

# Bismuth Subsalicylate

## Livestock

### **Executive Summary**

Bismuth subsalicylate was petitioned for use in livestock as an adsorbent, an anti-diahrreal aid, and as relief for ulcers. Bismuth subsalicylate is the active ingredient in Pepto-Bismol and is most commonly used by organic farmers for livestock, particularly cattle, with onset diarrhea from bacterial infections. The EPA issued a federal registered document and the FDA reviewed environmental assessments for 167 chemicals including bismuth subsalicylate and found no significant impact on the environment.

Bismuth subsalicylate is not officially listed anywhere in the NOP final rule. The NOP says at section 205.238 that “the producer of an organic livestock operation must not: (2) administer any animal drug, other than vaccinations, in the absence of illness. Organic farmers are not allowed to give unnecessary medicines to livestock. As in section 205.600 of the NOP final rule, “any synthetic substance used as a processing aid or adjuvant will be evaluated against the following criteria: (2) the substance’s manufacture, used and disposal do not have adverse effects on the environment and are done in a manner compatible with organic handling.” Bismuth subsalicylate is not explicitly listed in section 205.603 as a synthetic substance neither allowed for use in organic livestock production nor is it listed in section 205.604 as a prohibited substance.

### **Summary of TAP Reviewer’s Analyses<sup>1</sup>**

<i>Synthetic/ Nonsynthetic</i>	<i>Allow without restrictions?</i>	<i>Allow only with restrictions? (See Reviewers’ comments for restrictions)</i>
Synthetic (3)	Yes (1) No (2)	Yes (2) No (1)

### **Identification**

**Chemical names:** Bismuth Subsalicylate

**Chemical formula:** C<sub>7</sub>H<sub>5</sub>BiO<sub>4</sub>

**Molecular weight:** 362.10

**CAS no.** 14887-18-9 (an-hydrous)

**Other Names:** Pepto-bismol; Bismatrol; Helidac (combination drug); OXO(SALICYLATO)BISMUTH BISMUTH SALICYLATE, BASIC SALICYLIC ACID, BISMUTH BASIC SALT STABISOL (2-HYDROXYBENZOATO-O(1), O(2)OXO-BISMUTH (9CI) TRIS(2-HYDROXYBENZOATO)TRIOXOTRIBISMUTH BISMUTH OXYLSALICYLATE <sup>2</sup>

### **Characterization**

#### **Composition:**

<sup>1</sup> This information was referenced from <http://www.ams.usda.gov/nop/regtext.htm>

<sup>2</sup> This information was referenced from [http://157.98.10.135/NTP\\_Reports/NTP\\_Chem\\_HS\\_HTML/NTP\\_Chem1/Radian14882-18-9](http://157.98.10.135/NTP_Reports/NTP_Chem_HS_HTML/NTP_Chem1/Radian14882-18-9)

Odorless, white powder

### **Properties:**

**Melting Point:** not found

**Boiling Point:** not applicable

**Solubility in Water:** almost insoluble in water, decomposes in boiling water

**Specific Gravity:** 3.058

**pH** (aqueous solution): 8-9

**Stability:** stable

Thermal decomposition may produce toxic and irritating fumes. Bismuth subsalicylate may cause eye, skin, and upper respiratory tract irritation.<sup>3</sup>

### **How Made:**

Bismuth subsalicylate, pepto bismol, was originally developed 100 years ago around the start of the 20<sup>th</sup> century. The pepto bismol formula was developed by a doctor in his New York home. "He made it from pepsin, bismuth salicylate, zinc salts, salol and oil of wintergreen, along with a colorant to make it pink, and he called it Mixture Cholera Infantum." It was found that bismuth subsalicylate, the active ingredient in pepto bismol, was what made the product work; now listed as the product's active ingredient. Procter and Gamble is the primary manufacturer of Pepto-Bismol. Due to proprietary reasons, P&G will not disclose formulation information for this product to the general public.<sup>4</sup>

### **Specific Uses:**

Bismuth subsalicylate, better known as pepto-bismol, has several uses. The main uses of pepto-bismol include treating peptic ulcers and preventing/managing diarrhea in humans and animals (which may include domestic animals as well as livestock). Bismuth subsalicylate may also be used as a coloring agent in cosmetics, giving products a pearl like shine. Bismuth subsalicylate is used in the manufacture of cellulose-base, polystyrene and phenol-formaldehyde resins and is also used in heat-sensitive paper coatings and as stabilizer. It can be used therapeutically to treat Lupus erythematosus.<sup>5</sup> "Bismuth subsalicylate is considered to have an important role in relapsing gastric ulcer[s]."<sup>6</sup> Bismuth subsalicylate helps to coat the ulcer, allowing it to heal. "Bismuth subsalicylate, the ingredient in Pepto-Bismol, decreases the secretion of fluid into the intestine and inhibits the activity of bacteria. It not only controls diarrhea, but relieves the cramps that often accompany diarrhea."<sup>7</sup>

### **Action:**

Bismuth subsalicylate is prescribed to treat indigestion, heartburn, diarrhea, and duodenal ulcers. Bismuth subsalicylate stimulates the passage of fluid and electrolytes across the wall of the intestinal tract, and binds or neutralizes the toxins of some bacteria, rendering them nontoxic. It decreases intestinal inflammation and increases the activity of intestinal muscles and lining. It normally takes effect within 30-60 minutes.<sup>8</sup> In the gastrointestinal tract, bismuth subsalicylate is converted into insoluble bismuth salts as well as salicylic acid. Salicylate, extensively absorbed (greater than 90%), is excreted in human and animal urine.<sup>9</sup>

These are the human dosage recommendations.

<sup>3</sup> This information was referenced from <http://www.aerchem.com/html/products/msds/0044.PDF>

<sup>4</sup> This information was referenced from <http://www.pepto-bismol.com/history.htm> --Conducted phone interviews with Procter and Gamble representative, June 12, 2002

<sup>5</sup> This information was referenced from <http://www.uhe.com/bismuth.htm>

<sup>6</sup> Copied directly from <http://toxnet.nlm.nih.gov/cgi-bin/sis/search/?/temp/~AAA8taahH:2>

<sup>7</sup> Directly referenced from <http://www.ehendrick.org/healthy/00037810.html>

<sup>8</sup> This information was referenced from [http://www.wholehealthmd.com/refshelf/drugs\\_view/0,1524,64,00.html#How\\_It\\_Works](http://www.wholehealthmd.com/refshelf/drugs_view/0,1524,64,00.html#How_It_Works)

<sup>9</sup> This information was referenced from <http://alt1.csa.com/htbin/ids52/procskel.cgi>

**ADULT:**

- Diarrhea: 525 milligrams (30 milliliters regular liquid or 2 tablets) every 30 minutes to 1 hour, up to a maximum of 8 doses daily, by mouth (1-4)
- Diarrhea, maximum strength liquid: 30 milliliters (1050 milligrams) every 1 hour, for a maximum of 4 doses daily, by mouth (1-4)
- Upset Stomach, suspension (liquid): 30 milliliters, four times daily, by mouth, for 3 weeks (5)
- Helicobacter Pylori: 265 milligrams (2 tablets), four times daily, by mouth, along with antibiotic therapy (6,7)
- Indigestion (upset stomach): 525 milligrams (30 milliliters regular liquid or 2 tablets) every 30 minutes to 1 hour up to a maximum of 8 doses daily, by mouth (1-4)
- Traveler's Diarrhea: 525 milligrams (30 milliliters regular liquid or 2 tablets) every 30 minutes to 1 hour, up to a maximum of 8 doses daily, by mouth (1)
- Traveler's Diarrhea prevention: 2 chewable tablets four times daily up to 3 weeks. Begin treatment one day before departure (17)
- Stomach Ulcer: 600 milligrams, three times daily, by mouth (8)

**CHILDREN:**

- Diarrhea, Upset Stomach, 3 to 6 years old, suspension (liquid): 5 milliliters (1/3 tablet) every 30 minutes to 1 hour up to a maximum of 8 doses daily, by mouth (1)
- Diarrhea, Upset Stomach, 6 to 9 years old, suspension (liquid): 10 milliliters (2/3 tablet) every 30 minutes to 1 hour up to a maximum of 8 doses daily, by mouth (1)
- Diarrhea, Upset Stomach, 9 to 12 years old, suspension (liquid): 15 milliliters (1 tablet) every 30 minutes to 1 hour up to a maximum of 8 doses daily, by mouth (1)<sup>10</sup>

The maximum daily dose is 4.2 grams (2). Should a dose be missed, the individual should take the missed dose as soon as it is remembered unless it falls within 2 hours of the next scheduled dose. The patient should skip the missed dose, should this be the case. Only a doctor should authorize an increase in the dosage size or amount.<sup>11</sup>

The following are desired actions for farmers of livestock with digestive problems.

**FOR VETERINARY USE ONLY**

A palatable oral solution for use as an aid in the control of non-specific diarrhea.

**USE ONLY AS DIRECTED****DOSAGE:**

May be repeated until condition improves.

Horses, Cattle- 6 to 10 ounces every 2 to 3 hours.

Foals, Calves - 3 to 4 ounces every 2 to 3 hours.

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<sup>10</sup> Copied, unaltered from <http://www.cooperfitness.com/content/support/pharmaceutical/altmed/Detail.asp?DocID=1280>

<sup>11</sup> This information was referenced from <http://www.healthcentral.com/mhc/top/001852.cfm>

Dogs, Cats- 1 to 3 tablespoons every 1 to 3 hours<sup>12</sup>

For livestock, those animals which over consume highly digestible feed (grains in particular), or are suddenly exposed to legumes, need to be treated immediately to prevent permanent damage to the digestive tract or secondary complications. Bismuth subsalicylate should be administered because it acts as both an antacid and helps bind certain toxins. Animal dosage is based upon animal weight and is extrapolated from human (150 pounds) dosage regulations on the bottle. Treatment regiment consists of adding the amount recommended for a 24 hour period and dividing by the number of times per day the animal will be treated.<sup>13</sup> Most ulcers are caused by *H. pylori* bacterium found in the stomach. This is the greatest cause of ulcers because *H. pylori* survives in the stomach by producing urease, an enzyme, which generates neutralizing substances in the stomach enabling the bacteria to survive. *H. pylori* attacks and breaks down vital stomach mucus lining and can also enable the stomach to produce more acid. *H. pylori* causes weakness of stomach defensive mechanisms, inflammation, and increased acid content which all lead to the ulcer formation.<sup>14</sup>

### **Combinations:**

Bismuth subsalicylate is incompatible with strong oxidizing agents. There are no known food interactions with bismuth subsalicylate. Adverse interactions occur with Salicylate-containing herbs including meadowsweet, poplar, and wintergreen.<sup>15</sup> Bismuth subsalicylate should not be taken with doxycycline, used for therapeutic purposes (ie. gastric ulcers).<sup>16</sup> Bismuth subsalicylate may potentially be harmful if you are allergic to any of the following drugs:

- Carprofen (e.g., Rimadyl)
- Diclofenac (e.g., Voltaren)
- Diflunisal (e.g., Dolobid)
- Fenoprofen (e.g., Nalfon)
- Floctafenine (e.g., Idarac)
- Flurbiprofen taken by mouth (e.g., Ansaid)
- Ibuprofen (e.g., Motrin)
- Indomethacin (e.g., Indocin)
- Ketoprofen (e.g., Orudis)
- Ketorolac (e.g., Toradol)
- Meclofenamate (e.g., Meclomen)
- Mefenamic acid (e.g., Ponstel)
- Naproxen (e.g., Naprosyn)
- Oxyphenbutazone (e.g., Tandearil)
- Phenylbutazone (e.g., Butazolidin)
- Piroxicam (e.g., Feldene)
- Sulindac (e.g., Clinoril)
- Suprofen (e.g., Suprol)
- Tiaprofenic acid (e.g., Surgam)
- Tolmetin (e.g., Tolectin)
- Zomepirac (e.g., Zomax)<sup>17</sup>

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<sup>12</sup> This information was referenced from <http://www.med-pharmex.com/bismuth1.htm>

<sup>13</sup> This information was referenced from <http://members.aol.com/lamainfoex/backissues/overeating.html>

<sup>14</sup> This information was referenced from <http://gi.bsd.uchicago.edu/diseases/other/ulcers.html>

<sup>15</sup> This information was referenced from [http://www.gnc.com/health\\_notes/Drug/Bismuth\\_Subsalicylate.htm#Interaction-Summary](http://www.gnc.com/health_notes/Drug/Bismuth_Subsalicylate.htm#Interaction-Summary)

<sup>16</sup> This information was referenced from <http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~AAA8taahH:2>

<sup>17</sup> This information was referenced from [http://www.type40.com/Jolynne/drug\\_pepto-bismol.html](http://www.type40.com/Jolynne/drug_pepto-bismol.html)

“Bismuth subsalicylate should not be taken with aspirin or any other medicine that contains salicylate. This drug may also interact with other drugs, such as blood thinners (warfarin, for example), methotrexate, the antigout medicine probenecid, and the antidiabetes drug tolbutamide. In addition, bismuth subsalicylate may interact with any drug that interacts with aspirin.”<sup>18</sup>

## **Status**

### **Historic Use by Organic Farmers:**

Farmers most widely use bismuth subsalicylate in the treatment of diarrhea in baby calves. Other affected animals may include lambs, goats, and llamas. Several diarrhea-causing pathogens may cause Salmonella, Cryptosporidium, Giardia and E. coli, which are among the leading cause of death in young livestock. Most calves experience diarrhea in the first few days or weeks of life, making care the utmost priority for farmers. I will further discuss the uses of bismuth subsalicylate in baby calves particularly. Enteric Colibacillosis is a condition marked by diarrhea within the first seven days of a calf's life. The feces are fluid or pasty and maybe white to pale yellow in color. Critical time for calves with this condition is five days in which they either survive or die. High risk candidates for enteric colibacillosis are those calves and lambs who experience a colostrum deficiency. The risk for infection increases as animals remain in a pathogen- containing, dirty environment. E. coli causes enteric colibacillosis. Diarrhea stricken calves lose vital nutrients potassium, sodium, and chloride, in part due to an extreme loss of water in the body. Farmers use a fluid treatment for maximum results. Severe dehydration involves the use of IV fluids while mild dehydration (less than 8%) can be effectively treated by administering fluids orally. Electrolyte solutions should be alternated every 6 hours with cow's whole milk. Oral electrolyte treatments (solutions) rehydrate the animal and restore necessary electrolytes. Farmers use bismuth subsalicylate, pepto bismol or corrective mixture, as an electrolytic solution. Farmers normally administer 2-4 ml/kg orally every six hours. The animal's feces may become in color. Farmers are also concerned with Salmonellosis, another diarrhetic problem treated with bismuth subsalicylate. Salmonellosis affects all species of vertebrates but is most common in young, old, and debilitated animals and humans. Lambs recently shipped to feedlots and calves from 1-12 weeks are the most at risk for contracting the disease. Salmonellosis mortality rates are high in young stock. Adult livestock normally contract the disease in herds while an epidemic occurrence is possible. Symptoms of salmonellosis include fever, depression, extensive diarrhea, and reduce milk production rates in cows. "Diarrhea is caused by inflammatory changes produced by invasion into and destruction of intestinal epithelium." Young stock treatment includes antibiotics, fluid therapy, and oral bismuth subsalicylate. Adult treatment discourages antibiotic use and focuses on orally or IV administered doses of bismuth subsalicylate. Separating sick animals from those that are healthy should be done immediately.<sup>19</sup>

### **OFPA, USDA Final Rule:**

OFPA, 1990, states:

#### ***6509 ANIMAL PRODUCTION PRACTICES AND MATERIALS.***

##### **Health Care.**

(1) **Prohibited Practices.** For a farm to be certified under this chapter as an organic farm with respect to the livestock produced by such farm, producers on such farm shall not

- (A) use subtherapeutic doses of antibiotics;
- (B) use synthetic internal paraciticides on a routine basis; or
- (C) administer medication, other than vaccinations, in the absence of illness.

<sup>18</sup> Directly referenced from <http://www.ehendrick.org/healthy/00037810.html>

<sup>19</sup> This information was referenced from <http://lam.vet.uga.edu/LAM/LM000154.HTML#Cryptosporidiosis>

For organic certification, farmers must cease medication administration when symptoms are no longer present.<sup>20</sup>

Bismuth Subsalicylate is currently under review by the USDA. There is no official ruling at this time and are petitioned to be reviewed in September 2002.<sup>21</sup> Bismuth subsalicylate is not officially listed anywhere in the NOP final rule. The NOP says at section 205.238 that “the producer of an organic livestock operation must not: (2) administer any animal drug, other than vaccinations, in the absence of illness. Organic farmers are not allowed to give unnecessary medicines to livestock. As in section 205.600 of the NOP final rule, “any synthetic substance used as a processing aid or adjuvant will be evaluated against the following criteria: (2) the substance’s manufacture, used and disposal do not have adverse effects on the environment and are done in a manner compatible with organic handling.” Bismuth subsalicylate is not explicitly listed in section 205.603 as a synthetic substance allowed for use in organic livestock production nor is it listed in section 205.604 as a prohibited substance.<sup>22</sup>

## **Regulatory: EPA/NIEHS/Other Sources**

### **FDA:**

[Code of Federal Regulations]

[Title 21, Volume 5]

[Revised as of April 1, 2001]

From the U.S. Government Printing Office via GPO Access

[CITE: 21CFR330.5]

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TITLE 21--FOOD AND DRUGS

CHAPTER I--FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES--Continued

PART 330--OVER-THE-COUNTER (OTC) HUMAN DRUGS WHICH ARE GENERALLY RECOGNIZED AS SAFE AND EFFECTIVE AND NOT MISBRANDED--Table of Contents

Subpart A--General Provisions

Sec. 330.5 Drug categories.

Monographs promulgated pursuant to the provisions of this part shall be established in this part 330 and following parts and shall cover the following designated categories:

- (a) Antacids.
- (b) Laxatives.
- (c) Antidiarrheal products.
- (d) Emetics.

Bismuth subsalicylate is listed as an approved antidiarrheal drug as of April 1, 2001.<sup>23</sup>

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<sup>20</sup> This information was referenced from <http://www.ams.usda.gov/nop/orgact.htm>

<sup>21</sup> This information was referenced from <http://www.ams.usda.gov/nop/MaterialsMay2002.pdf>

<sup>22</sup> This information was referenced from <http://www.ams.usda.gov/nop/regtext.htm>

<sup>23</sup> This information was referenced from <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?FR=330.5>

## TITLE 21--FOOD AND DRUGS

## CHAPTER I--FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES

## PART 201--LABELING--Table of Contents

## Subpart B--Labeling Requirements for Prescription Drugs and/or Insulin

Sec. 201.59 Effective date of Secs. 201.56, 201.57, 201.100(d)(3), and 201.100(e).

July 1, 1983..... July 1, 1981..... Antidiarrheals..... HFD-110

The FDA issued a recall for bismuth subsalicylate, pepto bismol, posted May 13, 1998.

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**Enforcement Report****RECALLS AND FIELD CORRECTIONS: DRUGS -- CLASS II**

g) Pink Bismuth (Bismuth subsalicylate 262 mg/tablespoon) in 6 fluid ounce bottles

RECALLED BY Manufacturer, by letter on or about April 1, 1998. Firm-initiated recall ongoing. DISTRIBUTION Michigan, Mississippi, North Carolina, Georgia, California, Ohio, Illinois, New York. QUANTITY Undetermined. REASON Lack of good manufacturing practice controls.<sup>24</sup>

"FDA has proposed that products containing bismuth subsalicylate have labeling warning not to give the drug to children and teenagers who have or are recovering from chickenpox, flu symptoms (nausea, vomiting or fever), or flu."<sup>25</sup>

"November 12, 1996

**FDA PUBLISHES FINAL RULE ON EXTRALABEL DRUG USE IN ANIMALS**

In the November 7, 1996 *Federal Register*, FDA published a final rule to allow veterinarians to prescribe extralabel uses of certain approved animal drugs and approved human drugs for animals under certain conditions. This action implements the Animal Drug Use Clarification Act of 1994 (AMDUCA). This regulation provides veterinarians with greater flexibility in the use of approved drugs in animals. These regulations put AMDUCA into effect on December 9, 1996.

The notice of proposed rulemaking published in the *Federal Register* on May 17, 1996. FDA received and considered approximately 110 comments in preparing the final rule.

Prior to the enactment of AMDUCA, the Federal Food, Drug, and Cosmetic Act (the Act) required users of approved new animal drug products to follow the exact directions on the labeling of the drug. This extralabel use restriction precluded use of an approved drug in species or for indications (disease or other conditions) not listed in the labeling, use of an approved drug at dosage levels higher than those stated on the label, and other extralabel purposes. In addition, the Act did not provide for the use of human drugs for treating animals.

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<sup>24</sup> This information was referenced from <http://www.fda.gov/bbs/topics/ENFORCE/ENF00537.html>

<sup>25</sup> This information was referenced from <http://www.empowermentzone.com/tummy.txt>

Because of AMDUCA, the Federal Food, Drug, and Cosmetic Act will now permit veterinarians, like physicians, to prescribe extralabel uses of approved drugs for their patients. Although certain restrictions have been placed on veterinarians prescribing animal and human drugs in an extralabel manner, these restrictions generally apply only to the use of drugs extralabelly in food-producing animals. The key constraints are that any extralabel use must not result in violative residues in food-producing animals, the use must be by or on the order of a veterinarian within the context of a veterinarian-client-patient relationship, and the use must be in conformance with the new regulations.

AMDUCA includes a number of provisions that permit the Agency to restrict extralabel use in certain circumstances. For example, if there is a finding that there is a reasonable probability that an extralabel use may present a risk to public health from drug residues in animal-derived food, the Agency may establish a safe level for a residue for such extralabel use by regulation or order and may require the development of analytical methods for residue detection. If, after affording an opportunity for public comment, FDA finds that an extralabel animal drug use presents a risk to public health or that no analytical method has been developed and submitted, the Agency may prohibit such extralabel use. The following prohibitions currently apply to the uses of drugs in food-producing animals:

Chloramphenicol  
 Clenbuterol  
 Diethylstilbestrol (DES)  
 Dimetridazole  
 Ipronidazole  
 Other nitroimidazoles  
 Furazolidone (except for approved topical use)  
 Nitrofurazone (except for approved topical use)  
 Sulfonamide drugs in lactating dairy cattle (except approved use of sulfadimethoxine, sulfabromomethazine and sulfaethoxypyridazine)

Neither AMDUCA nor the implementing regulations are intended to lessen the responsibility of the manufacturer, the veterinarian, or the food producer with regard to drug residues. Under AMDUCA, any amount of residue resulting from an extralabel use would constitute a violation of the Act if a safe level or tolerance has not been established.

Title 21 of the *Code of Federal Regulations* is now amended to add a new part 530, titled "Extralabel Drug Use in Animals." "

Bismuth subsalicylate is allowed for extralabel animal used in food-producing animals because it is not explicitly prohibited.<sup>26</sup>

## **EPA**

The EPA issued a federal registered document and the FDA reviewed environmental assessments for 167 chemicals including bismuth subsalicylate and found no significant impact on the environment. NEPA requires all Federal agencies to include in every proposal for major Federal actions significantly affecting the quality of the human environment, a detailed statement assessing the environmental impact of, and alternatives to, the proposed action and to make available to the public such statements. (See 42 U.S.C. 4332, 40 CFR 1506.6, and 21 CFR 25.51(b).)

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 Federal Register: May 18, 1998 (Volume 63, Number 95) [Notices] [Page 27300-27303] From the Federal Register Online via GPO Access [wais.access.gpo.gov] [DOCID:fr18my98-81] -----

<sup>26</sup> This information copied directly from <http://www.fda.gov/cvm/index/amducca/amducatoc.htm>



----- DEPARTMENT OF HEALTH AND HUMAN SERVICES Food and Drug Administration [Docket No. 98N-0286] Environmental Assessments and Findings of No Significant Impact AGENCY: Food and Drug Administration, HHS. ACTION: Notice.

**Helidac (bismuth subsalicylate tablets, metronidazole 50-719 tablets, and tetracycline hydrochloride capsules)** <sup>27</sup>

**OTA:** bismuth subsalicylate is listed as a material of NOSB review and has been deemed synthetic and an allowable material (organic trade association)<sup>28</sup>

**OSHA:** None (29CFR 1910.1200)

**ACGIH:** None

**NIOSH Criteria Document:** None

**NFPA Hazard Rating:**

Health (H): None

Flammability (F): None

Reactivity (R): None <sup>29</sup>

**HSDB:** bismuth subsalicylate is a chemical that has shown reproductive effects in animal studies or have been investigated as mutagens, tumorigens, or reproductive effectors <sup>30</sup>

**Livestock Medicines Act**  
**Loi sur les médicaments pour le bétail**

REVISED REGULATIONS OF ONTARIO

REGULATION 730

*Amended to O. Reg. 291/97*

**GENERAL**

*This Regulation is made in English only.*

1. In this Regulation,

"biological" means a bacterin, vaccine, toxoid, antiserum or antitoxin prepared for use in the prevention or treatment of livestock diseases. R.R.O. 1990, Reg. 730, s. 1.

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<sup>27</sup> This information was referenced from <http://www.epa.gov/fedrgstr/EPA-IMPACT/1998/May/Day-18/i13045.htm>

<sup>28</sup> This information was referenced from [https://www.ota.com/rule\\_list\\_of\\_materials\\_for\\_nosb\\_revie.htm](https://www.ota.com/rule_list_of_materials_for_nosb_revie.htm)

<sup>29</sup> This information was referenced from [http://157.98.10.135/NTP\\_Reports/NTP\\_Chem\\_HS\\_HTML/NTP\\_Chem1/Radian14882-18-9.html](http://157.98.10.135/NTP_Reports/NTP_Chem_HS_HTML/NTP_Chem1/Radian14882-18-9.html)

<sup>30</sup> This information was referenced from <http://www.nwu.edu/research-safety/pdfs/cbslappb.pdf>

2. Subject to the *Food and Drugs Act* (Canada) and the Food and Drug Regulations made thereunder, the drugs and classes of drugs designated in the Schedule are designated as livestock medicines for the purposes of the Act and this Regulation. R.R.O. 1990, Reg. 730, s. 2.

3. (1) The following classes of licences are established:

1. Class 1.

2. Class 2.

R.R.O. 1990, Reg. 730, s. 3 (1); O. Reg. 291/97, s. 1 (1).

(2) A livestock medicine set out in the Schedule is designated as a livestock medicine that may be sold by the holder of a Class 1 licence at the holder's established place of business.

(3) A Class 2 licence authorizes the holder of a Class 1 licence to sell at a temporary place of business the livestock medicines that the holder is authorized to sell at the holder's established place of business. O. Reg. 291/97, s. 1 (2).

(4) Revoked: O. Reg. 291/97, s. 1 (2).

4. (1) The applicant for a Class 1 licence shall send to the Director an application accompanied by payment of the fee of \$75.

(2) A Class 1 licence is valid up to and including July 31 after it is issued. O. Reg. 291/97, s. 2.

5. (1) The holder of a Class 1 licence may obtain a Class 2 licence by sending to the Director an application accompanied by payment of the fee of \$50.

(2) A Class 2 licence is valid only for the period shown on it. O. Reg. 291/97, s. 2.

5.1 A licence is not transferable. O. Reg. 291/97, s. 2.

6. (1) A licence is issued on the terms and conditions that the licensee,

(a) shall continue to have an established place of business for the storage and sale of livestock medicines;

(b) shall keep for sale or sell livestock medicines only at the established or temporary place of business described on the licence;

(c) shall not keep for sale or sell any livestock medicines after the expiration date indicated by the manufacturer on the label thereof;

(d) shall not repackage or relabel livestock medicines;

(e) shall not deliver a livestock medicine except for dairy sanitizers, teat dips and udder washes to a livestock owner without an order from that owner authorizing the delivery evidenced by an invoice prepared by the licensee in advance of delivery;

(f) shall keep refrigerated all livestock medicines that require refrigeration;

(g) shall store in the manner prescribed by this Regulation all livestock medicines that do not require refrigeration; and

.....

(i) shall not sell a livestock medicine to any person other than an owner of livestock or for any purpose other than the treatment of livestock. R.R.O. 1990, Reg. 730, s. 6 (1); O. Reg. 636/91, s. 2 (1, 2); O. Reg. 291/97, s. 3 (1).

(2) A Class 2 licence shall be issued only for a temporary place of business that is located on premises where livestock are assembled in connection with an agricultural exhibition, a horse show or the holding of horse races. O. Reg. 291/97, s. 3 (2).

**7.** (1) A licensee who maintains, handles or stores livestock medicines shall keep them in a refrigerator, cabinet or other storage facility that is used solely for that purpose.

(2) A licensee shall ensure that livestock medicines, whether they require refrigeration or not, are maintained at the temperatures prescribed for them by the manufacturer and that they do not come in contact with food or medicine for human consumption. O. Reg. 636/91, s. 3.

(3) The licensee shall maintain every refrigerator, cabinet or other storage facility in a clean and sanitary condition. O. Reg. 291/97, s. 4.

**8.** (1) Every licensee shall,

(a) sell every livestock medicine in the container in which it is received by the licensee;

(b) in the case of any livestock medicine bearing a warning or caution on the label, draw the attention of the purchaser to the warning or caution; and

(c) immediately after the expiration date indicated by the manufacturer on the label of a livestock medicine, remove the livestock medicine from sale and keep it separate from other livestock medicines until it is disposed of in a manner approved by the Director.

(2) No licensee shall engage in any practice by which a livestock medicine is held out as an inducement for the purchase of livestock medicines or other goods, or by which other goods are held out as an inducement for the purchase of livestock medicines.

(3) No licensee shall store or permit to be stored any food or medicine for human consumption in a refrigerator, cabinet or facility used for the storage of livestock medicines. R.R.O. 1990, Reg. 730, s. 8.

**9.** (1) Every licensee shall keep accurate records of the livestock medicines sold by the licensee, and the record of each sale shall include,

(a) the date of the sale;

(b) the name and address of the purchaser;

(c) the brand name and quantity; and

(d) the lot numbers of any biologicals.

(2) Every record of a sale of livestock medicines shall be kept for a period of at least two years. R.R.O. 1990, Reg. 730, s. 9.

**10.** No advertising in respect of livestock medicines by a licensee shall exceed the claims or information set out on the manufacturer's label. R.R.O. 1990, Reg. 730, s. 10.

**11.** (1) Where an inspector seizes, removes or detains any livestock medicine under clause 3 (5) (c) of the Act, the inspector shall,

(a) attach thereto a tag bearing a serial number and the words "Ont. Detained";

(b) forthwith thereafter notify the owner or the person who had possession thereof in writing of,

(i) the seizure, and

(ii) the grounds on which the seizure was made; and

(c) direct that the livestock medicine be detained in the place where it was found or be removed to another place designated by him or her.

(2) Where a livestock medicine is detained, no person shall,

(a) remove the tag attached to it; or

(b) sell, offer to sell, move or allow or cause to be moved such livestock medicine.

(3) Where an inspector is satisfied that,

(a) the licensee is not contravening the Act or this Regulation with regard to a livestock medicine that is detained; or

(b) the person whose livestock medicine is detained is authorized to sell livestock medicines to owners of livestock for the treatment of livestock,

the inspector shall remove the attached tag and release the livestock medicine from detention.

(4) Where,

(a) after a hearing, the Director finds,

(i) that there is a contravention of the Act or this Regulation by the licensee whose livestock medicine is detained, or

(ii) that the person whose livestock medicine is detained is not authorized to sell livestock medicines to owners of livestock for the treatment of livestock; or

(b) a person is convicted of an offence against the Act or this Regulation in respect of livestock medicine that is detained,

the Director may direct that the livestock medicine be destroyed or disposed of in such manner as he or she considers advisable.

(5) Any proceeds realized from the disposal of livestock medicine under subsection (4) shall be paid to the Minister of Finance. R.R.O. 1990, Reg. 730, s. 11.

**12.** Where a licence is refused, suspended or revoked, any livestock medicines in the possession of the applicant or licensee shall be removed and disposed of under the supervision of an inspector by,

(a) their sale to a person authorized to sell livestock medicines;

(b) their return to the supplier of the livestock medicines; or

(c) any other method satisfactory to the Director. R.R.O. 1990, Reg. 730, s. 12.

**13.** In addition to the grounds mentioned in section 6 of the Act, the Director may refuse to renew or may suspend or revoke a licence where the licensee sells any drug other than a livestock medicine. R.R.O. 1990, Reg. 730, s. 13. <sup>31</sup>

### **Status Among U.S. Certifiers**

Oregon does not have specific limitations on materials used for crops and livestock. If the materials comply with USDA regulations, they are deemed acceptable for use in the state of Oregon. (Contact- Ron McKay) <sup>32</sup>

Pennsylvania is in accordance with guidelines proposed by OMRI.  
(Contact- Martha Melton- state certifier) <sup>33</sup>

Minnesota does not have specific limitations on materials used for crops and livestock. If the materials comply with USDA regulations, they are deemed acceptable for use in the state of Minnesota. (Contact- Mary Hanks- state certifier) <sup>34</sup>

### **International**

**IFOAM:** Basic standards 2002- not explicitly listed as approved food additive or processing aid<sup>35</sup>

**Italy:** Section PZ.01 Rev. 00

6.4 In case synthetic drugs are used, the safety interval to be applied is twice the one showed on the on the product's wrapping, with a minimum interval of six days for milk, and 30 days for meat. <sup>36</sup>

**EU:** EC reg. no 2092/91 + Council proposal 8697/98 does not reference synthetic drugs as restricted substances in their standards <sup>37</sup>

**Codex:** Bismuth subsalicylate is not specified on Basic Standards list but in 1993 a law was passed Controlling the use of veterinary medicines (no. 38) <sup>38</sup> Codex Alimentarius Alinorm 99/22 Does not reference synthetic drugs as restricted substances in their standards <sup>39</sup>

**Canada:** there are no Canadian regulations for bismuth; it is not a WHIMS controlled product <sup>40</sup>

<sup>31</sup> Copied directly from [http://192.75.156.68/DBLaws/Regs/English/900730\\_e.htm](http://192.75.156.68/DBLaws/Regs/English/900730_e.htm)

<sup>32</sup> Information was referenced from a phone interview with Ron McKay, State Certifier, June 5, 2002.

<sup>33</sup> Information was referenced from a phone interview with Martha Melton, State Certifier, June 5, 2002

<sup>34</sup> Information was referenced from a phone interview with Mary Hanks, State Certifier, June 12, 2002

<sup>35</sup> This information was referenced from [http://www.ifoam.org/standard/ibs\\_final02.html](http://www.ifoam.org/standard/ibs_final02.html)

<sup>36</sup> This information was referenced from <http://www.aiab.it/associazione/disciplinari/pdf/PZ0100ing.pdf>

<sup>37</sup> This information was referenced from [http://www.organic-research.com/LawsRegs/db/db\\_medicine\\_int.asp](http://www.organic-research.com/LawsRegs/db/db_medicine_int.asp)

<sup>38</sup> This information was referenced from [http://www.codexalimentarius.net/standard\\_list.asp](http://www.codexalimentarius.net/standard_list.asp)

<sup>39</sup> This information was referenced from [http://www.organic-research.com/LawsRegs/db/db\\_medicine\\_int.asp](http://www.organic-research.com/LawsRegs/db/db_medicine_int.asp)

<sup>40</sup> This information was referenced from <http://www.conostan.com/msds/bismuth.pdf>

## **Section 2119 OFPA U.S.C. 6518(m)(1-7) Criteria**

1. *The potential of the substance for detrimental interactions with other materials used in organic farming systems.*

Bismuth subsalicylate is a benign substance which if used in accordance with FDA regulations for drug use, it is considered safe. Adverse interactions occur with Salicylate-containing herbs including meadowsweet, poplar, and wintergreen. Wintergreen is also known as methyl salicylate. This is used in sports cream rubs and normally will not be used by organic farmers in livestock. The risk of detrimental interactions is minimal. Meadowsweet is an herbal medicine that is used in the aid of diarrhea as well as a stomach corrector. Bismuth subsalicylate and meadowsweet should not be mixed.<sup>41</sup>

2. *The toxicity and mode of action of the substance and of its break down products or any contaminants, and their persistence and areas of concentration in the environment.*

Bismuth is being produced and used as an alloying component, a catalyst for acrylic fibers, and in fire detection safety devices. This production may cause bismuth to be released into the environment through water waste streams. Bismuth used in pharmaceuticals including bismuth subsalicylate may be released into the environment as well. "Its production and use in pharmaceutical compounds such as bismuth subsalicylate and bismuth subnitrate may also lead to its release to the environment (1, SRC)." "Bismuth was found in the effluent of an aluminum processing plant in India at concentrations between 10 and 42 mg/kg. Effluent in municipal sludge contained 1.3 to 2.2 ppm of bismuth. Production of bismuth metal, oxide and nitrate lead to the formation and ejection of aerosols of these compounds at [concentrations] of 3.7 to 17.1 mg bismuth/cu m."<sup>42</sup> The primary minerals of Bi are mainly bismuthinite (Bi<sub>2</sub>S<sub>3</sub>) which commonly exists in hydrothermal deposits with other sulphide minerals, and bismite (Bi<sub>2</sub>O<sub>3</sub>). Bismuth is considered a rare metal in the Earth's crust and its higher concentrations commonly found in argillaceous sediments, do not exceed 0.5 mg/kg. However, Bi accumulation in coals and in graphite shale of up to about 5 mg/kg has been reported (Kabata-Pendias and Pendias, 1984). Levinson (1974) and Bowen (1979) compiled the mean Bi content of different rock types (Table 2-15).

Table 2-15. Average concentrations of Bi in the earth's crust and rocks (mg/kg).

Levinson (1974) Bowen (1979)

Earth's crust 0.170.048

ultramafic igneous 0.02-

basaltic igneous 0.150.031

granodiorite -

granitic igneous 0.100.065

shales and/or clays 0.180.48

limestones 0.17

<sup>41</sup> This information was referenced from <http://www.botanical.com/botanical/mgmh/m/meadow28.html>

<sup>42</sup> This information was referenced from <http://www.cas.org/ONLINE/DBSS/hsdbss.html>

sandstones- 0.18

phosphorites-<0.05-0.4

coal-0.05

The study of Bi concentrations in plants has not been undertaken extensively. Both Fergusson (1990) and Bowen (1979) reported that Bi concentrations in plants were less than 0.06 mg/kg (DW). Bismuth levels in plants grown on uncontaminated land are shown in Appendix 1-11. Bismuth levels in plants grown on soils contaminated by past mining activities do not exceed 0.2 mg/kg (DW) (Li and Thornton, 1993b). Bismuth, however, is likely to be concentrated at some contaminated sites due to its high concentration in some coals and sewage sludge. Bismuth concentrations in fresh water are around 0.02 mg/l (Bowen, 1979) and its content in ground water and surface water is about 0.005 mg/l (Rose *et al.*, 1979). Some Bi levels in water are also shown in Appendix 1-12. As with Sb, concentrations of Bi in edible plants and its toxicity to plants, animals and humans have been poorly investigated.<sup>43</sup> “Major producers of Bismuth are Peru, Japan, Mexico, Bolivia and Canada. Bismuth is found free in nature and in such ores as bismuth glance and bismite which are primarily found in South America but are rare in the United States. In the United States bismuth is obtained as a by-product in refining lead, copper, tin, silver, and gold ores.”<sup>44</sup>

### 3. *The probability of environmental contamination during manufacture, use, misuse, or disposal of the substance.*

“Bismuth is a non-toxic metal that is approved by governments and environmentalists as safe.”<sup>45</sup> Although bismuth is flammable in its powder state, it is not regulated by OSHA nor is it considered a carcinogen. The disposal of bismuth should be in compliance with local, state, and government regulations and should be done in a manner not to stir up dust. Bismuth is insoluble in water and is not considered harmful to human health or the environment. Any bismuth products or byproducts should be contained in a tightly sealed container while not in use.<sup>46</sup> Bismuth has “been evaluated for RCRA characteristics and does not meet hazardous waste criteria if discarded in its purchased form.” Because bismuth is mixed with other substances and becomes transformed particularly in pharmaceutical use (making of bismuth subsalicylate) the resulting substance or product may potentially become hazardous and it becomes the manufacturer’s responsibility to determine whether it meets RCRA hazardous waste criteria. Proper disposal techniques should be administered for different bismuth containing substances based on processing terms.<sup>47</sup> Bismuth subsalicylate as used for dysentery treatment and ulcers is considered non hazardous to the environment. “Unlike most heavy metals, bismuth is recognized as **one of the environmentally safest elements, and is noncarcinogenic**. A growing number of industrial applications use bismuth as a substitute for more toxic metals like lead.”<sup>48</sup> “Bismuth Subsalicylate is the active ingredient in Pepto-Bismol. It is also used in other kinds [of] medicine, such as aspirin. Since bismuth is the poorest heat conductor of all metals except mercury, it is good to use in electrical fuses, automatic fire alarms, and sprinkler system because it won’t catch fire.”<sup>49</sup>

### 4. *The effects of the substance on human health.*

Possible side effects with overindulgence of bismuth subsalicylate include: temporary, harmless darkening of the tongue or stool; risk of Reye syndrome in children or teenagers who have or are recovering from flu or chickenpox; and ringing in the ears.<sup>50</sup>

<sup>43</sup> Copied directly from <http://venus.semyung.ac.kr/~jmc65/data/my-work/phd2.htm>

<sup>44</sup> Directly referenced from <http://www.carondelet.pvt.k12.ca.us/Family/Science/Nitrogen/bismuth.html>

<sup>45</sup> This information was referenced from <http://www.fabunet.com/bismuth/>

<sup>46</sup> This information was referenced from <http://www.conostan.com/msds/bismuth.pdf>

<sup>47</sup> This information was referenced from <http://www.conostan.com/msds/bismuth.pdf>

<sup>48</sup> Cited directly from <http://www.resource-world.net/Bi.htm>

<sup>49</sup> Directly referenced from [http://www.gfsnet.org/msweb/its\\_elementary\\_02%20copy/bismuth.htm](http://www.gfsnet.org/msweb/its_elementary_02%20copy/bismuth.htm)

<sup>50</sup> This information was referenced from <http://www.fda.gov/fdac/reprints/tummy.html>

**Minimum Fatal Dose Level:**

3(?). 3= MODERATELY TOXIC: PROBABLE ORAL LETHAL DOSE (HUMAN) 0.5-5 G/KG, BETWEEN 1 OZ & 1 PINT FOR 70 KG PERSON (150 LB).

[Gosselin, R.E., H.C. Hodge, R.P. Smith, and M.N. Gleason. *Clinical Toxicology of Commercial Products*. 4th ed. Baltimore: Williams and Wilkins, 1976.,p. II-93]\*\*PEER REVIEWED\*\*<sup>51</sup>

**-EMERGENCY PROCEDURES =====**

\*SKIN CONTACT: IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash all affected skin areas thoroughly with soap and water. If symptoms such as redness or irritation develop, IMMEDIATELY call a physician and be prepared to transport the victim to a hospital for treatment.

\*INHALATION: IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital. Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Respirator Recommendation.

\*EYE CONTACT: First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center. Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician. IMMEDIATELY transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop.

\*INGESTION: DO NOT INDUCE VOMITING. If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a hospital or poison control center. Be prepared to transport the victim to a hospital if advised by a physician. If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY transport the victim to a hospital.

\*SYMPTOMS: Symptoms of exposure to this compound may include headache, nausea, foul breath, blue-black line on the gums and stomatitis.

\*FIREFIGHTING: Not available<sup>52</sup>

“Salicylates have not been shown to cause birth defects in humans. However, studies in animals have shown that salicylates may cause birth defects.”<sup>53</sup>

5. *The effects of the substance on biological and chemical interactions in the agroecosystem, including the physiological effects of the substance on soil organisms(including the salt index and solubility of the soil), crops and livestock.*

“Bismuth is not expected to volatilize from moist or dry soil.” Bismuth used in pharmaceuticals including bismuth subsalicylate may be released into the environment as well. Bismuth has been found in surface waters and sediment.<sup>54</sup> The Kentucky State Implementation plan has said that bismuth may be potentially harmful to the animals, humans, and plants.

<sup>51</sup> This information was referenced from <http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?/temp/~AAAwkaOzQ:1>

<sup>52</sup> Copied, unaltered from [http://157.98.10.135/NTP\\_Reports/NTP\\_Chem\\_HS\\_HTML/NTP\\_Chem1/Radian14882-18-9.html](http://157.98.10.135/NTP_Reports/NTP_Chem_HS_HTML/NTP_Chem1/Radian14882-18-9.html)

<sup>53</sup> This information was referenced from [http://www.type40.com/Jolynne/drug\\_pepto-bismol.html](http://www.type40.com/Jolynne/drug_pepto-bismol.html).

<sup>54</sup> This information was referenced from <http://www.cas.org/ONLINE/DBSS/hsdbss.html>



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**401 KAR 63:020. Potentially hazardous matter or toxic substances.**

NATURAL RESOURCES AND ENVIRONMENTAL PROTECTION CABINET

Department for Environmental Protection

Division for Air Quality

Relates to: KRS Chapter 224

Pursuant to: KRS 13.082, 224.033

Necessity and Function: KRS 224.033 requires the Department for Natural Resources and Environmental Protection to prescribe regulations for the prevention, abatement, and control of air pollution. This regulation provides for the control of emissions of potentially hazardous matter and toxic substances.

**Section 1. Applicability.** The provisions of this regulation are applicable to each affected facility which emits or may emit potentially hazardous matter or toxic substances as defined in Section 2, provided such emissions are not elsewhere subject to the provisions of the regulations of the Division of Air Pollution.

**Section 2. Definitions.** Terms used in this regulation not defined herein shall have the meaning given to them in 401 KAR 50:010.

(1) "Classification date" means April 9, 1972.

(2) "Potentially hazardous matter or toxic substances" means matter which may be harmful to the health and welfare of humans, animals, and plants, including, but not limited to, antimony, arsenic, **bismuth**, lead, silica, tin, and compounds of such materials.<sup>55</sup>

The old Ottawa City Landfill has portions of which were under review by EPA. EPA collected soil samples from the landfill in November, 1989 which contained elevated levels of three radioactive metals (radium-226, lead-214, and bismuth-214). Although radioactive, bismuth is considered non-toxic to the environment.<sup>56</sup> Bismuth [concentrations] in surface soils in the vicinity of mines and smelters range from 0.4-122 mg/kg dry wt, 4.2 mg/kg; the background level of bismuth in soil is 0.3 mg/kg. Sediment from Lake St. Clair had mean [concentrations] of bismuth of 0.372 and 0.296 mg/kg. River sediment in La Rioja, Argentina, contained bismuth at concentrations between 0.001 and 1.90ug/g. Bismuth was detected, not quantified, in the sediment in Puget Sound, Washington.<sup>57</sup> Bismuth should not be flushed directly into surface water or sewer systems. Generally speaking, bismuth is not harmful to the environment but may be a slight hazard in its powder form due to its flammability. "Overall the behaviour of Bi in soils and its distribution and uptake in plants is not fully understood."<sup>58</sup>

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<sup>55</sup> This information was referenced from <http://www.epa.gov/region4/air/sips/ky/63-020.htm>

<sup>56</sup> This information was referenced from <http://www.epa.gov/superfund/sites/npl/nar1303.htm>

<sup>57</sup> This information was referenced from Copied directly from <http://www.cas.org/ONLINE/DBSS/hsdbss.html>

<sup>58</sup> This information was referenced from <http://venus.semyung.ac.kr/~jmc65/data/my-work/phd2.htm>

6. *The alternatives to using the substance in terms of practices or other available materials.*

This first line of diarrhea treatment is compensating for fluid and electrolyte loss. Ninety percent of duodenal ulcers and seventy percent of gastric ulcers, occurring in both humans and livestock, are caused by *Helicobacter pylori* (H. pylori). Currently, the best remedy for H. pylori is a combination of a proton pump inhibitor, PPI, and two antibiotics. H. pylori eradication therapies include bismuth subsalicylate as well as amoxicillin, lansoprazole, clarithromycin, and metronidazole. Tetracycline is also a widely used alternative to bismuth subsalicylate for treating bacteria induced rectal and digestive problems.<sup>59</sup> A very common plant grown and cultivated in the U.S. as well all over the world is *Symphytum officinale*, also known as Comfrey. Comfrey is widely used as an alternative to bismuth subsalicylate. “For livestock, it is recommended as a treatment for internal hemorrhaging, ulcers, arthritis, broken bones, and rheumatism.” It is beneficial to add molasses to Comfrey when treating livestock ulcers. The normal dosage for livestock broken bones is two handfuls of “well bruised” roots/day.<sup>60</sup>

7. *Its compatibility with a system of sustainable agriculture.*

Bismuth is considered non-toxic to the environment and has actually been implemented as an alternative use to lead ammunition for the military and private use. The use of bismuth for ammunition is beneficial because it eliminates “adverse effects on outdoor ecosystems and reduce[s] costs of any cleanups.” The decomposition of bismuth may form carbon oxides, other bismuth compounds, or other non carbon oxides. Carbon monoxide may be produced if bismuth undergoes an incomplete combustion or decomposition. Elemental bismuth does contain petroleum hydrocarbons which, under the Clean Water Act, is considered hazardous if spilled into navigable waters.

## TAP DISCUSSION

**Reviewer 1** [Ph.D., M.S., Research interest: swine nutrition. Professor of Animal Science, University of Missouri-Columbia]

### Summary

Below are my recommendations for the use of bismuth subsalicylate in “organic” livestock production:

One important fact that must be considered is that bismuth (Bi) is a “heavy metal”, right next to lead (Pb) in the Periodic Table. Bismuth is obtained as a byproduct from the processing of lead, copper and tin ores, and has many industrial uses. Bismuth forms salts with more than a dozen anions (The Merck Index, Merck & Co., Inc. Rahway, NJ), of which most are insoluble in water and alcohol, including subsalicylate.

Bismuth subsalicylate is synthesized chemically for commercial purposes. It “binds or neutralizes” toxic bacteria to control scours (diarrhea) in farm animals. One possible mode of action of bismuth subsalicylate is that it controls these harmful bacterial populations by reducing the bacterial population. This is logical because most bismuth salts would become toxic to all living organisms, especially animals, if ingested continuously at some minimum daily amount for some minimum time period, probably weeks or a few months.

Therefore, the use of bismuth subsalicylate SHOULD BE RESTRICTED to short-term use for bacterial scours of YOUNG farm animals (e.g. weanling pigs and baby calves). It should not be approved for use in older animals as a substitute for “poor management” (e.g. over feeding grain or legumes to cattle), except as prescribed by a veterinarian to treat or save animals in emergency situations.

Summary of recommendations for use of bismuth subsalicylate in farm animals:

<sup>59</sup> This information was reference from [http://www.anthem.com/anthem/affiliates/anthemcbnsnv/formulary/gastrointestinal\\_drugs.htm](http://www.anthem.com/anthem/affiliates/anthemcbnsnv/formulary/gastrointestinal_drugs.htm)

<sup>60</sup> This information was referenced from <http://www.ansci.cornell.edu/plants/medicinal/comf.html>

- (1) Approve for short-term use by farmers to control scours of young farm animals at weaning.
- (2) Do not approve for farmer use with older growing and/or adult farm animals for problems that occur because of "poor management".
- (3) However, approve for use by veterinarians as required for farm animals of all ages for short-term use in emergency situations.

**Reviewer1 Conclusions**

Bismuth subsalicylate is synthesized chemically for commercial purposes. Bismuth subsalicylate is synthetic.

**Reviewer 1 Recommendations to NOSB**

Bismuth subsalicylate should be approved with restrictions.

**Reviewer 2** *[The reviewer has a Ph.D. in Food Engineering and is presently a faculty member in Food Science Department in a university on the west coast.]*

**Comments on Database**

The following information needs to be corrected or added to the database:

No additional information is required.

**Summary**

The report discusses that organic farmers feed bismuth subsalicylate to livestock to cure diarrhea and provide relief from ulcers. It appears that bismuth subsalicylate is a life saver for baby calves suffering from Colibacillosis (diarrhea within the first seven days of calf's life). The substance is also used to treat Salmonellosis in young animals. It is currently under review by USDA and is neither listed as an allowed synthetic substance nor a prohibited substance. FDA proposes a labeling warning that products containing bismuth subsalicylate not be given to children and teenagers recovering from chickenpox, flu symptoms or flu. EPA has found it to have no significant adverse effect on the environment. HSDB considers this substance to have shown adverse reproductive effects in animals. This point needs more discussion, but is mentioned only in a single sentence in the report. The report discusses adverse interaction of this substance with other materials used in organic farming. For example, bismuth subsalicylate has adverse interactions with salicylate containing drugs such as meadowsweet, poplar and wintergreen. There is also a discussion on the alternatives substances with a similar use. The drugs with which bismuth subsalicylate should not be administered to animals are also listed.

My only concern about this report is that most of the information has been gathered from websites. Only a few scientific journals have been cited. Although it is credible to cite reports listed on websites such as NIH, FDA etc., a lot of information has also been gathered from websites of non profit and commercial organizations. Especially, the information presented in the first few pages on uses of bismuth subsalicylate was gathered mainly from commercial websites. Such information could be biased and incomplete. Given that information obtained from these websites is based upon scientific methods, I would recommend considering bismuth subsalicylate as an allowable substance for use by organic farmers. However, it is important to administer the right dosage amounts, administering it with compatible substances and following other precautionary measures listed in the report. Further research/discussion on its adverse effects as a carcinogen, mutagen and its effect on animal reproductive system is also needed.

**Reviewer 2 Conclusions**

Bismuth subsalicylate is synthetic.

**Reviewer 2 Recommendations to NOSB**

Assuming all information in report obtained information from non-biased and scientifically supported websites, bismuth subsalicylate should be approved with restrictions.

**Reviewer 3** [*Ph.D., Professor of Organic and Biological Polymer Chemistry, Louisiana State University*]

**Comments on Database**

The following information needs to be corrected or added to the database:

No additional information is required.

The Technical Advisory Panel's review of bismuth subsalicylate, its chemistry and applications is adequate to understand how the compound would be useful in livestock production.

**Summary**

Bismuth subsalicylate is the bismuth salt of salicylic acid. Bismuth is recognized as one of the environmentally safest elements, and is noncarcinogenic. Salicylic acid is more commonly known as "aspirin", a well known organic compound. Bismuth subsalicylate acts by binding temporarily to the body, or to some body contaminant until it is removed. By binding in either of these two modes, bismuth subsalicylate passivates a body disturbance or toxin until it can be removed. It is this property of passivation for which bismuth subsalicylate is recognized in humans and animals.

A key issue is whether bismuth subsalicylate adds or changes the host organism in any permanent way. Bismuth subsalicylate does not remain in the host organism permanently and it does not cause a permanent change. Therefore, it does not require restricted use.

**Reviewer 3 Conclusions**

Bismuth subsalicylate is synthetic.

**Reviewer 3 Recommendations to NOSB**

Bismuth subsalicylate should be approved without restrictions.