



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Memorandum

Date January 9, 2007  
From [REDACTED]  
Subject Consumer Complaint # 57398 Follow-up Investigation, FAN 907013 and Sample # 426119  
To [REDACTED]

Complainant: [REDACTED]

Manufacturer: New England Compounding  
Center  
697 Waverly St  
Framingham, MA 01702  
FEI 3003623877

On 12/06/07, I was assigned to investigate FDA complaint # 57398. This complaint originated from Dr. [REDACTED] reported to FDA's Office of Emergency Operations on 12/05/07 that the patients he treated with epidural injections of betamethasone (Celestone) had adverse reactions between August and October, 2007. Dr. [REDACTED] faxed copies of the description of complaints from several of his patients to the Office of Emergency Operations. See attachment 1 for copies of the facsimile.

On 12/11/07, I met with [REDACTED] in his office located at [REDACTED]. An FDA 482, Notice of Inspection was issued and FDA credentials were displayed to Dr. [REDACTED]. Dr. [REDACTED] is a board certified neurologist with a sub-specialty in pain management. See attachment 2 for a copy of Dr. [REDACTED] medical license.

February 25, 2008

Complainant is [REDACTED]. He operates a pain management clinic in [REDACTED]. He noted adverse reactions in over 100 patients he treated with betamethasone injectable. Adverse reactions included increased fibromyalgia pain and flu-like symptoms. Some patients were hospitalized. Betamethasone (Celestone) was manufactured by New England Compounding Center in Framingham, MA. Dr. [REDACTED] described some vials of betamethasone injected into patients as being discolored and having particles. Sample 426119 consisting of 51/5 ml vials of betamethasone collected during investigation.

Referred to New England District for follow-up as appropriate.

[REDACTED]  
NOL-DO/Mandeville RP

O (with exhibits & CR): NWE-DO Consumer Complaint Coordinator thru NOL-DO CCC  
CC: NOL-DO Disk & NOL\_DCTM

explained he has been using injectable steroids by epidural route to treat patients for pain associated with herniated discs. noticed the patients who also had fibromyalgia had a decrease in the pain associated with the fibromyalgia after the steroid injections. He stated he began using injectable betamethasone via epidural methods for the off-label use in treating patients with fibromyalgia pain approximately two years ago. He stated the normal dose was 3-12mg.

stated the lot of betamethasone he received from New England Compounding Center on 3/28/07 had a decrease in efficacy. He said he contacted the compounding pharmacy, who told him there was nothing wrong with the medication. did not have any of the vials in his possession from this shipment.

In August, 2007, said greater than 100 patients that were treated with the betamethasone began complaining of increased fibromyalgia pain and moderate to severe flu-like symptoms. said he noticed some of the vials of betamethasone appeared to be discolored (less milky appearance than normal). Further, he said he noticed particles floating in the bottom of the vial. He said the lots in question were received on 08/20/07, 9/17/07 and 9/28/07. See collection report number 426119 for details of the lot numbers.

While interviewing I repeatedly asked him to give me exact dates and patient information. He was unable to sit at his desk for a very long period of time. He repeatedly walked in and out of the office and changed the subject of conversation. He stated he was being evicted from his current location because, "I was treating patients until late in the evenings." He repeatedly said that this incident has hurt his practice and reputation. He also asked me to give him something in writing stating this complaint was being investigated because he was being investigated by the Board of Medical Examiners for a questionable narcotic prescription he had written. I explained to him that the only document that I was authorized to give him was the FDA 482, Notice of Inspection.

asked ten patients that were affected to come meet with me at his office. I spoke with them and several patients complained of increased joint pain, worse than before the injections, nausea, and severe fatigue. There were several patients that were seen in the local emergency rooms and reported he was aware of at least four patients that were admitted to local hospitals. He provided contact information for all four patients who were hospitalized but I was only able to contact one patient. I obtained FDA Form 461, Authorization for Medical Records Disclosure from each of the patients I interviewed. See attachment 3 for copies of the FDA Form 461.

The following is a list of the patients interviewed with their complaints:

- generalized muscle pain that began one day following injection
- increased muscle pain and "flu-like" symptoms (aching feeling) following injection
- migraine headache following injection (seen in emergency department)
- increased muscle pain following injections
- unable to walk following injection "ached all over"
- "flu" symptoms, fever following injections
- "flu" symptoms, nausea, fatigue
- increased blood pressure, "flu" symptoms, "aching all over"
- increased muscle pain, unable to sleep, urinary incontinence
- increased pain, fatigue

I asked [redacted] if he reported these complaints to the compounding pharmacy. He stated he did not. He also stated he did not file any complaints with Med Watch. [redacted] said rather than reporting the adverse reactions to the compounding pharmacy, he changed suppliers. Currently he is receiving betamethasone from [redacted]

[redacted] provided me with vials of the questionable betamethasone, which were collected as sample number 426119. The vials are brown in color and I was unable to see the discoloring to which he referred.

Since I was unable to obtain complete specific information from [redacted] I asked him to provide me with a written timeline of events and asked for the medical records of the patients I interviewed, including medical history and the treatment records from March, 2007 until present. He said it would take some time to copy the records and write the timeline due to the office having to relocate. I agreed to meet with [redacted] after the Christmas and New Year's holidays to obtain the requested records.

On January 3, 2008, I arrived at [redacted] new office location of [redacted]. He did not have the records available I requested. He said he has been too busy to copy the records because he needed to go through all the records and update his documentation. He stated he has fallen behind on documenting because he has been working long hours treating his patients that were affected by the adverse reactions.

He revealed that on December 14, 2007, he had additional complaints from patients who were treated with betamethasone that was received from his new supplier. At this time, I documented the labeling on the vials he stated had problems. The betamethasone was labeled in part: "\*\*\*Betameth AC/PH 3/3.95mg/ml exp. 3/5/08 RX#16007981 12/31/07\*\*\*". He stated approximately 14 patients reported similar symptoms as with the betamethasone received from New England Compounding Center.

I asked [redacted] if he was still using the betamethasone. He stated he was because the alternate medication is Triamcinalone. He said the Triamcinalone makes his patients "fat" so he does not like to use it. I asked him why he was using the betamethasone if he suspected there were problems that were causing his patients adverse reactions and causing some patients to be hospitalized. He stated he has become "pretty good" at looking at the medication in the vials before using to see if the coloring is "good". He also said his technician is an "expert" at spotting any particles in the vials.

[redacted] provided me with a copy of an article that was written about his new treatment of fibromyalgia. The article was written in the [redacted] magazine describing the treatment success and patient testimonials. See attachment 4 for a copy of the article. The article states, [redacted] is thrilled by the results of his study so far" and [redacted] is expanding his study. If you suffer from fibromyalgia and would like to participate, please contact [redacted]. I asked [redacted] if he was conducting a study. He stated yes. I then asked him if he had a sponsor for the study. He stated he did not. I asked if he had a protocol and he stated yes, he was following the protocol of another study. I asked to see the protocol and then he stated he did not have one written. I asked if he had FDA or IRB approval to conduct the study and he stated he was not really

conducting a study, he was just collecting data. In addition, I asked [redacted] if he had consent forms from all the patients in the study and he said no. While questioning [redacted] about his study, he asked me if he was in trouble. I explained to him that I was unable to answer whether or not he was in trouble but I questioned if FDA and IRB approval was required even though betamethasone was an approved drug. He stated he did not call the FDA to discuss his study. He called FDA to find out if the betamethasone had a problem. He said he needed a "friend" during this time of hardship in his practice. I explained to him I was there to protect the public health and collect information regarding possible problems with the drug and to also report any possible violations of the FD&C Act.

I asked [redacted] how many injections of steroids can a patient have in a given time period. He stated the standard practice is three injections within six months. However, he added, he has never seen any research that supports this claim. He stated some of his patients receive more injections than the standard of care.

[redacted] asked me to interview another patient. Patient [redacted] explained she was being treated by [redacted] for back pain for approximately three years. She stated she received an injection of betamethasone on or about September 11, 2007. See attachment 5 for copies of [redacted] clinic record. She said on September 21, 2007, she was admitted to the emergency department at [redacted] at [redacted] for nausea, vomiting and diarrhea. In addition, she said she was admitted to [redacted] at [redacted] on September 24, 2007 for eleven days for right-sided weakness and a final diagnosis of Rhabdomyolysis. See attachment 6 for copies of [redacted] hospital records. She said [redacted] told her the symptoms were probably due to complications from the "bad shots". [redacted] signed and FDA Form 461, Authorization for Medical Records Disclosure to allow me to obtain medical records from the hospital.

At this time, I had [redacted] medical chart in my hands and requested copies of her medical records from [redacted]. He took the chart from me and said he was not going to provide any more records to me. I explained that if he did not provide the records it would be considered a refusal.

I was unable to thoroughly interview [redacted] due to repeated interruptions from [redacted] in his office. On January 8, 2008, I met with [redacted] at her residence to have her sign a FDA Form 463a, Affidavit describing the events of her hospitalizations and treatments from [redacted].

A voice mail was left on my office telephone on the evening of January 3, 2008 from [redacted] stating he remembered there were consent forms signed by his patients and he would fax them to me over the weekend. On January 4, 2008, a facsimile was received in the NOLDO Mandeville RP from [redacted]. It included signed consent forms that state, "By signing below, you hereby authorize the above information to be used in Fibromyalgia clinical studies performed by [redacted] or anyone acting on his behalf. I hereby acknowledge the above and consent to same." The facsimile also included a letter from [redacted] stating he researched the problems with the medication and discovered that "Celestone [betamethasone] suspension can undergo changes in particle size (decomposition of particles) which would produce a clearer appearance within the solution. Also, these larger particles (as would be expected with the introduction of a foreign substance into the body) act as irritants. Unfortunately, they develop. While the particles once injected are too large to diffuse out of the epidural space". See attachment 7 for original copies of the consent forms and the faxed letter. The letter also stated he would provide me with the requested records within one week.

On January 11, 2008 [REDACTED] called to say he did not have the records yet. I explained to him that I would be in his office on January 22, 2008 to pick up the records. If they were not available a refusal would be documented. He promised to have the records.

On January 22, 2008 [REDACTED] Consumer Safety Technician and I arrived at [REDACTED] office. We issued another FDA 482, Notice of Inspection and Ms. [REDACTED] displayed her credentials. Ms. [REDACTED] was present to document and witness any possible refusal from [REDACTED]

[REDACTED] provided typed procedure notes for two patients. I requested medical records for all 10 patients I interviewed on December 11, 2007 and [REDACTED] medical records. He said he had been working on creating the documents for at least a week. He did not have all the records that I requested. I explained to him that I needed the records and he said he was not going to provide me any more records.

The following is a synopsis of the number of procedures performed by [REDACTED] for the two patients he provided records for:

[REDACTED] (see attachment 8)  
8/27/07- 9 mg celestone  
9/4/07- 6 mg celestone  
9/4/07- 6 mg celestone  
9/25/07- 6 mg celestone  
9/25/07- 6 mg celestone  
9/25/07- 6 mg celestone  
1/12/08- 15 mg celestone  
1/14/08- 6 mg celestone  
1/17/08- 12 mg celestone

[REDACTED] - (see attachment 9)  
7/27/07- 6 mg celestone  
7/27/07- 6 mg celestone  
8/10/07- 6 mg celestone  
8/10/07- 6 mg celestone  
8/24/07- 6 mg celestone  
8/24/07- 6 mg celestone  
9/13/07- 6 mg celestone  
9/13/07- 6 mg celestone  
10/1/07- 4.5 mg celestone  
10/1/07- 4.5 mg celestone  
12/27/07 6 mg celestone  
12/27/07 6 mg celestone  
12/29/07 4.5 mg celestone  
12/29/07 6 mg celestone  
1/14/08 9 mg celestone

He showed me two vials of betamethasone in attempt to show me the discoloration. I requested to hold the vials so I could photograph the labeling but [REDACTED] refused to give me the vials, stating he did not want to get anyone in trouble.

Before leaving [REDACTED]'s office, I again requested copies of [REDACTED] medical records. I offered to copy them myself, but [REDACTED] agreed to give them to me. I also requested original copies of the consent forms that were faxed to the Mandeville RP, which he provided.

I explained to [REDACTED] that the findings of this investigation would be forwarded to my supervisor for review and possibly forwarded to NOL-DO's compliance branch. I explained that any further communication with NOL-DO should be directed to NOL-DO's compliance branch.

Please note a name change occurred during this investigation. [REDACTED] and [REDACTED] Investigator are one in the same.

**ATTACHMENTS**

- Attachment 1: Patient complaint facsimile
- Attachment 2: Medical license
- Attachment 3: FDA Form 461, Authorization for Medical Records Disclosure
- Attachment 4: Magazine article
- Attachment 5: [REDACTED] clinic records
- Attachment 6: [REDACTED] hospital records
- Attachment 7: Faxed letter and consent forms
- Attachment 8: [REDACTED] procedure notes
- Attachment 9: [REDACTED] procedure notes
- FDA 482, Notice of Inspection dated 12/11/07
- FDA 482, Notice of Inspection dated 1/22/08
- FDA Form 484, Receipt for Samples
- FDA Form 463a, Affidavit signed by [REDACTED]
- FDA Form 463a, Affidavit signed by [REDACTED]

[REDACTED]

[REDACTED] Investigator  
NOL-DO Mandeville Resident-Post