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CDC HEALTH UPDATE

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Update: Additional Contamination Identified in Medical Products from New England Compounding Center

Summary: As part of the ongoing investigation of the multistate outbreak of fungal meningitis and other infections, the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) continue to test medical products from the New England Compounding Center (NECC) in Framingham, Mass. CDC and FDA are reporting today additional microbial contamination identified in NECC products, which updates the November 1, 2012 Health Alert Network advisory. This update includes the following key points:

- CDC and FDA have identified additional microbial contamination in unopened vials of betamethasone, cardioplegia, and triamcinolone solutions distributed and recalled from NECC.
- These include bacteria known as *Bacillus*, and fungal species including *Aspergillus tubingensis*, *Aspergillus fumigatus*, *Cladosporium* species, and *Penicillium* species.
- Although rare, some of the identified *Bacillus* species can be human pathogens. Some of the fungal organisms identified, particularly *Aspergillus fumigatus*, are known to cause disease in humans. It is not known how product contamination with these organisms could affect patients clinically.
- To date, although CDC has received reports of illness in patients who have received the medications listed in the table below, including some patients who had evidence of meningeal inflammation, CDC and public health officials have no reports of laboratory-confirmed bacterial or fungal meningitis, spinal, or paraspinal infections caused by these products.
- The available epidemiological and laboratory data do not, at this time, support evidence of an outbreak of infections linked to usage of non-methylprednisolone NECC products.
- CDC's recommendations to healthcare providers for diagnosing and treating symptomatic patients who have received NECC products have not changed as a result of these findings.
- CDC continues to recommend that clinicians remain alert for the possibility that infections may have resulted from injection of NECC products, and that routine laboratory and microbiologic tests, including bacterial and fungal cultures, should be obtained as deemed necessary by treating clinicians.
- Clinicians should continue to report infections potentially related to NECC products to FDA's MedWatch and to state health departments.

Background

On September 26, 2012, NECC voluntarily recalled three lots of preservative-free methylprednisolone acetate (PF) 80mg/ml[1] associated with the multistate outbreak of fungal meningitis and other infections. As previously confirmed by CDC and FDA, the fungus *Exserohilum rostratum* was identified from two different lots of NECC-supplied, preservative-free methylprednisolone acetate (Lot #06292012@26 and Lot #08102012@51); testing on the third implicated lot of preservative-free methylprednisolone acetate (Lot #05212012@68) has yet to identify fungal growth. Two types of fungus not known to be human pathogens were also identified from product from the two tested lots, namely *Rhodotorula laryngis* and *Rhizopus stolonifer*. Among these fungal organisms, only *Exserohilum rostratum* has been associated with human infections in this outbreak.

On October 6, NECC expanded its recall to include all products in circulation that were distributed from its facility in Framingham, Mass. As part of the ongoing investigation, FDA and CDC have been testing various NECC products for evidence of contamination. Laboratory testing at CDC and FDA has found bacterial and/or fungal contamination in unopened vials of betamethasone, cardioplegia, and triamcinolone solutions distributed and recalled from NECC, as shown in the table below.

Laboratory-Confirmed Organisms from Product Samples Associated with NECC Recalled Lots of Betamethasone, Cardioplegia, and Triamcinolone Solutions

Medication	Lot Number	Bacterial and Fungal Contamination
Betamethasone 6 mg/mL injectable –5 mL per vial	08202012@141	*Paenibacillus pabuli/amolyticus, Bacillus idriensis, Bacillus flexus, Bacillus simplex, Lysinibacillus* sp., *Bacillus niacini, Kocuria rosea, Bacillus lentus*
Betamethasone 6 mg/mL injectable –5 mL per vial	07032012@22	*Bacillus niabensis, Bacillus circulans*
Betamethasone 12 mg/mL injectable – 5 mL per vial	07302012@52	*Bacillus lentus, Bacillus circulans, Bacillus niabensis, Paenibacillus barengoltzii/timonensis*
Betamethasone 6mg/mL injectable – 5 mL per vial	08202012@44	*Bacillus lentus, Bacillus firmus, Bacillus pumilus*
Betamethasone 6 mg/mL injectable – 5 mL per vial	08152012@84	*Penicillium* sp., *Cladosporium* sp.
Triamcinolone* 40mg/mL injectable – 1 mL per vial	06062012@6	*Bacillus lentus, Bacillus circulans*
Triamcinolone 40 mg/mL injectable – 2 mL per vial	08172012@60	*Aspergillus tubingensis, Penicillium* sp.
Triamcinolone 40mg/mL injectable – 10 mL per vial	08242012@2	*Aspergillus fumigatus*
Cardioplegia solution 265.5 mL per bag	09242012@55	*Bacillus halmapalus/horikoshii, Brevibacillus choshinensis*

*Identification of other bacteria for this product is pending.

Recommendations to Healthcare Providers

FDA released a MedWatch Safety Alert on October 15 stating that the sterility of any injectable drugs, including ophthalmic drugs that are injectable or used in conjunction with eye surgery, and cardioplegic solutions produced by NECC is of significant concern. The safety alert further advised healthcare providers to follow-up with patients who were administered any of these products purchased from or distributed by NECC on or after May 21, 2012. A sample notification letter to assist with this process is available.

CDC's recommendations to healthcare providers for diagnosing and treating symptomatic patients who have received NECC products have not changed as a result of the laboratory findings reported here. CDC continues to recommend that clinicians remain vigilant for the possibility that infections may have resulted from injection of NECC products, and that routine laboratory and microbiologic tests, including bacterial and fungal cultures, should be obtained as deemed necessary by treating clinicians.

There has been no prior systematic surveillance for adverse events following epidural steroid injections; however, infection is a known, although likely rare, risk that has been documented in the medical literature. To date, although CDC is aware of reports of illness in patients who have received these medications, including some patients who had evidence of meningeal inflammation, CDC and other public health officials have no reports of laboratory-confirmed bacterial or fungal meningitis, or spinal or paraspinal infections caused by these products. The available epidemiological and laboratory data do not, at this time, support evidence of an outbreak of infections linked to usage of non-methylprednisolone NECC products.

However, because it is possible that some of the organisms listed in the table above can cause human disease, clinicians should continue to include bacterial and/or fungal infection in the differential diagnosis when evaluating symptomatic patients who were exposed to these medications, including consideration of empiric antifungal therapy.

Consultation with an infectious disease specialist is strongly encouraged to help make treatment decisions in these cases. If the evaluation of these patients is suggestive of fungal infection, please consult existing CDC treatment guidance associated with this outbreak.

Physicians should continue to report infections potentially related to NECC products to FDA's MedWatch and to state health departments.

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[1] NECC lots of methylprednisolone acetate (PF) 80mg/ml:

Methylprednisolone Acetate (PF) 80 mg/ml Injection, Lot #05212012@68, BUD 11/17/2012
Methylprednisolone Acetate (PF) 80 mg/ml Injection, Lot #06292012@26, BUD 12/26/2012
Methylprednisolone Acetate (PF) 80 mg/ml Injection, Lot #08102012@51, BUD 2/6/2013

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