



### **FDA Drug Safety Communication: FDA requests label changes and single-use packaging for some over-the-counter topical antiseptic products to decrease risk of infection**

#### **Safety Announcement**

**[11-13-2013]** The U.S. Food and Drug Administration (FDA) is requesting label and packaging changes to enhance the safe use of certain over-the-counter (OTC) topical antiseptic products. This request is the result of our ongoing evaluation of infrequent but continuing reports of infections resulting from antiseptic products labeled for preoperative or preinjection skin preparation. When used properly, topical antiseptics are safe and effective products to reduce the number of bacteria on patients' skin prior to surgery or injections. However, most often, contamination of topical antiseptics occurs when organisms are introduced into the product by users. Therefore, health care professionals and patients should follow all label directions to decrease the chances of infection.

To further reduce the risk of infection with improper topical antiseptic use and the possibility of these products becoming contaminated with bacteria during use, we are requesting that manufacturers package antiseptics indicated for preoperative or preinjection skin preparation in single-use containers. The antiseptics in these single-use containers should be applied only one time to one patient. We also recommend that health care professionals and patients do not dilute antiseptic products after opening them. Applicators and any unused solution should be discarded after the single application.

In order to provide users with important information about contamination that may occur during the manufacturing process, we are also asking manufacturers to voluntarily revise the product labels for topical antiseptics to indicate whether the drug is manufactured as a sterile or nonsterile product. We believe this will assist health care professionals in making informed decisions about using these products. Topical antiseptics are not required to be manufactured as sterile and so may become contaminated with bacteria during manufacturing. Labeling stating a product is sterile means it was treated with a process during manufacturing to eliminate all potential microorganisms.

However, even topical antiseptics manufactured with a sterile process, can become contaminated if proper care is not taken when using them. Health care professionals and patients should follow all label directions to decrease the chances of infection. The term nonsterile on the product label means it was not sterilized during manufacturing; it does not mean the product contains harmful bacteria. All topical antiseptics are required to be manufactured under FDA's Current Good Manufacturing Practice (cGMP) regulations,

which contain minimum requirements for the methods, facilities, and controls used in manufacturing, processing, and packing of a drug product.

All topical antiseptic products should always be used according to the directions on the label. Health care professionals should consider these topical antiseptics as a possible source of infection when trying to determine the cause of postoperative or postinjection infections. In past years, outbreaks associated with the use of contaminated topical antiseptics have led to some product recalls (see Data Summary). Reported outcomes ranged from localized infections at injection sites to more widespread infections resulting in death.

We are continuing to evaluate this safety issue and will take additional actions as needed. As part of our evaluation, we held a public meeting on December 12, 2012, to gather comments on how to address microbial contamination of antiseptic drug products indicated for preoperative or preinjection skin preparation. The *New England Journal of Medicine* also published an article we wrote to raise awareness of potential contamination of these products.<sup>1</sup>

We have prepared a list of [questions and answers](#) to provide more information about this safety issue.

### **Facts about topical antiseptic products**

- Over-the-counter (OTC) topical antiseptic drugs for use according to the label instructions to reduce the number of bacteria on the skin prior to surgery or injections.
- Commonly used products contain isopropyl or ethyl alcohol, povidone iodine, poloxamer iodine, benzalkonium chloride, benzethonium chloride, or chlorhexidine gluconate as a single agent or in combination with alcohol.
- These products are marketed as solutions, swabs, pads saturated with a solution, and applicators containing a solution.
- Currently available as both single-use and multiple-use products.

### **Additional Information for Patients and Caregivers**

- When used properly, over-the-counter (OTC) topical antiseptics are safe and effective products to reduce the number of bacteria on the skin prior to surgery or an injection.
- To reduce the risk of infection, ensure the products are used according to the directions on the label.
- Topical antiseptics packaged in single-use containers should only be applied at one time to one patient. Applicators and any unused solution, even if it is not identified for single use, should be discarded after that application. These products should not be diluted after opening.
- All topical antiseptics are required to be manufactured under Current Good Manufacturing Practice (cGMP) regulations, which contain minimum

- requirements for the methods, facilities, and controls used in manufacturing, processing, and packing of a drug product.
- A “nonsterile” label does not mean the product contains harmful bacteria, but rather that its contents have not been sterilized, or treated with a process during manufacturing to eliminate all potential microorganisms.
  - Talk to your health care professional about how to properly use topical antiseptics, or if you have any questions or concerns about them.
  - Report side effects from topical antiseptics to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

### **Additional Information for Health Care Professionals**

- Over-the-counter (OTC) topical antiseptics are not required to be manufactured as sterile drug products and may become contaminated with bacteria during manufacture or use.
- When used properly, topical antiseptics are safe and effective products for patient preoperative or preinjection skin preparation.
- To reduce the chances of patient infection, ensure these products are used according to the directions on the label.
- Preoperative or preinjection topical antiseptics packaged in single-use containers should only be applied at one time to one patient. Applicators and any unused solution should be discarded after that application.
- Topical antiseptic products should not be diluted after opening.
- All topical antiseptics are required to be manufactured under Current Good Manufacturing Practice (cGMP) regulations, which require manufacturers to have appropriate procedures in place to prevent the presence of objectionable microorganisms in drug products that are not manufactured as sterile.
- Consider topical antiseptics as a possible source of infection when trying to determine the cause of postoperative or postinjection infections.
- Report adverse events involving topical antiseptics to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

### **Data Summary**

Outbreaks associated with the use of contaminated topical antiseptics have been reported in the medical literature and to the Centers for Disease Control and Prevention (CDC).<sup>2-4</sup> Clinical infections have also been reported to FDA, leading to some product recalls. The reported outcomes ranged from localized infections at injection sites to systemic infections that resulted in death. FDA has reviewed reports of four deaths, five cases of wound infection, seven cases of peritonitis, 10 cases of septic arthritis, 14 cases of indwelling catheters requiring replacement, 16 cases of injection site infection, and 32 cases of bacteremia. These infections have been confirmed to be caused by contaminated antiseptic products. Affected products included all commonly used antiseptic ingredients, including alcohol, iodophors, chlorhexidine gluconate, and quaternary ammonium products. Organisms implicated in the outbreaks included *Bacillus cereus*, *Burkholderia*

*cepacia*, *Pseudomonas aeruginosa*, *Achromobacter xylosoxidans*, *Ralstonia pickettii*, *Serratia marcescens*, and *Mycobacterium abscessus*.<sup>1</sup>

We are aware of two mechanisms by which contamination of topical antiseptic products may occur. Extrinsic contamination, which appears to be the more common mechanism, occurs when microorganisms are introduced into the antiseptic by the user. This may occur as a result of dilution of the product with contaminated water, failure to use appropriate aseptic techniques during handling, or storing antiseptic solutions under non-sterile conditions. Intrinsic contamination occurs during the manufacturing process. In these cases, microorganisms have been isolated from pharmaceutical water supplies and non-sterile manufacturing environments. Once introduced into the product during manufacturing, these organisms may remain viable and multiply.

## References

1. Chang CY, Furlong L-A. Microbial stowaways in topical antiseptic products. *N Engl J Med* 2012;367:2170-3.
2. Weber DJ, Rutala WA, Sickbert-Bennett EE. Outbreaks associated with contaminated antiseptics and disinfectants. *Antimicrob Agents Chemother* 2007;51:4217-24.
3. Contamination of alcohol prep pads with *Bacillus cereus* group and *Bacillus* species — Colorado, 2010. *MMWR Morb Wkly Rep* 2011;60:347.
4. Allergy injection-associated *Mycobacterium abscessus* outbreak — Texas, 2009 (<http://idsa.confex.com/idsa/2010/webprogram/Paper2955.html>)