SUMMARY

An inspection of this facility was conducted at the request of CDER Office of Compliance, Division of New Drug Labeling and Compliance, to specifically investigate the manufacture and distribution of Nicardipine IV bags (Attachment 7). The inspection was conducted under the Pharmacy Compounding Assignment, PAC 56D015 and FACTS ID 1188430.

This was the first FDA inspection for this company at this facility. There was no prior information to review in Central File.

This inspection determined that this facility repacks liquid prescription and OTC drug products, they admix epidural solutions for use in facilities, and they admix any other drug product as requested by their customer. They do not apply patient names to these individual products. The only product that they make from a prescription with a specific patient name is dialysis solutions which are used in patients with acute renal failure within an ICU.

The firm currently admixes Nicardipine IV bags in four different dosages for use by any of their customers. There are (b)(4) different customers currently purchasing the IV Nicardipine bags. The individual customers acquire the Nicardipine vials and send them to Ameridose for admixing. Ameridose does not purchase the Nicardipine directly. They are providing a controlled mixing service for their customers. The firm plans to continue to mix Nicardipine if requested by their customers. Ameridose applies a 75 day beyond use date on each bag of Nicardipine. The firm would not provide FDA a physical sample of Nicardipine as they stated that Ameridose does not own the Nicardipine. There was no FDA 483 issued at the close of the inspection.

The following Documentary Samples were collected during this inspection to document interstate shipment:

1. DOC Sample 462551, for Nicardipine 25mg/250ml, lot 05112010@396
2. DOC Sample 462552, for Nicardipine 20mg/200ml, lot 05112010@14
3. DOC Sample 462553, for Nicardipine 50mg/250ml, lot 06302010@437
4. DOC Sample 462554, for Nicardipine 40mg/200ml, lot 06042010@221

A copy of the Affidavit and Collection Reports are attached to this report (Attachments 2-6).

Throughout this report, Ameridose, LLC will be referred to as Ameridose.

A copy of this report should be sent to Mr. Gregory Conigliaro, Vice President and General Manager, and mailed to the address listed below.

ADMINISTRATIVE DATA

Inspected firm:	Ameridose, LLC
Location:	205 Flanders Rd Westborough, MA 01581-1032
Phone:	888-820-0622
FAX:	508-475-0421
Mailing address:	205 Flanders Rd Westborough, MA 01581-1032
Dates of inspection:	7/8/2010, 7/15/2010
Days in the facility:	2
Participants:	Debra M. Emerson, Investigator Stacey S. Degarmo, Investigator

On 7/8/10, Investigator Emerson and Investigator Degarmo displayed their credentials to Mr. Gregory Conigliaro, Vice President and General Manager, and a FDA-482, Notice of Inspection was then issued to Mr. Gregory Conigliaro, Vice President and General Manager. Mr. Conigliaro was identified as the most responsible person available at the initiation of the inspection.

Also in attendance on 7/8/10 were Mr. Samuel Penta, Ms. Cheryl Lathum, and Mr. Leo McKenna from the Massachusetts Board of Registration in Pharmacy.

Investigator Degarmo was present for the inspection on 7/8/10.

On 7/15/10, Ms. Sophia Pasedis, read the form 463a, Affidavit, made two corrections to the Affidavit, and then she signed the Affidavit.

This report was written by Investigator Emerson unless otherwise noted.

HISTORY

This is the first FDA inspection for this company at this facility. Ameridose opened this facility in December 2008.

INTERSTATE COMMERCE

The firm currently manufactures and repackages drug product for customers inside and outside of Massachusetts. The firm ships product locally to customers via couriers and also ships overnight via (b) (4) The firm ships to customers outside Massachusetts via (b) (4)

Shipping records were provided by Ms. Pasedis to document that four different dosages of Nicardipine which were distributed via interstate commerce: Nicardipine 25mg/250ml NS, 20mg/200ml NS, 50mg/250ml NS, and 40mg/200ml NS. All shipping records were incorporated with the batch records and entered as Documentary Samples 462551 thru 462554. Copies of the collection reports are included as Attachments 3-6.

JURISDICTION

The firm currently repacks and manufactures prescription drug products which are FDA regulated drug products.

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED

(Written by Inv. Degarmo and Inv. Emerson)

Gregory Conigliaro, Vice President and General Manager. Mr. Conigliaro has been with the firm and in his current role since it opened in July 2006. He is one of four owners of the company. He stated that he is responsible for the overall day to day management of the firm and works closely with Ms. Pasedis on regulatory affairs and compliance matters.

Sophia Pasedis, Vice President Regulatory Affairs and Compliance. Ms. Pasedis reports to Mr. Greg Conigliaro. Ms. Pasedis has been with the firm since its inception about 5 years ago. She has been in her current role for approximately 3 years. She stated that her responsibilities include the overall compliance of both facilities; oversight of the standard operating procedures; and acts as Pharmacist in Charge/Manager of Record for the Framingham facility

Melanie Cerullo, Vice President of Quality Assurance. Ms. Cerullo reports to Mr. Greg Conigliaro. Ms. Cerullo has been with the firm and in her current role since October 1, 2007. She has 5 direct reports. Ms. Cerullo's responsibilities include all of quality including chemistry, micro training, new products, and environmental monitoring.

Mr. Conigliaro provided a list of all Amerisode Owners (Exhibit 1 p. 1-2):

Carla R. Conigliaro
Barry J. Cadden

Lisa M. Conigliaro
Gregory A. Conigliaro

Mr. Conigliaro provided a list of top Ameridose management (Exhibit 1 p. 3-4). Ms. Pasedis provided a copy of their 2010 electronic Establishment Registration (Exhibit 2).

Pages were printed off the Ameridose website (Exhibit 3) which documents in part that Ameridose is an "FDA registered manufacturer", "meets cGMP requirements", and uses "NDC barcoding".

MANUFACTURING/DESIGN OPERATIONS

This facility is approximately (b) (4) square feet in size, with (b) (4) square feet in warehouse space, (b) (4) square feet for the clean rooms, and (b) (4) square feet for shipping. The warehouse has (b) incoming receiving bays (b) (4) The warehouse has (b distribution bays, (b) (4) (b) (4) This facility has (b) (4) clean rooms with (b) (4) (b) (4), a few of these hoods in the facility are (b) (4) (b) (4) comes in and certifies the hoods every (b) (4) They have a separate penicillin room, with a separate air handling unit that is vented to the outside. They have a separate caged area where all narcotics are processed. There is a QA lab on site. A copy of the firm's floor plan was obtained (Exhibit 4).

This facility no longer repackages tablets. This facility does not manufacture total parenteral nutrition (TPN). Most products made at this facility are products requested by their customers and they are not patient specific and are not labeled with patient names on the label. This facility does repackage liquids. They use commercially available parenteral drug products to make various IV dosage products as requested by their customers. This facility also makes epidural products.

There is one product that Ameridose makes which is patient specific: Citrate Veno Venous Hemofiltration (CVVH). This is a dialysis solution which is made patient specific and is labeled with patient names. This product is used in intensive care units for patients in acute renal failure.

Nicardipine IV bags

Ms. Pasedis stated that they started making the IV Nicardipine bags in 2006 at the request of one of their customers located in (b) (4) Ms. Pasedis stated that they used commercial Nicardipine vials which were provided to them by their individual customer. Ms. Pasedis stated that they have supplied the IV Nicardipine bags to (b) different customers. Mr. Conigliaro provided a list of all customers that have received the Nicardipine in 2010 (Exhibit 5). Mr. Conigliaro stated that he returned from vacation last week and received a letter from EKR Therapeutics (Exhibit 6) alleging that Ameridose is manufacturing unapproved injectable prescription drug product, Nicardipine. Mr. Conigliaro stated that this is a trade complaint. Mr. Conigliaro stated that they do

not purchase the Nicardipine vials, their customers purchase the IV vials and they send the vials to Ameridose and Ameridose mixes the IV bags for them. Ms. Pasedis stated that she "had no idea Cardene IV was on the market". The firm continues to admix Nicardipine for their customers as requested.

Mr. Conigliaro was asked for a list of all shipments or orders for Nicardipine. Mr. Conigliaro provided this list (Exhibit 7). It is important to note that Ameridose started making and shipping the IV Nicardipine in December 2006. The customers provide the Nicardipine vials and Ameridose orders the IV bags from (b) (4) which they use for all customers.

Ms. Pasedis stated that they used a beyond use date (BUD) of 7 days when they initially started making the Nicardipine IV bags back on 2006. The procedure entitled: Beyond-Use Dating (BUD) of Sterile Products, Version 1-3 (Exhibit 8-10) were collected. Version 1 of this procedure was in effect when Nicardipine was initially made by Ameridose and Version 3 is the current in place procedure. The procedures have been modified over the years. They changed from 7 days to 45 days on 12/22/06 at the conclusion of testing for Nicardipine lot 10182006@75. In 2007, they started product verification testing. In April 2007, they changed the beyond use date to 60 days based on customer request per Ms. Pasedis. Today they are using a 75 day beyond use dating for all Nicardipine mixed by Ameridose, this changed in October 2009. Ms. Pasedis was asked if the firm had data to support this beyond use dating. Ms. Pasedis provided the following:

- Certificate of Analysis for Nicardipine 100mcg/ml, lot 10182006@75 (Exhibit 11). Please note the following: the firm could not produce the batch record for this lot to confirm that the material used in this testing is the same material which is used today, testing occurred on day 5, 15, 30, 45 and 60 only for potency.
- Product Verification report for Nicardipine 25mg/250ml NS bag, lot 07252007@72 (Exhibit 12) this was for a 60 day beyond use date. Please note the following: the firm could not produce the batch record for this lot to confirm that the material used in this lot is the same material which is used today, only physical characteristics were evaluated on day 2 and day approx. day 60, as well as sterility which was performed once and reported on 12/3/07, and the firm did not test potency as part of this stability testing.
- Certificate of Analysis for Nicardipine 100mcg/ml, lot 03102009@218 (Exhibit 13). This was the only lot which was tested out to 90 days for potency in the IV bag. Ms. Pasedis stated that they changed their beyond use date to 75 days to be conservative instead of using the full 90 days as the lot was tested thru. A copy of the mixing record for the lot was provided (Exhibit 14).
- Certificate of Analysis for Nicardipine 100mcg/ml, lot 03102009@214 (Exhibit 15). This lot which was tested out to 90 days is made in a syringe. Ms. Pasedis stated that they test in different devices and at present, they are not selling Nicardipine in this syringe.

Ms. Pasedis was asked for the data to support the Nicardipine 200mcg/ml concentration and she stated that the firm has never tested the Nicardipine in the 200mcg/ml concentration.

Ms. Pasedis stated that either facility can make these IV Nicardipine bags. However, the clean room at the Framingham facility is currently shutdown. Once operational, the Nicardipine can be made in either facility.

Ms. Pasedis explained that the Nicardipine bags, once mixed, are placed in a UV protectant overwrap and then these bags are placed in a cardborad box for shipping. Ms. Pasedis stated that they have not received any complaints on Nicardipine going back to the initial admixing in 2006.

On 7/15/10, Mr. Conigliaro provided a letter to FDA (Exhibit 17) which outlines their response to the allegations made by EKR Therapeutics.

NDC Numbers

Ms. Pasedis explained that the firm will apply an NDC number to any product that they manufacture at the request of their individual customer. The firm has approximately 1800 different NDC numbers. Ms. Pasedis explained their NDC numbering, the first five numbers are the firms labeling code, the next four numbers are the product code, and the last 2 numbers are the size. Ms. Pasedis explained that the firm does not list any of these NDC numbers with FDA. Ms. Pasedis explained that the firm issues these NDC numbers thru an internal Ameridose committee. These same NDC numbers are used at both the Framingham and Westborough facilities.

The NDC numbers used for Nicardipine IV bags are the following:

Nicardipine 25mg/250ml, on 7/26/07 Ameridose issued the following NDC: 24200-0110-10
Nicardipine 20mg/200ml, on 2/26/10 Ameridose issued the following NDC: 24200-0111-11
Nicardipine 50mg/250ml, on 6/2/10 Ameridose issued the following NDC: 24200-0112-10
Nicardipine 40mg/200ml, on 6/3/10 Ameridose issued the following NDC: 24200-0113-11

MANUFACTURING CODES
(Written by Inv. Degarmo)

The firm has defined their own lot numbering system based on the date manufactured and a sequential numbering system. For example, lot number AABBCCCC@X, is determined by the following:

(b) (4)
[redacted]

REFUSALS

There were no refusals encountered during this inspection.

GENERAL DISCUSSION WITH MANAGEMENT

At the conclusion of the inspection, Mr. Gregory Conigliaro, Vice President and General Manager; Ms. Sophia Pasedis, Vice President Regulatory Affairs and Compliance; and Ms. Melanie Cerullo, Vice President of Quality Assurance; were present. There was no FDA 483 issued and there were no discussion items. I explained that this inspection would not cover the firm for their annual cGMP inspection and that FDA would return at some point to conduct a GMP inspection.

SAMPLES COLLECTED

The following Documentary Samples were collected during this inspection to document interstate shipment:

1. DOC Sample 462551, for Nicardipine 25mg/250ml, lot 05112010@396
2. DOC Sample 462552, for Nicardipine 20mg/200ml, lot 05112010@14
3. DOC Sample 462553, for Nicardipine 50mg/250ml, lot 06302010@437
4. DOC Sample 462554, for Nicardipine 40mg/200ml, lot 06042010@221

A copy of the Affidavit and Collection Reports are attached to this report (Attachments 2-6).

ATTACHMENTS

1. FDA 482, Notice of Inspection, dated 7/8/10
2. FDA 463a, Affidavit, dated 7/15/10
3. DOC Sample 462551, Collection Report
4. DOC Sample 462552, Collection Report
5. DOC Sample 462553, Collection Report
6. DOC Sample 462554, Collection Report
7. E-mail and letter (13 pages)

EXHIBITS COLLECTED

1. Ameridose Owners (4 pages)
2. Establishment Registration (6 pages)
3. Documents printed from Ameridose Website (3 pages)
4. Ameridose floor plan
5. Firms receiving Nicardipine in 2010
6. Copy of Letter Ameridose received from EKR Therapeutics (7 pages)
7. Listing of all Nicardipine sales (8 pages)
8. Procedure: Beyond-Use Dating (BUD) of Sterile Products, Version 1 (3 pages)
9. Procedure: Beyond-Use Dating (BUD) of Sterile Products, Version 2 (5 pages)
10. Procedure: Beyond-Use Dating (BUD) of Sterile Products, Version 3 (6 pages)
11. Certificate of Analysis for Nicardipine 100mcg/ml, lot 10182006@75
12. Product Verification for Nicardipine 100mcg/ml, lot 07252007@72
13. Certificate of Analysis for Nicardipine 100mcg/ml, lot 03102009@218
14. Nicardipine Worksheet lot 03102009@218 (8 pages)
15. Certificate of Analysis for Nicardipine 100mcg/ml, lot 03102009@214
16. Nicardipine Worksheet lot 03102009@214 (7 pages)
17. Letter from Ameridose dated 7/15/10 (4 pages)

Debra M. Emerson, Investigator

Stacey S. Degarmo, Investigator