

Identifying and Responding to Medical-Product Associated Illness Outbreaks Focus on Pharmacy Compounding

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Division of Healthcare Quality Promotion

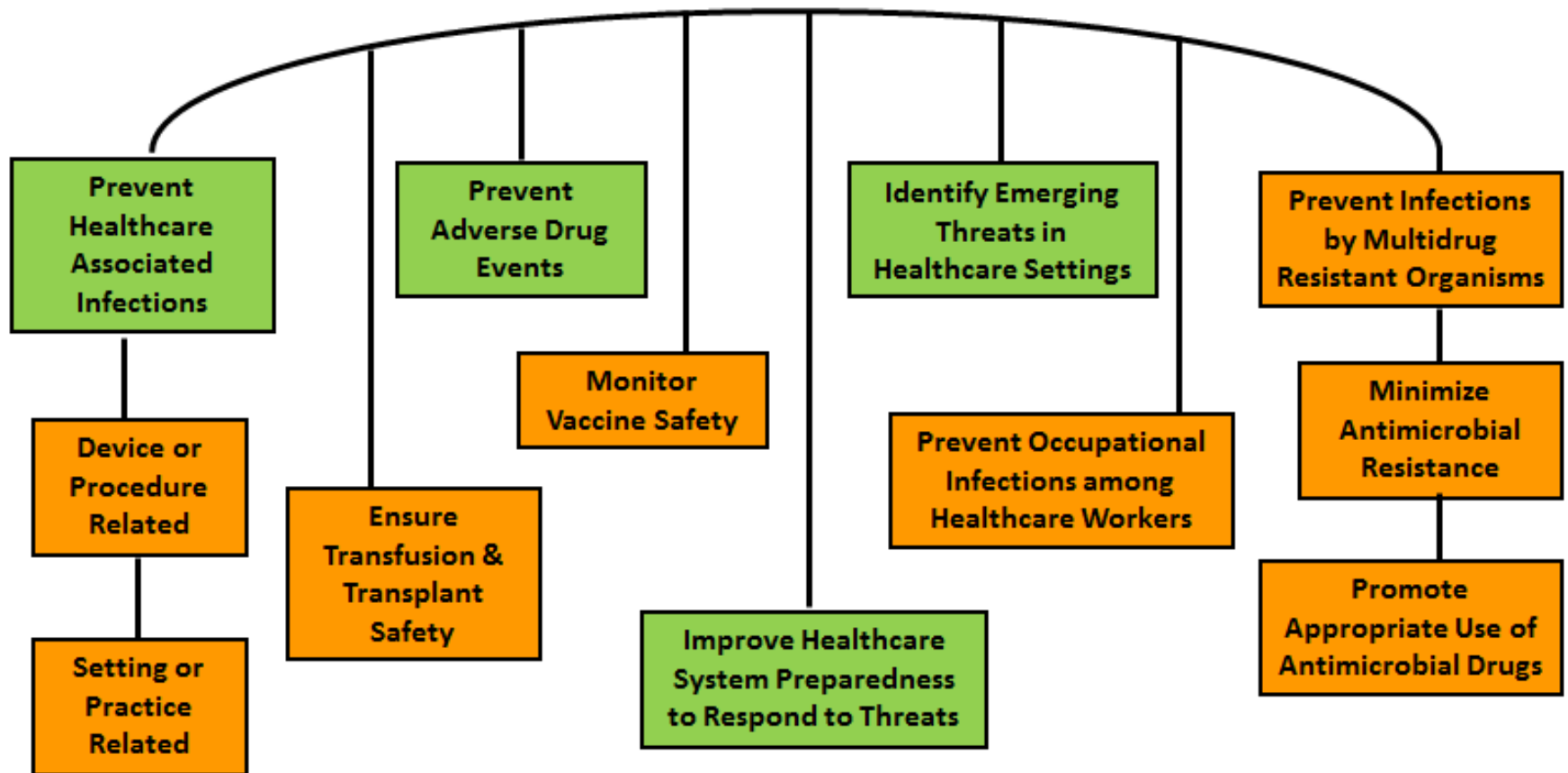


Overview

- ❑ Pharmacy-compounded sterile preparations are an important component of our healthcare system
- ❑ Identification and investigation of contaminated medications is a core public health activity
- ❑ CDC, along with FDA and state/local public health partners, has been increasingly responding to outbreaks linked to pharmacy compounding
- ❑ Monitoring the safety of non-manufactured (e.g. compounded) injectable medications poses challenges

CDC/DHQP Major Goals

Safe Healthcare is Our Priority



CDC Healthcare Outbreak Response Activities

Division of Healthcare Quality Promotion (DHQP)

- ❑ Responsibility for investigating infections and other adverse events related to healthcare delivery
- ❑ Consults (mostly with state health departments) are a major part of our daily activity
 - Cases, clusters, infection control breaches
- ❑ Over the past five years, we have averaged about one field investigation (“Epi-Aid”) per month
- ❑ Medical product-associated outbreaks
 - Many outbreaks and clusters potentially involve contamination of parenteral medications

Injectable Medications Intrinsic vs. Extrinsic Contamination

- ❑ Safe healthcare delivery relies on supply of safe sterile injectable medications (free of intrinsic contamination)
 - Oversight required to assure injectable medications are supplied in a sterile form
 - Majority are manufactured → FDA
 - Maintain sterility from point of manufacture or production to point of administration
 - Extrinsic contamination can result from mishandling of medications during preparation and administration



CDC addresses and promotes “Injection Safety” through guidelines and educational efforts

Investigations Involving Injectable Medications: Intrinsic vs. Extrinsic Contamination

- ❑ Infections may signal a wider problem
 - Require investigation by public health partners
 - Association with injections vs. other procedures
 - Multiple drug products are often involved

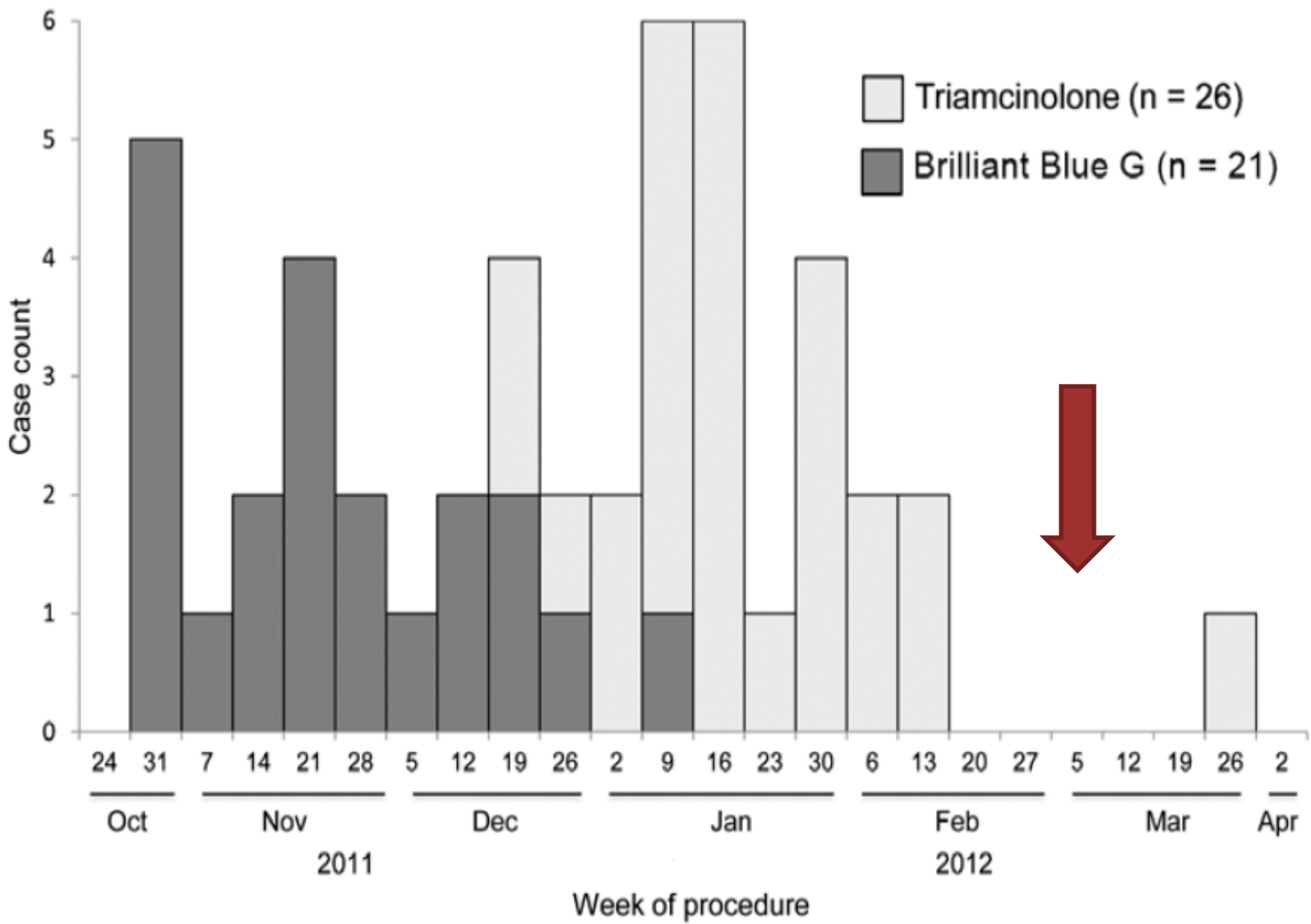
- ❑ Example: case of endophthalmitis in a patient who received injections at an eye clinic
 - Could represent EXTRINSIC contamination from clinic error
 - Could represent INTRINSIC product contamination, especially if compounded product was source of injectable medication

Fungal Endophthalmitis Associated with Compounded Products

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- March 2012 – CA health department notified of a cluster of 9 cases of fungal endophthalmitis
- All case-patients had vitrectomy procedures at a Los Angeles ambulatory surgery center during October-December 2011
- Local health department determined all cases associated w/ single lot of Brilliant Blue G dye from a FL compounder
- Multistate investigation involving CDC, FDA, pharmacy boards and health departments

Epidemic curve of confirmed and probable cases of postprocedural fungal endophthalmitis, by week of procedure



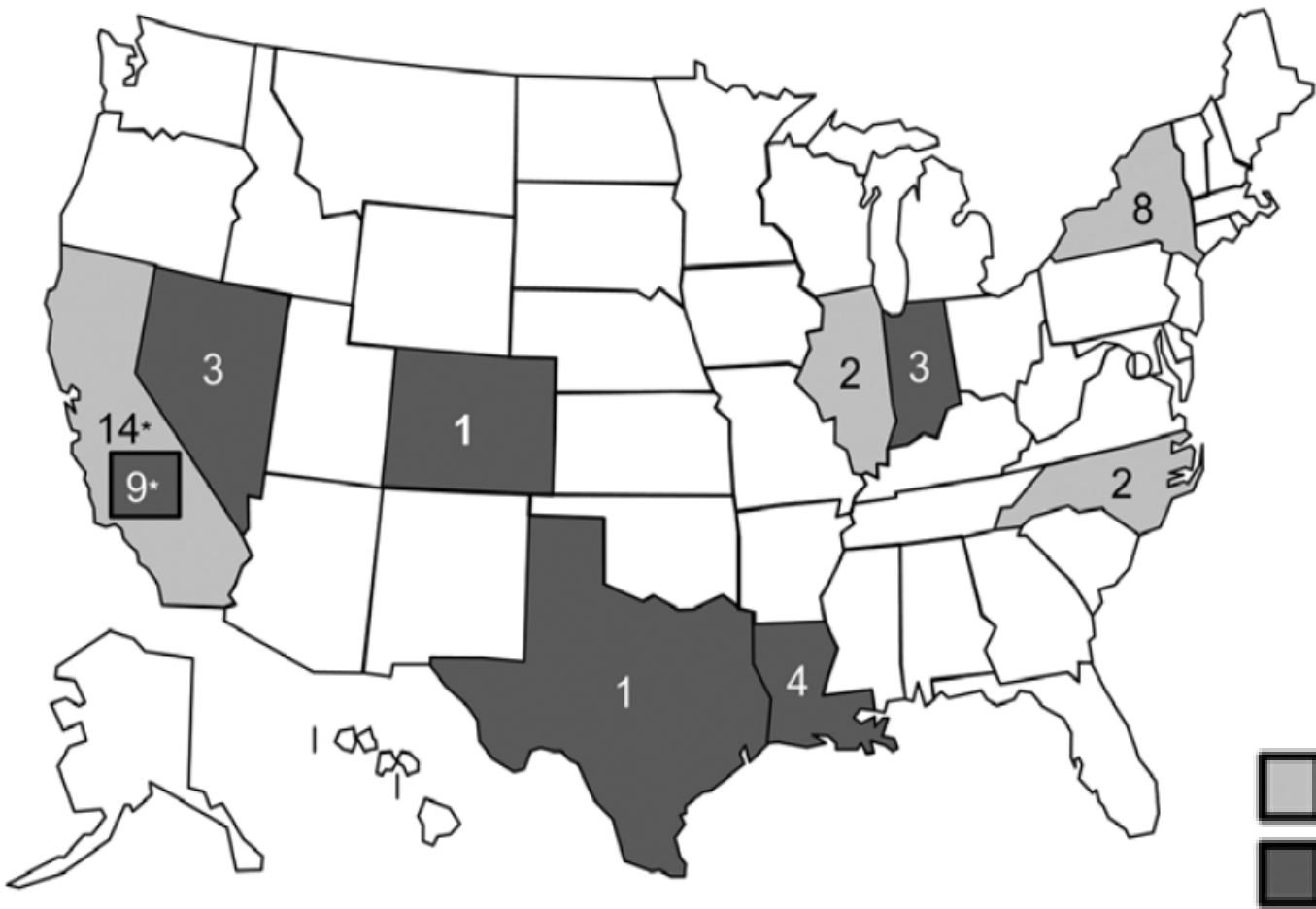


Figure 1. Confirmed and probable cases of postprocedural fungal endophthalmitis, by state, United States, 2011–2012. Infections occurred after exposure to a product from Franck’s Compounding Lab (Ocala, FL, USA), through March 2012, when the implicated product was recalled. *In California, cases were associated with exposure to each product.

Triamcinolone (n = 26)
 Brilliant Blue G (n = 21)



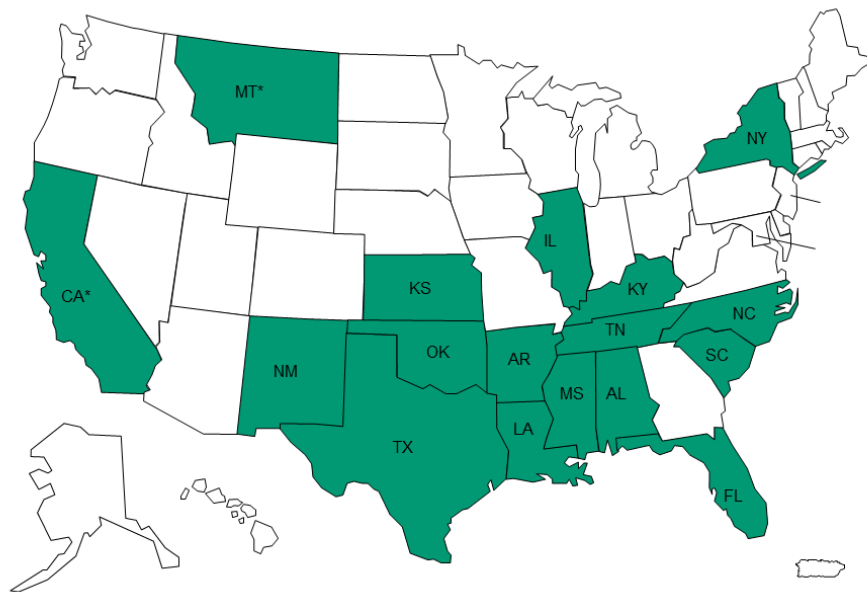
Main Street Family Pharmacy – Newbern, Tennessee

Source: Tom Wilemon, The Tennessean

Multistate Investigation of Suspected Infections Following Steroid Injections, 2013

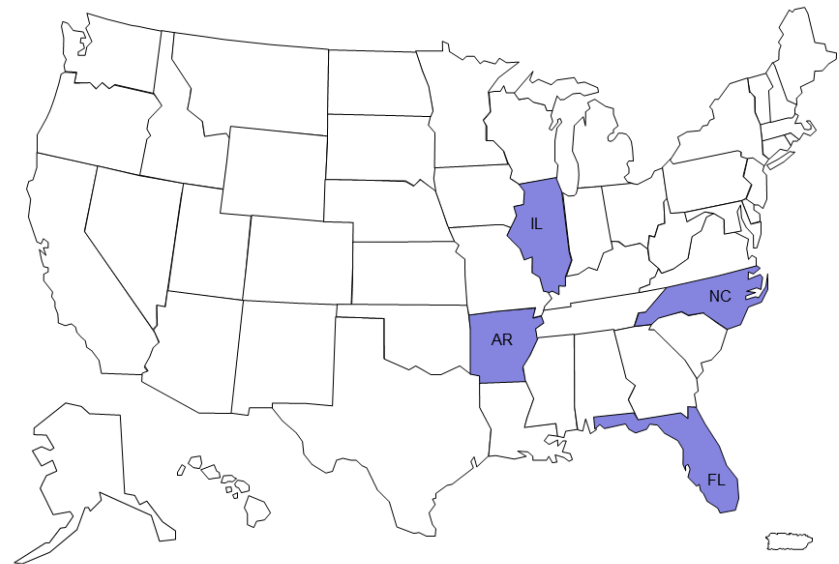
- During April-May, several patients presented with cyst or abscess, months after receipt of injections at a primary care clinic
 - Illinois Health Department notified
 - Patients received steroid injections (methylprednisolone acetate, MPA) from compounded 10 ml preservative-free “multi-dose” vials
- Two North Carolina patients with skin abscesses following receipt of steroid injections reported to MedWatch
 - Same medication and same compounding pharmacy as Illinois cases
 - Triggers a rapid and coordinated response involving various components of FDA and its field offices, CDC, state health departments and pharmacy boards
- Main Street Family Pharmacy recalled injectable steroids on May 24; extended to all sterile products on May 28

B-12 0.5ml prefilled syringe	HCG 310 iu prefilled syringes	Methylpred 80mg 1ml
Adenosine 35mg/ml 30ml	HCG 320 iu prefilled syringes	Methylpred 80mg PF 1ml
Adenosine 3mg 2ml	HCG 330 iu prefilled syringes	Methylpred 80mg PF 5ml
Adenosine 3mg/ml 4ml	HCG 340 iu prefilled syringes	Methylpred 80mg w/lidocaine 10ml
Adenosine 8mg/ml 2ml Vial	HCG 350 iu prefilled syringes	Methylpred 80mg w/lido 30ml
Adenosine Monophosphate 50mg/ml 30ml	HCG 380ium PFS	Mic .05ml prefilled syringe
Adenosine Monophosphate 35mg/ml 10ml	HCG 370 iu prefilled syringe	Mic 25/50/50 30ml
Adenosine Monophosphate 50mg/ml 10ml	HCG 380 iu prefilled syringes	Mic/Cyanocobalamin 25/50/50 50ml
AMIC-12 10ml	HCG 390iu prefilled syringes	MIC 25/50/50 formula w/333mg B-12 10ml
AMIC-12 10ml w/out lido	HCG 40,000u	Mic 30ml
AMP injection 30ml	HCG 400 iu prefilled syringes	Mic B-Complex 30ml
B-12 (compounded) 30ml	HCG 450 iu prefilled syringes	Mic B-Complex 50ml
B-12 mixture (Methylcobalamin 5mg/Folic Acid 5mg 8ml w/ 1 ml lidocaine	HCG 5,000U	Mic B w/Amp Mix 50ml
B-12 PFS	HCG 50 iu prefilled syringes	Mic Combo w/methylcobalamin (Methionine/Inositol/Choli
Betamethasone 4mg 10ml sodium phosphate	HCG 500 SL tablet	Mic Ultra (Methionine Free) 10ml
Betamethasone 8mg 10ml	HCG 500/B-12 300 tablet	Mic Ultra 30ml- Sulfur Free
Beta NA Phosphate, Beta Acetate (PF) 8mg 10ml	HCG 500/Test 200 troches (soy base)	Mic Ultra 10ml
Betamethasone 8mg PF 10ml	HCG 5000iu	Mic Ultra 30ml
Betamethasone 7mg 10ml	HCG 5000iu kit (Needle & 5ml syringe, Bacteriostatic Water 30ml,2 Alcohol prep pads	Mic Ultra 50ml
Betamethasone 9mg 10ml	HCG 500u/ml w/methylcobalamin 1mg/ml 10ml	Mic Ultra 50ml- Sulfur Free
Betamethasone 9mg PF 1ml	HCG 80 iu prefilled syringes	Mic Ultra 50ml- Sulfur Free w/ Lido
Betamethasone Acetate 9mg/ml PF 10ml/MDV	HCG 7000u	Mic w/B-12 30ml
Betamethasone 10mg 10ml	HCG 8,000u	Mic w/B-12 50ml
Bi-Mix 10ml	HCG 80 iu prefilled syringes	Mic w/B6/B12/Lido 50ml
Brompheniramine 10mg 10ml	L-Arginine 100mg/ml 30ml	Mitomycin 0.02%
Depo-Testadiol 10ml	L-Carnitine 30ml	Mitomycin 0.04% 2.5ml
Dexamethasone 10mg (PF) 1ml	L-Carnitine 500mg/ml 50ml	Mitomycin C 1/2 Strength
Dexamethasone 16mg 10ml	L-glutamine 30mg/ml 30ml vial	Mitomycin 20mg
Dexamethasone 16mg 30ml	L-glutathione 200mg/ml 30ml vial	Mitomycin 2ml (full Strength)
Dexamethasone Acetate 8mg/Phosphate 4mg 10ml	Lidocaine 2% MPF 2ml-compounded	Mitomycin 40mg Compounded
Dexamethasone 8/4 30ml	Lidocaine 4%/Phenylephrine 1% 1ml	Mitomycin C
Dexamethasone 8mg 10ml	Lidocaine 4%/Phenylephrine 1% 5ml	Post-menopausal HCG Pk (250iu, 270iu, 290iu, 310iu)
Dexamethasone LA 16mg 10ml	Lincomycin 300mg (Preservative Free) 10ml	Post-menopausal HCG Pk 2nd month (310iu, 320iu, 320iu)
Dexamethasone LA 8mg 10mlml	Lincomycin 300mg w/lidocaine 10ml	Post-menopausal HCG Pk 3rd month (340iu, 340iu, 350iu)
Dexamethasone 4mg 30ml	Lipo-Shot 30ml	Pre-menopausal HCG PK (200iu, 220iu, 240iu, 260iu)
Dexamethasone LA 16mg 30ml	Lipo B = Mic w/B5 12.5/B6 25/B12 .25/Lido 50ml	Pre-menopausal HCG PK 2nd month (270iu, 280iu, 290iu)
Double Strength PGE1 40mcg/ml 2ml	Lipo B Complex 30ml	Pre-Menopausal 3rd month (310iu, 320iu, 330iu, 340iu)
Double Strength PGE1 40mcg/ml 10ml	Lipo B Complex 50ml	Single Strength PGE1 20mcg 2ml
Estradiol Cypionate 40mg 10ml	Lipo Blast (Mic w/B1,B2,B3,B5,B6,B7,B12, AMP & Lido) 50ml	Single Strength PGE1 20mcg/ml 10ml
Estradiol Valerate 40mg 10ml	Lipo Blast w/o adenosine (Mic w/B1,B2,B3,B5,B6,B7,B12, & Lido) 50ml	Taper A prefilled syringes
Estradiol Cypionate 5mg 10ml	Lipo C 30ml	Taper Pack B
Estradiol Pellet 20mg	Mic w/B5/B6/B12/Lido/Amp 50ml	Taper Pack C
Estradiol Pellet 37.5mg	Mic w/B-12 .25/AMP 12.5mg/Lidocaine 50ml	Testosterone 200mg 10ml (compounded)
Estradiol Pellet 50mg	Lipotonix B	Testosterone 200mg 30ml (compounded)
Estradiol Pellets 10mg	Lipotonix Plus-Mic B Complex Fat Burner 30ml	Testosterone 210mg 10ml (compounded)
Estradiol Pellets 12.5mg	Lipotonix Plus 10ml	Testosterone Cypionate 300mg/ml 10ml
Estradiol Pellets 12mg	Lipotonix Plus 30ml	Testosterone Cypionate 250mg 10ml
Estradiol Pellets 15mg	Lipotonix Plus 30ml w/o methionine	Testosterone Cypionate 210mg 10ml
Estradiol Pellets 25mg	Lipotonix Plus w/Procaine/Chromium 10ml	Testosterone Cypionate 300mg/ml 10ml
Estradiol Pellets 31mg	Lipotropic 1.5ml PFS	Testosterone Pellet 112.5mg
Estradiol Pellets 8mg	Lipotropic 10ml	Testosterone Pellet 112mg
Glutathione "Reduced" 200mg/ml 30ml	Lipotropic 10ml with B-12 and L- Carnitine	Testosterone Pellet 12.5mg
Gluthione 150mg/ml 30ml	Lipotropic 1ml PFS	Testosterone Pellet 87.5mg
Gomenol 10ml	Lipotropic 2ml PFS	Testosterone Pellets 100mg
HCG + Mannitol 5000u	Lipotropic 30ml	Testosterone Pellets 125mg
HCG 100 iu prefilled syringes	Lipotropic 30ml w/o methionine	Testosterone Pellets 200mg
HCG 10000u	Lipotropic 50ml	Testosterone Pellets 220mg
HCG 1000iu PFS	Lipotropic 50ml w/L-Carnitine	Testosterone Pellets 225mg
HCG 11,000U	Lipotropic 50ml w/o methionine	Testosterone Pellets 25mg
HCG 110 iu prefilled syringes	MALE HCG PK (250, 280, 270, 280iu)	Testosterone Pellets 37.5mg
HCG 11000u/Methylcobalamin 8mg 10ml	MALE HCG PK 2nd month (290, 300, 310, 320iu)	Testosterone Pellets 50mg
HCG 11000 w/B-12 (cyanocobalamin)	MALE HCG PK 3rd month (320, 330, 340, 350iu)	Testosterone Pellets 75mg
HCG 12000u	Medroxyprogesterone 150mg PF 1ml	Testosterone Propionate 100mg/ml 10ml
HCG 125 iu prefilled syringes	Medroxyprogesterone 150mg w/lidocaine 10ml	Tetracaine 2%/Pontocaine 60ml
HCG 140 iu prefilled syringes	Medroxyprogesterone 150mg/ml 10ml	Tri-Mix 10ml
HCG 15,000u	Medroxyprogesterone 150mg w/lidocaine 1ml	Tri-Mix 5ml
HCG 15000u w/b-12	Medroxyprogesterone (PF) 150mg/ml 10ml	Triamcinolone Acetonide 10mg PF 5ml
HCG 1500iu PFS	Medroxyprogesterone 150mg w/lidocaine 5ml (compounded)	Triamcinolone Diacetate 40mg 2ml Preservative Free
HCG 170 iu prefilled syringes	Methylcobalamin 100mcg/ml 30ml	Triamcinolone 40mg/ml 5ml



Health departments determined 96 facilities in 17 states received recalled MPA. 81 facilities in 15 states administered MPA; these were provided instructions on product recall/testing, patient notification, case finding and reporting

A total of 26 patients in 4 states developed a suspected infection associated with injection of a product, labeled as sterile, that was distributed by the Main Street Family Pharmacy (Newbern, TN) since December 1, 2012



Additional Findings and Messages

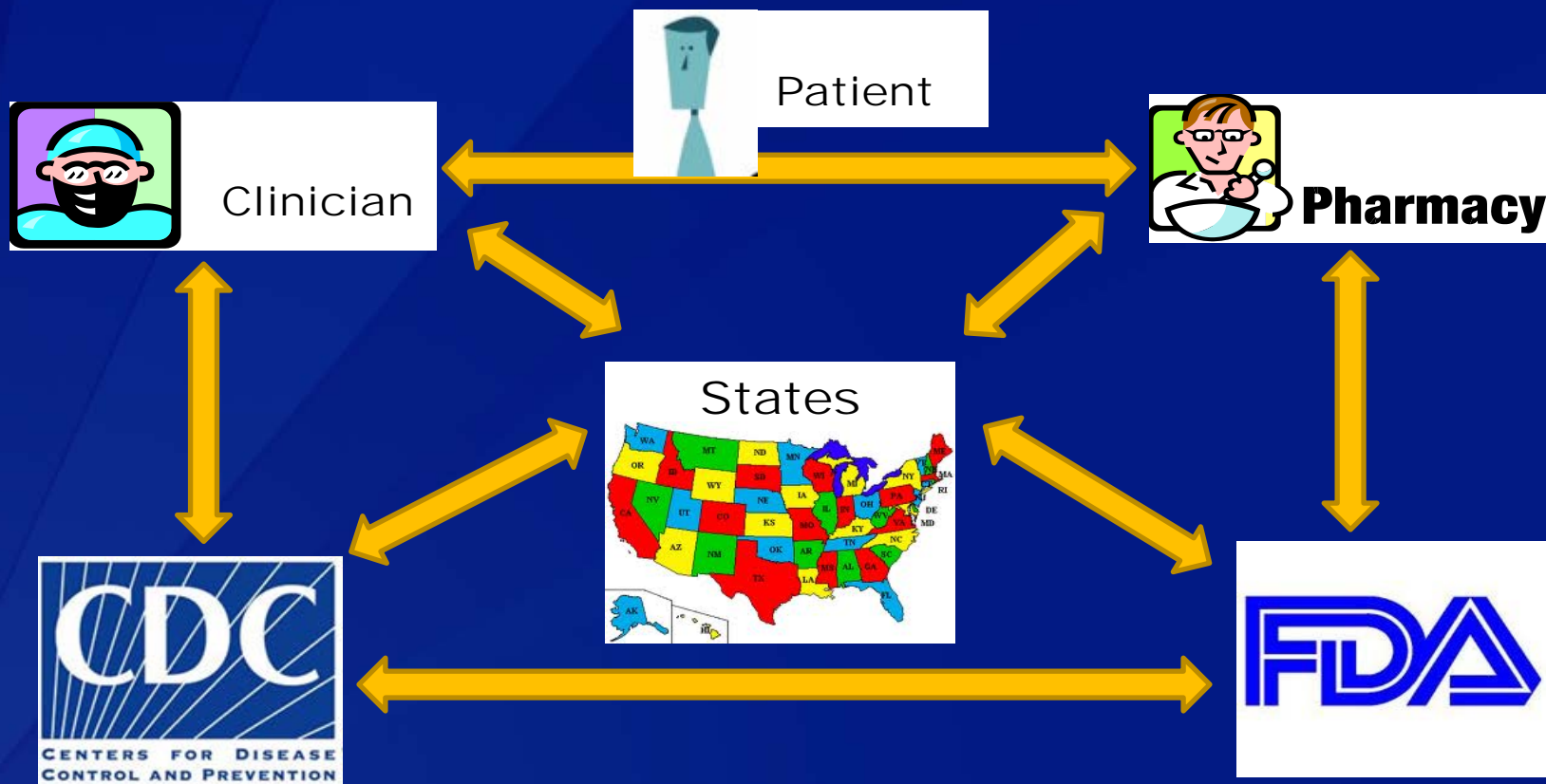
- CDC and FDA identified bacteria and fungi cultured from unopened vials of preservative-free MPA

Medication	Lot Number	Preliminary Microbial Identification
PF MPA 80 mg/mL – 10 mL per vial	011413dan	<i>Bacillus pumilus</i> , <i>Bacillus cereus/thuringiensis/mycoides*</i> , <i>Roseomonas gilardii</i> , <i>Acinetobacter ursingii</i> , <i>Alternaria sp.</i> , <i>Cladosporium sp.</i>
PF MPA 80 mg/mL – 10 mL per vial	010913dan	<i>Bacillus licheniformis</i> , <i>Penicillium sp.</i>

- Healthcare providers were reminded of their responsibilities
 - Ensure that all recalled products from MSFP are no longer in use
 - Complaints from patients exposed to products from MSFP should be promptly reported to FDA MedWatch and health department
 - Use individual containers of compounded or preservative-free medicine for a single-patient only
 - Promptly report to MedWatch any infection that might be related to a medication or medical device, even absent a recognized outbreak

Detecting and Responding to Pharmacy Compounding Outbreaks

Shared responsibility which requires coordination and timely flow of information



Summary & Closing Thoughts

- ❑ Shared goal: robust system for identifying – and investigating – adverse events that are potentially associated with medications produced and distributed under 503A/B
- ❑ State and local health departments have a firm legal foundation to respond to, request information from, and investigate potential disease outbreaks and cases of reportable diseases
- ❑ This hinges on signal detection and reporting
 - Will require investment in educating and equipping healthcare providers and patients (the end users)

Thank You

www.cdc.gov/HAI

For more information please contact Centers for Disease Control and Prevention

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Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348

E-mail: cdcinfo@cdc.gov Web: www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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“Response Takes Many Forms”

Examples from the CDC Side

- First 24 hours: Devised response strategies, arranged and managed partner communications, and assisted with series of press releases from FDA and 3 state health departments
- Days 2-4: Developed case report forms, a risk-based patient-centered notification framework, and scripts for facilities to use when contacting patients
- Over the following weeks, actively coordinated and led the multi-state health department response, which involved: conference calls with affected states, FDA, and the TN Board of Pharmacy; laboratory testing of clinical specimens as well as speciation of bacterial and fungal contaminants detected by FDA in product samples; media interviews; development and frequent updates of a dedicated CDC web site (<http://www.cdc.gov/hai/outbreaks/TN-pharmacy/index.html>); and monitoring overall progress at the state and facility levels