National Organic Standards Board
Livestock Subcommittee
Discussion Document: Use of Parasiticides in Organic Livestock Production
August 18, 2015

I. INTRODUCTION:
The use of synthetic parasiticides in organic production is strictly confined to emergencies. Synthetic parasiticides cannot be used routinely, but sick animals must be treated. Typically farmers bring clean animals into their herds or flocks, select breeds which have high resistance to parasites, and manage their land, especially pastures, in a manner which reduces the likelihood of parasite infection. If an increased parasite load is noted in fecal egg counts, farmers have a broad array of alternative treatments available. But when all else fails and animals are not doing well, the farmer, working with the veterinarian, may need to use one of the synthetic parasiticides on the National List.

At the present time, there are three (3) substances on the National List which are approved for use as parasiticides for organic livestock: Ivermectin, Moxidectin and Fenbenzadole. All three of these materials are presently being reviewed as part of the regular five-year Sunset process. All three materials have annotations and other language limiting usage. Such language was developed when Ivermectin was first added to the National List. Recent data and information indicates that if Moxidectin and Fenbenzadole remain on the National List, milk withholding and other restrictions could be modified in a manner which would be beneficial to the sick animal in emergency situations, without jeopardizing the quality of the organic product. In conventional milk production there is no withholding for fenbenzadole or moxidectin, but for organic milk there is a 90-day withholding period. Organic slaughter stock may never be treated with synthetic parasiticides.

Public comment is requested to guide the NOSB in determining if a proposal is needed to modify the withholding period, especially for milk, and/or allow the skin and fleece of animals treated with a parasiticide to be sold as organic.

II BACKGROUND:
In October 1999 the NOSB voted on three parasiticides for inclusion on the National List. Only Ivermectin had sufficient votes be added to the List. The votes were: Ivermectin 8-3-0, Fenbendazole 5-6-0, and Levamisole 0-11-0.

In April 2004, the NOSB voted to add Moxidectin to the National List by a vote of 11-1-1-1. The annotation "for control of internal parasites only" was included for Moxidectin for the given reason that "there is much less chance of any kind of contamination if it is used for internal parasites versus external." Moxidectin was added to the National List in 2012 (77 FR 28742).

Each of the parasiticides was added to the National List with the annotation of a 90-day Withholding period.

In December 2007, after much public comment and consultation, the NOP agreed that the NOSB could require double FDA withdrawal times, or double FARAD times (when appropriate), for a number of livestock materials.

As a proposed compromise to satisfy the intent of the NOSB, many commenters suggested that

> USDA should consider amending the annotations of Atropine, Butorphanol, Flunixin, Furosemide, Tolazoline, and Xylazine by establishing extended withdrawal periods, calculated using withdrawal times from the Food Animal Residue Avoidance Databank (FARAD).The FARAD is a National Food Safety Project administered through the USDA Cooperative State Research, Education, and Extension Service. It is a system designed to provide livestock producers, extension specialists, and veterinarians with practical information on how to avoid drug, pesticide and environmental contaminant residue problems. FARAD is a repository of comprehensive residue avoidance information. It is also sanctioned to provide ''withholding period'' (also known as withdrawal period) estimates to the U.S. Pharmacopeia-Drug Information (USP–DI) Veterinary Medicine Advisory Committee. Commenters suggested that USDA account for an extra margin of at least double the withdrawal times of FARAD to safely capture the intent of the NOSB.USDA agrees with the position…
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> Based on public comment, USDA consulted further with the FDA, concerning the ability to extend the withdrawal period on these approved drugs. Based on our consultations, USDA agreed to clarify the rationale for extending the FDA established withdrawal period. Secondly, USDA agreed to clarify the language used to authorize the use of the substances by indicating the extended withdrawal periods (at least two-times that required by the FDA) were only relevant for use of the substances under the NOP regulations. Therefore, to clarify our rationale for extending the withdrawal periods established by the FDA, we acknowledge that this determination was not based on scientific research or risk assessments. The decision to extend the FDA withdrawal periods (or any other withdrawal period) for the use of Flunixin and Furosemide (and other substances) was based on consumer preference and the recommendations of the NOSB. FDA exercises full responsibility for determining and enforcing the withdrawal intervals for animal drugs. No food safety arguments are used or implied to support the use of extended withdrawal periods authorized under the NOP regulations. Rather, we determined that extended withdrawal periods are more compatible with consumer expectations of organically raised animals. (72 FR 70479)

In May 2008, Fenbendazole was approved by the NOSB for addition to the National List by a vote of 14-0 and added to the National List in 2012 (77 FR 28472).

Three technical reports have been prepared on synthetic parasiticides: a 1999 Technical Advisory Panel (TAP) Report on Fenbendazole and Ivermectin; a 2003 TAP Report of Moxidectin; and a 2015 Technical Evaluation Report on all three parasiticides (Fenbenzadole, Ivermectin and Moxidectin) that was requested by this Livestock subcommittee for our Sunset Review of parasiticides.

III RELEVANT AREAS OF THE RULE:
The USDA organic regulations at 7 CFR part 205 provide guidance on livestock production practices to prevent the need for the use of synthetic parasiticides, and on regulation of the use of parasiticides in organic livestock production:

§205.238 Livestock health care practice standard.

(a) The producer must establish and maintain preventive livestock health care practices, including:
(1) Selection of species and types of livestock with regard to suitability for site-specific conditions

and resistance to prevalent diseases and parasites;
(2) Provision of a feed ration sufficient to meet nutritional requirements, including vitamins, minerals, protein and/or amino acids, fatty acids, energy sources, and fiber (ruminants);
(3) Establishment of appropriate housing, pasture conditions, and sanitation practices to minimize the occurrence and spread of diseases and parasites;

(b) When preventive practices and veterinary biologics are inadequate to prevent sickness, a producer may administer synthetic medications: Provided, That, such medications are allowed under §205.603. Parasiticides allowed under §205.603 may be used on:
(1) Breeder stock, when used prior to the last third of gestation but not during lactation for progeny that are to be sold, labeled, or represented as organically produced; and
(2) Dairy stock, when used a minimum of 90 days prior to the production of milk or milk products that are to be sold, labeled, or represented as organic.

§205.603 Synthetic substances allowed for use in organic livestock production.

(a) As disinfectants, sanitizer, and medical treatments as applicable.
(18) Parasiticides—Prohibited in slaughter stock, allowed in emergency treatment for dairy and breeder stock when organic system plan-approved preventive management does not prevent infestation. Milk or milk products from a treated animal cannot be labeled as provided for in subpart D of this part for 90 days following treatment. In breeder stock, treatment cannot occur during the last third of gestation if the progeny will be sold as organic and must not be used during the lactation period for breeding stock.
(i) Fenbendazole (CAS #43210-67-9)—only for use by or on the lawful written order of a licensed veterinarian.
(ii) Ivermectin (CAS #70288-86-7).
(iii) Moxidectin (CAS #113507-06-5)—for control of internal parasites only.

IV DISCUSSION:

Parasiticide Uses:

Fenbenzadole:

The US Food and Drug Administration Center for Veterinary Medicine and the US Department of Agriculture National Organic Program permit oral administration of fenbendazole in dairy cattle for the removal and control of lungworm (Dictyocaulus viviparus); brown stomach worm (Ostertagia ostertagi), barberpole worm (Haemonchus contortus and H. placei), small stomach worm (Trichostrongylus axei), hookworm (Bunostomum phlebotomum), threadnecked intestinal worm (Nematodirus helvetianus), small intestinal worm (Cooperia punctata and C. oncophora), bankrupt worm (Trichostrongylus colubriformis) and nodular worm (Oesophagostomum radiatum); in beef cattle (beef) for the removal and control of stomach worm (Ostertagia ostertagi) and tapeworm (Moniezia benedeni); in goats for the removal and control of stomach worms (Haemonchus contortus and Teladorsagia circumcincta); in swine for the removal and control of lungworms (Metastrongylus apri and M. pudendotectus), roundworms (Ascaris suum), nodular worms (Oesophagostomum dentatum, O. quadrispinulatum), small stomach worms (Hyostrongylus rubidus), whipworms (Trichuris suis) and kidney worms (Stephanurus dentatus) and in turkeys for the removal and control of round worms (Ascaridia dissimilis) and cecal worms (Heterakis gallinarum). Currently, fenbendazole is sold by Merck Animal Health as Panacur® and Safe-Guard®. It is available in liquid suspension, as granules, as a paste and in blocks. Products are dispensed both by veterinarian's prescription and over the counter, but must be used in organic production only under veterinary supervision. For swine, turkeys, and wild sheep the NADA (141-144, 140-954, 136-116, 131-675) for fenbendazole is for use in medicated feed only. Other 300 uses for these animals are extralabel. Furthermore, the use of fenbendazole in medicated feed for domestic 301 sheep in food production is not

permitted by the FDA (TR 2015 284-302).

Ivermectin:
The US Food and Drug Administration Center for Veterinary Medicine and the US Department of Agriculture National Organic Program permit topical, subcutaneous and oral administration of ivermectin in cattle for the treatment and control of gastrointestinal nematodes: Haemonchus placei, Ostertagia ostertagi, O. lyrata, Trichostrongylus axei, T. colubriformis, Cooperia oncophora, C. punctata, C. pectinata, Oesophagostomum radiatum, Nematodirus helvetianus, N. spathiger, Bunostomum phlebotomum, lungworms: Dictyocaulus viviparous, grubs Hypoderma bovis, H. lineatum, sucking lice: Linognathus vituli, Haematopinus eurysternus, Solenopotes capillatus, mites: Psoroptes ovis (syn. P. communis var. bovis), Sarcoptes scabiei var. bovis, in reindeer for treatment and control of warbles (Oedemagena tarandi), in swine for treatment and control of gastrointestinal roundworms: Ascaris suum; red stomach worm, Hyostrongylus rubidus; nodular worm, Oesophagostomum species; threadworm, Strongyloides ransomi, somatic roundworm larvae-threadworm, Strongyloides ransomi, lungworms: Metastrongylus species, lice: Haematopinus suis, mites: Sarcoptes scabiei var. suis and ear mites: Otodectes cynotis, in american bison for the treatment and control of grubs: Hypoderma bovis and in sheep for treatment and control gastrointestinal roundworms: Haemonchus contortus, H. placei, Ostertagia circumcincta, Trichostrongylus axei, T. colubriformis, Cooperia oncophora, C. curticei, Oesophagostomum columbianum, O. venulosum, Nematodirus battus, N. spathiger, S. papillosus
Chabertia, Trichuris ovis, lungworms: Dictyocaulus filaria and all larval stages of the nasal bot Oestrus ovis. Ivermectin is marketed by Merial, Inc. and other companies under a number of pharmaceutical labels. It is available as a drench, in liquid solution, for medicated feed, as a sustained release bolus and as a paste. Products are dispensed both by veterinarian's prescription and over the counter (TR 2015, 303-321).

Moxidectin:
The US Food and Drug Administration Center for Veterinary Medicine and the US Department of Agriculture National Organic Program permit topical, subcutaneous and oral administration of moxidectin in cattle for treatment and control of internal and external parasites, gastrointestinal roundworms: Ostertagia ostertagi, Haemonchus placei, Trichostrongylus axei, T. colubriformis, Cooperia oncophora, C. pectinata, C. punctata, C. spatulata, C. surnabada, Bunostomum phlebotomum, Oesophagostomum radiatum, Nematodirus helvetianus, lungworms: Dictyocaulus viviparus, cattle grubs: Hypoderma bovis, H. lineatum, mites: Chorioptes bovis, Psoroptes ovis, P. communis var. bovis, lice: Linognathus vituli, Haematopinus eurysternus, Solenopotes capillatus, Bovicola(Damalinia) bovis and horn flies: Haematobia irritans and in sheep for the treatment and control of Haemonchus contortus, Teladorsagia circumcincta, T. trifurcata, Trichostrongylus axei, T. colubriformis, T. vitrinus, Cooperia curticei, C. oncophora, Oesophagostomum columbianum, O. venulosum, Nematodirus battus, N. filicollis, and N. spathiger. Moxidectin is sold by Boehringer Ingelheim Vetmedica, Inc. as Cydectin. It is available in liquid solution. Products are dispensed over the counter (TR 2015, 322-332).

<u>Regulated approvals:</u>
The use of fenbendazole for food animals is approved under six FDA new animal drug applications (TR 2015, Table 3). It is dispensed over the counter. The use of ivermectin for food animals is approved under nineteen FDA new animal drug applications. It is dispensed both by veterinary prescription and over the counter. The use of moxidectin is approved under three new drug approval applications. It is available over the counter (TR 2015, 243-248).

Once a NADA is approved, the FDA, under the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA), can permit the use of the approved drug under specific conditions outside the designated or intended label use, e.g. use in species not listed in the labeling, use for indications (disease or other

conditions) not listed in the labeling, use at dosage levels, frequencies, or routes of administration other than those stated in the labeling, and deviation from the labeled withdrawal time based on these different uses (FDA, 1994). This "off-label" or extralabel use is only permitted in the context of a valid veterinarian-client-patient relationship and is limited to treatments when the health of an animal is threatened or suffering or death may result from failure to treat. A valid veterinarian-client-patient relationship is one in which: (1) A veterinarian has assumed the responsibility for making medical judgments regarding the health of (an) animal(s) and the need for medical treatment, and the client (the owner of the animal or animals or other caretaker) has agreed to follow the instructions of the veterinarian; (2) There is sufficient knowledge of the animal(s) by the veterinarian to initiate at least a general or preliminary diagnosis of the medical condition of the animal(s); and (3) The practicing veterinarian is readily available for follow up in case of adverse reactions or failure of the regimen of therapy. Such a relationship can exist only when the veterinarian has recently seen and is personally acquainted with the keeping and care of the animal(s) by virtue of examination of the animal(s), and/or by medically appropriate and timely visits to the premises where the animal(s) are kept (TR 2015, 249-266)

For example, there is not an FDA approved use for fenbendazole in domestic sheep; however, it is used under veterinary supervision for this purpose. Furthermore, the National List permits the use of fenbendazole only under veterinary supervision (§ 205.603(a)(18)(i)). There are some limitations for the AMDUCA including extralabel use of an approved new animal or human drug by a lay person (except when supervised by a veterinarian). (TR 2015, 266-268).

International Use and Restrictions - TR 2015, 432-507:

The organic standards of Canada prohibit the use of parasiticides with exceptions: If no alternative treatment exists a parasiticide may be administered under veterinary supervision as directed by the standard and mandated by law. Treated livestock with a withdrawal period equivalent to double the label requirement or 14 days, whichever is longer is still considered organic. Organic status for chronically infected animals is discontinued.

The Canadian Organic Standard requires organic livestock operations to have a comprehensive plan to minimize parasite problems in livestock, including monitoring and emergency measures. Normally, parasiticides cannot be administered to meat, dairy or laying animals, but in emergencies, production operations can use them: (1) if parasites are detected, (2) under veterinary instructions, (3) with double the label withdrawal time or 14 days whichever is longer, (4) with one treatment for slaughter animals under one year and two treatments for older animals (requiring more treatments will lose organic status), (5) but dairy animals requiring more than two treatments lose organic status and require a 12 month transition, (6) but dairy animals cannot be organic for slaughter, (7) and a dam may be treated during gestation, (8) and poultry flocks can be treated, but laying hens with more than one treatment per 12 months lose organic status and (9) the operator must provide a written action plan with amendments to the parasite control plan.

The organic standards of CODEX Alimentarius, the European Economic Community, Japan, and IFOAM also do not allow routine use of parasiticides, but they allow some provisions for emergency uses of parasiticides if preventative animal husbandry practices and natural remedies have been used and not found to be effective.

Like the Canadian standards, IFOAM organic standards require that when livestock are treated with synthetic parasiticides the required withdrawal time is not less than double the withdrawal period required

by legislation, or a minimum of 14 days, whichever is longer. The organic standards of Japan and CODEX Alimentarius both require a withdrawal period of double the period required by legislation or a minimum of 48 hours.

Alternatives:

There are many natural alternative parasiticides being used in organic livestock production today. Natural parasiticides include homeopathic remedies, diatomaceous earth and many herbs with anthelminthic properties. Table 10 of the 2015 TR lists over 50 botanical and alternative de-wormers. The efficacy of most of these natural alternatives is not well documented, and more research is needed. However, there does seem to be a lot of potential for the development of effective natural parasite control systems in the future.

Confusion in present annotation language:

There are some inherent contradictions and problems in the way the three parasiticides are listed and annotated on the National List:

1. Fenbendazole, which is considered the most environmentally benign, is annotated to require the "written order of a licensed veterinarian". Ivermectin and Moxidectin have no such requirement. That may lead producers to choose a more environmentally detrimental parasiticide for convenience.
2. Moxidectin is annotated "for control of internal parasites only." However, Moxidectin is widely used as a pour-on, and when used in that form for control of internal parasites it is also a de facto control for external parasites. Moreover, as mentioned above, the annotation "for control of internal parasites only" was apparently written based on incorrect information on the half-life of Moxidectin in the soil.
3. §205.603(a)(18) requires a 90-day withholding period for organic milk or milk products from a treated animal. There seems to be wide consensus that 90 days is much too long of a withholding period, because 1) it may motivate a producer to withhold needed treatment of an animal because of the severe consequences of a 90-day withdrawal, and 2) Fenbendazole and Moxidectin have no milk withdrawal time for use in conventional production. There is no scientific rationale for the 90-day withholding. The 90 days reflects a desire to assure consumers that organic standards exceed conventional use of restricted materials.

V REQUEST FOR PUBLIC COMMENT

1. Should the milk withholding period be modified for any or all of the parasiticides? If so, how many days for Moxidectin, Fenbenzadole and Ivermectin?

2. Should minimal use of parasiticides be allowed in organic slaughter stock such as is permitted under Canadian Organic standards with one treatment for slaughter animals under one year old and two treatments for older animals (requiring more treatments will lose organic status)?

3. Should sheep fleece and wool be allowed to be certified organic even if use of parasiticides was necessary at some time in the animal's life?

4. Should use of moxidectin be changed to allow both internal and external use?

5. Should use of parasiticides be allowed only under veterinarian advice?

Vote in Subcommittee

Motion to accept the discussion document on annotation changes for paraciticides
Motion by: Jean Richardson
Seconded by: Francis Thicke
Yes: 6 No: 0 Abstain: 0 Absent: 0 Recuse: 0