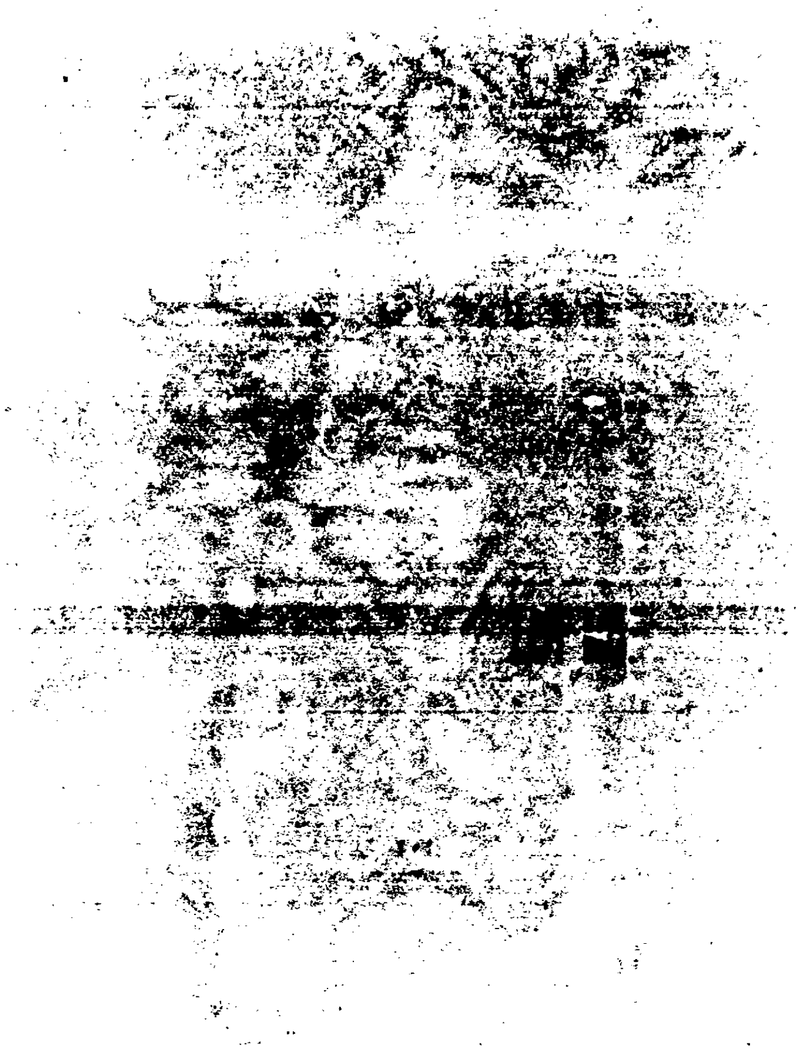


(DICHLORVOS*)

EQUINE ANTHELMINTIC

10 PACKETS, 3.35 oz. (95 g.) EACH

CAUTION! KEEP OUT OF REACH OF CHILDREN

VETERINARY USE ONLY. U.S. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

See other Precautions on Side Panel.

*2,2 Dichlorovinyl Dimethyl Phosphate U.S.D.A. Reg. No. 201-257

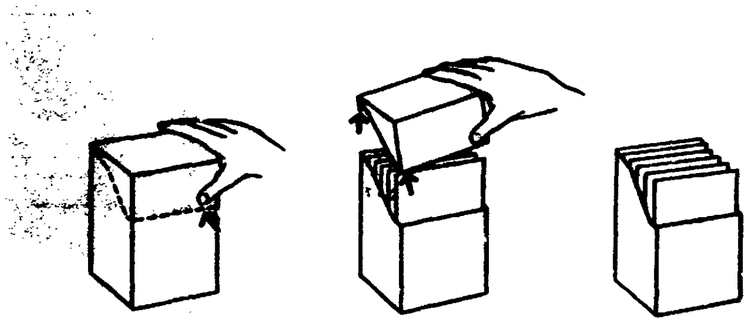
SHELL

ACTIVE INGREDIENT		
Dichlorvos* (2,2-dichlorovinyl dimethyl phosphate)	16.6 g.	(17.5%)
INERT INGREDIENTS	78.4 g.	(82.5%)
TOTAL	95.0 g.	(100.0%)

SHELL CHEMICAL COMPANY

U.S. Patents Nos. 2,956,073; 3,166,472; 3,310,769

Made in U.S.A. ACD-62D 4-71



TO DISPLAY: PUSH THUMB INTO PERFORATION
AND TEAR AWAY.

[redacted]

ATTENTION:
SEE PACKAGE INSERT FOR COMPLETE
USE DIRECTIONS.

SHELL CHEMICAL COMPANY
A Division of Shell Oil Company
AGRICULTURAL DIVISION
SAN RAMON, CALIFORNIA 94583

STORE IN A COOL PLACE (LESS THAN 80° F.)

EQUIGARD®10

(DICHLORVOS*)

EQUINE ANTHELMINTIC

NET CONTENTS: 50 PACKAGES, 3.35 oz. (95 g.) EACH

SHELL CHEMICAL COMPANY
A Division of Shell Oil Company
AGRICULTURAL DIVISION
SAN RAMON, CALIFORNIA, U.S.A. 94583

ACL 1139A 4/71

U.S. Patent Nos. 2,956,074 3,166,472 3,418,769 Made in U.S.A.

SHELL

LOT NO.

CAUTION! KEEP OUT OF THE REACH OF CHILDREN

VETERINARY USE ONLY. U.S. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

ACTIVE INGREDIENT		
Dichlorvos* (2,2-dichlorovinyl dimethyl phosphate)	16.6 g.	(17.5%)
INERT INGREDIENTS	78.4 g.	(82.5%)
TOTAL	95.0 g.	(100.0%)

U.S.D.A. Reg. No. 201-257

(DICHLORVOS*)
EQUINE ANTHELMINTIC

NET CONTENTS: 50 PACKAGES, 3.35 oz. (95 g.) EAC

SHELL CHEMICAL COMPANY
A Division of Shell Oil Company
AGRICULTURAL DIVISION
SAN RAMON, CALIFORNIA, U.S.A. 94583

U.S. Patent Nos. 2,956,073; 3,166,472; 3,318,769

ACL-1139A 4-71
Made in U.S.A.

SHELL

LOT NO.

INDICATIONS: For the removal and control of bots (Gastrophilus intestinalis, G. nasalis), large strongyles (Strongylus vulgaris, S. equinus, S. edentatus), small strongyles (of the genera Cyathostomum, Cylicocercus, Cylicocyclus, Cylicodontophorus, Triodontophorus, Poteriostomum, Gyalocephalus), pinworms (Oxyuris equi), and for Ascarids (Parascaris equorum) in horses other than foals (sucklings and young weanlings).

ACTIVE INGREDIENT		
Dichlorvos* (2,2-dichlorovinyl dimethyl phosphate)	16.6 g.	(17.5%)
INERT INGREDIENTS	78.4 g.	(82.5%)
TOTAL	95.0 g.	(100.0%)

U.S.D.A. Reg. No. 201-257

ACCEPTED
June 4, 1971
UNDER THE FEDERAL INSECTICIDE, FUNGICIDE AND RODENTICIDE ACT FOR ECONOMIC POISONS REGISTERED UNDER NO. 201-257
TO ARTWORK ONLY

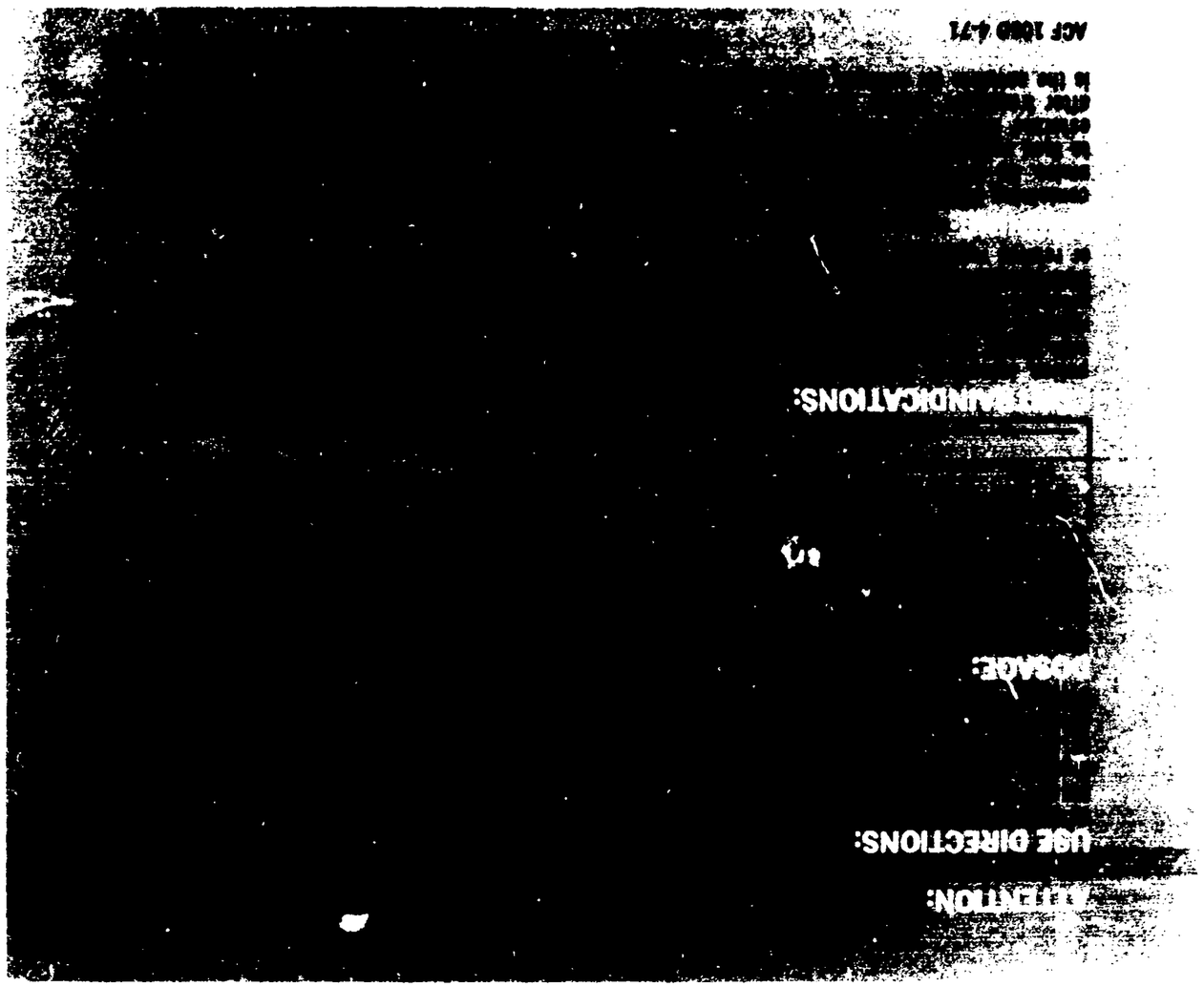
(DICHLORVOS*)
EQUINE ANTHELMINTIC
NET WEIGHT: 3.35 oz. (95 g.)

CAUTION! KEEP OUT OF REACH OF CHILDREN

VETERINARY USE ONLY. U.S. Federal law restricts this drug to use by or on the order of a licensed veterinarian. See other Precautions on Back Panel.

SHELL

SHELL CHEMICAL COMPANY
A Division of Shell Oil Company
AGRICULTURAL DIVISION
SAN RAMON, CA. 94583



STORE IN A COOL PLACE (LESS THAN 80° F.)

CAUTION! KEEP OUT OF REACH OF CHILDREN

VETERINARY USE ONLY. U.S. Federal law restricts this drug to use by or on the order of a licensed veterinarian. See other Precautions on Back Panel.

esterase inhibitor. Do not use this product in animals simultaneously or within a few days before or after treatment with or exposure to cholinesterase inhibiting drugs, pesticides or chemicals. Atropine is the antidote for animals. Atropine and 2-PAM are human antidotes.

Made in U.S.A. — U.S. Patent Nos. 2,956,073; 3,166,472; 3,318,769

ACF 105D 4-71

SHELL CHEMICAL COMPANY
A Division of Shell Oil Company
AGRICULTURAL DIVISION
SAN RAMON, CA. 94583

with the preparation. The removal of subclinical ascarid infections from older horses is an integral part in the control of **Parascaris equorum** by reducing the incidence of contamination to which the young animals are exposed.

Critical studies have demonstrated consistent high efficacy against horse bots (**Gastrophilus intestinalis, G. nasalis**), provided all water is withheld four (4) to six (6) hours prior to administration and for three (3) hours after ingestion of the preparation. Variable efficacy against bots has been observed when water is available **ad lib.** The availability of water has no detrimental effect on activity against the other parasites.

The removal of the minute pinworm **Probstmayria vivipara,** following treatment with EQUIGARD (dichlorvos) has been determined in critical anthelmintic assays. The parasite is reportedly found in equines throughout the world. **Probstmayria vivipara** is unique in that the females of the species deposit living larvae that are almost fully developed. These larvae are capable of completing their development to maturity without leaving the host. The infections of this specie may number millions in a single host animal, but the clinical significance and pathogenicity are unknown at this time.

In the case of individual reluctance to consume medicated grain, sweetening agents such as molasses or honey may be added or the application of a small amount of Vicks Vapo Rub or similar preparations on the muzzle frequently will overcome such difficulties. (1,3,9,10,11)

CONTRAINDICATIONS

Horses **severely debilitated** or suffering from diarrhea or severe constipation, infectious disease, toxemia or colic should not be treated until such conditions are corrected with proper therapy. Do not administer in conjunction with or within one (1) week of administration of muscle relaxant drugs (i.e., succinylcholine), phenothiazine derived tranquilizers, or central nervous system depressant drugs. Horses should not be subjected to insecticide treatment for five (5) days prior to or after EQUIGARD (dichlorvos) treatment. Do not administer to horses afflicted with Chronic Alveolar Emphysema (Heaves) or related respiratory conditions. There are no other known contraindications for this preparation.

ATTENTION

EQUIGARD (dichlorvos) in critical anthelmintic and clinical studies has demonstrated excellent anthelmintic activity against the gastrointestinal parasites of major importance in horses in the United States. The drug is not a substitute for proper sanitary measures or management, but should be used in conjunction with such practices. When used in this capacity, EQUIGARD (dichlorvos) can be a valuable tool for the improvement of individual and herd health through the control and reduction in rate of contamination by parasite eggs in paddocks, pastures and other grazing areas.

Horses will become reinfected following treatment if they are returned to contaminated areas. The rate and degree of infection will be directly correlated to the life cycle of the parasite and exposure rate. Retreatment schedules with EQUIGARD (di-

per kilogram of body weight, have been observed to be reversed within twenty-four (24) to forty-eight (48) hours without antidotal or supportive therapy. The sign of toxicity from such dosages, most frequently observed that was of longer duration was a diarrhea. This condition was corrected with one (1) week's time without the aid of antidotal or supportive therapy.

The reversal of toxic signs comes about because the degradation of dichlorvos by the horse proceeds at a relatively constant rate below a threshold maximum. Mortality only results when the subject's detoxification threshold is suddenly reached or exceeded resulting in overwhelming the body's detoxification mechanism. (1,2,4,5,7,8,10)

PHARMACOLOGY

The primary known pharmacologic effect of EQUIGARD (dichlorvos) is its ability to inhibit the enzyme cholinesterase. This action allows for overstimulation of the parasympathetic nervous system by the resultant accumulation of acetylcholine. The severity of the action is directly related to dosage.

Horses of all ages, when administered the recommended dosage of EQUIGARD (dichlorvos) show a detectable drop in whole blood, red blood cell and plasma cholinesterase values one (1) to three (3) days post-treatment time. The magnitude of cholinesterase depression varies from horse to horse but is not of sufficient magnitude to interfere with normal neuro-physiological functions.

Normal or above normal cholinesterase values are often achieved within one (1) to three (3) weeks time in horses receiving active ingredient dosages of two hundred (200), four hundred (400), eight hundred (800) and sixteen hundred (1600) mg. per kilogram of body weight. Similar observations have been made in mares receiving two (2) to four (4) treatments at recommended dosages prior to foaling.

The significance of plasma or red blood cell cholinesterase depression in the

and congestion of the lungs, fatty degeneration of the liver, with marked hyperemia and inflammation of the gastrointestinal tract. Histopathological examination of tissues was consistent with the gross pathological findings. Nerve tissue showed no evidence of demyelination or other abnormalities. (1,2,3,10)

USE DIRECTIONS

EQUIGARD (dichlorvos) is designed to be administered in the grain portion of the ration. Preconditioning horses by fasting is not necessary or recommended. The preparation is generally consumed more rapidly if administered in a limited amount of the normal grain portion. The remainder of the grain may be offered after consumption of the medication. The preparation should be added to the feed immediately prior to administration.

The weight of each animal should be carefully determined and EQUIGARD (dichlorvos) added to the grain at the following dosage rates:

DOSAGE TABLE

Package Size	Active Ingredient (Dichlorvos) Grams	Lbs. Body Weight Treatment/Package
#2	3.2	200
#3	4.7	300
#5	8.3	500
#10	16.6	1,000

Horses of odd weights may be treated with a package or combination of packages that will provide a dosage of fourteen point two (14.2) mg. to eighteen point five (18.5) mg. of active ingredient per pound of body weight.

Critical anthelmintic studies in the horse have shown that one-half ($\frac{1}{2}$) of the above single recommended dosage of EQUIGARD (dichlorvos) and repeated eight (8) to twelve (12) hours later, provides equivalent anthelmintic efficacy and spectrum of that obtained by the single recommended dosage. This split dosage schedule of EQUIGARD (dichlorvos) eight (8) to twelve (12) hours apart has been demonstrated to be beneficial in the treatment of the very aged, emaciated or debilitated subjects or those reluctant to consume medicated feed. In suspected cases of severe ascarid infection sufficient to cause concern over mechanical blockage of the intestinal tract, the split dosage should be utilized.

The efficacy of EQUIGARD (dichlorvos) against **Parascaris equorum** has not been evaluated in foals (sucklings and young weanlings) due to their known variance in grain consumption and therefore, EQUIGARD (dichlorvos) is not recommended for them. The number of ascarids present in horses typically diminishes with the increasing age of the subject but it has been documented that horses of all ages may harbor this parasite. Critical anthelmintic assays conducted in horses, other than nursing foals harboring **Parascaris equorum** populations, have demonstrated consistent high anthelmintic efficacy as achieved against such ascarid infections.

PATHOLOGY

The administration of varying dosages of unformulated dichlorvos orally or parenterally for varying periods of time to rats, rabbits, swine and dogs produced no significant gross or histopathological changes in any of the organs or tissues. Occasionally large oral dosages of the active ingredient will cause hyperemia and congestion of the stomach mucosa.

Post mortem examinations of horses succumbing to lethal doses of EQUIGARD (dichlorvos) show varying degrees of gross pathology which is dosage related. Horses receiving EQUIGARD dichlorvos at twenty (20) times the recommended dosage or eight hundred (800) mg. of active ingredient per kilogram showed bronchial inflammation and alveolar congestion, congestion of the spleen and gastrointestinal tract and fatty degeneration of the liver. Horses in this dosage group exhibited eight (8) to ten (10) days post medication time.

Horses receiving dosages of sixteen hundred (1600) mg. of active ingredient per kilogram of body weight or forty (40) times the recommended dosage expired in one (1) to two (2) days time and exhibited more pronounced gross pathological changes. These changes were characterized by petechial hemorrhages, emphysema

such as molasses or honey may be added or the application of a small amount of Vicks Vapo Rub or similar preparations on the muzzle frequently will overcome such difficulties (1,3,9,10,11)

CONTRAINDICATIONS

Horses **severely debilitated** or suffering from diarrhea or severe constipation, infectious disease, toxemia or colic should not be treated until such conditions are corrected with proper therapy. Do not administer in conjunction with or within one (1) week of administration of muscle relaxant drugs (i.e., succinylcholine), phenothiazine derived tranquilizers, or central nervous system depressant drugs. Horses should not be subjected to insecticide treatment for five (5) days prior to or after EQUIGARD (dichlorvos) treatment. Do not administer to horses afflicted with Chronic Alveolar Emphysema (Heaves) or related respiratory conditions. There are no other known contraindications for this preparation.

ATTENTION

EQUIGARD (dichlorvos) in critical anthelmintic and clinical studies has demonstrated excellent anthelmintic activity against the gastrointestinal parasites of major importance in horses in the United States. The drug is not a substitute for proper sanitary measures or management, but should be used in conjunction with such practices. When used in this capacity, EQUIGARD (dichlorvos) can be a valuable tool for the improvement of individual and herd health through the control and reduction in rate of contamination by parasite eggs in paddocks, pastures and other grazing areas.

Horses will become reinfected following treatment if they are returned to contaminated areas. The rate and degree of infection will be directly correlated to the life cycle of the parasite and exposure rate. Retreatment schedules with EQUIGARD (di-

per kilogram of body weight, have been observed to be reversed within twenty-four (24) to forty-eight (48) hours without antidotal or supportive therapy. The sign of toxicity from such dosages, most frequently observed that was of longer duration was a diarrhea. This condition was corrected with one (1) week's time without the aid of antidotal or supportive therapy.

The reversal of toxic signs comes about because the degradation of dichlorvos by the horse proceeds at a relatively constant rate below a threshold maximum. Mortality only results when the subject's detoxification threshold is suddenly reached or exceeded resulting in overwhelming the body's detoxification mechanism. (1,2,4,5,7,8,10)

PHARMACOLOGY

The primary known pharmacologic effect of EQUIGARD (dichlorvos) is its ability to inhibit the enzyme cholinesterase. This action allows for overstimulation of the parasympathetic nervous system by the resultant accumulation of acetylcholine. The severity of the action is directly related to dosage.

Horses of all ages, when administered the recommended dosage of EQUIGARD (dichlorvos), show a detectable drop in whole blood, red blood cell and plasma cholinesterase values one (1) to three (3) days post-treatment time. The magnitude of cholinesterase depression varies from horse to horse but is not of sufficient magnitude to interfere with normal neuro-physiological functions.

Normal or above normal cholinesterase values are often achieved within one (1) to three (3) weeks time in horses receiving active ingredient dosages of two hundred (200), four hundred (400), eight hundred (800) and sixteen hundred (1600) mg. per kilogram of body weight. Similar observations have been made in mares receiving two (2) to four (4) treatments at recommended dosages prior to foaling.

The exact significance of plasma or red blood cell cholinesterase depression in the horse is not known. Other animal species have been observed to survive long periods of time with no detectable whole blood cholinesterase values. Such measurements at best, serve only to indicate that over a period of time small but significant amounts of the drug were absorbed from the digestive system into the bloodstream.

The cholinergic properties of dichlorvos increase the rate of peristalsis of the intestinal tract. The degree of this action is related to dosage. The recommended therapeutic dosage of EQUIGARD (dichlorvos) may produce several loose stools. These are transitory and result in early expulsion of dichlorvos-susceptible gastrointestinal parasites. Dosages greater than that recommended for high anti parasitic efficiency may cause diarrhea.

Measurements of blood clotting time, per cent hematocrit, total leucocyte and differential leucocyte counts in horses receiving dosages of two hundred (200), four hundred (400), eight hundred (800) and sixteen hundred (1600) mg. of dichlorvos per kilogram of body weight or repeated recommended dosages have shown no significant differences in pre-treatment and post-treatment values.

Studies in healthy horses have shown that dichlorvos does not interfere with liver function at five (5) or ten (10) fold greater dosage than the recommended anthelmintic dosage as measured by sulfobromophthalein (BSP) clearance rates, serum

glutamic pyruvic transaminase (SGPT) and serum glutamic oxalic transaminase (SGOT) measurements.

The liver is the primary site of detoxification of dichlorvos in the body. An impairment by toxicants, parasites or infectious disease processes of this organ's function, lowers the tolerance for the drug in the body.

Phenothiazine derived tranquilizers or succinylcholine should not be administered shortly in advance of, in conjunction with, or within one (1) week of the administration of EQUIGARD (dichlorvos). Phenothiazine derived tranquilizers have shown a potentiating effect with organophosphates in rats and have been suspected of such action in man. Succinylcholine has been noted to increase the toxicity of given pharmacological effective dosages of organophosphates in horses.

EQUIGARD (dichlorvos) should not be administered to horses suffering from Chronic Alveolar Emphysema (Heaves) or related respiratory conditions in order to avoid acute respiratory embarrassments. (1,2,3,4,5,6,7,9,12)

REPRODUCTION

Pregnant mares receiving recommended anthelmintic dosages of EQUIGARD (dichlorvos) every two (2) months throughout gestation with a maximum of five (5) treatments, showed no adverse signs and all delivered normal foals at full term. The foals at thirty (30) days post-parturient time appeared normal and enjoyed a development rate comparable to the controls. Signs of toxicity, abortion or stillbirths were not observed. Similar mares treated with recommended dosages immediately after foaling, likewise, exhibited no reactions or changes in lactation resulting in adverse effects in the foals. The administration of fifty (50), one hundred (100) and two hundred (200) mg. of the active ingredient per kilogram of body weight to pregnant mares at various stages of gestation produced no observable deleterious effects to the mares or foals. (1,3,8)

PATHOLOGY

The administration of varying dosages of unformulated dichlorvos orally or parenterally for varying periods of time to rats, rabbits, swine and dogs produced no significant gross or histopathological changes in any of the organs or tissues. Occasionally, large oral dosages of the active ingredient will cause hyperemia and congestion of the stomach mucosa.

Post-mortem examinations of horses succumbing to lethal doses of EQUIGARD (dichlorvos) show varying degrees of gross pathology which is dosage related. Horses receiving EQUIGARD (dichlorvos) at twenty (20) times the recommended dosage or above single recommended dosage of EQUIGARD (dichlorvos) and repeated eight (8) to ten (10) days post-medication time.

Horses receiving dosages of sixteen hundred (1600) mg. of active ingredient per kilogram of body weight or forty (40) times the recommended dosage expired in one (1) to two (2) days time and exhibited more pronounced gross pathological changes. These changes were characterized by petechial hemorrhages, emphysema and congestion of the lungs, fatty degeneration of the liver, with marked hyperemia and inflammation of the gastrointestinal tract. Histopathological examination of tissues was consistent with the gross pathological findings. Nerve tissue showed no evidence of demyelination or other abnormalities. (1,2,3,10)

USE DIRECTIONS

EQUIGARD (dichlorvos) is designed to be administered in the grain portion of the ration. Preconditioning horses by fasting is not necessary or recommended. The preparation is generally consumed more rapidly if administered in a limited amount of the normal grain portion. The remainder of the grain may be offered after consumption of the medication. The preparation should be added to the feed immediately prior to administration.

The weight of each animal should be carefully determined and EQUIGARD (dichlorvos) added to the grain at the following dosage rates.

DOSAGE TABLE

Package Size	Active Ingredient (Dichlorvos) Grams	Lbs. Body Weight Treatment/Package
#2	3.2	200
#3	4.2	300
#5	6.6	500
#10	16.6	1,000

Horses of odd weights may be treated with a package or combination of packages that will provide a dosage of fourteen point two (14.2) mg. to eighteen point five (18.5) mg. of active ingredient per pound of body weight.

Critical anthelmintic studies in the horse have shown that one-half (1/2) of the above single recommended dosage of EQUIGARD (dichlorvos) and repeated eight (8)

Measurements of blood clotting time, per cent hematocrit, total leucocyte and differential leucocyte counts in horses receiving dosages of two hundred (200), four hundred (400), eight hundred (800) and sixteen hundred (1600) mg. of dichlorvos per kilogram of body weight or repeated recommended dosages have shown no significant differences in pre-treatment and post-treatment values.

Studies in healthy horses have shown that dichlorvos does not interfere with liver function at up to ten (10) fold greater dosage than the recommended anthelmintic dosage, as measured by sulfobromophthalein (BSP) clearance rates, serum

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EQUIGARD (dichlorvos) should not be administered to horses suffering from Chronic Alveolar Emphysema (Heaves) or related respiratory conditions in order to avoid further respiratory embarrassments. (1 2.3.4 5.6.7.9 12)

REPRODUCTION

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[illegible]	[illegible]	[illegible]
[illegible]	16.6	1,000

Horses of other weights may be treated with a package or combination of packages that will provide a dosage of fourteen point two (14.2) mg. to eighteen point five (18.5) mg. of active ingredient per pound of body weight.

Critical anthelmintic studies in the horse have shown that one-half (½) of the active single recommended dosage of EQUIGARD (dichlorvos) and repeated eight (8) to twelve (12) hours later provides equivalent anthelmintic efficacy and spectrum to that obtained by the single recommended dosage. This split dosage schedule of EQUIGARD (dichlorvos) eight (8) to twelve (12) hours apart has been demonstrated to be beneficial in the treatment of the very aged, emaciated or debilitated subjects or those reluctant to consume medicated feed. In suspected cases of severe ascarid infection sufficient to cause concern over mechanical blockage of the intestinal tract, the split dosage should be utilized.

The efficacy of EQUIGARD (dichlorvos) against **Parascaris equorum** has not been evaluated in foals (sucklings and young weanlings) due to their known variance in grain consumption and therefore, EQUIGARD (dichlorvos) is not recommended for them. The number of ascarids present in horses typically diminishes with the increasing age of the subject, but it has been documented that horses of all ages may harbor this parasite. Critical anthelmintic assays conducted in horses, other than nursing foals harboring **Parascaris equorum** populations, have demonstrated consistent high anthelmintic efficacy is achieved against such ascarid infections

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Critical studies have demonstrated consistent high efficacy against horse bots (**Gastrophilus intestinalis, G. nasalis**), provided all water is withheld four (4) to six (6) hours prior to administration and for three (3) hours after ingestion of the preparation. Variable efficacy against bots has been observed when water is available **ad lib.** The availability of water has no detrimental effect on activity against the other parasites.

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In the case of individual reluctance to consume medicated grain, sweetening agents such as molasses or honey may be added or the application of a small amount of Vicks Vapo Rub or similar preparations on the muzzle frequently will overcome such difficulties. 1 3 9 10 11

CONTRAINDICATIONS

Horses **severely debilitated** or suffering from diarrhea or severe constipation, infectious disease, toxemia or colic should not be treated until such conditions are corrected with proper therapy. Do not administer in conjunction with or within one (1) week of administration of muscle relaxant drugs (i.e., succinylcholine), phenothiazine derived tranquilizers or central nervous system depressant drugs. Horses should not be subjected to insecticide treatment for five (5) days prior to or after EQUIGARD (dichlorvos) treatment. Do not administer to horses afflicted with Chronic Alveolar Emphysema (Heaves) or related respiratory conditions. There are no other known contraindications for this preparation.

ATTENTION

EQUIGARD (dichlorvos) in critical anthelmintic and clinical studies has demonstrated excellent anthelmintic activity against the gastrointestinal parasites of major importance in horses in the United States. The drug is not a substitute for proper sanitary measures or management, but should be used in conjunction with such practices. When used in this capacity, EQUIGARD (dichlorvos) can be a valuable tool for the improvement of individual and herd health through the control and reduction in rate of contamination by parasite eggs in paddocks, pastures and other grazing areas.

Horses will become reinfected following treatment if they are returned to contaminated areas. The rate and degree of infection will be directly correlated to the life cycle of the parasite and exposure rate. Retreatment schedules with EQUIGARD (di-

per kilogram of body weight have been observed to be reversed within twenty four (24) to forty-eight (48) hours without antidotal or supportive therapy. The sign of toxicity from such dosages, most frequently observed that was of longer duration was a diarrhea. This condition was corrected with one (1) week's time without the aid of antidotal or supportive therapy.

The reversal of toxic signs comes about because the degradation of dichlorvos by the horse proceeds at a relatively constant rate below a threshold maximum. Mortality only results when the subject's detoxification threshold is suddenly reached or exceeded resulting in overwhelming the body's detoxification mechanism. 1 2 4 5 7 8 10

PHARMACOLOGY

The primary known pharmacologic effect of EQUIGARD (dichlorvos) is its ability to inhibit the enzyme cholinesterase. This action allows for overstimulation of the parasympathetic nervous system by the resultant accumulation of acetylcholine. The severity of the action is directly related to dosage.

Horses of all ages when administered the recommended dosage of EQUIGARD (dichlorvos) show a detectable drop in whole blood, red blood cell and plasma cholinesterase values one (1) to three (3) days post-treatment time. The magnitude of cholinesterase depression varies from horse to horse but is not of sufficient magnitude to interfere with normal neuro-physiological functions.

Normal or above normal cholinesterase values are often achieved within one (1) to three (3) weeks time in horses receiving active ingredient dosages of two hundred (200), four hundred (400), eight hundred (800) and sixteen hundred (1600) mg. per kilogram of body weight. Similar observations have been made in mares receiving two (2) to four (4) treatments at recommended dosages prior to foaling.

The exact significance of plasma or red blood cell cholinesterase depression in the horse is not known. Other animal species have been observed to survive long periods of time with no detectable whole blood cholinesterase values. Such measurements at best serve only to indicate that over a period of time small but significant amounts of the drug were absorbed from the digestive system into the bloodstream.

The cholinergic properties of dichlorvos increase the rate of peristalsis of the intestinal tract. The degree of this action is related to dosage. The recommended therapeutic dosage of EQUIGARD (dichlorvos) may produce several loose stools. These are transitory and result in early expulsion of dichlorvos susceptibe gastrointestinal parasites. Dosages greater than that recommended for high anti parasitic efficiency may cause diarrhea.

In a study conducted by Drummond and Jackson dosages of twenty five (25) mg and fifty (50) mg per kilogram of body weight unformulated dichlorvos administered to horses via stomach tube, produced signs of toxicity. The signs of toxicity at the twenty five (25) mg per kilogram dosage level became apparent within fifteen (15) minutes and were mild and of short duration. The higher dosage produced signs of toxicity within fifteen (15) minutes of administration which were of a more severe nature and were apparent for two (2) days. When unformulated dichlorvos was administered in feed, signs of toxicity were not observed.

The oral LD_{50} of EQUIGARD (dichlorvos) administered in feed is unknown. Horses do not consume sufficient quantities to produce acute toxic effects resulting in death. When offered feed containing five (5) to forty (40) times the recommended anthelmintic dosage of the drug, the maximum consumption observed in a single horse was six hundred forty-eight (648) mg active ingredient per kilogram of body weight. The LD_{50} for forced oral administration of EQUIGARD (dichlorvos) was found to be more than eight hundred (800) and less than sixteen hundred (1600) mg of active ingredient per kilogram of body weight.

The most frequent signs of dichlorvos toxicity in horses are hypermotility of the intestine with diarrhea, pupillary contraction (miosis), dyspnea, generalized perspiration, severe abdominal pain and neurological manifestations characterized by lethargy, ataxia, muscular fasciculations and paralysis. These signs are followed by a fall in blood pressure and respiration rates, the latter apparently being the immediate cause of death.

The cardinal signs of toxicity produced by massive single doses of EQUIGARD (dichlorvos) on the order of four hundred (400) to eight hundred (800) mg of dichlorvos

chlorvos) are at the discretion of the veterinarian whose decision should be based on accurate fecal examinations, clinical symptoms, herd history and management.

WARNING

Use contents immediately after opening package. Do not store unused drug or feed containing EQUIGARD (dichlorvos). Avoid contact with the skin. Do not use in animals other than horses, ponies and mules. Do not use in horses, ponies and mules intended for food purposes. Do not allow fowl access to feed containing this preparation or to fecal excrement from treated animals.

EQUIGARD (dichlorvos) is a cholinesterase inhibitor. Do not use this product in animals simultaneously or within a few days before or after treatment with or exposure to cholinesterase inhibiting drugs, pesticides or chemicals. Atropine is the antidote for animals. Atropine and 2-PAM are human antidotes.

CAUTION

Keep out of the reach of children. For veterinary use only. U. S. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

PACKAGE SIZES

Package No.	Active Ingredient		
#2	3.2 Gram Package	10 Packages Box	10 Boxes Carton
#3	4.7 Gram Package	10 Packages Box	10 Boxes Carton
#5	8.3 Gram Package	5 Packages Box	10 Boxes Carton
#10	16.6 Gram Package	5 Packages Box	10 Boxes Carton

STORE PACKAGES IN A COOL PLACE (LESS THAN 80 F)

U. S. Patent Nos. 2 956 073, 3,166,472, 3,318 769

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SHELL CHEMICAL COMPANY
A Division of Shell Oil Company
AGRICULTURAL DIVISION
SAN RAMON, CALIFORNIA, U. S. A. 94583

ACL 1210A 4-71

EQUIGARD®

(DICHLORVOS)

EQUINE ANTHELMINTIC

DESCRIPTION

EQUIGARD® (dichlorvos) Equine Anthelmintic is a highly effective anthelmintic recommended for the removal and control of bots (**Gastrophilus intestinalis, G. nasalis**), large strongyles (**Strongylus vulgaris, S. equinus, S. edentatus**), small strongyles (of the genera **Cyathostomum, Cylicocercus, Cylicocyclus, Cylicodontophorus, Triodontophorus, Poteriostomum, Gyalocephalus**) and pinworms (**Oxyuris equi**). EQUIGARD (dichlorvos) has been demonstrated to be active against the ascarid (**Parascaris equorum**) in those animals consuming sufficient grain to ingest the therapeutic dosage. Due to known variability in grain consumption, EQUIGARD (dichlorvos) is not recommended for foals (sucklings and young weanlings) nor has

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EQUIGARD (dichlorvos) is an uncoated, grain-shaped resin pellet approximating one-eighth ($\frac{1}{8}$) inch in length and one-twentieth ($\frac{1}{20}$) inch in diameter, the active ingredient of which is 2,2-dichlorovinyl dimethyl phosphate (dichlorvos). The preparation is designed for administration to horses in limited amounts of the grain portion of the ration. The design is such that when used according to directions, the active ingredient release rate is sufficient to provide for high anti-parasitic efficiency, but not of such magnitude to exceed the degrading (detoxification) capacity of the horse. This provides a wide margin of safety for use in horses. Its use in animals other than the horse, pony and mule is contraindicated. (1,3,4,5,7,8,9,10,11)

PALATABILITY

EQUIGARD (dichlorvos) at recommended dosage levels administered in grain has been found to be palatable to the majority of horses. An occasional horse has been observed that refuses grain with any added foreign substance. In cases of individual reluctance to consume medicated feed, acceptability may be increased by the addition of flavoring agents such as molasses or honey to the feed or by applying a small amount of Vicks Vapo Rub or a similar preparation on the muzzle of the animal. (1,3,8,9,10,11)

RAPIDITY OF ACTION: PARASITE EXPULSION TIME

EQUIGARD (dichlorvos) pellets are non-digestible and may be observed in feces from treated horses as soon as ten (10) hours following administration. The average time for the first appearance of pellets following administration is about twenty four (24) hours. Dead parasites first appear in the stool eighteen (18) to twenty-four (24) hours after administration and continue for another forty-eight (48) to seventy-two (72) hours. Strongyle egg counts start to decrease after twenty-four (24) hours and usually drop to zero (0) within forty-eight (48) to seventy-two (72) hours following treatment (3,8,9,10,11)

STABILITY

The active ingredient, 2,2-dichlorovinyl dimethenyl phosphate, is a volatile substance which is susceptible to destruction by oxidizing agents and hydrolysis. EQUIGARD (dichlorvos) is stable when stored in original, unopened packages at temperatures below 80 F. It is recommended that EQUIGARD (dichlorvos) be added to the grain portion of the ration immediately prior to administration. Unused contents in opened packages of grain containing the preparation should not be stored for future use

TOXICOLOGY

The oral LD_{50} of unformulated dichlorvos for animals falls in a range from fifty (50 to three hundred sixteen (316) mg. per kilogram of body weight.

In a study conducted by Drummond and Jackson, dosages of twenty-five (25) mg. and fifty (50) mg. per kilogram of body weight, unformulated dichlorvos administered to horses via stomach tube, produced signs of toxicity. The signs of toxicity at the twenty-five (25) mg. per kilogram dosage level became apparent within fifteen (15) minutes and were mild and of short duration. The higher dosage produced signs of toxicity within fifteen (15) minutes of administration which were of a more severe nature and were apparent for two (2) days. When unformulated dichlorvos was administered in feed, signs of toxicity were not observed.

The oral LD_{50} of EQUIGARD (dichlorvos) administered in feed is unknown. Horses do not consume sufficient quantities to produce acute toxic effects resulting in death. When offered feed containing five (5) to forty (40) times the recommended anthelmintic dosage of the drug, the maximum consumption observed in a single horse was six hundred forty-eight (648) mg. active ingredient per kilogram of body weight. The LD_{50} for forced oral administration of EQUIGARD (dichlorvos) was found to be more than eight hundred (800) and less than sixteen hundred (1600) mg. of active ingredient per kilogram of body weight.

The most frequent signs of dichlorvos toxicity in horses are hypermotility of the intestine with diarrhea, pupillary contraction, photophobia, generalized perspira-

WARNING

Use contents immediately after opening package. Do not store unused drug or feed containing EQUIGARD (dichlorvos). Avoid contact with the skin. Do not use in animals other than horses, ponies and mules. Do not use in horses, ponies and mules intended for food purposes. Do not allow fowl access to feed containing this preparation or to fecal excrement from treated animals.

EQUIGARD (dichlorvos) is a cholinesterase inhibitor. Do not use this product in animals simultaneously or within a few days before or after treatment with or exposure to cholinesterase inhibiting drugs, pesticides or chemicals. Atropine is the antidote for animals. Atropine and 2-PAM are human antidotes.

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PALATABILITY

EQUIGARD (dichlorvos) at recommended dosage levels administered in grain has been found to be palatable to the majority of horses. An occasional horse has been observed that refuses grain with any added foreign substance. In cases of individual reluctance to consume medicated feed, acceptability may be increased by the addition of flavoring agents such as molasses or honey to the feed, or by applying a small amount of Vicks® Vapo-Rub or a similar preparation on the muzzle of the animal. (1,3,8,9,10,11)

RAPIDITY OF ACTION: PARASITE EXPULSION TIME

EQUIGARD (dichlorvos) pellets are non-irritating and may be observed in feces from treated horses as soon as ten (10) hours following administration. The average time for the first appearance of pellets following administration is about twenty-four (24) hours. Dead parasites first appear in the feces between 18 to twenty-four (24) hours after administration and continue for another forty-eight (48) to seventy-two (72) hours. Strongyle egg counts start to increase after twenty-four (24) hours and usually drop to zero (0) within forty-eight (48) to seventy-two (72) hours. (3,8,9,10,11)

STABILITY

The active ingredient 2,2-dichlorovinyl dimethyl phosphate is a volatile substance which is susceptible to destruction by oxidizing agents and hydrolysis. EQUIGARD (dichlorvos) is stable when stored in airtight, unopened packages at temperatures below 80° F. It is recommended that EQUIGARD (dichlorvos) be added to the grain portion of the ration immediately prior to administering. Unused, opened packages of grain containing the preparation should not be stored for future use.

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The cardinal signs of toxicity produced by excessive dosages of EQUIGARD (dichlorvos) on the order of four hundred 400 to five hundred 500 mg. of dichlorvos are at the discretion of the veterinarian based on accurate fecal examinations, clinical symptoms, history and observation. The most frequent signs of dichlorvos toxicity in horses are hypermotility of the intestine with diarrhea, pupillary contraction, pulse rate increased, perspiration, severe abdominal pain and neurological manifestations characterized by ataxia, muscular fasciculations and palsy. These signs are followed by a fall in blood pressure and respiration rates, the latter apparently being the immediate cause of death.