ENVIRONMENTAL IMPACT ANALYSIS REPORT

NADA 7-891

3-Nitro® Premixes

3-Nitro®-10, 3-Nitro® Pig-Pak, 3-Nitro®-20,
3-Nitro®-50, and 3-Nitro®-80

For Increased Rate of Weight Gain and Improved Feed Efficiency For Growing Chickens, For Growing Turkeys, and Growing-Finishing Swine. For Improved Pigmentation of Growing Chickens and Growing Turkeys. An Aid In the Treatment of Swine Dysentery (Hemorrhagic Enteritis or Bloody Scours).

SALSBURY LABORATORIES, INC.
2000 Rockford Road
Charles City, Iowa 50616

March 2, 1981

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A. DATE:

March 2, 1981.

B. NAME OF APPLICANT/PETITIONER:

Salsbury Laboratories, Inc.

C. ADDRESS:

2000 Rockford Road
Charles City, Iowa 50616.

D. ENVIRONMENTAL INFORMATION:

1. Describe the Proposed Action:

a. Purpose of the Action:

The proposed action is the manufacture of 3-Nitro® Premixes (3-Nitro®-10, 3-Nitro® Pig-Pak, 3-Nitro®-20, 3-Nitro®-50, and 3-Nitro®-80), active ingredient Roxarsone, which will be administered via the feed to growing chickens and growing turkeys for increased rate of weight gain, improved feed efficiency, and improved pigmentation, and to growing-finishing swine for increased rate of weight gain and improved feed efficiency, and as an aid in the treatment of swine dysentery (Hemorrhagic Enteritis or bloody scours).

The products, 3-Nitro® Premixes, are made by blending the active ingredient, 3-Nitro-4-Hydroxyphenylarsonic Acid (Roxarsone), with the inactive ingredient, grain by-products. 3-Nitro®-10 is packaged in a 50-pound bag, 3-Nitro® Pig-Pak is packaged in a 12-ounce pouch, 3-Nitro®-20 is packaged in a 50-pound bag, 3-Nitro®-50 is packaged in a 20-pound bag and a 50-pound bag, and 3-Nitro®-80 is packaged in a 50-pound bag.

3-Nitro®-10 and 3-Nitro® Pig-Pak contain 10% Roxarsone, 3-Nitro®-20 contains 20% Roxarsone, 3-Nitro®-50 contains 50% Roxarsone, and 3-Nitro®-80 contains 80% Roxarsone. The products are administered via the feed to growing chickens, growing turkeys, and growing-finishing swine.

For increased rate of weight gain, improved feed efficiency, and improved pigmentation for growing chickens and growing turkeys, use:

Product	Amount per Ton	Roxarsone Concentration in Finished Feed
3-Nitro®-10	1/2 lb (8 oz) to 1 lb (16 oz)	0.0025% to 0.005% (22.7 gm to 45.4 gm)
3-Nitro®-20	4 oz (1/4 lb) to 8 oz (1/2 lb)	0.0025% to 0.005% (22.7 gm to 45.4 gm)
3-Nitro®-50	1.6 oz (1/10 lb) to 3.2 oz (1/5 lb)	0.0025% to 0.005% (22.7 gm to 45.4 gm)
3-Nitro®-80	1 oz (1/16 lb) to 2 oz (1/8 lb)	0.0025% to 0.005% (22.7 gm to 45.4 gm)

For increased rate of weight gain and improved feed efficiency in growing-finishing swine, use:

Product	Amount per Ton	Roxarsone Concentration in Finished Feed
3-Nitro®-10	1/2 lb to 3/4 lb	0.0025% to 0.00375% (22.7 gm to 34.1 gm)
3-Nitro® Pig-Pak	3/4 lb (12 oz)	0.00375% (34.1 gm)
3-Nitro®-20	4 oz (1/4 lb) to 6 oz	0.0025% to 0.00375% (22.7 gm to 34.1 gm)
3-Nitro®-50	1.6 oz (1/10 lb) to 2.4 oz	0.0025% to 0.00375% (22.7 gm to 34.1 gm)
3-Nitro®-80	1 oz to 1-1/2 oz	0.0025% to 0.00375% (22.7 gm to 34.1 gm)

As an aid in the treatment of swine dysentery, use:

Product	Amount per Ton	Roxarsone Concentration in Finished Feed
3-Nitro®-10	4 lb	0.02% (181.5 gm)
3-Nitro®-20	2 lb	0.02% (181.5 gm)
3-Nitro®-50	12.8 oz (4/5 lb)	0.02% (181.5 gm)
3-Nitro®-80	8 oz (1/2 lb)	0.02% (181.5 gm)

b. Environment to be Affected if the Action is Taken:

The environment affected by the 3-Nitro® Premixes is a portion of the growing chicken and growing turkey population and a portion of the swine population.

3-Nitro® Premixes have been marketed by Salsbury Laboratories, Inc., as an approved drug since March 23, 1951. The product has been marketed and used since that time.

The continued marketing of the 3-Nitro® Premixes will not change the overall use pattern or the existing market for the product subject to this Environmental Impact Analysis Report.

2. Discuss the Probable Impact of the Proposed Action on the Environment, Including Primary and Secondary Consequences:

a. Describe the Probable Adverse and Beneficial Envrionmental Effects of the Use, Consumption, and Disposal of the Article That is the Subject of the Action, Including, But Not Limited To, the Following Areas of Environmental Impact (Where Applicable):

(1) Pollution (Air, Water, Soil):

(a) Air:

The use of 3-Nitro® Premixes in growing chickens, growing turkeys, and swine has had neither an adverse nor a beneficial effect on air quality.

Roxarsone does not diffuse from the 3-Nitro® Premixes, the drug dosage form, nor does it diffuse

from the medicated feed or the excreta of the medicated animals.

(b) Water:

The use of 3-Nitro® Premixes in growing chickens, growing turkeys, and swine has had neither an adverse nor a beneficial effect on water quality.

Poultry and swine excreta is not permitted to be discharged into waterways, so there is no direct addition of the residual product to the water. Inadvertent pollution of water streams with poultry and swine waste should not result in the contamination of water.

Morrison (1969) reported that the arsenic content of ground water was apparently unaffected by treatment of the soil with poultry house litter, and he stated that this was in agreement with published data for natural arsenic levels in the water. The data was obtained by taking samples of soil from a control field (no litter used) and samples of soil and water from a field treated for 20 years with arsenical-containing poultry house litter. Total arsenic assays were performed on the samples. The amount of arsenic found in the drainage water samples from the treated field was 0.29 p.p.m., while the average of the three control samples was 0.97 p.p.m.

(c) Soil:

The use of 3-Nitro® Premixes in growing chickens, growing turkeys, and swine has had neither an adverse nor a beneficial effect on soil.

In comparing the arsenic content of soil samples from a control field (no litter used) and from a field treated for 20 years with arsenical-containing poultry house litter, Morrison (1969) found 2.65 p.p.m. arsenic and 1.83 p.p.m. arsenic, respectively. Total arsenic assays were performed on the samples. Morrison concluded that the arsenic content of the soil was apparently unaffected by treatment of the soil with poultry house litter. He further stated that this was in agreement with published data for natural arsenic levels in soil.

(2) Solid and Liquid Wastes (Compliance):

The use of 3-Nitro® Premixes in growing chickens, growing turkeys, and swine has had neither an adverse nor a beneficial effect on solid and liquid wastes.

As indicated above, 2.a.(1)(b) and (c), the disposal of poultry and swine wastes by treatment of the soil with litter has had no effect on the arsenic content of soil or water.

In that this is the primary way in which litter is disposed of, it can be concluded that the use of 3-Nitro® Premixes has not effected the solid or liquid waste problems.

(3) Toxic Substances (Heavy Metals, Pesticides, Radiation):

3-Nitro® Premixes (Roxarsone) have been adequately researched for safety in domestic animals and man.

Kerr, Cavett, and Thompson (1963) evaluated the acute and subacute toxicity of 3-Nitro-4-Hydroxyphenylarsonic Acid. The acute oral toxicity was studied in four species: the chicken, the turkey, the rat, and the dog. The acute intraperitoneal toxicity studies were conducted in the chicken and in the rat. The subacute toxicity was studied in two species: the chicken and the rat.

The acute oral LD_{50} was reported to be 100 mg/kg in three-week-old chickens, and 123 mg/kg in twelve-week-old chickens. In turkeys, the acute oral LD_{50} was 61 mg/kg. In the rat, it was 155 mg/kg, and in dogs, it was 50 mg/kg.

The acute intraperitoneal LD_{50} was 34 mg/kg in chickens and 66 mg/kg in rats.

The thirteen-week subacute toxicity studies in chickens and rats at 25, 50, 100, 200, and 400 p.p.m. showed that the highest dosage caused mortality in both species. The 200 p.p.m. dosage did not affect the growth or feed utilization of either species. The chicken showed a postural effect at the 200 p.p.m. dosage. There was no effect on the rat hematology at any dosage, and no microscopic pathology attributable to the compound could be detected in either species.

Chronic oral toxicity studies in dogs, rats, and mice; a chronic dermal toxicity study in mice; and a subcutaneous toxicity study in mice were reported by Prier, Nees, and Derse (1963).

They found that no detectable effect resulted from the oral ingestion, over a two-year period, of 3-Nitro-4-Hydroxyphenylarsonic Acid at levels of 50 and 100 p.p.m. in the dog or mouse. In the rat, no effect was seen at 50 p.p.m., and a mild, and only early, growth rate depression was the sole result of ingestion at the 200 p.p.m. level.

A single massive subcutaneous injection induced no toxic findings over a two-year observation period.

A topical application at approximately one mg per mouse, three times a week for one year, was without effect over the two-year observation period.

Salsbury Laboratories, Inc., Research Division, Biological Development Department, conducted a three-generation study in rats (RRT-55-70). In this study, groups of rats in each generation were given 0, 50, 100, and 200 p.p.m. 3-Nitro-4-Hydroxyphenylarsonic Acid continuously in their feed.

The results reported show no essential difference between the groups in fertility, ratio of dead pups to number of pups born, litter size, and pup body weights at weaning. Caesarean sections were conducted on some of the rats in the F_{1B}, F_{2B}, and F_{3B} generations. The examination of the dams and the fetuses did not reveal any indication of mutagenicity and teratogenicity attributable to Roxarsone.

Under the conditions of this experiment, Roxarsone was not embryo toxic, mutagenic, nor teratogenic when given continuously in the feed to rats at dosage levels of 50, 100, and 200 p.p.m. during the three-generation study.

Moody and Williams (1965) reported on the metabolism of 3-Nitro-4-Hydroxyphenylarsonic Acid in hens.

They reported that when administered orally to hens, it was relatively slowly excreted. At a dose level of about 19 mg/kg, nearly 50% was excreted in 24 hours;

at 38 mg/kg, 37%; and at 75 mg/kg, about 25%. About nine to eleven days were required for the complete excretion of a single oral dose of 75 mg/kg.

On intramuscular injection, they found the compound to be lethal at a dose of 38 mg/kg. However, it was much more rapidly excreted on injection than on oral dosing, and of an intramuscular dose of 19 mg/kg, 80% was excreted in 24 hours, and over 95% in three days.

The only transformation product of 3-Nitro-4-Hydroxyphenylarsonic Acid found in the excreta was 3-Amino-4-Hydroxyphenylarsonic Acid, and this amounted to 18% of the dose (nearly 25% of the output) in three days after an oral dose of 19 mg/kg.

Moody and Williams further reported that on injection, 3-Nitro-4-Hydroxyphenylarsonic Acid was mainly excreted unchanged, and the amount of the amino compound excreted being only about 4% of the dose.

They also found that the extent of reduction depended upon diet, with it being lower in starved hens than in well-fed hens. The reduction of 3-Nitro-4-Hydroxyphenylarsonic Acid appeared to take place mainly in the crop, and it appeared that this organ also controlled the elimination of the compound when given orally. A comparison of the elimination of the drug with that of polyethylene glycol suggested that it was poorly absorbed in the hen. Analyses of the total arsonic acid and total arsenic excretion indicated that the compound was stable in vivo.

From the discussion of the results of the safety tests reported above, it can be concluded that, from a toxic substances standpoint, 3-Nitro® Premixes will have neither an adverse nor a beneficial effect on the environment.

(4) Populations (Human, Animal, Plant):

Human exposure to the 3-Nitro® Premixes (Roxarsone) can occur only by the consumption of the 3-Nitro® Premix-medicated feed or by the ingestion of excreta from medicated animals.

Plant life will be exposed only as the 3-Nitro® Premix (Roxarsone) in the excreta is used to spread on crop land.

(a) Humans:

The only probably adverse effect on the human population arising from the use of 3-Nitro® Premixes (Roxarsone) in poultry and swine feeds is the residues of the compound which may be present in the food of man.

The safety of Roxarsone is further addressed in 2.a.(3) above.

This product is on the market, and specific tolerances for residues in food-producing animals have been set. These tolerances are published in 21 CFR § 556.60 Arsenic, and read as follows:

> Tolerances for total residues of combined arsenic (calculated as As) in food are established as follows:
>
> (a) In edible tissues and in eggs of chickens and turkeys:
>
> (1) 0.5 part per million in uncooked muscle tissue.
>
> (2) 2 parts per million in uncooked edible by-products.
>
> (3) 0.5 part per million in eggs.
>
> (b) In edible tissues of swine:
>
> (1) 2 parts per million in uncooked liver and kidney.
>
> (2) 0.5 part per million in uncooked muscle tissue and by-products other than liver and kidney.

Therefore, there is no adverse effect on the human population from this action.

(b) Animals:

As discussed in the previous section on toxic substances, D.2.a.(3), Roxarsone reveals an adequate margin of safety in animals.

To substantiate the safety of Roxarsone for the target species (chickens), a study was conducted by Salsbury Laboratories, Inc., Research Division, Pharmaceutical Development and Analysis Department (TR-382-73, December 7, 1973, unpublished) to determine the total arsenic residues in chickens medicated with Roxarsone. In the study, 150 medicated birds were observed for signs of toxicity during a ten-day medication period. The birds received 3-Nitro-4-Hydroxyphenylarsonic Acid at a level of 0.008%, which is four times higher than the recommended production level for the product in question. There was no mortality observed, nor were there any signs of toxicity observed. Furthermore, there were no gross pathological lesions indicative of a toxic effect of the drug in any of the birds posted for tissue samples at the termination of the trial.

Another report which supports the safety of Roxarsone to animals is the paper by Kerr, Cavett, and Thompson (1963), discussed above, D.2.a.(3). This study includes the results of an over-dosage study in chickens conducted for a thirteen-week period at 25, 50, 100, 200, and 400 p.p.m. Roxarsone which shows the drug to have in excess of a two-times margin of safety.

To further substantiate the safety of Roxarsone for the target species (swine), a study was conducted by Salsbury Laboratories, Inc., Research Division, Pharmaceutical Development and Analysis Department (TR-391-75, October 24, 1975, unpublished) to determine the total arsenic residues in swine medicated with Roxarsone. In the study, eight swine, weighing approximately 75 pounds each, were medicated with Roxarsone at the prophylactic level (0.00375%) for ten days prior to the initiation of the treatment level. The swine were then medicated with Roxarsone at twice the treatment level (0.02%) for six days. There was no mortality observed, nor were there any signs of toxicity observed. Furthermore, there were no gross pathological lesions indicative of a toxic effect of the drug in any of the pigs posted for tissue samples at the termination of the trial.

Therefore, it can be concluded that the 3-Nitro® Premixes are safe for animals, and there will be no adverse effects on the animal population from this action.

(c) Plants:

Morrison (1969) reported on the distribution of arsenic in crops raised on soils fertilized with litter containing organoarsenicals. The study reported that, although measurable amounts of arsenic (15 to 30 p.p.m.) were found in the litter, the arsenic content of the soil and crops was unaffected by the use of litter as fertilizer.

Morrison found that the arsenic content of the forage crops studied contained less than 0.2 p.p.m. arsenic regardless of the extent of litter treatment of the soil.

Therefore, it can be concluded that there will be no adverse effect on the plant population from this action.

(5) Human Values:

The quality of the environment in terms of the human values, e.g., the effects on public health, effects on endangered species, effects on historical places, and compliance with local ordinances, will not be adversely affected by the projected use of 3-Nitro® Premixes.

(6) Food Contamination:

3-Nitro® Premixes are fed to growing chickens, growing turkeys, and swine. Consequently, the only probable effect on food contamination is the residues of the compound which may be present in the meat of chickens, turkeys, and swine.

3-Nitro® Premixes are currently on the market, and specific tolerances for residues in food-producing animals have been set. These tolerances are published in 21 CFR § 556.60 Arsenic. Refer to D.2.a.(4)(a).

Therefore, there is no adverse effect on food contamination.

(7) Natural Resources:

There will be no adverse environmental effects on the use and/or accessibility of natural resources as a result of the use of the 3-Nitro® Premixes.

(8) Energy:

There will not be a direct impact on the energy supply or the utilization of that energy supply as related to the proposed use of the 3-Nitro® Premixes.

b. Describe Measures Taken to Avoid or Mitigate Potential Adverse Environmental Effects:

If the 3-Nitro® Premixes are used in accordance with label directions, adverse environmental consequenses are not likely to occur. To insure the proper use, the label bears a Precaution Statement, a Warning Statement, and a Poison-Arsenic Statement to further emphasize the proper use of the 3-Nitro® Premixes.

c. Analyze the Environmental Impact of the Manufacturing Process(es) of the Article that is the Subject of the Requested Action:

The manufacturing of the 3-Nitro® Premixes takes place in the Day Mixer.

The Day Mixer has a completely-enclosed dust-collecting system. The dust-collecting system has a State of Iowa Permit Number 76-A-063. The dust collected is saved and incorporated into future batches of the product in accordance with Good Manufacturing Practices.

The Day Mixer is vacuum-cleaned, and the cleanings are saved and incorporated into future batches of the product in accordance with Good Manufacturing Practices.

(1) An Identification of the Pollutants Expected to be Emitted:

Specific answers to this item were submitted to our 3-Nitro®-W New Animal Drug Application (NADA 93-025) File in a letter dated May 21, 1979.

This data and information are protected from disclosure by 18 U.S.C. 1905 or 21 U.S.C. 331(j), and need not be included in the environmental documents

prepared under 21 CFR Part 25. See: 21 CFR § 25.1(l) and the FEDERAL REGISTER, Volume 44, No. 239, Tuesday, December 11, 1979, page 71747, 21 CFR § 25.30(b).

(2) A Citation of Applicable Federal, State, and Local Emission Requirements:

(a) Air:

Air emissions are controlled by the Iowa Department of Environmental Quality (IDEQ).

The Iowa Department of Environmental Quality (IDEQ) makes an annual inspection of all air emissions.

We are in compliance.

(b) Waste Water:

Waste water discharges are controlled by the Iowa Department of Environmental Quality (IDEQ).

The Salsbury Laboratories' waste water is discharged to the Charles City Municipal Wastewater Treatment Plant. This plant is permitted by the Iowa Department of Environmental Quality (IDEQ) under the National Pollutant Discharge System (NPDES). Their Permit Number is 34-05-0-01. The State of Iowa is authorized to issue this permit by the Environmental Protection Agency (EPA) under the Clean Water Act.

(c) Landfill:

Salsbury Laboratories' Environmental Protection Agency (EPA) I.D. Number is IAD005275540.

Salsbury Laboratories' solid waste disposal is under contract with a waste acceptance firm, and the waste is disposed of near Livingston, Alabama.

The Landfill is owned by Chemical Waste Management, Inc., a wholly-owned subsidiary of Waste Management, Inc. Chemical Waste Management, Inc.

is permitted by the Environmental Protection Agency (EPA), and their EPA I.D. Number is ALT000622464. They are also permitted by the State of Alabama under a Hazardous Waste Disposal Facility Permit Number 78.1.

(3) A Certification that Such Emissions Will Comply With Said Requirements:

This statement is to certify that the Salsbury Laboratories' emissions, referred to above, will comply with the cited requirements.

Therefore, it can be concluded that the manufacturing process(es) will have no adverse effects on the environment.

d. Specific Data, Including Pertinent References, Shall be Included to Substantiate the Information Provided Above:

(1) Cavett, J. W., "Biochemical Studies of Arsenicals", Dr. Salsbury's Laboratories, 1960. (Unpublished).

(2) Food and Cosmetic Toxicology, 2:211-247, 1964, "More on Organic Arsenicals".

(3) Kerr, K. B., J. W. Cavett, and Owen L. Thompson, "The Toxicity of an Organic Arsenical, 3-Nitro-4-Hydroxyphenylarsonic Acid. I. Acute and Subacute Toxicity", Toxicology and Applied Pharmacology, 5:507-525, 1963.

(4) Kerr, K. B., J. R. Narveson, and F. A. Lux, "Toxicity of an Organic Arsenical, 3-Nitro-4-Hydroxyphenylarsonic Acid: Residues in Chicken Tissues", Agricultural and Food Chemistry, 17(6):1400, November/December 1969.

(5) Kerr, K. B., Research Technical Memorandum No. 143, "Evaluation of the Safety of Roxarsone Residues in Chicken Tissues for Human Consumption", Salsbury Laboratories, 1969. (Unpublished).

(6) Kerr, K. B., "Arsenic and Arsenical Residues in Soil", Dr. Salsbury Laboratories. (Unpublished).

(7) McGuire, W. C., Research Technical Memorandum No. 69, "Evaluation and Usage of Dr. Salsbury's Products in Game Birds", Dr. Salsbury's Laboratories, 1962. (Unpublished).

(8) Moody, J. P., and R. T. Williams, "The Metabolism of 4-Hydroxy-3-Nitrophenylarsonic Acid in Hens", Food and Cosmetics Toxicology, 2:707:715, 1964.

(9) Morehouse, Neal F., and Orley J. Mayfield, "The Effect of Some Aryl Arsonic Acids on Experimental Coccidiosis Infection in Chickens", Journal of Parasitology, 32(1): 20-24, February 1946.

(10) Morehouse, Neal F., "Accelerated Growth in Chickens and Turkeys Produced by 3-Nitro-4-Hydroxyphenylarsonic Acid", Poultry Science, 28(3):375-384, May 1949.

(11) Morehouse, Neal F., and F. McKay, "On the Chemotherapeutic Action of 3-Nitro-4-Hydroxyphenylarsonic Acid Against the Coccidium Eimeria Tenella in Chickens", Iowa Academy of Science, 48:507-516, 1951.

(12) Morehouse, Neal F., Research Technical Memorandum No. 38, "Progress Report on the Use of 3-Nitro Products in the Feed of Ring-Neck Pheasants", Dr. Salsbury's Laboratories, 1956. (Unpublished).

(13) Morehouse, N. F., Research Technical Memorandum No. 48, "Experimental Administration of 3-Nitro to Calves", Dr. Salsbury's Laboratories, 1957. (Unpublished).

(14) Morehouse, Neal F., Max W. Moeller, and Donald E. Dexheimer, "Arsonic Acids for Swine. A Review of Published Information on the Effect of Arsonic Acids on Growth, Feed Utilization, the Prevention and Control of Swine Dysentery, and on Other Factors Influencing the Development of Swine", Dr. Salsbury Laboratories, July 1, 1962. (Unpublished).

(15) Morrison, J. L., "Arsenic Residues in Tissues of Swine Medicated with 3-Nitro®-10 at Various Levels", Dr. Salsbury Laboratories, 1967. (Unpublished).

(16) Morrison, Joseph L., and Glenn M. George, "Dry Ashing Method for the Determination of Total Arsenic in Poultry Tissues", Journal of Association of Official Analytical Chemists, 52:930-932, September 1969.

(17) Morrison, Joseph L., "Distribution of Arsenic from Poultry Litter in Broiler Chickens, Soil, and Crops", Agricultural and Food Chemistry, 17:1288-1290, November/December 1969.

(18) Morrison, J. L., "The Effect of the Use of Poultry Litter on the Arsenic Content of Feathers, Soil, and Crops", Dr. Salsbury Laboratories, 1969. (Unpublished).

(19) Prier, R. F., P. O. Nees, and P. H. Derse, "The Toxicity of an Organic Arsenical, 3-Nitro-4-Hydroxyphenylarsonic Acid. II. Chronic Toxicity", Toxicology and Applied Pharmacology, 5(4):526-542, 1963.

(20) Rueber, H. W., and F. A. Lux, "Veterinary Arsenicals", Iowa State University Veterinarian, 28(1):13-18, 1966.

(21) Salsbury Laboratories, New Drug Application Allowing the Use of Roxarsone in Parakeets and Pigeons. Transmittal Letter, dated June 13, 1954.

(22) Salsbury Laboratories' Research Division, Biological Development Department. Rat Reproduction Test No. RRT-55-70, "A Three-Generation Study in Rats Given 3-Nitro-4-Hydroxyphenylarsonic Acid (Roxarsone) in Their Feed", 1970. (Unpublished).

(23) Salsbury Laboratories, "Total Arsenic Residues in Turkeys Medicated with Roxarsone in the Feed at Various Levels". (Unpublished).

(24) Salsbury Laboratories' Research Division, Pharmaceutical Development and Analysis Department. Research Report No. TR-382-73, "Total Arsenic Residues in Chickens with Ren-O-Sal® Tablets for Drinking Water (Roxarsone)", December 7, 1973. (Unpublished).

(25) Swinehart, Carl, Coordinator, "A New Look at Organic Arsenicals", Feed Age, 10(5):39-51, May 1960.

(26) Walde, Eunice C., Research Technical Memorandum No. 26, "3-Nitro-4-Hydroxyphenylarsonic Acid", Dr. Salsbury Laboratories, 1955. (Unpublished).

(27) Zietlow, David C., and Joseph L. Morrison, Research Technical Memorandum No. 145, "A Method for the Analysis of Nitro Arsonic Acids and Their Amino Metabolites in Animal Tissues", Salsbury Laboratories, 1969. (Unpublished).

All unpublished references have been submitted to our 3-Nitro-4-Hydroxyphenylarsonic Acid Master File (MF-19) and/or our New Animal Drug Application File (NADA 7-891).

3. Describe the Probable Adverse Environmental Effects That Cannot Be Avoided:

To the best of our knowledge, there are no known probable adverse environmental effects from the manufacture or use of the 3-Nitro® Premixes when the manufacturer's directions are followed for the manufacturing procedures as well as for the use of the product.

4. Evaluate Alternatives to the Proposed Action:

Roxarsone, the active ingredient of the 3-Nitro® Premixes, is certainly one of the most efficient, if not the most efficient, compound available to the animal production industry as related to increased rate of weight gain, improved feed efficiency, and improved pigmentation in growing chickens, growing turkeys, and swine.

There are other products available as alternates to the proposed action; however, they are more effective because of their antibiotic claims. Their primary use is not in the area of increased rate of weight gain, improved feed efficiency, or improved pigmentation.

5. Describe the Relationship Between Local Short-Term Use of the Environment with Respect to the Proposed Action and the Maintenance and Enhancement of Long-Term Productivity:

The use of the 3-Nitro® Premixes does not result in any long-term cumulative losses or pose long-term risks to health or safety.

The short-term benefits; therefore, are not at the expense of long-term deterioration of the environment.

6. Describe Any Irreversible and Irretrievable Commitment of Resources That Would Be Involved if the Proposed Action Should Be Implemented:

Other than the insignificant amount of energy consumed in the manufacturing process, there are no known irreversible or irretrievable commitment of resources involved in the proposed action.

7. Discuss the Objections Raised by Other Agencies, Organizations, or Individuals That Are Known to the Applicant:

There are no known objections to the proposed action.

8. If the Proposed Action Should Be Taken Prior to 90 Days From the Circulation of a Draft Environmental Impact Statement or 30 Days from the Filing of a Final Environmental Impact Statement, Explain Why:

   No known reason.

9. Risk-Benefit Analysis:

   The manufacture and use of the 3-Nitro® Premixes as specified in this proposed action will have no adverse effect on the environment in terms of risk.

   This action presents no new risks to the environment since we have been manufacturing and distributing this product for many years, and it has been the subject of an Approved New Animal Drug Application since March 23, 1951.

   The lack of risk associated with the 3-Nitro® Premixes is further attested to by the fact that specific tolerances for residues in food-producing animals have been approved and published in 21 CFR § 560.60, Arsenic. Refer to D.2.a.(4)(a).

   As stated previously, the 3-Nitro® Premixes provide the benefits of increased rate of weight gain, improved feed efficiency, and improved pigmentation for growing chickens and growing turkeys, as well as increased rate of weight gain and improved feed efficiency in growing-finishing swine and as an aid in the treatment of swine dysentery (Hemorrhagic Enteritis or bloody scours).

   Resulting from the previously described benefits is the final benefit to the consumer of meat at a lower cost because the grower can more efficiently produce animal protein with the aid of the 3-Nitro® Premixes.

E. CERTIFICATION:

The undersigned Applicant/Petitioner certifies that the information furnished in this Environmental Impact Analysis Report is true, accurate, and complete to the best of his knowledge.

March 2, 1981
(date)

Robert R. Baron, Ph.D.
Government Relations Manager
Salsbury Laboratories, Inc.