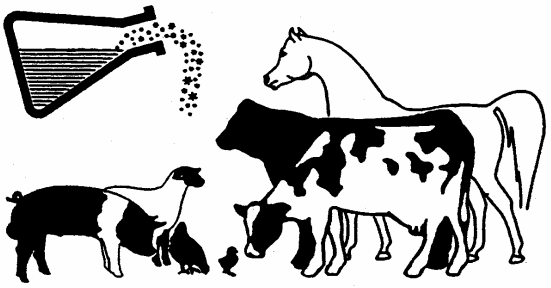
HANDBOOK

for Veterinary Drug Dispenser Licence

DECEMBER 1996



BRITISH COLUMBIA

Ministry of Agriculture,
Fisheries and Food

Handbook for Veterinary Drug Dispenser Licence

Including Section on Specific Medicants for Bee Diseases

DECEMBER 1996

Developed by

Animal Health Branch
Ministry of Agriculture, Fisheries and Food 1767 Angus Campbell Road Abbotsford, British Columbia V3G 2M3

Canadian Cataloguing in Publication Data Main entry under title:
Handbook for veterinary drug dispenser licence including section on specific medicants for bee diseases

ISBN 0-7726-1878-X

1. Veterinary drugs - British Columbia - Handbooks, manuals etc. 2. Bees - Diseases - British Columbia .Handbooks, manuals, etc. I. British Columbia. Animal Health Centre.

SF917.H36 1993 636.0895 C93-092305-7

HANDBOOK FOR
VETERINARY DRUG DISPENSER LICENCE

LICENCE CLASSIFICATION

A - Open Shops Including Apiary Supplies

B - Apiary Supplies Only

C - Open Shops and Medicated Feeds

EXAM REQUIREMENTS

A - Sections 1, 2, 3 and 4	1 1/2 hours
B - Sections 1, 2 and 4	1 hour
C - Sections 1, 2 and 3	1 hour

PASS: 75% overall for A, B and C Licenses.

HANDBOOK SECTIONS FOR STUDY

Section 1 Pages 1 - 7	Legislation Concerning Veterinary Drugs and Medicated Feeds
Section 2 Pages 12 - 18	Use of Veterinary Drugs Listed in Table 11
Section 3 Pages 19 - 25	Some Consequences of Misuse of Veterinary Drugs
Section 4 Pages 28 - 31	Specific Directives for the Sale of Veterinary Drugs for the Control of Bee Diseases

FOREWORD

This handbook has been compiled to provide applicants for the Veterinary Drug Dispenser Licence with a source of information on how veterinary drugs and biologicals (vaccines and bacterins) should be handled, stored and used.

People have benefited greatly from the use of pharmaceuticals. For example, small pox has been eradicated and polio and diphtheria controlled through the use of vaccines. Pneumonia is not the almost certain killer that it once was in either humans or animals. In poultry, the routine use of vaccines to control virus diseases and medication to control coccidiosis has permitted much more intensified and economic production.

There is a down side to all of this, some people have tried to replace good animal husbandry by the use of biologicals and drugs. This is not only uneconomic but also has lead to the production of disease organisms which are resistant to many antibiotics.
The Swann Report in the late 1960's pointed out there was an increasing number of disease causing organisms becoming resistant to an ever increasing number of drugs. Treatment of some common infections with certain drugs was no longer effective, leading to prolonged illness, even death in both humans and animals.

The Report also recommended that antibiotics which were used in human medicine should not be used to treat animals. Fortunately, this recommendation was not enforced, on the understanding that antibiotics used on livestock would be more carefully controlled.

The sale of veterinary drugs in specially licensed businesses, permitted under the *Veterinary Drug & Medicated Feed Act* of British Columbia, began in 1968. Mainly to provide the livestock producer with access to some pharmaceuticals in remote areas of the province where there was no veterinary or pharmacist service. The *Pharmacists, Pharmacy Operations and Drug Scheduling Act is* administered on behalf of the Ministry of Health by the College of Pharmacists, but the sections pertaining to veterinary drugs are administered by the Ministry of Agriculture, Fisheries and Food. It is up to you and us to make sure this trust is not abused, otherwise we may lose the privilege.

You can do your part by understanding what is in this handbook, adhering to the regulations, handling the drugs properly and making sure the farmer who purchases the drug knows what animal it can be used on, the precautions on use and the withdrawal time.

TABLE OF CONTENTS

LEGISLATION CONCERNING VETERINARY DRUGS AND MEDICATED FEEDS

For our purposes, there are three Acts which control the sale of veterinary drugs and medicated feeds. These are:

1. ***The Feeds Act*** - administered by the Plant Products Division, Agriculture and Agri-Food Canada
2. ***The Food & Drug Act*** - administered by Health Canada
3. ***The Pharmacists, Pharmacy Operations and Drug Scheduling Act*** - administered by the College of Pharmacists of British Columbia

The Feeds Act provides standards which permit the inclusion of medicines or drugs in feeds for farm animals, birds and fish that are used for human consumption. The standards state:

- which drugs can be included in animal, fish or poultry feeds;
- specifies the animal, fish or bird for which the medicated feed can be prepared;
- lists the maximum permissible level of drug permitted in the final ration;
- directions for use of the medicated feed;
- cautions in the use of the medicated feed and lists necessary warnings;
- the maximum amount of drug permitted may be at a treatment, preventive or growth stimulating level.

The pharmaceuticals which can be added to feed, at the levels and under the conditions set out in the Medicating Ingredient Brochures (see below) are listed in Schedule A, Table 1 of the *Pharmacists, Pharmacy Operations and Drug Scheduling Act* of B.C. If a person wished to properly mix a medicated feed, where would that person find the information that she/he must have? The answer is in the Compendium of Medicating Ingredient Brochures (MIB), which is prepared and updated by the Plant Products Division, Agriculture and Agri-Food Canada. Appendix A and B, of this Handbook, provide examples of MIB 33 and MIB 37 as they appear in the Compendium of Medicating Ingredient Brochures, August 1990. It can be seen that directions for their use are specific.

The Food and Drug Act authorizes which drugs may be sold in Canada and, through the regulations, provides the conditions and standards under which they may be prepared for sale. For instance, all drugs listed in Schedule F Part 1 of the Food and Drug Regulations may be sold only on a prescription. Because drugs like Micotil (timicosin) are included in Schedule F Part 1, it is necessary that its sale adhere to the requirement of a prescription for all purposes.

The *Pharmacists, Pharmacy Operations and Drug Scheduling Act* permits the use of drugs in this province through its power to regulate who may be licensed to sell them. The Act may be more restrictive than the Federal *Food And Drug Act* but it cannot be less restrictive. A non-prescription drug under the *Food and Drug Act* could be made a prescription under the *Pharmacists, Pharmacy Operations and Drug Scheduling Act* but as a rule an attempt is made to follow the *Food and Drug Act* schedule.

The *Pharmacists, Pharmacy Operations and Drug Scheduling* Act of British Columbia goes one step further in that Sections 63 to 69 inclusive give the British Columbia Minister of Agriculture, Fisheries and Food the authority to control the sale of veterinary drugs by persons other than a pharmacist or a registered veterinarian. It gives the Minister of Agriculture, Fisheries and Food the authorization to set up two types of regulations relating to veterinary drugs:

1. The sale of veterinary drugs and medicated feeds and the manufacture of medicated feeds.

2. The establishment and duties of an advisory committee.

The Veterinary Drug and Medicated Feed Regulations are administered by the Chief (Provincial) Veterinarian. The regulations specify the different classes of licenses and list the requirements that have to be met by each class of licence and regulates those who may be licensed. The Regulations are included with this Handbook.

A Veterinary Drug Licence may be issued to holders of a Medicated or Limited Medicated Feed Licence, the operator of a registered hatchery, a person in areas of limited service, and to persons whom the Minister of Agriculture, Fisheries and Food considers appropriate. The Advisory Committee on veterinary drugs makes this decision on behalf of the Minister.

Products exempt from the Regulations under the *Pharmacy Operations and Drug Scheduling Act* include worming preparations for cats and dogs and limited preparations labeled "For Aquarium Use Only". Other preparations for pets are not exempt.

Four classes of licenses may be issued:

1. **Limited Medicated Feed Licence** for a business where medicated feeds are sold but not manufactured, i.e., purchased as bagged medicated feed. The annual fee is $12.00 (at the time of writing - subject to change) and expires on March 31st each year. The licensee is required to record all purchases of medicated feed that have been imported for sale from another province or another country in the Veterinary Drug Purchase Register.

   The original copy of the Veterinary Drug Purchase Register must be forwarded to the Chief (Provincial) Veterinarian before February 28th each year to cover all out-of-Province purchases for the previous calendar year.

2. **Medicated Feed Licence** authorizes the licensee to manufacture and to sell feeds medicated with veterinary drugs listed in Schedule A, Table 1 to the limit shown in the M.I.B. Upon the written order (prescription) of a registered veterinarian, the licensee may manufacture medicated feeds with veterinary drugs in strengths above those listed in the M.I.B. and with veterinary drugs not listed in Schedule A, Table 1.

   The annual fee is $55.00 (at the time of writing - subject to change) and expires on March 31st each year. The licensee is required to record all drug purchases in the Veterinary Drug Purchase Register. This must be kept up-to-date as each batch of drugs are purchased. The original copy and a copy of all prescriptions filled shall be forwarded to the Chief (Provincial) Veterinarian before February 28th each year to cover all purchases for the previous calendar year.

3. **Veterinary Drug Licence** authorizes the licensee to sell the veterinary drugs listed in Schedule A, Table 11. Licenses may be limited to certain products, i.e., hatcheries may only sell poultry products, tack shops are usually restricted to horse wormers and wound dressings, in which case it is specified **on the licence.** The annual fee is $55.00 (at the time of writing - subject to change) and expires on March 31st of each year. The licensee is required to record all drug and biological purchases in the Veterinary Drug Purchase Register as they are received. The original copy shall be forwarded to the Chief Veterinarian before February 28th each year to cover all purchases for the previous calendar year.

4. **Veterinary Drug Dispenser Licence** is issued to a person who passes an examination. The exam covers the properties, use and abuse of veterinary drugs and related information. Every Medicated Feed Licensee or Veterinary Drug Licensee must have a Veterinary Drug Dispenser present at all times at the premises where business is carried on

   - when and where medicated feeds are being manufactured, or;
   - when open for business for the sale of veterinary drugs.

The Veterinary Drug Dispenser Licence is normally valid for five (5) years (fee, $12.00 at time of writing, subject to change) and must then be renewed by re-examination. Reexamination may be required for any licensee at any time at the request of the Chief (Provincial) Veterinarian.

This means that businesses that have a Medicated Feed Licence or a Veterinary Drug Licence must have a person holding a current Veterinary Drug Dispenser Licence on the premises during the manufacture of medicated feeds or for the sale of veterinary drugs on the premises during working hours .

Under the *Pharmacists, Pharmacy Operations and Drug Scheduling Act* and Regulations of B.C. it is illegal for a drug wholesaler to sell directly to a farmer. It is also illegal for drugs to be transported in British Columbia except by a wholesaler to a properly licensed outlet, veterinarian or pharmacist. Farmers may transport or have delivered, drugs purchased by them from a B.C. licensed veterinary drug retail outlet, veterinarian or pharmacist to their farm for their own use.

These regulations do not affect the sale of veterinary drugs by pharmacists or registered veterinarians.

SIGNIFICANT TERMS IN PHARMACY AND VETERINARY MEDICINE

The sale of veterinary drugs carries with it certain responsibilities, and implies that the sellers have some knowledge of the products. In order to add to this knowledge, one must understand some of the terms which are used in regard to these products. All drugs and biological products are used to treat or prevent diseases.

1) Diseases may be classified as:

a. Non-Infectious

Sporadic: These are diseases which appear from time to time and usually only affect one animal in the herd. Such diseases as bloat, founder, urinary calculi, and broken bones are examples of this.

Metabolic and nutritional: These are diseases caused by an upset in the body function of the animal and nutritional imbalances. Milk fever, pregnancy disease of ewes, white muscle disease and hypomagnesemia are diseases of this category.

Poisonous: Almost any chemical eaten in excess may cause poisoning and varying types of disorders. Poisonous plants, such as Timber Milk Vetch, Ragwort and Water Hemlock, among others, are of concern in British Columbia. Animals receiving excess doses of drugs or medicinal chemicals can also show toxic reactions.

b. Infectious:

These include diseases which are caused by an infectious agent. The disease is not spread directly from one animal to another. In this classification are such diseases as blackleg, lump jaw, pulpy kidney disease, foot rot and edema disease of swine.

c. Contagious:

Diseases which are caused by an infectious agent and will spread from one animal to another. Included in this group are most of the viral diseases, shipping fever, pinkeye, ringworm, and scours of newborn animals.

d. Parasitic:

Parasites (worms and insects) may be regarded as a form of animal life that has become adapted to live on or in animals larger than themselves. The parasite nourishes itself at the expense of the host and causes disease by robbing the host of its nourishment or by causing tissue damage.

The majority of livestock losses are caused by infectious, contagious and parasitic **diseases. These are caused by agents known as bacteria, viruses and parasites.** There are other disease causing agents such as chlamydia, rickettsia and mycoplasma. In this Handbook we will concentrate on bacteria, viruses and parasites.

2) Other Terms (Definitions):

a. Antigen:

A protein introduced into the body which is recognized as foreign. The body reacts to this foreign protein by producing antibodies which assist in the removal of the foreign protein. Infectious agents (antigens) introduced into the body stimulate an antibody response which assists in the control and removal of the infectious agents from the body.

b. Antibody:

A protein produced by the body in response to a foreign protein (antigen). Antibodies which are developed in response to infectious agents control and remove these agents. **Immunity** or resistance to disease is dependent upon the presence of antibodies against a particular infectious agent.

c. Viruses:

Infectious agents which require DNA or RNA from a host's cell to multiply. During this process they disrupt the function of the cell and often destroy it. The damage caused by the virus may cause the animal to be ill or die, or it may only reduce the resistance of the animal and make it more susceptible to bacterial disease. **At the present time, we do not have drugs which will significantly overcome viruses in the living host.**

d. Bacteria:

Living microscopic organisms that do not require a living cell to multiply as viruses do. A healthy animal has bacteria in its gut; these are known as normal gut flora and are necessary for the animal's digestive process. However, other bacteria called pathogens, if present, may cause disease.

The invasion of the animal body by pathogenic bacteria and viruses results in a constant battle between the host and invading organisms. If the organisms are able to overcome the resistance of the host, disease ensues. **Factors such as the nutritional status of the animal, the stress it is subjected to and sanitary conditions will also affect the ability of the animal to overcome the pathogen.**

The host is able to build up immunity or resistance to bacteria and viruses by the production of antibodies. When exposed to bacteria, referred to in this context as an antigen, the animal body produces antibodies. These antibodies are able to neutralize or destroy antigens. However, these antibodies are specific for that particular antigen. The animal body must produce antibodies for each antigen it encounters.

When an animal is vaccinated, antibody production is stimulated for that particular antigen (bacteria or virus). Later, when the animal is exposed to that bacteria or virus enough antibodies are often present to overcome the infection. Similarly, when an animal recovers from an infection it will build up antibodies to that infection. **An animal understress, poor nutrition, animals which have just been through saleyards and transported, castrated, dehorned, branded, or are just weaned, usually respond poorly to vaccination and may not produce enough antibody to overcome the invading pathogen.**

e. Immunity:

Having enough antibodies to overcome exposure to any particular disease causing organism is known as immunity.

Active immunity: When an animal is vaccinated with antigens, which have been altered so as not to cause disease, the body is stimulated to produce its own antibodies. Recovery from an infection has the same effect.

Passive immunity: When an animal receives **antibodies** produced in another animal, those antibodies help to protect the animal against a specific disease. In this case the animal is not stimulated to produce its own antibodies. A good example of this is mother's colostrum (first milk) which contains antibodies which protect the newborn.

Active immunity takes ten days to two weeks to develop, however, it lasts a long time - sometimes a lifetime. Passive immunity protects immediately but lasts a very few weeks.

f. Anaphylactic Reaction:

When an animal becomes over sensitive to a protein and will react violently to reject the protein when it is administered. Many pharmaceuticals contain protein which are foreign to the host and they may cause an anaphylactic reaction in over-sensitized animals.

g. Gram Positive/Gram Negative Bacteria:

Bacteria can be seen under the microscope and can be grown on various media such as agar. They can be stained with different dyes, which aid in their identification. One common staining method is known as Gram's stain. Depending on the colour imparted to the bacteria, they are referred to as being Gram positive or Gram negative. Staphylococci and streptococci are examples of Gram positive organisms; coliforms, pasteurella and brucella are examples of Gram negative organisms.

h. Narrow Spectrum/Broad Spectrum Antibiotics:

Some drugs are effective mainly against Gram positive organisms and others against Gram negative. For example, penicillin is effective against Gram positive organisms and streptomycin is effective only against Gram negative organisms. These are referred to as narrow spectrum antibiotics. Tetracyclines, Tylosin and Erythromycin will destroy certain Gram positive **and** Gram negatives and are referred to as broad spectrum antibiotics. However, because an antibiotic has a narrow spectrum it does not mean it is less effective against bacteria which are susceptible to it than a broad spectrum antibiotic. In fact, it is often more effective against susceptible bacteria.

i. Sensitivity Testing:

Bacteria exposed to certain drugs or antibiotics may develop a resistance to that drug. Bacteria isolated from a laboratory specimen are grown on agar and small discs impregnated with specific antibiotics are applied to the agar plate. If the bacteria are unable to grow in close apposition to these discs, it indicates that the bacteria are sensitive to the drug. This procedure is known as sensitivity testing and is done to determine the most appropriate antibiotic for treatment of a particular disease.

j. Bacteriostatic/Bactericidal Antibiotics:

Some drugs will inhibit bacteria from growing and multiplying, and are known as bacteriostatic. Other drugs that kill the bacteria are known as bactericidal.

k. Vaccines/Bacterins:

The words vaccines and bacterins are often used interchangeably. When bacteria gain entrance to the body they stimulate antibody production. Not all bacteria stimulate a good strong production of antibodies. Hence we are unable to vaccinate for all diseases, and some vaccines produce a better immunity than others. Some bacterins or vaccines will produce life long immunity with one dose. Others may require two or more doses with annual re-vaccination. It is important to follow the instructions on the label.

A good vaccination program is an important part of disease prevention. Bacterins are produced by growing the bacteria, killing it and diluting it to a standard concentration.

Modified-live vaccines are produced by growing the organism in suitable media. The organisms are kept alive, but are altered so that they are much less likely to cause disease. Modified-live vaccines are **not included** on Schedule A, Table 2 and **cannot be sold** by Licensed Veterinary Drug Outlets. Vaccines are also produced by killing the organism and using the whole organism in the vaccine or a portion of the organism. These products can be sold by Licensed Veterinary Drug Outlets. Bacterins and vaccines require 10-15 days or longer to produce adequate immunity. They are not intended to cure disease, but to prevent it. **Their use is not a substitute for good sanitation and animal husbandry.**

l. Toxoids/Antitoxins:

Some organisms produce toxins or poisons which cause disease in the animal. Toxoids are produced from these toxins. They have their antigenic factor maintained or enhanced but their poisonous effect is reduced or eliminated. They act like vaccines producing an active immunity.

Antitoxins are products which neutralized the toxins produced by the bacteria. They act immediately but are short-lived. They produce a passive immunity.

USE OF VETERINARY DRUGS LISTED IN TABLE 11

Biologicals

Under the *Pharmacists, Pharmacy Operations and Drug Scheduling Act,* the Veterinary Drug and Medicated Feed Regulations, Schedule A, Table 2 lists the veterinary drugs which may be sold by licensees. The first group listed are biologicals. They include vaccines, bacterins and toxoids as discussed earlier. When given to an animal or bird, both vaccines and bacterins stimulate the production of antibodies against that disease and thus help to prevent the appearance of symptoms. A toxoid is a suspension of a toxin (or poison) produced by a bacterium, which has had its poisonous effect reduced or destroyed. It stimulates the animal to produce antibody in this case known as an antitoxin.

It should be remembered that vaccines, bacterins and toxoids prevent disease, but have little value in treatment. Biologicals, to maintain their effectiveness, should be kept under refrigeration (but not frozen) at all times. Animals under "stress" including poor nutrition may not respond to the administration of biologicals adequately to protect them against disease.

Route of administration is on the label of the product and it is important to follow those instructions.

1.) Killed virus vaccines in animals that have not been vaccinated before require two doses approximately 21 days apart. Failure to administer the second dose within the time frame stated on the label will result in inadequate protection from the vaccine.
2.) Animals that have received two doses in the required time period must be vaccinated annually in order to provide continued protection.
3.) Beef Quality Assurance Programs promote the administration of bacterins and vaccines subcutaneously. **Do not use vaccines and bacterins subcutaneously unless that route of administration is stated on the label.**

Examples of biologicals

Avian Encephalomyelitis Vaccine

This is a vaccine which is used to prevent a nervous disease of young poultry. It is not sold by licensees in general, but is included in Schedule A Table 2 of the Regulation for the use of hatcheries licensed under the Regulations.

Bovine Virus Diarrhea Vaccine

Bovine Virus Diarrhea (BVD) is associated with respiratory disease, diarrhea, abortions and brain defects in newborn calves. It has also been shown to reduce the body defence mechanism, reducing the animal's resistance to other diseases.

Bovine Respiratory Synctiai Virus Vaccine

Bovine Respiratory Synctial Virus (BRSV) is associated with respiratory disease in cattle. The vaccine is often included with BVD, IBR, P13 vaccine.

Clostridial Bacterins and Toxoids

Diseases caused by the Clostridia family of bacteria include **Blackleg, Malignant Edema, Enterotoxemia, and Tetanus** (Lockjaw). These biologicals are used widely in cattle and sheep.

Blackleg is common and affects young animals.

Malignant Edema is seen less often; it affects animals of all ages.

Enterotoxemia is an infection of the gut. It is most often seen under feedlot conditions when animals are given an abundance of "heavy" feed. It occurs in sheep and occasionally in young calves and pigs.

Treatment of the three preceding diseases is of little use. Frequently, no symptoms are seen and the livestock owner finds a number of dead animals. Prevention is most important.

Tetanus is not a prominent disease in British Columbia. However, most producers have lost a calf or pig from Lockjaw after castration. A tetanus toxoid is injected to prevent infection and should be given at least 2 weeks before surgery is anticipated. Tetanus antitoxin can be used at the time of surgery but the protection is short lived.

As these diseases are caused by bacteria that are closely related, bacterins are manufactured which combine protection against two or more of the infections. There are 2-way, 7-way and 8-way bacterins.

Erysipelas Bacterins

Erysipelas is a disease of pigs and turkeys. It is common in British Columbia.

This product also comes in a vaccine and as oral preparation to be given in the drinking water.

Infectious Bovine Rhinotracheitis Vaccine

This virus disease of cattle is also called IBR or Rednose. It produces respiratory disease and also is a cause of abortion.

Because IBR is enzootic, the vaccine should have widespread use in all cattle.

Infectious Bronchitis Vaccine

Infectious Bronchitis is a virus disease of poultry. Like Avian Encephalitis vaccine, it is included in Schedule A Table 2 of the Regulations for the benefit of licensed hatcheries and may not be stocked by other licensed businesses.

Mink Botulism Toxoid - Mink Distemper Vaccine - Mink Virus Enteritis Vaccine

These veterinary drugs may be classed as specialty items for the mink raising industry. Purchases are made through one licensed outlet in British Columbia. The licensed outlet obtains the required doses from a supplier specializing in the production of these vaccines. Thus there is no interest by other licensees to stock these biologicals.

Newcastle Disease

Newcastle Disease is a virus disease of poultry. Hatcheries are licensed to supply and use Newcastle vaccine.

Parainfluenza Vaccine (P13)

This vaccine is included in the IBR vaccine and is associated with respiratory diseases of cattle.

Pasteurella Bacterin - Toxoid

Pasteurella infection of cattle is another name for Shipping Fever and Shipping Fever may be termed a contagious pneumonia of livestock.

Staphylococcus Bacterin

Staphylococcus is another class of bacteria which is of major importance to livestock. It can cause a severe mastitis in cattle, Blue Bag in sheep, and is the frequent germ in boils, abscesses and other infections.

The bacterin is not a good antibody producer and its effectiveness is debatable. Staphylococcus is also capable of producing a toxin (poison) which can cause serious symptoms and, upon occasion, death in the infected animal. However, livestock owners may request a Staphylococcus bacterin, having experienced "good luck" with its use.

Staphylococcus bacterin is another which can be combined with other bacterins in a "shotgun" approach to prevent disease.

Streptococcus Bacterin

Streptococcus bacterin is produced for pigs in which certain strains cause illness and death.

Streptococcus equi Bacterin

Streptococcus equi is the cause of Strangles and which goes by the more common name of Horse distemper. This bacterin is not entirely effective in controlling an outbreak of Horse Distemper, but its use may lessen the number of new cases as well as reducing the severity of the symptoms.

Vibriosis Bacterin (Campylobacter)

Vibriosis is a venereal disease of cattle and sheep.

There are also vaccines for farmed fish included in Schedule A Table 2 such as Aeromonas salmonicida bacterin, Vibrio anguillarum bacterin, Vibrio ordalii bacterin, Vibrio salmonicida bacterin and Yersinia ruckeri bacterin.

Antibiotics

Although the term antibiotic means any substance that opposes growth, it is now used in a restricted sense to describe those products of the growth of certain fungi and bacteria that possess the property of inhibiting the growth of disease causing microorganisms. This phenomenon has been known for many years (over 80), but is was not until the isolation of penicillin in a pure form in 1940 and the discovery of its therapeutic activity that research really went ahead. Several hundred antibiotics have since been isolated, but many were either too toxic to animal tissues or not efficient enough to be developed commercially. Some are bactericidal, that is they actively kill certain bacteria (penicillin is an example of this) while others are bacteriostatic, that is they inhibit the multiplication but do not kill bacteria (oxytetracycline is an example):

Penicillin

Penicillin is produced by the growth of the mold **Penicillin notatum.** At least ten different penicillins have been identified. Penicillin used for treatment is mostly Penicillin G and the sodium salt is preferred because of its stability.

Penicillin is measured in units and is based on the potency of pure crystalline penicillin G, i.e. one international unit is 0.0006 milligrams of the pure salt. Thus, 5,000 units weigh three one thousandths of a gram (3 milligrams).

Penicillin is rapidly excreted and the difficulty is to maintain adequate blood levels without continuous or frequent injections. Various methods are therefore devised to retard the absorption of penicillin from the site of injection. At first it was suspended in oil, but now the more insoluble mixture of procaine and penicillin suspended in water, or with aluminum stearate suspended in oil, is used. The effect is to delay the reaching of a maximum blood level which, although lower than with crystalline penicillin, will remain longer.

Penicillin is destroyed by acids and alkalis and by penicillinase, an enzyme produced by many bacteria, some of which may also be found in non-sterile distilled water. Thus, because of gastric acidity, enzyme destruction and absorption on to food, its action, when given by mouth, is unreliable. In addition to injection, it may be used locally in the form of creams or ointments. Some preparations lose their activity even when refrigerated and the recommended methods of storage and handling must be adhered to.

Penicillin is active against a number of gram-positive bacteria, but within these groups of sensitive organisms may be strains of resistant organisms of the same species. Also the sensitivity of a strain outside the body (in vitro) may not apply to the same organism when inside body tissues (in vivo). If used with other antibiotics, such as tetracycline, an antagonism may occur which destroys the activity of both antibiotics.

Streptomycin and Dihydrostreptomycin

Streptomycin is an antibiotic obtained from the growth of *Streptomyces griseus* and is usually supplied as the hydrochloride, sulphate, or calcium chloride double salt. Serious drawbacks are its toxicity and the tendency to produce resistant strains of organisms, especially when used in chronic conditions requiring a long course of treatment. It is mainly effective against gram-negative bacteria and is bactericidal at high concentrations, but may cause toxic reactions.

Dihydrostreptomycin sulphate or hydrochloride are about equal therapeutically, but less toxic than Streptomycin. Preparations available may be mixtures of streptomycin and dihydrostreptomycin and are often available combined with penicillin.

Tetracyclines

Those available are chlortetracycline and oxytetracycline. Oxytetracycline is available in both oral and injectable forms. It is important to follow the label instructions in regard to the dosage, the route administered and the volume administered per injection site.

Chlorotetracycline is obtained from cultures of *Streptomyces aureofaciens* and is a yellow crystalline substance available as the soluble hydrochloride. It has a fairly wide range of activity against cocci and both Gram-negative and Gram-positive bacteria, but its main area of use is against some chlamydia and rickettsiae. However, as it alters normal intestinal flora if given to cattle, sheep or goats, it will seriously interfere with rumen digestion. It is therefore used mainly in young calves, lambs and goats before rumen development has occurred. Bacterial populations in the gut are in competition with one another. **A normal gut flora (i.e., bacteria which normally inhabit the gut and are beneficial) tends to inhibit pathogens in the gut from multiplying and causing disease. If the gut flora are knocked out by the use of antibiotics, pathogens, if resistant to that antibiotic, have a much better chance of multiplying and causing disease.**

Oxytetracycline is obtained from cultures of *Streptomyces rimosus.* It too has a wide range of activity but, unfortunately, has also created similar problems to chlorotetracycline if given orally.

The preceding section is a brief account of the more common antibiotics. A large amount of work has been done in regard to the emergence of resistance to antibiotics in bacteria which were previously sensitive. It is sufficient to know that certain resistant bacteria have the ability to transfer this resistance to other sensitive bacteria which then multiply and pass on this resistance genetically. This causes a problem when resistant bacteria come in contact with pathogens, they may pass on their resistant characteristic to the pathogen. A drug which worked before may not work now. This resistance may also be passed from animal bacteria to human bacteria, which could result in a human infection which is non-responsive to treatment.

Chemotherapeutics

Chemotherapy is the treatment of disease with chemical agents, but it is restricted today to the use of chemical agents that have a specific action on the organism causing disease. For instance, quinine in the treatment of malaria is an early example.

Sulphonamides

In 1935 the introduction of sulphonamides opened up a whole new field of chemotherapeutics having a wide range of activity against pathogenic organisms. Although a large number have been produced, the number now in regular use is quite small. The choice of any sulphonamide depends on the concentration that is effective in the blood and its rate of absorption and excretion. This influences the frequency of dosage, their individual toxic effects and their antibacterial action. They may interfere with digestion and vitamin production in the animals by destroying the normal gut flora. Some alter the oxygen carrying hemoglobin of blood, and some form insoluble substances which damage the kidneys.

Effectiveness is based on maintaining an adequate concentration in the blood. The most common route of giving them is by mouth. Those listed in Schedule A Table 2 are the ones most commonly used. The correct dosage rate must be adhered to, for once the necessary blood concentration is allowed to fall, the bacteriostatic effect of the drug is lost.

Antiparasitic Drugs

Amprolium, nithiazide, 2-4-diamino-5-(chlorophenyl)-6- ethylprimidine, and dimetridazole are chemicals used as aids in the prevention and treatment of parasites causing coccidiosis and blackhead in chickens and turkeys. Their use and claims are controlled by the Medicating Ingredient Brochures when mixed in feeds. Where they are added by the owner to feed or water, the directions must be adhered to and it must be realized that they are an aid to management - not a substitute.

Phenothiazine, piperazine salts, tetramisole, ivermectin and the benzimidazoles are drugs which kill or inactivate intestinal worms. No one wormer is effective against all species of worms and each has its advantages. While they are the least toxic to healthy mammals when used correctly, it must be remembered that they are poisons and caution is necessary when dosing individuals which may be severely affected by parasitism. Individual reactions, such as anaphylactic shock, occasionally occur in normal animals, even when dosed according to weight and condition. Worms can also build up a resistance to these drugs.

Carbadox

This compound, probably better known by the trade name "Mecadox", was used primarily as a growth promoter in pigs and is therefore sold as "Mecadox Premix 10". As it is claimed to inhibit some bacteria it is also marketed as, a suspension, "Mecadox Scours Treater", for treating certain diarrheas in piglets. However, specific warnings to which the purchaser's attention should be drawn, are as follows:

DO NOT feed to swine over 35 kg (75 Ibs) body weight. DO NOT feed within 5 weeks of slaughter.

DO NOT use in feeds containing bentonite.

Injectable Vitamin and Mineral Preparations

Injectable A & D

Vitamin A promotes good health by stimulating healthy tissues (said healthy tissues being more disease resistant) in the animal.

Vitamins A & D are essential to good health in the animal. They are readily available in green forage but are often deficient in cured forage fed in winter.

Vitamin B Preparations

There are many different types of vitamin B (e.g. riboflavin, thiamine, nicotinic acid, pantothenic acid, etc.). While they, like vitamin A, are essential for good health, they are seldom found in short supply as most are produced normally in the paunch of ruminants. Thus, you will not find much demand for injectable vitamin B, but there could be some demand by horse owners.

Selenium - Vitamin E

This is a mixture of the trace mineral selenium and vitamin E. Selenium is deficient in most areas of British Columbia, although, there are local pockets where there are toxic levels. Severe deficiencies can cause death in an animal, mild deficiencies will interfere with the animal's ability to fight infections. Selenium and vitamin E are synergistic (they help each other). This product should only be used where it is known that the diet is deficient in selenium. In such cases a reasonable attempt should be made to correct the deficiency in the diet. Whenever possible one should avoid injections as referenced in the previous comments regarding Beef Quality Assurance.

Injectable Iron

Pigs are born with insufficient iron and sow's milk does not contain enough iron to fulfill the baby pig's needs. Therefore, iron must be supplied. In recent years it has become popular to inject iron rather than feed it by mouth.

Calcium Solutions

Milk Fever is a common problem of dairy cattle and is due to a sudden drop in circulating calcium within the blood system of just calved cows. This veterinary drug is usually given intravenously, i.e. into the bloodstream through a vein, and requires skill to administer. Purchasers should be advised to use calcium solutions with caution as they can adversely affect the heart and kill when given too quickly.

Calcium solutions may also include phosphorous and magnesium and, therefore, can be used to correct deficiencies of these minerals.

Sodium Iodide Solution

This antibacterial solution is given intravenously for the treatment of Actinomycosis (Lump Jaw) and Actinobacillosis as well as other chronic diseases. As with calcium solutions, they must be administered with extreme caution as sudden death may result.

Miscellaneous Veterinary Drugs

The veterinary drugs included in this section are made available primarily for three conditions affecting cattle. The barium chloride, silicones, surfactants and tartar emetics are found in preparations to treat bloat; the propylene glycol and sodium proprionate for the prevention or treatment of acetonemia (ketosis) and zeranol, better known as Ralgro, is a growth stimulant used to increase the efficiency of finishing cattle.

Chlorhexidine

Chlorhexidine (Hibitane) is an antiseptic and general disinfectant used in a number of preparations. As with all disinfectants, the most efficient and effective dilution is the one recommended on the label. General cleaning and disinfecting/sanitizing agents which do not have a D.I.N. are not restricted.

SOME CONSEQUENCES OF MISUSE OF VETERINARY DRUGS

The rational use of veterinary drugs demands a knowledge not only of the disease to be treated, but also the nature and extent of the infection. Unfortunately, this is not always the case and they are often used in a hit and miss fashion.

Over the years, many bacteria have become resistant, either by mutation or by the transferable resistance syndrome. This phenomena poses many problems, but it is known that where the use of antibiotics and chemotherapeutics is restricted, the resident bacterial population in a herd or flock may regain some of its previous sensitivity. Antibiotics and chemotherapeutics should never be used as a substitute for good husbandry.

Apart from the fact that some diseases do not now respond to treatment because of bacterial resistance, the big concern is a public health one. Animals in general are believed to be the reservoir of those salmonella types that cause human food poisoning and the multiple resistance now found in outbreaks of this disease may have been acquired when the strains were in the animal community. This may eventually lead to the banning of all drugs used for treatment from use as feed additives, and much greater restrictions on their use for treatment. To a greater or lesser extent this is already happening and many countries are considering severe restrictions for all antibiotics however used. Resistant organisms in animals may be transferred to man by direct contact or through contaminated food.

However, this is only one aspect of the effects of misuse. Another big problem is that of drug residues in food for human consumption. Firstly, there may be allergic reactions in hypersensitive people or this hypersensitivity may develop due to exposure. Secondly, toxic reactions, which may be acute or chronic, may occur. Thirdly, some drugs are carcinogenic i.e. cause the formation of cancers, and there is the danger of acute or chronic exposure to these. Fourthly, resistant organisms may develop in people by continued exposure to drug residues in food. Also, any residues above certain tolerances (which may be set at zero) are considered adulterants and it is illegal to sell adulterated food. Consumers are aware of these problems and are concerned about the food they eat. We must make sure that the drugs used in animals are not *abused otherwise the consumer will lose confidence in animal food products.*

In considering the dose of any drug the uninformed often think that if a certain amount of a drug is good, then double the dose should be twice as good. This is not true and an example would be aqueous penicillin where doubling the dose prolongs the effective blood concentration by only one hour each time it is doubled; there is no direct relationship to dosage. Increasing the dose rate increases the withdrawal time but often not in relation to the increased dose. It can be much, much longer (see below). It is often thought that if a dose is missed in a course of treatment that no harm is done. In the case of sulphonamides, if the effective initial blood concentration is allowed to fall by missing a dose, then the subsequent maintenance dose rate may be unable to raise it to the effective level again. The expected response would, therefore, be lacking.

Dosing at too low a level may allow predominance of resistant organisms to develop which, when subsequent treatment is required, do not respond. Treatment with one antibiotic can lead to bacteria which are resistant to antibiotics other than that to which they have been exposed. An example of this is neomycin which, when fed to calves for one week, resulted in *Escherichia coli* bacteria which were also resistant to tetracyclines, streptomycin, neomycin, kanamycin and ampicillin. This resistance was capable of being transferred in the laboratory to other *E. coli* and *Salmonella.*

Multidose bottles are commonly used these days for antibiotics, chemotherapeutants, biologicals, vitamins and minerals. These are convenient and cheaper to produce. However, it must be remembered that as soon as the rubber stopper is pierced by a needle there is a strong potential for contamination of the product by organisms. In a matter of hours, under the right conditions these organisms can have multiplied rapidly in the bottle - producing an infectious "soup". This can destroy the product or even cause severe disease, anaphylactic reaction or death in the animal when it is next used.

Thus, it can be seen that the decision to use antibiotics or chemotherapeutics in any given case should not be made lightly and veterinary advice should be obtained whenever possible so that both the correct drug and the correct dosage may be used.

The injection of drugs intramuscular (IM, into the muscle) causes tissue damage. This tissue damage shows up in meat products as scarring or some times as an abscess. These injection site lesions cost the meat industry millions of dollars in lost product because these sites have to be cut out. There is the direct loss of meat product and the loss of prime cuts because they have to be sold as lesser quality cuts when injection sites are cut out.

Sound health management programs will reduce the number of animals that require treatment. Beef and Pork Quality Assurance Programs are designed to reduce injection site lesions. Injection sites should be clean, a clean sharp needle should be used and the volume should not exceed 20 ml per injection site (label may state less). Large volumes injected in one site not only cause damage but they also affect the absorption of the drug and make the withdrawal time invalid (see below). Injections should not be given in the same area when giving repeated injections.

Finally, every licensee must realize that it is a privilege to handle and use these drugs, it is not a right. Remember, the next child that fails to respond to medicines when desperately needed, may be yours.

UNLAWFUL VETERINARY DRUGS MOST FREQUENTLY FOUND IN BUSINESSES

It is felt desirable to include a brief outline of the veterinary drugs most frequently found available for sale in licensed businesses and yet they are not listed in Schedule A Table 2.

Hormones

Under Schedule A of the *Pharmacists, Pharmacy Operations and Drug Scheduling Act,* hormones can be sold only by prescription. They are also restricted by Schedule F of the *Food and Drug Act.* Examples of these drugs are:

Stilbestrol (Diethylstilbestrol) is a sex hormone. It favorably influences weight gains in cattle and has been used in livestock rations and as a stimulant for many years. However, it has been proven carcinogenic, that is, cancer producing. The use of stilbestrol in animals was stopped in Canada on January 1, 1973.

Oxytocin is a very powerful muscle stimulant. Its chief use is to force the let down of milk in nursing cows. Unfortunately, it stimulates other muscles besides those in the mammary gland. The use of oxytocin, without a careful evaluation of the patient, has brought about the death of an animal on occasion.

Cortisone is dangerous because it has the ability to mask symptoms and give a false sense of well-being. When cortisone is used with an inappropriate antibiotic, an overwhelming infection can occur. This is because cortisone interferes with the immune response, one of the basics of body defence against disease.

The unlawful sale of cortisone usually involves its combination with mastitis ointments. Prednisolone follows a similar pattern to cortisone and is usually combined with neomycin in mastitis infusions.

Tranquilizers

Tranquilizers are not included in Table 2 of the Regulations because they are mood changers and also they disguise symptoms. The sins which have been committed by the use of tranquilizers are many - for example, in the selling of a balky horse or a kicking cow. In the hands of unscrupulous persons tranquilizers are an aid to illegal transactions in the livestock trade.

Phenylbutazone

Phenylbutazone is an anti-inflammatory agent which relieves rheumatic conditions as well as inflamed muscles and tendons. It masks symptoms and gives temporary relief from pain. An animal treated with phenylbutazone may appear and act normal, but in the meantime it could be further damaging already damaged tissues. It has been made a prescription item for all species under the *Food & Drug Act* and cannot be sold by Licensed Veterinary Drug Outlets.

Trichlorfon

Trichlorfon is an organophosphate which is specific for certain internal parasites of horses. All organophosphates are absorbed into the whole of the body system, have residual problems. While we don't commonly eat horses in this country, the sale of this drug by licensees, other than in the paste form under the Regulations, is forbidden. Furthermore,' as it is a poison, there are problems of leftover feed being eaten by other species with fatal results.

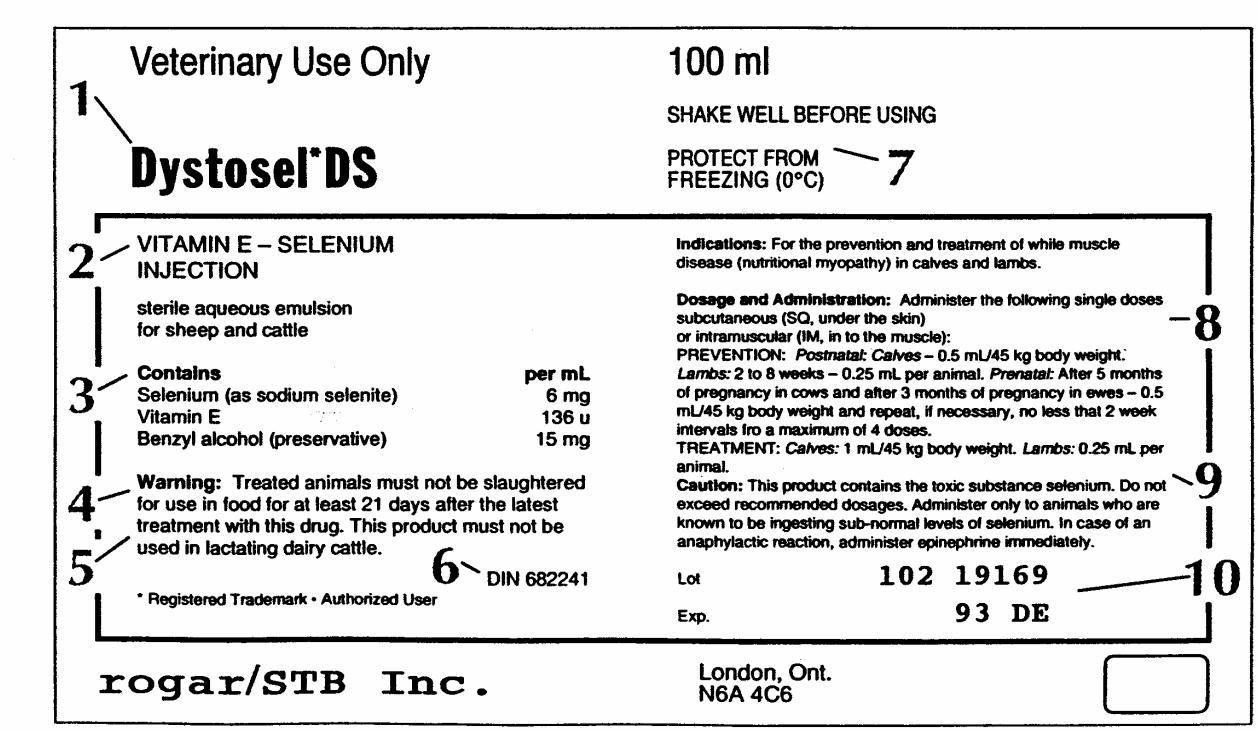
SOME CONSEQUEN LABELLING

Products are licensed according to the contents and instructions on the label. To use a product in any manner other than stated on the label is a violation. Only licensed veterinarians are allowed by law to deviate from the instructions on the label. When a veterinarian deviates from the label this is described as a prescription use. He is responsible for anything that should go wrong including residues. The following example looks at a label describing the key points.

An example of a label on a veterinary drug is included below. This illustrates ten things usually included in such a label. You should be aware of these as it is your responsibility to point them out to the purchaser.

1. Trade Name.
2. Generic Name.
3. Content of the bottle or package.
4. Withdrawal time.
5. Restrictions to its use.
6. DIN (Drug Registration Number).
7. Storage Instructions.
8. Dosage and method of administration.
9. Cautions.
10. Expiry date (the date after which the product must not be used).

1. TRADE NAME: This the name that the pharmaceutical company has chosen to call the product. It may contain the name of the drug that is in the product or it may not bear any relation to the drug. Many of the same or similar products which are designed to do the same job have names that are totally dissimilar.



Example:

Covexin-8 is a clostridial bacterin containing antigens against eight different clostridial organisms and is sold by Coopers. This product was originally sold by Burroughs Welcome who was bought out by Coopers. Coopers had their own 8-way clostridial bacterin (Tasvax-8) but they continued to sell both trade name products after the merger. This is a good example of the fact that trade names only have implications in marketing and little to do with what the product is used for.

Tasvax-8 is a clostridial bacterin containing the same eight antigens as in Covexin 8, manufactured by the same company.

2. GENERIC NAME: This identifies the active ingredient. In the case of the Covexin-8 and the Tasvax-8, the product is a Clostridial Bacterin. The specific clostridial antigens contained in the product will be listed under the **Active Ingredients.**

3. CONTENT AND CONCENTRATION (active ingredients): This will tell you what is in the product and the amounts. For the above example it lists the antigens that are present.

In the case of the example label it states the amount of vitamin E and selenium present. As well it includes the carrier, Benzyl Alcohol (the substance in which the active drug is dissolved or suspended) and the amount present. The concentration is expressed as the amount present in each millilitre (ml) or in the case of powders it is the amount present per gram. (Note that ml and cc (cubic centimetre) are the same volume measurement. It takes 1000 mls (cc) to make a litre.)

4. WITHDRAWAL TIME: This is usually labeled **Warning** and states the amount of time after the last treatment before the animal may be slaughtered, or a product from it (such as milk) can be used for human consumption.

The withdrawal time is only applicable if the directions are followed exactly. If the dosage is changed, if the method of administration is changed or the route changed (intramuscular/oral etc.) or it is given to a different species of animal than is recommended on the label, the withdrawal time is no longer applicable. The safe withdrawal time is no longer known. **This is extremely important.**

If someone treats an animal differently than the label specifications and for some reason sends the animal to slaughter, or its product to market, after the label withdrawal time there is a strong possibility that this animal will have residues and make it unfit for human consumption.

5. RESTRICTIONS: These instructions are usually included under **Warning.** It will state here what animals or class of animals that this product cannot be used on. In this example the product is not to be used in lactating dairy cattle. Depending upon the product, you may see here "not for use in food producing animals".

6. DRUG IDENTIFICATION NUMBER (DIN): This is a coded number that appears on the label of all products licensed by the Bureau of Veterinary Drugs, Health and Welfare Canada. All veterinary pharmaceutical products in Canada carry this number except for patent medicines which are not restricted drugs and do not require a licence to sell them. This number is recorded in all poison control centres. If there is a case of accidental poisoning there is no confusion created by using trade names or generic names. The emergency treatment procedures etc. are recorded for each DIN number.

Biologicals (vaccines, bacterins and toxoids) do not carry a DIN number. They are licensed by Agriculture and Agri-Food Canada and carry an Ag. Can. Est. Licence No. (Agriculture and Agri-Food Canada Establishment Licence Number.)

7. STORAGE INSTRUCTIONS: These directions are extremely important to ensure that the product maintains its effectiveness.

These must be followed by the producer using the product and storing it at home. It is your responsibility as the retailer to ensure that that the product is stored in the manner recommended and to point out the storage recommendations to your customer. It is your responsibility to sell a viable product to your customer.

If you receive a shipment from your supplier that requires refrigeration and it arrives without cold packs, you are accepting an inferior product. The same can be said for frozen product in the winter. Do not accept shipments from a transport company that do not meet the storage instructions on the product. This is also true in accepting customer returns such as unopened vaccine. You have no idea how this product was stored after it left your premises. This product may be totally useless if it has not been stored properly. When you are selling a product to your customer that requires refrigeration it is in your best interest and the usefulness of the drug to provide some method of keeping that product cool until it can be refrigerated at home.

The following are storage terms and associated temperatures:

Refrigerate - 2-8 degrees C.

Cool Place - 8-15 degrees C.

Protect from excessive heat - store below 40 degrees C.

If there are no specific instructions drugs should be protected from moisture, excessive heat and freezing. Drugs should not be stored in direct sunlight. Drugs that have been exposed to excessive heat or freezing in transportation should not be accepted.

8. DOSAGE: The dose to be administrated and the route stated (IM, SC, oral, etc) has been used in the trials to substantiate the label claims. If these instructions are not followed then the label is not valid and instructions such as the withdrawal time are no longer valid. The dosage is usually stated in ml/kg of body weight.

9. CAUTIONS: These are designed to draw attention to any potential adverse reactions from the product to make sure that the user is aware of these potential reactions and prepared to act in the case of an adverse reaction.

10. EXPIRY DATE: Clinical tests have been done to determine the "shelf life" of the product. Remember you are selling a consistent, quality product that has been designed to produce a specific result. If you use an out-dated product the company has said that after this time this product no longer meets the label information and is not suitable for use.

To sell out-dated product is to sell someone a product that you have no idea of its quality. Veterinary pharmaceuticals are purchased to do a particular job and it is not a bargain to purchase out-dated drugs.

It is important to regularly check the expiry dates on your inventory and to rotate stock to avoid having expired stock. As well it is important to check the expiry date when unpacking shipments from the wholesaler. If the product does not have a reasonable shelf-life left, you may be left with unsold out-dated product. If you are selling short dated product, you are not providing your customers with good service as they may not be able to use the product before it becomes out-dated.

IT IS YOUR RESPONSIBILITY TO POINT OUT TO YOUR CUSTOMER THE WARNINGS ASSOCIATED WITH THE PRODUCT.

THE SALE OF PHARMACEUTICALS IS A PRIVILEGE NOT A RIGHT, RESPONSIBLE SALES OF VETERINARY PHARMACEUTICALS WILL RESULT IN YOU MAINTAINING THAT PRIVILEGE, FAILURE TO DO SO WILL RESULT IN A LOSS OF THAT PRIVILEGE.

THE PURCHASE REGISTER

The Regulations require that a holder of a Medicated Feed Licence who mixes feeds or a holder of a Veterinary Drug Licence shall keep a register of all purchases made by the licensee. For this purpose, the Ministry of Agriculture, Fisheries and Food supplies a Veterinary Drug Purchase Register (Form V.7) in which it is necessary to legibly record, in order of date, all purchases of veterinary drugs showing:

- date of purchase;
- name of supplier;
- quantity purchased;
- the generic name;
- trade or brand name;
- the name of the manufacturer of veterinary drugs purchased.

It is required that the veterinary drugs purchased to manufacture medicated feed (Schedule A Table 1) be kept in a separate Veterinary Drug Purchase Register to those veterinary drugs (Schedule A Table 2) to be sold from a licensed business. The original copy of the Purchase Register is to be sent to the Chief (Provincial) Veterinarian before February 28th each year to cover the purchases in the previous calendar year. Failing to do this may lead to a suspended licence and refusal to renew any Medicated Feed Licence or Veterinary Drug Licence in the next fiscal year.

It is also required that holders of Limited Medicated Feed Licenses register in the Purchase Register medicated feeds purchased from another Province or country and sold in British Columbia. The Chief Veterinarian must receive this purchase Register before February 28th each year.

Note: The Veterinary Drug Purchase Register must be kept current, drugs etc. should be added as they are received.

There are two very important reasons why the Veterinary Drug Purchase Register is necessary:

1. Having available a written register whereby the Ministry of Agriculture, Fisheries and Food can ascertain what veterinary drugs are being purchased and sold by licensees. The veterinary drugs that can be sold legally are those listed in the Schedule A Tables 1 and 2 of the Regulations. The exception is permitted under section 4 of the Regulations where a holder of a Medicated Feed Licence may sell, only upon the written order of a registered veterinarian, feeds medicated with veterinary drugs in strengths listed above those authorized under the Feeds Act (Canada) and feeds medicated with other veterinary drugs not listed in Schedule A Table 1.

2. Having available a written register showing the total amount of each veterinary drug sold during a given calendar year. During 1974, for instance, there were 18,746 doses of Newcastle-Bronchitis vaccine used in poultry, 103,900 lbs. of Furazolidone (NF 180) mixed in poultry feeds (now banned for use in food - producing animals) and 20,250 cc's of Erysipelas bacterin sold for use in pigs. These examples will indicate that valuable information regarding veterinary drugs is made available for use by the Ministry of Agriculture, Fisheries and Food.

The main purpose of this section of the Handbook is to try and standardize the reporting of veterinary drugs in the Veterinary Drug Purchase Register returns. The main problems are in five areas:

1. In the "Quantity Purchased" column, reporting must be standardized to pounds, cc's, ml's, gallons, ounces, grams and doses. There is no way that accurate totals, as to amounts, can be arrived at when the "Quantity Purchased" column includes designations such as bags, barrels, packages, #, 2's, tablets, drums and so on. Appendix C shows a very poor tabulation of amounts when using the designations in the previous sentence. One can see that it is impossible to arrive at a reasonably accurate total of the actual sales due to the many different ways that quantities are shown. In Appendix C, the total doses for poultry vaccines are fine, but the rest is impossible.

   Appendix D shows a Purchase Register completed neatly and properly.

2. In the "Veterinary Drug" column, it is required that only those veterinary drugs listed in Schedule A Table 2 be entered in the "Veterinary Drug" column. There is no call to include saddles, halters, udder balm, oral vitamins and minerals, horse shoes and so on.

3. In the "Veterinary Drug" column, the generic name must be included. The generic names are those actually listed in Schedule A Table 2. Unless this is done, there is considerable difficulty in knowing what the medical ingredients are. Unless the generic name is included, how can one decide if any Schedule A Table 2 veterinary drugs are in things such as cowpest powder, horse wormer, mastitis ointment, pink eye bomb, calf scour oblets, dehorning paste, udder rub, teat dilators, pig saver, ringo, scour boluses and a host of other terms? One can be sure that there are Schedule A Table 2 veterinary drugs in things such as mastitis ointment, horse wormer and calf scour oblets, but there is no way of knowing what they are unless the generic name (Schedule A Table 2) is included.

4. In report "Quantity Purchased", all of the poultry vaccines are listed according to the "doses" used. This is fine and it must remain this way.

   When it comes to reporting "Quantity Purchased", for all other vaccines and bacterins used in animals, the amounts must be reported in "cc's" or "ml's" . This is essential as Blackleg, Corynebacteria and Pasteurella bacterins and IBR vaccines are being reported in both "cc's" or "ml's" and "doses". in order to standardize, report all bacterins and vaccines in "cc's" or "ml's", except those sold by hatcheries and used for poultry diseases.

5. In order to save time and space, trade names can be used provided that the ingredients are listed at least once on the Purchase Register. For instance, if the term "Triple Bacterin" is used and a statement is made that this product includes C1 chauveii-septicum and pasteurella, then for the entire *year* the brand name "Triple Bacterin" can be used. This applies to other products such as Coopervac, TwoWay Bacterin and so on.

It is realized that much of the difficulty of properly completing the Veterinary Drug Purchase Register is due to problems of continuity of staff in each licensed business. Sometimes, the task is delegated to a stenographer or clerk and, in most cases, this person has not been properly apprised of what is required in the recording of veterinary drugs. Packs of V7 forms are available from the Animal Health Branch (address shown at beginning of this Handbook).

Better continuity and adequate knowledge is the aim of the Ministry of Agriculture, Fisheries and Food and provides additional impetus to the need to issue Veterinary Drug Licenses to businesses where a qualified person has completed a course of study and has passed an examination.

This Handbook contains the information that will enable an applicant for a Veterinary Drug Dispenser Licence to pass an examination. It will also provide a useful source for continual reference after the Licence has been issued.

The examination consists of 50 questions which must be answered in one hour (75 questions in one and one half hours if bee products are included). The pass mark is 75% and you may bring this handbook into the examination with you. Most people pass the examination; of those who do not, it is usually because they have not studied this Handbook and fail to complete a significant number of questions to pass.

Good Luck!!

*SPECIFIC DIRECTIVES FOR THE SALE OF VETERINARY DRUGS FOR THE CONTROL OF BEE DISEASES

Individuals or businesses wishing to sell veterinary medicines for the control of bee diseases should be familiar with the Veterinary Drug and Medicated Feed Regulations. The only drugs these licensees are authorized to sell are Fumagillin and "Tetracyclines for oral use only" (Terramycin) which are included in Schedule A Table 2 of the Regulations.

The honeybee, *Apis mellifera* falls prey to a number of diseases, most of which are contagious either between individual bees within a hive or between bee hives. These may be caused by a wide range of pathogens -bacteria, protozoans, fungi, viruses and parasitic mites. As a general rule, infectious agents attack only one stage of the bee, i.e. the larval stage or the adult stage. Bee diseases are usually classified as brood diseases or adult diseases. The brood diseases are: American foulbrood, European foulbrood, chalkbrood, sacbrood and stone brood. Adult diseases include Nosema disease, Bee paralysis and Acarine disease. American and European foulbroods and Nosema disease are the only bee diseases that are treated with veterinary medicines.

'* **This section should only be studied if you are going to sell products for bees.**

Pharmaceuticals Used in Apiary Production

A) Antibiotics

Although the term **antibiotic** means any substance that opposes growth, it is now used in a restricted sense to describe those products of the growth of certain fungi and bacteria that possess the property of inhibiting the growth of disease causing microorganisms. This phenomenon has been known for many years (over 80), but it was not until the isolation of penicillin in a pure form in 1940 and the discovery of its therapeutic activity that research really went ahead. Several hundred antibiotics have since been isolated, but many were either too toxic to animal tissues or not efficient enough to be developed commercially. Thus, relatively few are available for practical use.

In the last fifteen years, a large amount of work has been done in regard to the emergence of resistance to antibiotics in bacteria which were previously sensitive. It is sufficient to know that certain resistant bacteria have the ability to transfer this resistance to other sensitive bacteria which then multiply and pass on this resistance genetically. Thus, the problem arises that if the bacteria in a normal environment becomes resistant and disease causing bacteria are introduced, they could pick up this resistance and the treatment, which has worked previously, then becomes ineffective.

Tetracyclines

Tetracyclines have been used to control American and European foulbroods since 1951. Those available for bees are tetracycline and oxytetracycline in the soluble forms of tetracycline hydrochloride and oxytetracycline hydrochloride. These antibiotics are available under such trade names as: Terramycin Animal Formula, Tetra-Sol, Onycin, Intracin, Polyotic and others. The proper concentration of active material must be 55 milligrams per gram (55 mg/g) or 25 grams per pound of formulation. The concentration is marked on the package. Care must be taken that the soluble form is purchased which should also be marked on the package.

The soluble tetracyclines are relatively unstable once in solution and remain effective only for about 2 weeks, especially during summer weather. On the other hand, if stored properly in the powdered form they are effective until the expiry date.

Fumagillin

Fumagillin is used in the prevention and control of Nosema disease in bees. It is an antibiotic produced by the fungus *Aspergillus fumigatus* and was originally developed for use in human medicine but was discarded. It was found effective against Nosema disease in 1952. It is marketed in a formulation under the trade names, Fumidil-B, Noceemafix, Nosemax and so on. Five grams of these formulations contain 100 mg of the active ingredient, fumagillin, and is sold in two sizes. A small bottle is marked .5 g of active ingredient while the large bottle is marked 9.5 g. These figures refer to the amount of fumagillin in the formulation. As in the case with the tetracyclines, fumagillin should not be used after the expiry date and it should be stored inn a cool dry place such as in a refrigerator.

B) Chemotherapeutics

Chemotherapy is the treatment of disease with chemical agents, but it is restricted today to the use of chemical agents that have a specific action on the organism causing disease. For instance, quinine in the treatment of malaria is an early example.

Sulphonamides

In 1935 the introduction of sulphonamides opened up a whole new field of chemotherapeutics having a wide range of activity against pathogenic organisms. Although a large number have been produced the number now in regular use is quite small.

Sodium Sulfathiazole (sulfa)

Sodium Sulfathiazole, sometimes referred to as "sulfa" by beekeepers, was found effective in preventing American foulbrood in 1944. However, the very properties of stability in solution and its long shelf life which made it useful in veterinary medicine have caused residue problems in honey.

For this reason, and because it has never been registered for use in bees in Canada, it is not recommended and should not be used. It is now not allowed to be sold for bees by licensees, and if it is used seizure of the honey and severe repercussions could occur.

Precautionary Measures in Treating Beehives with Veterinary Drugs

Care must be taken to ensure that no medications get into honey that will be extracted for human use. The tetracyclines may be fed as late as June 1st since their activity lasts only 14 days in solution. All medication must be removed six weeks before extracting is to begin, or by June 15. Any medicated honey will be consumed by the bees by extracting time and not be available for human consumption.

Special attention must be paid to feeding only the proper dosage. Overdosing will not increase the effectiveness of the medicant and may cause harm to adult bees and brood. It also increases the likelihood of honey contamination. Underdosing is equally detrimental. If sufficient dosage levels are not maintained, the medication will be ineffective. Furthermore, exposing pathogens to sublethal levels of antibiotics fosters development of resistant strains.

Bee Diseases

American Foulbrood

American foulbrood (AFB) is caused by the bacterium *Bacillus larvae.* AFB has been the cause of concern to beekeepers for many years as this disease is quite capable of killing whole beehives and is extremely contagious. Before the use of medication AFB wiped out whole apiaries and occurred at a rate of about 10% in British Columbia. Many billions of infective spores are formed in each infected larva which may account for its contagiousness and persistence.

The soluble Tetracyclines are capable of preventing spore germination of *B. larvae.* However, they do not kill the spores. For this reason, these medications are normally used as preventive treatments only. Once a colony becomes infected it is usually destroyed since medication serves to mask the disease and not cure it. As a result, the B.C. Ministry of Agriculture, Fisheries and Food carries out routine inspection of beehives with the object of discovering and destroying infected colonies thus preventing the spread of AFB. This function is performed by apiary inspectors.

From March until June, Terramycin (55 mg/g) or other soluble tetracyclines at the proper strength may be administered at a dosage of 1 teaspoon per gallon of sugar syrup fed. **Care must be taken not to feed anymedication during the honeyflow.**

Dry feeding of Tetracyclines is practiced where syrup feeding is not necessary. One part tetracycline (55 mg/g) is mixed with 5 parts icing sugar and 2 tablespoons of the powder is sprinkled across the **ends** of the tops of the frames in the brood nest. Care must be taken not to sprinkle directly over the brood.

At this time antibiotic extender patties are not recommended or approved for use.

European Foulbrood (EFB)

EFB is caused by the bacterium *Streptococcus pluton.* If untreated this disease causes serious losses to beekeepers. Unlike AFB, *S. pluton* does not form spores although resistant stages can exist for lengthy periods.

The tetracyclines are effective preventatives to EFB and can also be used as a cure of the disease. They are administered in the same manner as for AFB.

Nosema Disease

Nosema disease is caused by the protozoan, *Nosema apis.* It attacks the lining of the mid-gut of the adult bee, having no effect on immature stages. It is a debilitating disease resulting in reduced honey crops, and reduced pollination effectiveness but rarely kills a colony. It reaches epidemic levels in spring, declining in summer and fall.

The antibiotic fumagillin has been found effective in decreasing the effects of Nosema disease. It is only effective when fed in sugar syrup. Ideally it should be fed in the fall and spring to overwintered colonies. If only fed once per year a fall treatment is more effective than spring treatment.

Dosage level is 1 slightly rounded teaspoon (5 grams) of the fumagillin formulation (100 mg of active fumagillin) per gallon of syrup. In the fall at least 1 gallon of medicated syrup should be fed and at least 1 gallon the following spring.

APPENDIX A

EXAMPLE

MEDICATING INGREDIENTS BROCHURE NO. 33 Page 1

Generic Name: **DIMETRIDAZOLE**

APPROVED BRANDS:
1. EMTRYL contains 300 g/kg of 1,2-dimethyl-5-nitroimidazole (Rhone-Poulenc Canada, Inc.)
2. DIMETRIDAZOLE 30% PREMIX contains 300 g/kg of 1,2-dimethyl-5nitroimidazole (Bio Agri Mix Ltd.)

APPROVED FOR USE: In meal or pellet feed for turkeys, swine.

APPROVED CLAIMS: For turkeys - Claims 1, 2 For swine - Claim 3

Claim 1: As an aid in prevention of death from Blackhead in turkeys.

LEVEL OF DRUG: 0.015% (150 mg/kg) of complete feed.

DIRECTIONS: Feed this medicated feed as the sole ration.

WARNING:
1. Eggs from treated birds must not be used as human food.
2. Discontinue the use of this medicated feed at least 5 days before treated turkeys are slaughtered for use in food.

CAUTION:
1. If unexpected deaths occur consult a veterinarian or poultry pathologist.

Claim 2: As an aid in the treatment of outbreaks of Blackhead in turkeys.

LEVEL OF DRUG: 0.05% (500 mg/kg) of complete feed.

DIRECTIONS: At the first sign of an outbreak, remove normal diet and feed this medicated feed as the

sole ration for 14 days. Follow this with rations containing preventive levels of medication.

WARNING:

1. Eggs from treated birds must not be used as food.
2. Discontinue the use of this medicated feed at least 5 days before treated turkeys are slaughtered for use in food.

CAUTION:

1. In an outbreak all turkeys inn a flock should be treated for the recommended period, whether or not visibly affected.
2. If unexpected deaths occur consult a veterinarian or poultry pathologist.

Generic Name: DIMETRIDAZOLE

Claim 3: As an aid in the prevention of Swine Dysentery for feeder pigs intended for slaughter only.

LEVEL OF DRUG: 0.015% (150 mg/kg) of complete feed.

DIRECTIONS: Feed this medicated feed as the sole ration continuously for at least 28 days during the period of risk.

WARNING: Discontinue the use of this medicated feed at least 5 days before treated swine are slaughtered for use in food.

CAUTION:

1. Do not feed to swine intended for breeding.
2. Do not use this medicated feed for the control of *Escherichia coli* or *Salmonella* infections. When in doubt consult a veterinarian.

Accepted Compatibilities: Dimetridazole is compatible with the following drug/drug combinations. For details refer to the MIB as indicated.

	For use in feed for:
1. amprolium (MIB #27)	turkeys
2. chlortetracycline hydrochloride (MIB #10)	turkeys
3. chlortetracycline hydrochloride *(MIB #34)*	turkeys
4. furazolidone (MIB #11)	turkeys
5. oxytetracycline hydrochloride (MIB #10)	turkeys
6. oxytetracycline hydrochloride *(MIB #35)*	turkeys
7. procaine penicillin and streptomycin (MIB #10)	turkeys
s **8.** zinc or methylene disalicylate bacitracin (MIB #10)	turkeys

s

APPENDIX B

EXAMPLE

MEDICATING INGREDIENT BROCHURE NO. 37 A

Generic Name: **ZINC BACITRACIN**

APPROVED BRANDS:

1. BACIFERM 50 contains zinc bacitracin at 110 g/kg (Pitman-Moore, Inc.)
2. BACITRACIN 50 (ZINC) contains zinc bacitracin at 110 g/kg (Canada Packers, Inc.)
3. ZINC BACITRACIN 50 contains zinc bacitracin at 110 g/kg (Rhone-Poulenc Canada, Inc.)

APPROVED FOR USE: In meal or pellet feed for chickens, swine.

APPROVED CLAIMS: For chickens - Claim 1. For swine - Claim 2, 3.

Claim 1: **For the reduction of early mortality of chicks.**

LEVEL OF DRUG: 0.011 % (110 mg/kg) of bacitracin from zinc bacitracin in the complete feed.

DIRECTIONS: Feed this medicated feed as the sole ration for 5-15 days.

CAUTION:

1. Do not use in feeds containing bentonite or other pellet binding agents. (Required only on premix and supplement labels).

Claim 2: **As an aid in the prevention of Bacterial Enteritis (Scours) (except Coliform Diarrhea) in swine**

LEVEL OF DRUG: 0.0055% (55 mg/kg) of bacitracin from zinc bacitracin in the complete feed.

DIRECTIONS: Feed this medicated feed as the sole ration.

CAUTION:

1. Do not use in feeds containing bentonite or other pellet binding agents. (Required only on premix and supplement labels).
2. Pigs refusing to eat should be treated individually.

Claim 3: **As an aid in treatment of Bacterial Enteritis (Scours) (except Coliform Diarrhea) in swine.**

LEVEL OF DRUG: 0.011 % (110 mg/kg) of bacitracin from zinc bacitracin in the complete feed.

DIRECTIONS: Feed this medicated feed as the sole ration for 5-15 days.

CAUTION: **1.** Do not use in feeds containing bentonite or only pellet binding agents. (Required only on premix and supplement labels).

2. Pigs refusing to eat should be treated individually.

Accepted Compatibilities: Zinc bacitracin is compatible with the following drug/drug combinations. For details refer to the MIB as indicated.

for use in feed for

1. penicillin as procaine penicillin (MIB #36)
streptomycin (MIB #36)

April/84

APPENDIX C

Poor Tabulation of Amount From "Quantity Purchased" Column

Key to Abbreviations:

N/B - Newcastle Bronchitis Vaccine
N/C - Newcastle Vaccine
I/B - Infectious Bronchitis Vaccine
M/D - Marek's Disease Vaccine
A/E - Avian Encephalomyelitis Vaccine
ILT - Infectious Laryngotracheitis Vaccine

N/B	2,180,000 doses
N/C	340,000 doses
I/B	298,000 doses
WD	16,000 doses
A/E	89,500 doses
ILT	245,500 doses
Erysipelas bacterin	13,800 cc
Aureomycin Bisulphate	3#
ESP	75# + 80
Electrolytes	25# + 25 + 50 lbs
Emtryl	300 tablets
Germex	6 gallons
Gallimycin Poultry Formula	14 drums
Gallimycin Sol	1,700 grams
Gallimycin Inject	100 cc
(BSO Bonded TM2)	100#
(ISO Bonded TM2)	100# + 50 bags + 50 lbs
(Bonded TM2)	45# + 45 bags + 35 lbs + 45
Kerol	2 gal
Klotogen	25# + 25
Medic Aid	240 ounces
NF 180	5#
MDS	4# + 5
Neo Med	10# + 5
Neotran	1,020 grams
Div. 5 Special	10# + 65 lbs
Western Fedd Special	275#
1 Stroke environ	31 gal
Sol Nitrofurazine	32#
Superdyne	352 ounces
Sulquin	1 gal + 60 ounces + 30/4
Spectam	230,400 cc
Sulpha plus	1 drum
Sulphamethazine	46 gal
Tranquillizer	50# + 10 bags
Tetramix	6# + 48 + 72 1's

APPENDIX D

Veterinary Drug Purchase Record

NOTE: Please Print **Licence No.**_____

NAME OF FIRM:_____ **Year**_____

Veterinary Drug

Date of Purchase	Supplier (Company Name & Address)	Quantity Purchased	Generic Name, Trade Name, and Name of Manufacturer)
Jan. 25	Franklin Laboratories	20/100 cc	PenStrep
Jan. 30	Franklin Laboratories	20/125 cc	Triple Bacterin-Cl. chauveii septicum, pasteurella
Feb. 15	Franklin Laboratories	10/100 cc	C-P Bacterin-Pasteurella & Corynebacteria
Feb. 16	Franklin Laboratories	20/1 ounce	P E Powder-Sulphathiazole & Sulphanilamide
Mar. 2	McClelland	5/100 cc	Bocine - IBR Vaccine
Mar. 15	McClelland	5/250 cc	3-Way Vaccine - Cl. chauveii septicum, pasteurella
Mar. 20	McClelland	10 1/4 lb	Tetracycline Soluble Powder
Mar. 30	McClelland	10/8 ounces	Pypzine Concentrate - Piperazine
Apr. 6	Viobin	10/30 cc	Scour-ade Solution - Furazolidone
Apr. 15	Viobin	10/1 lb	Sulphanilamide Powder
Apr. 20	Viobin	5/50 cc	Clostridium Chauveii-Septicus Bacterin
Apr. 30	Viobin	10/100 cc	Triple- Bacteri n-B lackleg, Mal. Edema & Shipping Fever
May 2	Franklin	10/100 cc	PenStrep
May 2	Franklin	10/125 cc	Triple Bacterin
May 2	Franklin	10/100 cc	C-P Bacterin
May 2	Franklin	10/1 ounce	P E Powder
June 2	McClelland	5/100 cc	Bocine
June 15	McClelland	5/250 cc	3-Way
June 20	McClelland	10 1/4 lb	T.S.P.
June 30	McClelland	10/8 ounces	Pypzine

APPENDIX D

Veterinary Drug Purchase Record

NOTE: Please Print **Licence No.**_____

NAME OF FIRM:_____ **Year**_____

Veterinary Drug

Date of Purchase	**Supplier (Company Name & Address)**	**Quantity Purchased**	**(Generic Name, Trade Name, and Name *of* Manufacturer)**
July 6	Viobin	5/30 cc	Scour-Ade
July 6	Viobin	5/1 lb	Sulphanilamide Powder
July 12	Viobin	10/50 cc	C & S Bacterin
July 12	Viobin	10/100 cc	Triple Bacterin