ENVIRONMENTAL ASSESSMENT

OXYTET SOLUBLE
(OXYTETRACYCLINE HYDROCHLORIDE SOLUBLE POWDER)

I.D. RUSSELL COMPANY, LABORATORIES
P. O. BOX 410001
KANSAS CITY, MO 64141

January 9, 1989

ENVIRONMENTAL ASSESSMENT

OXYTET WATER SOLUBLE POWDER FOR

CHICKENS, TURKEYS AND SWINE

1. Date: January 9, 1989

2. I.D. Russell Company, Laboratories

3. P. O. Box 410001

   Kansas City, MO 64141

4. Description of the Proposed Action:

   I.D. Russell Company, Laboratories has filed a supplemental application to an approved new animal drug application for oxytetracycline hydrochloride for the purpose of adding swine as a species to the label. The need for this action is to provide swine raisers with an alternate source of oxytetracycline for treating oxytetracycline-susceptible diseases in swine.

   The product will be manufactured at the I.D. Russell manufacturing facility which is located in Kansas City, MO 64141. OXYTET SOLUBLE will be used by swine producers throughout the United States, with Iowa, Illinois, Indiana, Minnesota, Missouri and Nebraska representing the highest production areas. The potential market for medication in 1986 was approximately 55 million animals. This potential is now being served by several antibiotics, of which oxytetracycline accounts for about 15% of the tetracyclines used. Pfizer, Inc. currently markets an oxytetracycline product for use in swine and other species which was approved by the Food and Drug Administration in 1952 and was reviewed by the National Academy of Science/National Research Council (NAS/NRC).

The approval of this product is not expected to increase the environmental oxytetracycline burden since the dosage and administration are similar to existing products administered according to the NAS/NRC recommendations, and because OXYTET SOLUBLE is expected to capture only a portion of the existing market share currently held by the Pfizer product and similar products marketed by other firms.

There are no special handling or storage requirements for OXYTET SOLUBLE. Stability studies of the product in market containers show that OXYTET SOLUBLE is stable for two years when stored at room temperature.

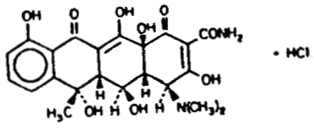
The product is mixed in drinking water prepared fresh daily per label directions and used as the sole source of drinking water. Swine producers who would use this product are quite familiar with the amounts of feed and water their herds use daily, and will therefore mix materials accordingly to avoid waste. Consequently, nearly all material prepared is consumed by the animals and little disposable wastage is generated.

Swine are generally housed in specially designed commercial facilities having slatted or solid concrete floors. Some are held in large penned areas having dirt floors. These facilities are generally rural in nature and not located in populated areas, thus the spaces around such facilities are open.

5. Identification of chemical substance that is the subject of the proposed action:

a. Physical and Chemical Properties

OXYTETRACYCLINE HYDROCHLORIDE



Chemical Name: 2-Naphthacenecarboxamide, 4-(dimethylamino)-1,4,4a, 5,5a, 6,11,12a-octahydro-3,5,6,10,12,12a-hexahydroxy-6-methyl-1,11-dioxo-,[4S-(4 α, 4a α, 5 α,5a α,6 β, 12a α]-,monohydrochloride

Empirical Formula: $C_{22}H_{24}N_2O_9.HCl$

Molecular Weight: 496.90

CAS Registry No.: 2058-46-0

Oxytetracycline is produced by a selected strain of *Streptomyces rimosus* on a medium consisting of water, proteins, and nutrient salts. The hydrochloride salt of oxytetracycline is a yellow, crystalline powder; odorless, hygroscopic, and having a bitter taste. It decomposes above 180°C and exposure to strong sunlight, or to temperatures above 90°C in moist air, causes darkening but no appreciable loss in potency.

Potency is affected in solutions of pH below 2 and is rapidly destroyed by alkaline hydroxide solutions. It is very soluble in water (1 g/mL) but the solution becomes cloudy or turbid due to liberation of oxytetracycline base. Half-lives of aqueous solutions of oxytetra-

cycline, in hours, at various pH levels are: pH 1.0=114; pH 2.5=134; pH 4.6=45; pH 5.5=45; pH 7.0=26; pH 8.5=33; pH 10.0=14. In alcohol the solubility is 1 g in 35 mL, but it is less soluble in anhydrous alcohol. It is insoluble in chloroform and ether.

6. Introduction of substances into the environment.

a. Impact of Manufacturing

The manufacturing process involves only the mixing together of an inert, water soluble bulking agent with oxytetracycline hydrochloride in a large blender constructed of non-reactive product contact parts. Since water is not used in the process, any oxytetracycline lost via the sewer system would be through clean-up, and the amount would be negligible. Water emissions from the I.D. Russell plant are subject to and are in compliance with the regulations of the City of Kansas City, Missouri, Water and Pollution Control Department, Division of Industrial Waste Control (Part II Administrative Code, Article V, Division 10, Pollution Control, and Part III Code of General Ordinances, Chapter 29, Sewers and Sewage Disposal, Article I).

Air emissions generated during the mixing of the two ingredients consist only of fine dust particles. These are trapped by appropriate dust collecting systems which are monitored by I.D. Russell Company on a scheduled basis. Air emissions will be subject to and in compliance with Section 112 of the Clean Air Act in general and with the City of Kansas City under the Air Quality Control Code, Article III, specifically Sections 18.85-18.90, Restrictions on Emissions.

Dry solid wastes generated during the production operations (paper, trash, etc.) will be disposed of at the Kansas City sanitary landfill and are expected to be minimal. The bulk containers consist of exterior metal or fiberboard drums with inner plastic bags which contain the oxytetracycline hydrochloride. These containers are thoroughly emptied for the mixing process and only minimal residues of material, which may cling to the sides of the bags, remain. It is estimated that less than 1.7 kg of oxytetracycline hydrochloride would be lost from each batch and disposed of as solid waste from emptying containers, mixing, filling market containers and cleaning of equipment.

Oxytetracycline hydrochloride and the inert carrier are not hazardous substances as defined and listed under Section 311(b)(2)(a) of the Federal Water Pollution Control Act; Section 3001 of the Solid Waste Disposal Act; Section 112 of the Clean Air Act; Section 306(a) of the Comprehensive Environmental Response, Compensation, and Liability Act; or the Department of Transportation hazardous material listing contained in 49 CFR Part 172.

In accordance with the enclosed Letter of Certification from I.D. Russell Company, Laboratories, industrial wastes discharged as a result of manufacturing OXYTET SOLUBLE are subject to the requirements of the City of Kansas City, Missouri, Water and Pollution Control Departments, Division of Industrial Waste

Control. I.D. Russell Company, Laboratories is in compliance with the applicable regulations promulgated by these regulatory entities.

I.D. Russell Company, Laboratories also complies with the regulations regarding occupational exposure and has made available to its employees the required OSHA Material Safety Data Sheets (MSDS). Copies of the MSDS for oxytetracycline hydrochloride are appended to this assessment.

b. Use and Disposal

The purpose of this amendment is to request approval for swine to be added as a species to the label which has already been approved for chickens and turkeys. Since this product is similar to an already approved product and is not to be administered at higher dosage levels, for longer durations, or for different indications than are currently in effect under the NAS/NRC guidelines, and because approval of this action is expected to result only in a redistribution of the market shares currently held by similar products, the amount of oxytetracycline hydrochloride added to the environment from usage or disposal of the subject product is not anticipated to increase appreciably. Assuming the most extravagant usage whereby all of the approximately 55 million head of swine produced annually in the U.S. will be treated at least once with oxytetracycline water soluble powder at the recommended dose level of 10 mg/lb. bwt/day for the maximum recommended period of 14 days, and stipulating an average animal weight of 200 lbs., the total annual usage of oxytetracycline water soluble powder from all sources would amount to approximately 1,540,000 kg.

List of Preparers:

Paul W. Carr, P.E.

SHOTWELL & CARR, INC.

Dallas, Texas 75234

Degree in Chemical Engineering and Licensed Professional Engineer. Thirteen years consulting to industries regulated by the Food and Drug Administration and Environmental Protection Agency.

Attachments:

1. I.D. Russell Company: Certification of Compliance with Emission Standards
2. I.D. Russell Company: Material Safety Data Sheets for OXYTET SOLUBLE
3. I.D. Russell Company: Proposed Product Labeling (70 gram pack only)

I. D. RUSSELL COMPANY, *Laboratories*

• BOX x • 411268
KANSAS CITY, MO. 64141
LOCAL PHONE 816-471-1845
TOLL-FREE 800-821-5811
TELEX 434372 WU Publx KSC

February 12, 1987

Dr. Charles E. Haines, Chief
Antimicrobial Drugs Branch
Div. of Therapeutic Drugs for Food Animals
New Animal Drug Evaluation
Center for Veterinary Medicine
Food & Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Sir:

This letter will certify that, to the best of our knowledge, I.D. Russell Company, Laboratories is in compliance with all applicable local, State and Federal requirements for materials expected to be emitted as a result of the manufacture of Oxytet Soluble.

Oxytetracycline hydrochloride and citric acid (the constituents of Oxytet Soluble) are not hazardous substances as defined and listed under section 311 (b)(2)(a) of the Federal Water Pollution Control Act, section 3001 of the Solid Waste Disposal Act, section 112 of the Clean Air Act, section 306 (a) of the Comprehensive Environmental Response, Compensation, and Liability Act, or the Department of Transportation hazardous materials listings contained in 49 CFR Part 172, and are therefore not regulated on a State or Federal level.

Industrial wastes discharged as a result of manufacturing of Oxytet Soluble are subject to the requirements of the City of Kansas City, Missouri Water and Pollution Control Department, Division of Industrial Waste Control. I.D. Russell is in compliance with the applicable regulations contained in Kansas City, Missouri, Part II Administrative Code, Article V, Division 10, Pollution Control, and Part III Code of General Ordinances, Chapter 18, Air Quality Control Code, Article III, specifically Sections 18.85-18.90, Restriction on Emissions, and Chapter 29, Sewers and Sewage Disposal, Article I, specifically Section 29.52, Wastes Prohibited in Sewers.

Sincerely,

Marva L. Weigelt

Marva L. Weigelt
Regulatory Compliance
Coordinator

*****MATERIAL SAFETY DATA SHEET*****

Manufacturer's Name: I.D. Russell Company, Laboratories

Address: Box 411268 Kansas City, MO 64141

Emergency Telephone #: 816/471-1845

Date Prepared or Revised: 01/28/87 (Rev.)

SECTION 1 - IDENTITY

Product Name: **OXYTET SOLUBLE**

Chemical Name and Synonyms: Oxytetracycline hydrochloride, 2-Naphthacene-carboxamide, 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6, 10,12,12a-hexahydroxy-6 methyl-1,11-dioxo-monohydrochloride, [4S(4α, 4aα, 5α, 5aα, 6β, 12aα)]

Chemical Family: Tetracycline antibiotics

CAS Registry Number: 2058-46-0

SECTION 2 - HAZARDOUS INGREDIENTS

Paints, Preservatives and Solvents:

Paints - NA
Preservatives - NA
Solvents - Less than 0.75% TLV - NA

Alloys and Metallic Coatings: NA

Hazardous Mixtures of Other Liquids, Solids or Gases: None

SECTION 3 - PHYSICAL & CHEMICAL CHARACTERISTICS (Fire & Explosion Data)

Boiling Point (°F): NA Vapor Pressure: NA

Specific Gravity (H_2O = 1): NA Vapor Density: NA

% Volatile by Volume: NA Evaporation Rate: NA

Solubility in Water: Freely soluble (1 g/10 ml)

Reactivity in Water/Air: Not reactive

Appearance and Odor: Yellow crystalline powder with mild odor

Flash Point (°F): NA

Extinguishing Media: Use dry chemical, water fog or CO_2

Special Fire Fighting Procedures: None

Unusual Fire and Explosion Hazards: None known

MSDS

SECTION 4 - PHYSICAL HAZARDS

Stability: Stable

Incompatability (Materials to Avoid): Aqueous reaction with caustic may create heat

Conditions to Avoid: None known

Hazardous Decomposition Products: None known

Hazardous Polymerization: Will not occur.

SECTION 5 - HEALTH HAZARDS

Threshold Limit Values: None established

Acute Effects of Exposure: May cause slight skin, eye and respiratory irritation.

Chronic Effects of Exposure: None established

Emergency and First Aid Procedures: Flush skin contact with water and flush eye contact immediately with water or physiological saline. Get medical care for eyes if irritation persists.

SECTION 6 - SPECIAL PROTECTION INFORMATION

Respiratory Protection: Nuisance dust mask

Ventilation: Local exhaust is satisfactory

Protective Gloves: Rubber or vinyl gloves desirable if gross contact likely

Eye Protection: Safety goggles.

Other Protective Equipment: Eyes, nose, mouth and exposed skin areas should be covered as needed to help prevent irritation. A safety eyebath should be available.

SECTION 7 - SPECIAL PRECAUTIONS AND SPILL/LEAK PROCEDURES

Precautions to be Taken in Handling and Storage:

Containers should be protected from physical damage. Store in dry place.

Steps to be Taken in Case Material is Released or Spilled:

Clean large amounts by vacuum, sweeping or shoveling. Flush small amounts with water.

Waste Disposal Method:

Dispose of in accordance with applicable local, county, state and federal regulations.

RUSSELL

MSDS

MSDS

Although the information and recommendations set forth herein (hereinafter "Information") are presented in good faith and believed to be correct as of the date thereof, I.D. Russell Company, Laboratories makes no representations as to the completeness or accuracy thereof. Information is supplied upon the condition that the persons receiving same will make their own determination as to its suitability for their purposes prior to use. In no event will I.D. Russell Company, Laboratories be responsible for damages of any nature whatsoever resulting from the use of or reliance upon Information. **No representations or warranties, either express or implied, of merchantability, fitness for a particular purpose or of any other nature are made hereunder with respect to Information or the product to which Information refers.**

This Material Safety Data Sheet has been adapted from Form OSHA-20 (Rev. May 1972).

RUSSELL

MSDS