipes are dry, non-woven, low-linting wipes. They are specifically designed to apply the Tristel Duo ULT foam onto the surface of a medical device. A user lays the Duo Wipe in one hand and applies 4 doses of the Tristel Duo ULT foam before closing their hand around the wipe and waiting for 10 seconds. The wipe can then be used to spread the foam in a massaging motion from one end of the device to the other 4 times. After the device is wiped, it is left undisturbed for 2 minutes.

Figure 7 - Duo Wipes in Tub and Flow Wrap Commercial Packaging

The Duo Test Strips are semi-quantitative chemical indicators used to determine whether the concentration of the Tristel Duo ULT high level disinfectant foam is above or below the minimum recommended concentration (MRC) (~90% v/v / ~280 ppm).

Tristel Duo ULT foam bottle is designed in a way that ensures measured dose delivery with each application generating active ingredient above the MRC.

The Duo Test Strips, when used in accordance with directions for use detect the MRC and above giving a color indication of a "PASS" and if the concentration is below the MRC a color indication of a "FAIL".

Figure 8 - The Duo Test Strips

Tristel Duo ULT, according to the directions of use, has passed the AOAC Sporicidal Activity Test in 12 hours and additional potency tests against mycobacteria, fungi, bacteria and viruses in 2 minutes at 20°C at a worst case concentration below the MRC at 80% v/v of the nominal concentration of Duo. The test results qualify Tristel Duo ULT as a high level disinfectant.

Tristel Duo ULT has been tested on a large number of materials and found to be compatible after a total of 120 hours immersion. Tristel Duo ULT is labeled for use on ultrasound probes only and is not intended for disinfection of other semi-critical medical devices.

Tristel Duo ULT is intended for use by qualified healthcare professionals (HCP) and reprocessing technicians. The HCP's intended use environments include a procedure room and

exam room. The reprocessing technicians' intended use environment includes a central processing unit. Each environment should include a designation between contaminated and clean work surfaces, a sink, a clock or another device to track time, and personal protective equipment such as gloves, masks with eye protection, and gowns.

SUMMARY OF BENCH STUDIES

REPROCESSING, STERILITY AND SHELF-LIFE

The Tristel Duo ULT high level disinfectant foam is not intended for either cleaning or sterilization, it is intended to disinfect cleaned, reusable, non-lumened ultrasound probes. Performance related to the high level disinfection was reviewed as a part of the performance testing. The device includes instructions for reprocessing ultrasound probes. Specifically, the sponsor has included reprocessing instructions that they have validated according to the FDA guidance "Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling".

The storage stability study is provided to support: (i) a two-year shelf life of the product from the date of manufacture of the unopened product; and (ii) a use period of six months of the opened container from the date of opening under the prescribed storage conditions of room temperature (15-25°C).

The transport stability study is provided to support the resilience to transport conditions (such as temperature, pressure, and humidity), environmental factors (such as freeze and thaw), and mechanical impact (such as drop effect on package integrity) and the capability of maintaining its composition (physical and chemical integrity).

BIOCOMPATIBILITY

The Tristel Duo ULT is categorized as a surface disinfectant, with contact to mucosal membranes, A-limited (<24hour), in accordance with Guidance for Industry and Food and Drug Administration Staff -Use of International Standard ISO10993-1,'Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process.'

Tristel Duo ULT (Duo) is based on Tristel's proprietary chlorine dioxide chemistry. The sponsor provided the following studies to assess the potential toxicity of Duo to a user (100% solution), Duo with Duo Wipes to the user, and Duo to a patient (i.e., residue levels). The results of these tests are deemed acceptable.

- Duo Working Solution (Genotoxic tests, Skin Irritation tests, Acute Eye Irritation tests, Duo Skin Sensitization tests, Acute Oral tests)
- Duo with Duo Wipes (Cytotoxicity, Dermal Irritation, Skin Sensitization)
- Duo Residues (Vaginal Mucosa Irritation Test, Rectal Mucosa Irritation Test, Dermal Irritation Test, Residues Cytotoxicity)

The sponsor provided the following studies on the exhaustive extractable and leachable to evaluate the potential adverse health risk from patient exposure to residues remaining on ultrasound probes:

- Trace metals,
- Volatile Organic Compounds (VOC),
- Semi-Volatile Organic Compounds (SVOC), and
- Non-Volatile Organic Compounds (NVOC).

The sponsor also provided the exposure and risk assessment for chlorine dioxide's inhalation toxicity, which met the acceptance criteria in accordance with the U.S. Occupational Safety and Health Administration (OSHA) legal airborne permissible exposure limit (PEL) for chlorine dioxide of 0.1 ppm averaged over eight hours and California Division of Occupational Safety and Health PEL of averaged 0.3 ppm over a 15-minute period.

SOFTWARE

The Tristel Duo ULT does not require software.

ELECTROMAGNETIC COMPATIBILITY & ELECTRICAL SAFETY

The Tristel Duo ULT does not require equipment or installation.

Human Factors

A simulated-use human factors (HF) study was provided in accordance with the guidance "Applying Human Factors and Usability Engineering to Medical Devices." It included participants representative of the intended healthcare professionals and reprocessing technicians. During the session, participants were presented with a simulated-use scenario where they were tasked with using the product to simulate reprocessing a reusable medical device (either an ophthalmic tonometer, a flexible nasoendoscope, or a transvaginal ultrasound probe). Following the session, participants answered questions and provided feedback regarding use-related issues and the product itself. The study included 27 assessments which evaluated the critical tasks for using the product and found that users understood.

The provided human factors validation testing results, analyses and conclusions established that Tristel Duo ULT is safe and effective for the intended users, its intended uses, and use environments.

PERFORMANCE TESTING – BENCH

The sponsor conducted the following performance tests to support that the device can achieve its intended use:

- Potency tests were provided, including sporicidal efficacy, mycobactericidal efficacy, fungicidal efficacy, bactericidal efficacy, virucidal efficacy, to qualify

the Tristel Duo ULT as a high level disinfectant, which has been confirmed by an independent laboratory.

- Simulated-use tests were provided, with a total of six skin surface ultrasound probes and a total of seven endocavity ultrasound probes were tested in triplicate. It demonstrated the penetrating capability of this high-level disinfectant along with other factors that may prevent or limit contact and effectiveness of the germicide.
- In-use tests were conducted under clinical condition with wild type bacteria and fungi from patient contaminated BK Medical endocavity ultrasound probes. It confirmed the results of simulated-use testing and high level disinfectant performance in clinical use conditions.
- The material compatibility testing with ultrasound device manufacturers was conducted and supportive of compatibility on various ultrasound probes and equipment. Manufacturers of ultrasound systems have evaluated compatibility of Tristel Duo ULT with their ultrasound devices assessing the impact Duo high level disinfectant has on the materials and functionality.
- A chemical indicator validation test was provided, with adequate performance testing and shelf life / stability testing, to support that the Duo test strip is appropriately designed to respond with a characteristic chemical reaction to the concentration of the germicide active ingredients of Tristel Duo ULT.

The device has been appropriately evaluated for performance on the bench.

LABELING

The labeling consists of Instructions for Use in user guide and packaging labels for all three components of Tristel Duo ULT, Duo Wipe, and Duo Test Strip. The instructions for use include the indications for use; a description of the device, contraindications, warnings, precautions; information on use-life; instructions for the safe use of the device (Duo ULT, Duo wipe, and Duo test strip), storage condition and stability information, user training, emergency and/or additional information, disposal; germicide classification scheme for labeling purposes; general information on selection and use of germicides for medical device reprocessing; material and device compatibility; mode of action of germicidal activity; precleaning agent compatibility; toxicology and adverse reactions.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a high level disinfectant foam:

Identified Risks to Health and Mitigation Measures

Identified Risks to Health	Mitigation Measures
Patient cross-contamination due to high level disinfectant (HLD) foam lacking adequate potency	Potency efficacy testing Simulated-use testing In-use testing Shelf life / Stability testing

	Reliability testing (device design verification/validation) Labeling
Disinfected device malfunction due to its incompatibility with HLD foam	Device and Material compatibility testing Labeling
Adverse tissue reaction to patient due to HLD foam's toxicity	Biocompatibility evaluation
Adverse event to end user due to use/user error caused by inappropriate labeling	Human factors testing, simulated-use testing, and in-use testing Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the foam or gel chemical sterilant/high level disinfectant is subject to the following special controls:

(1) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be evaluated under challenging conditions:
   (i) Storage stability testing must demonstrate the real time stability and dynamics of the device formulation within the expiration date (shelf life) of the unopened product and within a use period of the opened container from the date of opening under the proposed storage conditions.
   (ii) Transport stability testing must demonstrate device resilience to transport conditions (such as temperature, pressure, and humidity), environmental factors (such as freeze and thaw), and mechanical impacts (such as the effect of drops on package integrity).
   (iii) Potency testing must demonstrate sporicidal, mycobactericidal, fungicidal, bactericidal, and virucidal activities of the device.
   (iv) Simulated use testing must use the mycobacterium species most resistant to the germicide as the test organism on inoculated instruments to demonstrate a kill of at least 10^6 inoculated mycobacteria under the labeled contact time.
   (v) In-use testing must test clinical-relevant microorganism on clinically used instruments, in accordance with the labeled contact conditions for device high level disinfection, must confirm the results of simulated use testing.
   (vi) Compatibility testing with labeled devices and materials.
   (vii) Chemical indicator validation must demonstrate a characteristic chemical reaction to the concentration of the germicide active ingredients.

(2) The device must be demonstrated to be biocompatible.

(3) Usability / human factors validation testing must demonstrate that the device can be used correctly, based solely on the directions for use.

(4) Labeling must include:
   (i) Instructions for personal protective equipment to be used with the device.
   (ii) Directions for use including:
      (A) Instructions for preparation and use of the germicide; cleaning steps in preparation for high level disinfection; high level disinfections of cleaned

devices; rinsing, neutralizing, and removing residues, when needed; and reuse of the solution, if applicable.

(B) Chemical indicator for monitoring the Minimum Effective Concentration (MEC) or Minimum Recommended Concentration (MRC) of the product's active ingredient(s).

(iii) Storage conditions and expiration date information for stock solution, opened container, activated solution, and use-dilution.

(iv) A statement that the end user should be trained in the reprocessing (decontamination and sterilization or disinfection) of medical devices and in the handling of toxic substances, such as liquid chemical germicides.

(v) Instructions for disposal of the germicide and any neutralizers, including an instruction to check local and state regulations.

(vi) Germicide classification scheme.

(vii) General information on selection and use of germicides for medical device reprocessing.

(viii) Material and device compatibility and incompatibility information.

(ix) Microbial mode of action of germicidal activity.

(x) Precleaning agent / method compatibility and incompatibility with this device.

(xi) Toxicology profile of the final product formulation and information on adverse reactions following exposure to the product.

BENEFIT-RISK DETERMINATION

Benefit

The current paradigm for high level disinfectants is that they support, through testing, that the high level disinfectants will allow for the semi-critical devices to be high level disinfected to at least 6-log reduction of a mixed suspension of vegetative organisms and 6-log reduction of an appropriate mycobacteria. From an end user perspective, this may decrease reprocessing time, as this is a point of care product and does not require transport to a reprocessing room. The subject high level disinfectant, a chlorine dioxide based foam with two-minute contact time, is intended to be used at the point of care without the need for equipment or installation. With appropriate testing and controls in place, the probable benefit of this feature is that it will provide a new option to healthcare providers for high level disinfection of ultrasound devices. Proper use of this device is also likely to improve the time taken to reprocess ultrasound devices between patients and enable healthcare providers to serve more patients. These probable benefits were supported through non-clinical performance testing including potency testing, simulated-use, and in-use testing.

Risk

The identified risks have been mitigated with appropriate performance testing (for risks of inadequate potency), biocompatibility testing (for risks of solution/residue toxicity to healthcare provider/patient), as well as addressing human factors and the risk related to active ingredient concentration measurement.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

Benefit/Risk Conclusion

Based on the performance testing provided (in particular potency test, simulated-use test, in-use test, stability / shelf life test, biocompatibility test, human factor study, compatibility test, reliability test, and labeling. chemical indicator validation), the sponsor has adequately supported that the subject device is a high level disinfectant foam for manually reprocessing ultrasound probes. This feature will provide a new option for high level disinfection of ultrasound probes and is likely to improve the time needed to reprocess ultrasound probes between patients. This testing has also mitigated the probable risk of inadequate potency and the subsequent risk of infection resulting from exposure to inadequately disinfected ultrasound probes. Biocompatibility testing has mitigated the risk of adverse tissue reaction. Chemical indicator validation testing and labeling have mitigated the risk of using high level disinfectant at a concentration lower than MEC/MRC.

In conclusion, given the testing provided above, for the following indication statement:

> Tristel Duo ULT is a high level disinfect foam for reprocessing ultrasound probes. It can be used to high level disinfect endocavity transvaginal and transrectal probes, and skin surface transducers that may contact non-intact skin during use.
>
> Tristel Duo ULT is a high level disinfectant when used in accordance with the directions for use, including a disinfection contact time of 2 minutes, at room temperature and a concentration at or above Minimum Recommended Concentration (MRC).
>
> Tristel Duo ULT must be applied on the surface of an ultrasound probe using Duo Wipes.
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> Duo Wipes are intended to apply Tristel Duo ULT foam on the surface of ultrasound probes and to remove residue of the foam after high level disinfection.
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> Each dose of Tristel Duo ULT foam and each Duo Wipe are single use.
>
> The semi-critical ultrasound probes reprocessed by Tristel Duo ULT must first be cleaned according to a validated cleaning protocol or standard and following the device manufacturers' instructions.
>
> Tristel Duo ULT foam bottle is designed in a way that ensures measured dose delivery with each application generating active ingredient above the MRC.
>
> Minimum Recommended Concentration (MRC): ~90% v/v (~280ppm) at point of use. MRC of Tristel Duo ULT may be verified using Duo Test Strips.
>
> Tristel Duo ULT is intended to be marketed for prescription use.

The probable benefits outweigh the probable risks for the Tristel Duo ULT high level disinfectant. The device benefits patients and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the Tristel Duo ULT high level disinfectant is granted and the device is classified as follows:

Product Code: QWS
Device Type: Foam or gel chemical sterilant/high level disinfectant
Regulation Number: 21 CFR 880.6886
Class: II