United States Senate
COMMITTEE ON FINANCE
WASHINGTON, DC 20510–6200

July 13, 2006

Via Electronic Transmission

The Honorable Mark McClellan
Administrator
Centers for Medicare & Medicaid Services
Department of Health & Human Services
200 Independence Avenue, SW
Washington, DC 20201

Andrew C. von Eschenbach, M.D.
Acting Commissioner
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Administrator McClellan and Acting Commissioner von Eschenbach:

As Chairman of the Committee on Finance (Committee), I have a responsibility to the more than 80 million Americans who receive health care coverage under the Medicare and Medicaid programs to oversee the proper administration of these programs and ensure that taxpayer and beneficiary dollars are spent appropriately on safe and effective drugs and devices.

Thank you for providing briefings for my Committee staff as requested to address allegations of inappropriate pharmacy compounding of inhalational drugs. Specifically, the Committee received allegations that some pharmacies, in particular mail-order pharmacies, and durable medical equipment (DME) suppliers may be producing and/or providing unsafe and/or ineffective or less effective nebulizer medications by inappropriately compounding prescription drugs. The Committee recognizes that there are legitimate needs for compounded medications.[1] However, if these allegations are true, then the Committee is greatly concerned about the health and safety of the patients using these drugs as well as the financial impact that unsafe and/or ineffective compounded medications may have on the Medicare program in particular and our health care system generally.

The Committee initiated an investigation in March after my staff interviewed several former employees of a home care company that provides patients with compounded nebulizer medications. As part of the investigation, my staff spoke with and/or received information from representatives from the Centers for Medicare & Medicaid Services (CMS), the Food and Drug Administration (FDA), Astra Zeneca, Dey, LP, Sepracor, the International Academy of Compounding Pharmacists (IACP), Allergy & Asthma Network Mothers of Asthmatics, as well as individual compounding pharmacists. The Committee also received documents from patients and parents of children with respiratory conditions that require treatment with nebulizer medications.

[1]The FDA also states in its May 2002 compliance guide on pharmacy compounding (Sec. 460.200) that it "recognizes that pharmacists traditionally have extemporaneously compounded and manipulated reasonable quantities of human drugs upon receipt of an individually identified patient from a licensed practitioner," and these activities are not the subject of the FDA's compliance guide.

Based on the interviews and a review of information and documents received to date, my Committee staff have informed me of the following:

- During their interview with Committee staff, the former employees of a home care company in Florida described methods used by the company to substitute prescriptions for nebulizer medications with compounded products, without the knowledge of patients and/or their doctors. They showed my staff copies of pre-printed prescription order forms that were provided to physicians, and on some of these forms, the medications to be prescribed were pre-checked by the company. See attachment. The former employees also added that the company targeted Medicare patients because Medicare pays the same amount whether the product is brand name, generic or compounded.

- The former home care employees also informed my Committee staff that the company provided financial incentives for producing prescriptions for compounded medications. The employees received bonuses and commissions for each new compounded prescription filled per patient.

- In addition to the information provided by the former employees, the Committee received information about patients in other states who allegedly discovered that their pharmacy provided them with compounded inhalational drugs without their knowledge or their physician's knowledge. Some of these patients stated that they became ill or their condition did not improve after using the compounded drugs.

- Several pharmaceutical companies with whom my staff met said they independently tested drug samples obtained from physicians who realized that their patients received compounded drugs instead of the brand name medication they thought they had prescribed. The companies found that the drugs were not the prescribed dosage or concentration. They also found samples that failed sterility tests and were contaminated with the bacteria *Burkholderia cepacia*. According to the Centers for Disease Control and Prevention, *B. cepacia* poses little medical risk to healthy people, but individuals with weakened immune systems or chronic lung diseases may be susceptible to infections, including serious respiratory infections.

- My Committee staff were provided with pictures of vials of compounded inhalational drugs that were not packaged appropriately as well as vials that contained varying volumes of solution for a single prescription.

- My Committee staff were told that some of the compounding pharmacies or DME suppliers allegedly misled patients by telling patients that they were being provided generics or cheaper alternatives, even though there were no generics available for some of the brand name products.

- Some pharmacies or DME suppliers are allegedly using bulk chemicals that are not pharmacy grade or not obtained from a registered chemicals supplier.

- During meetings with my staff, representatives from both CMS and FDA acknowledged their concerns about inappropriate or illegal pharmacy

compounding. CMS staff stated that the compounding of inhalational drugs is a significant clinical issue that has accelerated over the last five years.

- FDA's May 2002 compliance guide states that the FDA believes an "increasing number of establishments with retail pharmacy licenses are engaged in manufacturing and distributing unapproved new drugs for human use in a manner that is clearly outside the bounds of traditional pharmacy practice…." However, neither FDA nor CMS knows the full extent of the problem, and it appears that neither agency has plans to determine the extent of the problem.

- CMS staff admit that CMS does not know how often and how much Medicare pays for compounded inhalational drugs because its reimbursement codes are "not precise enough" to allow the agency to distinguish payments for brand name and generics from compounded drugs.

- In response to some of the concerns regarding inappropriate pharmacy compounding of inhalational drugs, CMS created Healthcare Common Procedure Coding System (HCPCS) codes for non-compounded budesonide inhalation solution and budesonide powder compounded for inhalation solution. However, separate reimbursement codes are not available for other non-compounded and compounded inhalational drugs.

- FDA maintains that drug compounding activities are generally subject to FDA oversight, although according to FDA's compliance guide, "in practice,…the agency generally relies on states to regulate the limited compounding of drugs as part of the traditional practice of pharmacy." It is not clear from the compliance guide, however, where compounding ends and manufacturing begins. There is also concern that FDA does not have the means or the resources to identify the offending parties and must rely largely on third party complaints to initiate inspections and take enforcement actions. My staff were informed that a team of five FDA staff oversee all pharmacy compounding issues for the agency.

- CMS staff stated that as long as the compounded medication is provided by a licensed pharmacy pursuant to a valid prescription from a licensed health care provider, then Medicare pays. The Committee's concern, however, is that some of these prescriptions may be fraudulently obtained. In addition, a licensed pharmacy could still be engaging in questionable compounding activities. CMS advised my staff that the agency can instruct its regional contractors to write articles to educate DME suppliers, pharmacies, and physicians, but articles, as we well know, are not binding guidance.

- The FDA is reviewing a citizen petition filed on March 24, 2005, by the Consumer Health Alliance for Safe Medication (CHASM) that requests, among other things, that the FDA take action(s) related to the labeling and advertising of compounded inhalational drugs.

- My staff were informed that states lack the resources to hire well-trained pharmacy inspectors who can identify problematic facilities. They were also told that there is lack of consistent oversight at the state level.

- According to IACP, most state boards of pharmacy do not maintain a database of adverse event reports from pharmacists for compounded drugs. The Government Accountability Office (GAO) testified in 2003 that North Carolina is the only state that requires mandatory adverse event reporting involving prescription drugs, including compounded drugs. However, the North Carolina Board of Pharmacy's reporting system only requires that pharmacy managers report information to the board regarding prescription drugs that may have caused or contributed to the death of a patient.

- My Committee staff were informed that the pharmacy board in Missouri has a program for random testing of compounded drugs for safety, quality, and potency, but other states do not have similar programs. The GAO testified in 2003 that "the ability of states to oversee and ensure the quality and safety of compounded drugs may be affected by state-specific factors such as the resources available for inspections and enforcement."[2]

- The National Association of Boards of Pharmacy developed standards for good compounding practices, but implementation by state boards of pharmacy is voluntary, so there are varying standards and regulation across states.

- Concerns have been raised that in the effort to drive down drug costs, some pharmacies are using substitution laws to substitute prescriptions with compounded products without prior authorization from the physician and/or patient.

- Pharmacists engaged in legitimate compounding are concerned that one bad apple spoils the whole barrel. They are concerned that reductions in Medicare reimbursement for compounded nebulizer medications will shut down pharmacies engaged in small scale compounding for patients with a legitimate need for compounded medications. I am equally concerned.

In light of the serious concerns and issues regarding pharmacy compounding of inhalational drugs, I request that the FDA and CMS keep the Committee apprised of any developments or actions related to pharmacy compounding and the allegations discussed in this letter. Additionally, I would appreciate a response from your respective agencies regarding the following questions and proposals:

1. Pharmacies believe that it is the state boards of pharmacy that are responsible for regulating drug compounding; however, given the limitations in oversight by state boards of pharmacy, what is or should be the federal role in the regulation of pharmacy compounding?

2. Is the FDA considering modifications to its pharmacy compounding compliance guide to further clarify what activities fall under the category of drug manufacturing?

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[2]Statement of Janet Heinrich, before the Senate Committee on Health, Education, Labor, and Pensions, *Prescription Drugs: State and Federal Oversight of Drug Compounding by Pharmacies*, GAO-04-195T (October 23, 2003).

3. Does the FDA require additional and/or more explicit authorities to respond to allegations of inappropriate or illegal compounding of inhalational drugs, particularly in light of the district court ruling by Judge Robert Junell in *Medical Center Pharmacy v. Ashcroft,* on May 25, 2006, that compounded drugs are not considered unapproved products under the Food, Drug, and Cosmetic Act?

4. My staff were told that the Medicare reimbursement rate for inhalational drugs is a major driving force for large volume compounding of such drugs, and these large providers can be identified easily by CMS's DME regional carriers. As the agency responsible for oversight of DME suppliers, how often does CMS conduct audits of DME suppliers that provide compounded medications, and how are these audits initiated? Does CMS coordinate with FDA on audits and inspections?

5. It appears that one aspect of the solution to addressing some of the problems identified is raising awareness among health care providers who prescribe inhalational drugs of the inappropriate or illegal compounding of such drugs. For example, is the FDA considering alerting physicians by sending out Dear Healthcare Provider letters and/or issuing a public health advisory to advise physicians of how some pharmacies or DME suppliers are manipulating the system to "switch" a patient from a prescribed drug to a compounded drug?

6. The American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology proposed a resolution urging the American Medical Association (AMA) to request that the FDA take enforcement action against pharmacies that are mass manufacturing medications under the guise of compounding and that CMS reconsider paying for these medications. The resolution also calls for education of physicians regarding potential liability, since they are accountable for signing prescriptions for such medications, knowingly or unknowingly. Has FDA spoken with AMA or other professional societies to coordinate an educational campaign on this issue?

7. CMS staff informed my staff that changing and creating HCPCS codes is labor intensive. However, since the agency cannot distinguish payments for compounded inhalational drugs from payments for brand name or generic drugs, will CMS be considering modifications to how inhalational drugs are reimbursed?

8. Patients should be told when they are taking compounded inhalational drugs and why. Who is or should be responsible for ensuring that compounded medications are labeled appropriately so that there is full disclosure regarding the risks and benefits of the drugs that patients are taking?

9. Please keep the Committee apprised of FDA's actions related to CHASM's citizen petition.

10. What is CMS's position on maintaining reimbursement for nebulizers in Medicare Part B but restricting reimbursement for the inhalational drugs to Part D? What is CMS's position on accreditation of compounding pharmacies in order to receive Medicare reimbursement?

11. Has CMS considered requiring a determination of medical necessity for compounded inhalational drugs?

Thank you for your cooperation and your attention to this important matter. I would appreciate a response to the concerns and questions set forth in this letter by no later than August 3, 2006.

Sincerely,

Charles E. Grassley
Chairman

cc: The Honorable Daniel R. Levinson, Office of Inspector General, Department of Health and Human Services
American Medical Association
American Academy of Allergy, Asthma and Immunology
American Association for Respiratory Care
American College of Allergy, Asthma and Immunology

Enclosure

Prescription

[redacted]

[redacted]

Patient Name: _____ Date: _____

Address: _____

City: _____ State: _____ Zip _____ Date of Birth: _____

Phone: _____ Insurance ID# _____ SS# _____

Nebulizer Solution — Frequency

Nebulizer Solution						
☐ Albuterol Sufate 0.083% 3ml	☐ QID	☐ TID	☐ BID	☐ QD	☐ OTHER:	
☐ Ipratropium Bromide 0.02% 2.51	☐ QID	☐ TID	☐ BID	☐ QD	☐ OTHER:	
☑ Albuterol 2.5/Ipratropium 0.5mg 2ml (compounded)	☑ QID	☐ TID	☐ BID	☐ QD	☐ OTHER:	
☑ Budesonide 0.5mg 2.5ml (compounded)	☐ QID	☐ TID	☑ BID	☐ QD	☐ OTHER:	
☐ Albuterol 2.5mg/Ipratropium 0.5mg/ Budesonide 0.25mg 3ml (compounded)	☐ QID	☐ TID	☐ BID	☐ QD	☐ OTHER:	
☐ Albuterol 2.5mg/Ipratropium 0.5mg/ Triamcinolone 0.2mg 3ml (compounded)	☐ QID	☐ TID	☐ BID	☐ QD	☐ OTHER:	
Acetylcysteine 20% 4ml _____	Use ☐ 1ml ☐ 2ml ☐ 3ml ☐ 4ml ☐ _____					
	☐ QID	☐ TID	☐ BID	☐ QD	☐ OTHER:	
	☐ QID	☐ TID	☐ BID	☐ QD	☐ OTHER:	

QUANTITY: 1 MONTH SUPPLY or Other: _____ **REFILLS: 1 YEAR or Other** _____

DIAGNOSIS

☐ Asthma ☐ COPD ☐ Emphysema ☐ Chronic Bronchitis ☐ Other: _____

EQUIPMENT/SUPPLIES

☐ AsthmaPak asthma support equipment (spacing device, peak flow meter w/instructions)

☐ Nebulizer Compressor (Does patient currently own a nebulizer compressor?) ☐ Yes ☐ No

☐ Pari LC Jet Nebulizer Circuit

☐ Other: _____

I give permission to [redacted] to act as my agent in transmitting thhis written prescription to the pharmacy of the patients choice.

Physician Printed Name [redacted] UPIN: [redacted]

Address: [redacted]

City: [redacted] State: [redacted] Zip: [redacted]

Physician Signature: _____ Date: _____

THIS PRESCRIPTION MAY BE FILLED AT ANY PHARMACY OF YOUR CHOICE.