Why are ChloraPrep® patient preoperative skin preparation labels being updated?

In December 2013, the U.S. Food and Drug Administration (FDA) issued a letter requesting that manufacturers of skin antiseptic products add clarity to their label regarding the sterility of the solution. The request was rooted in a history of sporadic contamination outbreaks which have been associated with skin antiseptic products. ChloraPrep® has been used worldwide for millions of procedures with no documented case of intrinsic contamination causing a patient infection; however, because the solution in the ampoule does not go through a sterilization step, the ChloraPrep® label is being updated to indicate the solution inside the ChloraPrep applicator is non-sterile. The ChloraPrep applicator does undergo an ethylene oxide gas sterilization step after it is packaged, which sterilizes the applicator surfaces *(internal and external),* exterior glass ampoule surfaces, the applicator foam sponge and packaging.

History

In 2007, a review article was published summarizing over 50 years of documented patient infections which were caused by various germicides, including patient skin antiseptics and surface disinfectants.[1] A summary of the infections caused by skin antisepsic products is listed below:

Table 1. Overview of contaminated skin antiseptic products and the source of contamination

Patient skin antiseptic that caused a patient infection	Example Contaminant*(s)*	Source of contamination[1,2]
Alcohol prep pad	*Bacillus cereus* *Burkholderia cepacia*	• Contaminated alcohol • Dilution with contaminated water
Bulk chlorhexidine solution	*Pseudomonas spp.* *Burkholderia cepacia* *Ralstonia pickettii* *Serratia marcescens*	• Dilution with contaminated water • Over dilution
Chlorhexidine plus cetrimide	*Pseudomonas multivorans* *Stentrophomonas malt.*	• Dilution with contaminated water • Over dilution
Chloroxylenol	*Serratia marcescens*	• Contaminated soap and sink
Benzalkonium chloride/picloxydine	*Pseudomonas (various)* *Burkholderia cepacia* *Serratia marcescens* *Enterobacter aerogenes*	• Intrinsic contamination of antiseptic solution • Improper storage with cotton gauze • Dilution with contaminated water • Over dilution
Povidone-iodine	*Burkholderia cepacia*	• Intrinsic contamination of antiseptic solution
Poloxamer-iodone	*Pseudomonas aeruginosa*	• Intrinsic contamination of antiseptic solution
Triclosan	*Serratia marcescens*	• Intrinsic contamination of antiseptic solution

The AORN Seal of Recognition has been awarded to the CareFusion - CHP Label change program on February 20, 2015 and does not imply that AORN approves or endorses any product or service mentioned in any presentation, format or content. The AORN Recognition program is separate from the AORN, ANCC Accredited Provider Unit and therefore does not include any CE credit for programs.

CareFusion

History *(cont.)*

As a result of these documented cases, the FDA began an investigation. In 2009, the FDA held an advisory board meeting to discuss patient infections due to contaminated germicides.[3]

In 2010, an outbreak of patient infections occurred as a result of contaminated alcohol prep pads.[4] One case of sepsis in a four-year-old leukemia patient and one case of sepsis in an infant with heart disease were documented. Blood cultures of both patients grew *Bacillus cereus.* While there was no breach in infection control procedures, it was determined the alcohol prep pads were the source of the contamination that infected these patients.[4] Forty of 60 alcohol prep pads tested were positive for *B. cereus,* and all alcohol prep pads were made by the same manufacturer. These findings were confirmed by the CDC. In 2010, a two-year-old patient died from bacterial meningitis due to *B. cereus.*[5] The products were recalled in January 2011.[6]

FDA response

In December 2012, the FDA published an article in the *New England Journal of Medicine* discussing the issue of microbial contamination in antiseptic products.[2] Immediately following, the FDA held a public meeting on December 12, 2012, to gather comments on how to address microbial contamination of skin antiseptic drug products indicated for preoperative or pre-injection preparation. On November 13, 2013, the FDA issued a Drug Safety Communication[7] and requested that manufacturers of skin antiseptics do the following:

- Update their labels to indicate if the solution and applicator are sterile or non-sterile.
- Use single-use packaging to decrease the risk of infection.

The goal was to better educate clinicians on the products they use to prepare patients prior to injection or surgery and to limit sources of extrinsic contamination, such as accessing the same antiseptic container multiple times.

Today

ChloraPrep® Preoperative Skin Preparation products have never been documented to be intrinsically contaminated or cause a patient infection. The safety and consistency of ChloraPrep® is guaranteed through well-designed and controlled manufacturing and testing procedures conducted prior to release of the product.

Manufacturing excellence

CareFusion reduces contamination risks during ChloraPrep manufacturing to ensure skin antisepsis products are safe. Current good manufacturing practice (cGMP) guidelines were developed by the FDA to assure that a food or drug product is safe for use[8,9] and not contaminated. All ChloraPrep products are manufactured according to cGMP guidelines, and the ChloraPrep manufacturing facility is cGMP-compliant. Each step of the manufacturing process is tightly controlled. These steps assure that each ChloraPrep applicator will consistently perform as intended.

Extensive testing to ensure quality

In-process checks are performed throughout manufacturing to safeguard against errors, including testing of the ChloraPrep solution for microbial growth prior to applicator assembly. As a final manufacturing step, each lot of ChloraPrep undergoes ethylene oxide gas sterilization. This sterilizes the applicator surfaces *(internal and external),* exterior glass ampoule surfaces, the applicator foam sponge and packaging. A sterile applicator and wrapper allows ChloraPrep to be used in a sterile field. This includes ChloraPrep applicators that are packaged as stand-alone applicators or as part of a sterile procedure kit with other medical devices.

The CareFusion Quality Control Laboratory tests each chemical raw material component that goes into manufacturing ChloraPrep as well as every finished lot of ChloraPrep. This extensive testing guarantees every applicator meets established quality and safety specifications. These analyses include:

Chemical analysis:

The ChloraPrep solution is tested to ensure:

- The chlorhexidine concentration is 2% weight/volume.
- The isopropyl alcohol concentration is 70% volume/volume.
- Clear products have clear and colorless solutions.
- Tinted products exhibit the correct color.

Microbial analysis:

Each batch of ChloraPrep solution *(2% chlorhexidine w/v in 70% isopropyl alcohol v/v)* is tested to ensure it is free of microbial growth using Test Method based on United States Pharmacopeia (USP) general chapter <61> *(Microbiological Examination of nonsterile products; Microbial enumeration test)* and <62> *(Microbiological Examination of nonsterile products; Test for specified microorganisms).* These tests ensure the ChloraPrep solution is:

- Screened for growth of total aerobic microbes.
- Screened for growth of total yeast and mold counts.
- Screened for growth of various species of gram positive and gram negative bacteria.

Finally, the finished product is sterilized via exposure to ethylene oxide gas. Following ethylene oxide (EtO) sterilization, tests are performed to ensure the ethylene oxide gas sterilization process was effective in killing microbes.

Applicator integrity:

The quality team tests the physical integrity of the ChloraPrep applicator for:

- Integrity of the glass ampoule.
- Secure attachment of the foam sponge.

Package testing:

The quality team tests the integrity of the ChloraPrep applicator packaging, prior to release for commercial distribution to ensure a sterile barrier is formed per the validated processes and can be maintained for the shelf life of the product *(three years).*

CareFusion's priority is patient safety. We believe clinicians should understand and trust the tools they use. In an effort to improve patient safety, CareFusion will continue to improve clarity on product labels and provide single-use antiseptic applicators.

For more information, contact customer service at **800.323.9088**.

References

1 Weber et al. Outbreaks Associated with Contaminated Antiseptics and Disinfectants. *Antimicrobial Agents and Chemotherapy,* 2007, Vol. 51(12):4217-4224. **2** Chang et al. Microbial Stowaways in Topical Antiseptic Products. *New England Journal of Medicine,* 2012, Vol. 367(23): 2170-2173. **3** Kelly Pyrek. Sterility of Antiseptic Products: FDA investigates, Deliberated on Potential Recommendations. *Infection Control Today.* July 2013 Special Report. **4** Dolan et al. Contamination of Alcohol prep Pads with Bacillus cereus Group and Bacillus Species-Colorado, 2010. *CDC Morbidity and Mortality Weekly Report,* 2011, vol. 60(11): 347. **5** http://vitals.nbcnews.com/_news/2012/12/05/15702729-bacteria-in-antiseptic-skin-prep-fda-ponders-sterility?lite. Accessed 1-16-2015 **6** http://www.fda.gov/Safety/Recalls/ucm239219.htm **7** http://www.fda.gov/Drugs/DrugSafety/ucm374711.htm **8** http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch. cfm?CFRPart=211&showFR=1 **9** http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm090016.htm

carefusion.com

CareFusion

©2015 CareFusion Corporation or one of its subsidiaries. All rights reserved. ChloraPrep, CareFusion and the CareFusion logo are trademarks or registered trademarks of CareFusion Corporation or one of its subsidiaries. SU4665 (0215/PDF)