February 28, 2005

Nebraska FACE Investigation 2004-99

SUBJECT:

Cattle Rancher Hospitalized After Accidental Injection of Micotil

SUMMARY:

A 41-year-old cattle rancher became seriously ill as a result of an accidental injection of an animal antibiotic known as Micotil 300® which has no known antidote. On November 16, 2004, the rancher was preparing to vaccinate two calves with a 20 cc plastic disposable syringe in an outside lot using a squeeze chute. He vaccinated the first calf, then placed the syringe's plunger in his mouth, while reaching up to open the squeeze chute gate. The gate only partially opened, so he reached up with his left hand to use the end gate's "pipe" handle to fully open the chute. At this same instant, the calf lunged forward, flinging open the end doors, causing the closest pipe handle to strike his left hand, driving it backwards into the needle between his left thumb and first finger, injecting between 1 cc and 1.5 ccs. He immediately felt a burning sensation at the injection site. Within a couple of minutes he developed severe ringing in his ears and felt as though his tongue and lips were swollen. He called out for help.

His wife was exiting their house about 50 yards away and heard her husband call for help. She immediately called the Rocky Mountain Poison Control Center phone number listed on the Micotil packaging insert and was advised to place ice on the injection site and immediately get her husband to an emergency room. As his condition worsened, the cattle rancher was airlifted to a regional medical center and placed in Intensive Care Unit for two days. After his condition stabilized he was discharged.

The Nebraska Workforce Development, Department of Labor's Investigator concluded that to help prevent future similar occurrences:

- Veterinarians and animal health distributors, prior to releasing Micotil, should require the purchaser to sign a product information fact sheet that indicates Micotil can be fatal in humans, and that there is no antidote for this medication every time they purchase the product.

- Users of syringe-loaded medications should practice safe handling procedures during all phases of animal treatment.

- Veterinarians/Cattlemen, when practical, should consider using another less-hazardous antibiotic.

PROGRAM OBJECTIVE:

The goal of the Fatality Assessment and Control Evaluation (FACE) workplace investigation is to prevent future work-related deaths or injuries, by a study of the working environment, the worker, the task the worker was performing, the tools the worker was using, and the role of management in controlling how these factors interact.

This report is generated and distributed **solely** for the purpose of providing current, relevant education to employers, their employees and the community on methods to prevent occupational fatalities and injuries.

INTRODUCTION: On November 16, 2004, at approximately 3:30 p.m. a 41-year-old cattle rancher became severely ill as a result of an accidental injection of the bovine antibiotic Micotil 300®. The Nebraska Department of Labor was notified of the incident on November 17, 2004. The Nebraska FACE investigator met with the rancher and his wife on December 2, 2004. A site visit was conducted the same day. The local newspaper personnel that interviewed the family and wrote an extensive related article were also interviewed the same day.

The rancher is a self-employed cattleman/farmer/trucking company operator. He was born and raised on a farm and has been raising cattle his entire life. A total of 5 other personnel are employed at various times throughout the year with the ranching and trucking operations. The rancher was in good physical shape.

INVESTIGATION:

At approximately 3:30 p.m. on the day of the incident the victim was working alone outside in the lot. He had two calves that needed to be vaccinated. He used a Monoject® 20 cc disposable syringe with a 1 inch, 16 gauge needle to withdraw 14 ccs of Micotil. Each calf weighed approximately 600 pounds and would receive 7 ccs each.

The first calf was run into a Pearson® brand squeeze chute (see photo 1). The rancher patted the calf on the shoulder area where the injection was to be given to accustom the calf to the pressure of the needle. He made the subcutaneous (just below the skin, not into the meat) injection using his left hand without any problems and withdrew the syringe/needle.

He placed the extended plunger of the syringe between his lips, holding it by the extended plunger. The needle attached to the syringe was pointed outwards to the left. He reached up to release the calf but the doors did not open fully, so he reached up with his left hand to grab the pipe handle nearest him to open the doors. As he reached forward, the calf lunged forward, striking the doors, flinging them open. Both doors have handles made from steel pipe that swivel. As the doors flung outward, the pipe handle nearest the rancher struck his extended left hand, driving it back onto the unprotected needle between his left thumb and first finger, striking the bone. The impact caused the syringe's plunger to depress slightly, injecting the Micotil® into his hand. The rancher immediately looked at the syringe and saw that there were still approximately 5 ccs of Micotil® remaining, and there was some running down the outside of his hand. Based on this, he estimated that he had been injected with 1 to 1.5 ccs.

He immediately began to feel a burning sensation at the injection site. The sensation was slowly working its way up his left arm toward his shoulder area.

His wife came out of the house, approximately 50 yards from the rancher, and heard him shouting for help. She called the Rocky Mountain Poison Control Center after finding the toll-free number on a Micotil packaging insert. She was told to apply ice to the site and to transport her husband to the nearest emergency room, which was approximately 5 miles away.

The rancher was now feeling pain from the injection site through his left shoulder area. His left hand had begun to swell immediately, and within five minutes he was experiencing severe ringing in his ears and the sensation of his lips burning. He stated that his lips and tongue also felt swollen.

His wife transported him to the emergency room, arriving approximately 15-20 minutes after the injection. According to hospital personnel, although he seemed to be getting sleepy at the local hospital, his vital signs remained close to normal. At approximately 5 p.m. his condition worsened as he began developing chest pains along with severe lower abdominal extremity shakes/convulsions, and his blood pressure began to rapidly rise. He was administered a medication, Ativan, that quieted the convulsions. The decision was made to airlift him to a regional hospital approximately 45 land miles away, requiring a 15 minute air flight.

Five minutes into the airlift to the regional medical center his condition worsened and he was immediately taken to the intensive care unit upon arrival. Doctors contacted the Rocky Mountain Poison Control Center and searched the internet for treatment information. One consideration was amputation of the left hand to stop the spread of the Micotil®, but since the medication had moved up his arm into his upper extremities by the time he arrived that consideration was removed as a treatment option. He was given more Ativan to relax him and also medications for pain.

His wife drove to the hospital and was met by a social worker and other hospital staff . She was told to "prepare for the worst" and to call in their immediate family at once.

The mother of the Nebraska cattleman killed due to an accidental injection of Micotil® (FACE report NE 2003-04, *Cattleman Dies Due To Accidental Injection*) approximately 20 months before heard about the accident. She immediately contacted the local emergency room and was told the rancher had been air lifted to the regional medical center. She then was able to contact the rancher's doctors at the medical center, explain who she was, and to inform them that in November 2003 the Veterinary Drugs Directorate (VDD) of Canada had issued recommendations to Canadian hospitals for managing cardiac reactions associated with Micotil®. She scanned a copy of the document and emailed it to the attending doctors.

The rancher's condition was constantly monitored. His condition improved after two days in intensive care and he was discharged. Since his release, he has returned to full work capacity, although still experiencing muscle soreness in his left arm and shoulder areas, along with some fatigue.

Note: Information concerning specific medications and procedures administered at the hospital emergency room, during air transport, and at the medical center were not revealed to the investigator due to doctor/patient confidentiality guidelines of all agencies involved.

ANALYSIS/SYNOPSIS:

Cattle: The calves being vaccinated weighed approximately 600 pounds each.

Syringe/needle: The syringe in use that day was a 20 cc Monoject 200™ with a 16 gauge, 1" long needle.

The syringe originally contained 14 ccs of Micotil, 7 ccs per calf. One calf had been vaccinated, leaving 7ccs in the syringe. The rancher immediately looked at the syringe after the injection, noting that there were 5 ccs remaining. Due to some Micotil on the outside of his hand, the rancher estimated that 1-1.5 ccs of Micotil was injected into his left hand between his thumb and first finger.

Antibiotic: [1]Micotil®, which contains Tilmicosin phosphate, is used to control respiratory disease in cattle (bovine respiratory disease), more commonly called Dairy Calf Pneumonia (DCP), a very expensive and difficult-to-treat problem. It was designed to provide a single-injection therapy intended to reduce stress on the animal, thus requiring less labor since it is a low-volume dose used at a single injection site. It reaches effective concentration levels in lung tissue in two hours and maintains effective concentration levels throughout the respiratory tract for three to four days. It works with the animal's own immune system to destroy pathogenic bacteria.

Micotil® is an antibiotic that originally offered a lower cost per treatment than many other antibiotics for this condition available at the time. It was first introduced in Canada in 1990, then in the United States in 1992 and immediately gained wide acceptance. It is currently being marketed in many countries throughout the world.

A dosage of 1.5 mL per 100 lbs. of animal weight is recommended. It is to be injected subcutaneously (beneath the skin) in cattle. It can not be administered intravenously in cattle, as that proves fatal. The manufacturer states on all product literature that it is not to be used with automatically powered syringes, presumably due to its hazards to humans or possibly inefficiency to administer subcutaneous injections via this method. Most cattlemen use some form of disposable plastic syringe for injection.

Elanco is the only producer of Micotil®. It is sold, through a distributor, only to licensed veterinarians. The victim had used Micotil® since it first became available. He was aware that it was a dangerous drug, but was not aware that it could cause death in humans and that there was no antidote.

In addition to the March 2003 Nebraska Micotil-related fatality mentioned earlier in this report, another fatality occurred almost one year later in South Dakota. On April 24, 2003, a 50-year-old male farmer was attempting to inject a cow inside a head chute with Micotil®. The cow jerked and he injected himself with the drug. He was able to summon help, but died 3 ½ hours later.

RECOMMENDATIONS/DISCUSSION:

Recommendation #1: Veterinarians and animal health distributors, prior to releasing Micotil, should require the purchaser to sign an information fact sheet that indicates Micotil can be fatal in humans and that there is no antidote for this medication, <u>every time</u> they purchase the product.

Discussion: Following the Nebraska fatality in 2003 associated with Micotil, Elanco developed a new "*Micotil Client Dispensing Information*" pad to be used by the person prescribing the antibiotic (see photo 2). This form contains general information about the drug, along with a

HUMAN WARNINGS and **NOTE TO PHYSICIAN** sections explaining the possible dangers and treatment protocol for human exposure to Micotil. Proper handling and administrative procedures are also covered.

At the bottom of the form are two "signature lines", one for the Doctor and one for the Producer to sign, indicating that the dangers of Micotil have been explained by the doctor, and understood by the producer (in this instance the cattle rancher). Unfortunately, a single prescription may be good for several refills, and the same "producer" that originally picked up the drug may not be the same person picking it up the next time, using the same prescription. Veterinarians need to ensure that this document is filled out each and every time a bottle of Micotil is dispensed, not just when the prescription is originally written.

Recommendation #2: Users of syringe-loaded medications should practice safe handling procedures during all phases of animal treatment.

Discussion: Syringes, when not being used, should have the protective cap placed over the needle, or have the needle removed from the syringe and capped. During this incident, the protective cap had been removed to vaccinate the first calf, then the syringe was placed between the rancher's teeth while he used both hands to release the calf from the squeeze chute, allowing the next calf to enter the chute. Syringes should never be placed into one's mouth, the syringe should be recapped and placed out of the way while preparing the next calf for vaccination, and not uncapped until the animal if fully restrained.

Unfortunately not every cattleman in Nebraska always has the advantage of a head or squeeze chute while vaccinating cattle. Many times the calves are physically wrestled to the ground and restrained by the rancher and maybe another employee by sheer body weight and pressure. This atmosphere greatly increases the chance for an accidental exposure/injection to the needle tip and the medication it contains.

Recommendation #3: Veterinarians/Cattlemen, when practical, should consider using another less-hazardous antibiotic.

Discussion: [2]According to the Federal Drug Administration's (FDA) Center for Veterinary Medicine and their Office of New Animal Drug Evaluation (ONADE), Micotil is not the only FDA approved veterinary drug without an antidote, but there is no published list of those medications.

The FDA does not require an antidote for any new animal drug that is approved. In order to be approved, veterinary drugs must be safe for the animal, for humans who consume products from the animal, and for the environment. In addition, they must be effective for the animal. Also FDA regulations require that adequate directions be prescribed for the safe administration of the product, and for the establishment of a veterinarian/client/patient relationship.

The end-user (producer) can purchase Micotil from either a state licensed/registered veterinarian or an animal health distributor. In either situation, the end-user must have a valid prescription from a veterinarian before obtaining the product.

The FDA does not require that there be an antidote for animal drugs that can cause human fatalities should an exposure occur. While an antidote is one possible solution to an accidental poisoning, it is not necessary to make the administration of the product safe. The bottle that Micotil is sold in does carry warning labeling on the source bottle and the manufacturer also

inserts a warning sheet inside the container's box that states in part "Not for human use. Injection of this drug in humans has been associated with fatalities…". However, neither the warning sheet nor the label on the bottle warn that there is no antidote to this medication.

The minimum amount of this medication needed to cause a fatality when injected into a human is not known. Interviews conducted with both veterinarians and users during our investigation into the Nebraska fatality indicated that the persons interviewed believed any amount greater than 6 ccs could prove fatal, depending upon the route of exposure or injection, e.g. subcutaneous, intramuscular, intravenous, oral, etc. [3]This may be based on a case of unintentional human exposure that occurred several years ago in Nebraska. The subject, a 28-year-old male, using a 12-cc syringe with Micotil, was attempting to inject a steer but inadvertently injected less than half of the contents into his left forearm. He felt no ill effects until approximately five hours later when he developed severe chest pain and was transported to a nearby hospital where he was intubated. He was extubated approximately 10 hours after arrival and remained free of chest pains for the 3 days of hospitalization and was discharged.

Several veterinarians queried during the original Nebraska fatality investigation in 2003 indicated they personally did not want to use this product due to the possible fatal human consequences. They all indicated that needle sticks in their business is unfortunately all too common, and to use a substance that may have no treatment depending on the amount and route injected or ingested was not their choice. They felt that there were other drugs on the market that would produce the same results and were safer to work with. Many indicated that since this incident they have received numerous calls from not only their customers about Micotil, but also from concerned family members that were looking for alternative medications.

ATTACHMENTS:

Photo #1. Squeeze chute where calves were being vaccinated.
Photo #2. New Micotil dispensing pad with signature lines for Doctor and Producer.

REFERENCES:

1. Web site http://www.elanco.com Last accessed December 27, 2004.
2. Information is summarized from electronic correspondence with the Federal Drug Administration's Center for Veterinary Medicine.
3. Von Essen S. Unintentional Human Exposure to Tilmicosin (Micotil® 300) Journal of Toxicology Vol. 41, No. 3, pp. 229-233, 2003.

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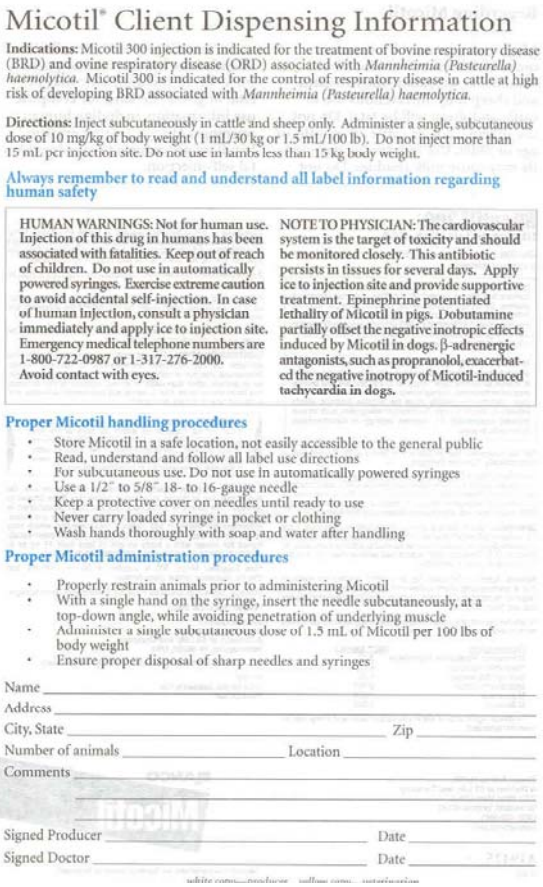
Metal handle that struck rancher's hand, knocking it into the syringe/ needle that he was holding in his mouth.

Where rancher was standing.

This is the Pearson brand chute that was being used to vaccinate the calves. The calves would enter from the right side of the chute, exiting to the left. The handle above the chute with the attached rope is used to pull one side of the chute towards the operator, thereby "squeezing" the calf. The rancher then reaches through the side bars to vaccinate the calf, then raises the handle, releasing the calf. As the calf bolts forward, the exit doors normally open. If the exit doors don't fully open, the handles on the exit doors can then also be used to open them. In this incident, the doors only partially opened when the overhead was released and the rancher was reaching for the exit door handles when the calf was able to bolt through them, knocking the metal pipe into his hand, driving it into his hand.

Photo 1.



Micotil® Client Dispensing Information

Indications: Micotil 300 injection is indicated for the treatment of bovine respiratory disease (BRD) and ovine respiratory disease (ORD) associated with *Mannheimia (Pasteurella) haemolytica*. Micotil 300 is indicated for the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia (Pasteurella) haemolytica*.

Directions: Inject subcutaneously in cattle and sheep only. Administer a single, subcutaneous dose of 10 mg/kg of body weight (1 mL/30 kg or 1.5 mL/100 lb). Do not inject more than 15 mL per injection site. Do not use in lambs less than 15 kg body weight.

Always remember to read and understand all label information regarding human safety

HUMAN WARNINGS: Not for human use. Injection of this drug in humans has been associated with fatalities. Keep out of reach of children. Do not use in automatically powered syringes. Exercise extreme caution to avoid accidental self-injection. In case of human injection, consult a physician immediately and apply ice to injection site. Emergency medical telephone numbers are 1-800-722-0987 or 1-317-276-2000. Avoid contact with eyes.

NOTE TO PHYSICIAN: The cardiovascular system is the target of toxicity and should be monitored closely. This antibiotic persists in tissues for several days. Apply ice to injection site and provide supportive treatment. Epinephrine potentiated lethality of Micotil in pigs. Dobutamine partially offset the negative inotropic effects induced by Micotil in dogs. β-adrenergic antagonists, such as propranolol, exacerbated the negative inotropy of Micotil-induced tachycardia in dogs.

Proper Micotil handling procedures

- Store Micotil in a safe location, not easily accessible to the general public
- Read, understand and follow all label use directions
- For subcutaneous use. Do not use in automatically powered syringes
- Use a 1/2" to 5/8" 18- to 16-gauge needle
- Keep a protective cover on needles until ready to use
- Never carry loaded syringe in pocket or clothing
- Wash hands thoroughly with soap and water after handling

Proper Micotil administration procedures

- Properly restrain animals prior to administering Micotil
- With a single hand on the syringe, insert the needle subcutaneously, at a top-down angle, while avoiding penetration of underlying muscle
- Administer a single subcutaneous dose of 1.5 mL of Micotil per 100 lbs of body weight
- Ensure proper disposal of sharp needles and syringes

Name _____

Address _____

City, State _____ Zip _____

Number of animals _____ Location _____

Comments _____

Signed Producer _____ Date _____

Signed Doctor _____ Date _____

Front of new Micotil Client Dispensing Information pad that includes signature lines at the bottom for both the Producer and the Doctor. One copy is kept by each after signing.

Photo 2.