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Single Dose Vial / Repackaging
FactFinder

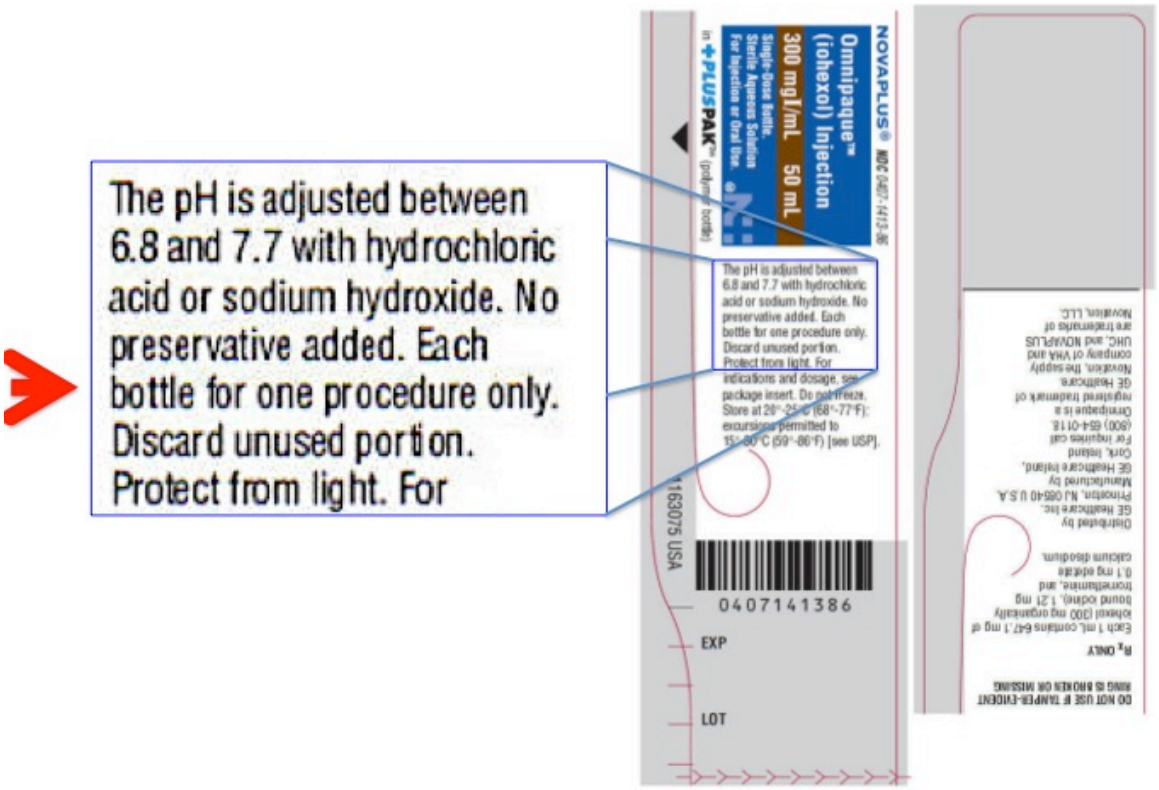
Committed to providing helpful information to International Spine Intervention Society members about key patient safety issues, the Society's Patient Safety Committee has developed a FactFinder series. FactFinders will explore and debunk myths surrounding patient safety issues. The intent of this inaugural FactFinder is to address some key issues relative to implementing the CDC recommendations prohibiting reuse of single dose vials, focusing on repackaging contrast. Also, in light of the current outbreak of Exserohilum rostratum and Aspergillus fumigatus meningitis, we have also added a myth related to oversight of compounding pharmacies.

Myth #1: "The recent fungal outbreak was indirectly the result of enforcement of the CDC single dose vial and safe injection policies."

Fact: The medication in question, methylprednisolone acetate, was widely available in single dose vials at a reasonable cost, and the source of the infection was not a breach in injection safety protocol. Rather, the source appears to be contamination of the medication vials at the compounding pharmacy, New England Compounding Center (NECC). Most providers using the NECC compounded methylprednisolone did so in order to obtain a specific preservative-free preparation that is not commercially available, and not to lower cost or obtain single dose vials.

Myth #2: "50 mL vials of Omnipaque are intended for use on more than one patient."

Fact: Each vial of iodinated contrast is meant for single use. It is stated clearly on the vial.



Myth #3: "If I draw up separate aliquots of contrast at the start of my day, it will bypass this issue and eliminate the risk of contamination."

Fact: Strict standards must be adhered to when drawing up syringes from a single dose vial. For most of us, the standards are prohibitive to the practice of drawing separate aliquots from a single dose vial.

The United States Pharmacopeia (USP) has addressed this topic thoroughly in their Standards – Chapter 797 (USP797).[1] A single dose vial can be divided and repackaged into smaller doses if proper techniques are observed. Proper techniques include the use of an ISO Class 7 room with laminar flow hood. Additionally, technicians must be wearing sterile gown, gloves, cap and booties. They are to enter the ISO Class 7 room through a "clean" anteroom. Simply gowning and gloving prior to dividing the aliquots is insufficient. The protocols established in USP797 require that the air particle counts are strictly monitored and maintained at or below specified levels. Furthermore, independent testing of these standards must be performed regularly and recorded for review. Failure to monitor or meet these standards may result in loss of accreditation from JCAHO and other certifying organizations.

Additionally, there are specifications for cleaning and disinfecting the sterile compounding areas, personnel training and competency evaluation of garbing,

aseptic work practices and cleaning/disinfection procedures, and viable and nonviable environmental sampling testing - all of which must be followed as described in the USP797 chapter.

Myth #4: "There is no evidence of any risk of infection or outbreak resulting from re-using a single dose vial in the injection suite."

Fact: There are several reported cases of outbreaks linked to reuse of single dose vials accompanied with other breaches in sterile technique during spinal procedures.[2-6] Radcliffe, *et al.,* reported a series of eight patients who developed methicillin-susceptible *Staphylococcus aureus* infections following epidural steroid injection.[2] Wong, *et al.*, described four confirmed (and eight suspected) cases of *Klebsiella pneumoniae* and *Enterobacter aerogenes* infections in patients receiving sacroiliac injections.[3] This again was attributed to the inappropriate re-use of single dose vials on multiple patients. There are also individual reports published by the New York State Department of Health, and Los Angeles Department of Health documenting hepatitis outbreaks in outpatient pain clinics from the inappropriate re-use of single dose vials.[4-6]

The most recent case, reported in Arizona and the basis of the CDC's Morbidity and Mortality Weekly Report (MMWR) in July, provided a definitive link between the outbreak and the reuse of a single dose vial.[7] As illustrated above, the use of single dose vials for multiple patients has causally contributed to infectious disease outbreaks from interventional pain procedures, resulting in severe morbidity and even mortality. While numerous breaches in appropriate sterile technique were cited in most of the investigations, the case reported in MMWR of a methicillin-resistant *Staphylococcus aureus* (MRSA) outbreak involving a pain management clinic in Arizona left little doubt that the common denominator was reuse of a single dose vial. The only other safety breach in this outbreak was failure to don a face mask during the procedures. However, the lack of face mask use could not have accounted for the outbreak. As the CDC report states, "All of the patients with MRSA infections received diluted contrast from the afternoon vial… The three patients with MRSA infections went to a local hospital 4–8 days after their outpatient pain remediation procedures. They required inpatient care for severe infections, including acute mediastinitis, bacterial meningitis, epidural abscess, and sepsis. Hospitalization ranged from nine to 41 days, with additional long-term care in an acute-care facility required for one patient. The fourth recipient of diluted contrast from the afternoon vial was found deceased at home, six days after treatment at the clinic. The cause of death was reported as multiple-drug overdose; however, invasive MRSA infection could not be ruled out."

Myth #5: "If I keep my drawn-up syringes of Omnipaque refrigerated, I can decrease the chance of contamination."

Fact: Refrigeration has not been shown to decrease contamination of single dose vials. Omnipaque does not need to be refrigerated, although it should be stored at 20°-25° (68°-77°F). Omnipaque is, however, light sensitive and should be stored away from direct sunlight – including after it has been appropriately divided into smaller doses such as syringes.

Myth #6: "I can have my local hospital or compounding pharmacy divide larger single dose vials into multiple smaller doses on a monthly basis and bypass this issue."

Fact: Any facility that meets or exceeds the USP797 Standards for repackaging and compounding may perform this procedure. Again, this requires the use of an ISO Class 7 room equipped with a laminar flow hood, and personnel properly dressed in full surgical attire. *Once Omnipaque has been repackaged, in the absence of sterility testing, it generally must be kept at controlled room temperature and used or disposed of within 48 hours.* If it is kept in a controlled refrigerated temperature it may be kept for 14 days, and if frozen, up to 45 days. It is imperative that any clinician or facility utilizing repackaged injectable medications review the policies and procedures of the compounding pharmacy to ensure USP797 Standards are met or exceeded.

The CDC position statement from May 2012 states that it may be appropriate to seek a compounding pharmacy to split single dose vials in times of critical shortage.[8] Clearly missing from the statement are any recommendations supporting the use of compounding pharmacies to reduce waste and curb cost associated with discarding 47 mL of a 50 mL single dose vial.

Myth #7: "Compounding pharmacies have the same FDA oversight as commercial manufacturers."

Fact: Unlike drug manufacturers, compounding pharmacies are not directly regulated by the FDA; rather, the state pharmacy boards are responsible for overseeing adherence to USP797 Standards. The FDA only becomes involved on a case-by-case basis. Critics of compounding pharmacies argue that state agencies are often understaffed and underfunded to adequately monitor such facilities.

Due to several critical drug shortages, many physicians have utilized compounding pharmacies to obtain medications. There are many compounding pharmacies that have excellent track records despite the lack of direct FDA oversight. The recent outbreak of *Exserohilum rostratum* and *Aspergillus fumigatus* meningitis highlights the need for increased monitoring and regulation to help ensure the safety of all compounding pharmacies. While it is not completely understood at this point whether there was a breach in adherence to USP797 Standards at the New England Compounding Center, failure of a compounding pharmacy to adhere to these standards may have widespread and devastating consequences.

References:

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