

## **PROPOSAL:**

# **1,3-DIBROMO-5,5-DIMETHYLHYDANTOIN (DBDMH)**

## **SUMMARY**

DBDMH is an antimicrobial chemical used in conventional slaughterhouses to control pathogenic bacteria such as *E. coli*.

Cornucopia supports the recommendation of the Handling Subcommittee to **reject** DBDMH's addition to the National List.

### ***Rationale***

- DBDMH is a chemical antimicrobial with potentially negative effects on human health and the environment. Many questions regarding its safety remain unanswered.
- DBDMH fails every criterion for inclusion on Section 205.605, including that it does not have GRAS (Generally Recognized as Safe) status with the FDA. The FDA considers DBDMH to be a “food contact substance” and the EPA considers it a pesticide.
- The petitioner withheld important information from the NOSB, the TR reviewer and the public. Withheld Confidential Business Information included an entire section titled “Effects on Human Health.”
- Alternatives exist, including those discussed at length in the TR: peracetic acid, hot water washing, chlorine and hydrogen peroxide.
- Furthermore, another alternative practice for controlling *E. coli* must be considered: grass-finishing ruminants. Research has established that 100% grass-finished ruminants, and grain-fed animals that are switched back to 100% forage for a period of time prior to slaughter, have demonstrably lower levels of *E. coli* contamination. This management model would greatly reduce the justification for using materials such as DBDMH in processing.

## **BACKGROUND**

DBDMH has been petitioned by Albemarle Corporation as an antimicrobial for use in meat processing, to control pathogenic bacteria including *E. coli*.

## *International regulations*

DBDMH is not allowed in any international organic regulations.

## **CONCERNS WITH DBDMH**

### ***Negative effects on the environment (fails 205.600(b)(2))***

First, it is important to note that very little information appears to exist regarding the environmental effects of DBDMH. This is made apparent in the TR, which lists only two sources in its discussion on DBDMH's environmental effects: the petitioner and the EPA (TR 281-309).

The Material Safety and Data Sheet (MSDS) on DBDMH states that the material is "very toxic to aquatic life." The MSDS also states, "An environmental hazard cannot be excluded in the event of unprofessional handling or disposal. Very toxic to aquatic life."

Since DBDMH breaks down to DMH and hypobromous acid (HBrO), it is important to consider the possible environmental effects of these two breakdown products.

According to the petitioner, Albemarle Corporation, in its Environmental Assessment report prepared for the FDA, "DMH is slightly toxic to fish and aquatic invertebrates."<sup>70</sup> It is interesting to note that this information, which was supplied to the FDA, was not included in its petition to the NOSB.

Furthermore, in its FDA notification, Albemarle calculated that the level of exposure to aquatic wildlife from DMH in wastewater from a poultry processing plant would be well below toxic and harmful levels. It is worth noting that the only information available on this topic is from the petitioner itself. It appears that the effects on wildlife of DMH have not been adequately studied and independently verified.

The other breakdown product is hypobromous acid (HBrO), a bromide, which is in fact the "active ingredient" of DBDMH. The TR cites Albemarle Corporation's claim that "no HBrO is expected to be released into wastewater," but again, this has not been independently verified since no independent information or data appears to exist.

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<sup>70</sup> Albemarle Corporation, Environmental Assessment.  
[http://www.fda.gov/downloads/Food/FoodIngredientsPackaging/EnvironmentalDecisions/UCM287539.pdf?utm\\_campaign=Google2&utm\\_source=fdaSearch&utm\\_medium=website&utm\\_term=1,3-dibromo-5,5-dimethylhydantoin&utm\\_content=9](http://www.fda.gov/downloads/Food/FoodIngredientsPackaging/EnvironmentalDecisions/UCM287539.pdf?utm_campaign=Google2&utm_source=fdaSearch&utm_medium=website&utm_term=1,3-dibromo-5,5-dimethylhydantoin&utm_content=9)

If hypobromous acid were to be released into wastewater, it could have negative effects on wildlife. A study by Dutch researchers found bromide affected reproductive health and endocrine function of crustaceans and fish:

“Bromide ion markedly impaired reproduction in both crustaceans and fish. Histologically no effects were observed in the long-term test with *Oryzias*, but in the reproduction test with *Poecilia*, hyperplasia of the thyroid, atrophy and degeneration of the musculature and regressive changes in the female reproductive tract were observed.”<sup>71</sup>

Albemarle Corporation has stated to the FDA that studies with sodium bromide are appropriate for determining the effects of hypobromous acid: “Since sodium bromide dissociates in water to yield the free sodium and bromide ions, the data on sodium bromide serve to provide useful information on the toxicity of the bromide ion, itself.”<sup>72</sup>

In an EPA Reregistration Eligibility Decision document for sodium bromide, the EPA noted: “The results indicate that sodium bromide, measured as bromine, is highly toxic to estuarine/marine organisms on an acute basis.”<sup>73</sup>

The EPA states that “chronic testing of sodium bromide is not required,” based on the assumption that “residues of sodium bromide (hypobromous acid) are short-lived.” The EPA states that “residues of [hypobromous acid] are highly toxic on an acute basis,” and then states that “ultimate biodegradation [will be] completed within a few weeks.” For this reason, the EPA waived the requirement for standard chronic toxicity tests. However, the effects of this “highly toxic” substance on aquatic wildlife, in the weeks before the material is completely degraded, must be considered. For this reason—to protect aquatic life from the toxicity of DBDMH’s breakdown product—the material should not be approved for use in organics.

### ***Negative effects on human health (fails 205.600(b)(3))***

#### *National Institutes of Health*

The National Institutes of Health, in a Haz-Map<sup>74</sup> listing for DBDMH, states that evidence exists of “thyroid hypofunction in repeated dose study of rats.”<sup>75</sup>

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<sup>71</sup> Canton JH, Wester PW, Mathijssen-Spiekman EAM (1983) Study on the toxicity of sodium bromide to different freshwater organisms. *Food and Chemical Toxicology* 21(4): 369-378.

<sup>72</sup>[http://www.fda.gov/downloads/Food/FoodIngredientsPackaging/EnvironmentalDecisions/UCM287539.pdf?utm\\_campaign=Google2&utm\\_source=fdaSearch&utm\\_medium=website&utm\\_term=1,3-dibromo-5,5-dimethylhydantoin&utm\\_content=9](http://www.fda.gov/downloads/Food/FoodIngredientsPackaging/EnvironmentalDecisions/UCM287539.pdf?utm_campaign=Google2&utm_source=fdaSearch&utm_medium=website&utm_term=1,3-dibromo-5,5-dimethylhydantoin&utm_content=9)

<sup>73</sup> [http://www.epa.gov/pesticides/chem\\_search/cleared\\_reviews/csr\\_PC-013907\\_30-Jun-05\\_a.pdf](http://www.epa.gov/pesticides/chem_search/cleared_reviews/csr_PC-013907_30-Jun-05_a.pdf)

<sup>74</sup> HazMap is an online database of chemicals by the National Institutes of Health. All information on the HazMap has been scientifically verified.

<sup>75</sup> <http://hazmap.nlm.nih.gov/category-details?id=9444&table=copytblagents>

The NIH Hazmap also lists the following for DBDMH: “inhalation may cause corrosive injuries to upper respiratory tract and lungs; toxic by ingestion.”<sup>76</sup>

*Environmental Protection Agency*

It is important to note that the EPA regulates DBDMH as a pesticide. It is used as a microbial control and disinfectant in water systems, ornamental ponds, swimming pools, toilet bowls, etc. The EPA recognizes the only food-use of DBDMH to be in the manufacture of food-contact paper and paperboard.<sup>77</sup>

The EPA reviewed DBDMH<sup>78</sup> in 2007 as a multi-purpose biocide. The EPA writes that the Reregistration Eligibility Decision (RED) does not cover any food-related uses other than use as a slimicide in food-contact paper and paperboard.<sup>79</sup> Therefore, it appears the EPA and FDA have not considered accumulative exposure to DBDMH.

In its Reregistration Eligibility Decision, the EPA considered the following toxicity data, from laboratory animal studies using DBDMH:

1,3-Dibromo-5,5-dimethylhydantoin			
870.1100 Acute oral toxicity-Rat	93076011, 00137105 (4334-012-01)	LD <sub>50</sub> = 760 mg/kg	III
870.1100 Acute oral toxicity-Rat	44988002, )	combined LD <sub>50</sub> = 448 mg/kg	II
870.1200 Acute dermal toxicity-Rabbit	93076025, 00137110 (4334-012-07)	LD <sub>50</sub> cannot be ascertained (study is classified as Unacceptable/non-guideline)	--
870.1200 Acute dermal toxicity-Rat	44988001	LD50 > 2000 mg/kg	III
870.1300 Acute inhalation toxicity-Rabbit	44988003	LC50 between 0.51-2.02 mg/L	II
Guideline No./ Study Type	MRID No. (TRID No.)	Results	Toxicity Category
870.2500 Primary dermal irritation-Rabbit	93076017, 00137109 (4334-012-05)	severe skin irritant	I
870.2500 Primary dermal irritation-Rabbit	44988004	corrosive	I
870.2600 Dermal Sensitization - guinea pig	44988005	non-sensitizer	N/A

**Category I** is “highly toxic and severely irritating,” and applies to two dermal irritations in rabbit studies.

<sup>76</sup> <http://hazmap.nlm.nih.gov/category-details?id=9444&table=copytblagents>

<sup>77</sup> <http://www.epa.gov/oppsrrd1/REDS/halohydantoin-red.pdf>

<sup>78</sup> EPA’s review covered halohydantoin and issued a Reregistration Eligibility Decision in September 2007. DBDMH is one of five halohydantoin covered in the RED.

<sup>79</sup> <http://www.epa.gov/oppsrrd1/REDS/halohydantoin-red.pdf>

**Category II** is “moderately toxic and moderately irritating,” and applies to the acute inhalation (rabbit) study and the acute oral toxicity (rat) studies.

**Category III** is “slightly toxic and slightly irritating,” and applies to the acute oral toxicity (rat) test and acute dermal toxicity (rat) test.

The EPA also raised concerns about one of the breakdown products of DBDMH, which is DMH. The EPA wrote: “Available metabolism data indicate that DMH and EMH are excreted unchanged in the rat. However, it is known that hydroxymethylhydantoin is a formaldehyde releaser.”

Ultimately, much remains unknown regarding these antimicrobial chemicals’ effects on human health. The EPA wrote that further studies would be needed, especially “to better characterize effects related to endocrine disruption.”

#### *Food and Drug Administration*

Both DBDMH and its breakdown product, HBrO, which is its active ingredient, are listed in the FDA’s food contact substance database. As with the FDA’s Generally Recognized As Safe (GRAS) system, the FDA does not require any independent safety testing or evaluation before a food contact substance can be used. As a result, virtually no information from independent sources is available regarding potential human health effects from eating foods treated with this chemical biocide.

The FDA database of Food Contact Substances contains the Albemarle Corporation notifications for HBrO<sup>80</sup> and DBDMH.<sup>81</sup> These notifications are remarkably lacking in safety test results. Not surprisingly, Albemarle assured the FDA that DBDMH and HBrO are safe, and since the FDA requires no independent safety testing, it has allowed its use in conventional food production.

#### *Scientific literature (peer-reviewed academic articles)*

OFPA requires that the potential impact on human health of breakdown products be considered as well. DBDMH breaks down to hypobromous acid (HBrO), which is a bromide. Albemarle writes in its petition to the FDA: “Since sodium bromide dissociates in water to yield the free sodium and bromide ions, the data on sodium bromide serve to provide useful information on the toxicity of the bromide ion, itself.”<sup>82</sup>

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<sup>80</sup><http://www.accessdata.fda.gov/scripts/fcn/fcnDetailNavigation.cfm?rpt=fcsListing&id=1197>

<sup>81</sup><http://www.accessdata.fda.gov/scripts/fcn/fcnDetailNavigation.cfm?rpt=fcsListing&id=1190>

<sup>82</sup>[http://www.fda.gov/downloads/Food/FoodIngredientsPackaging/EnvironmentalDecisions/UCM287539.pdf?utm\\_campaign=Google2&utm\\_source=fdaSearch&utm\\_medium=website&utm\\_term=1,3-dibromo-5,5-dimethylhydantoin&utm\\_content=9](http://www.fda.gov/downloads/Food/FoodIngredientsPackaging/EnvironmentalDecisions/UCM287539.pdf?utm_campaign=Google2&utm_source=fdaSearch&utm_medium=website&utm_term=1,3-dibromo-5,5-dimethylhydantoin&utm_content=9)

We searched the literature for toxicity and endocrine effects of sodium bromide. A study found that rats exposed to sodium bromide experienced “complex of changes in the endocrine system, thyroid activation being the most prominent.” A multi-generation study showed a decrease in fertility following high sodium bromide exposure. It would seem that one of the breakdown products of DBDMH may be a potential endocrine disruptor.<sup>83</sup>

*Centers for Disease Control and Prevention/National Institute for Occupational Safety and Health*

The CDC and NIOSH Occupational Health Guidelines<sup>84</sup> for DBDMH include the following:

- “Contact with water, strong acids, and easily oxidized materials such as ammonium salts, sulfides, etc., may cause fires and explosions and formation of toxic fumes of chlorine and nitrogen trichloride.”
- “Toxic gases may be released in a fire involving DBDMH.”
- “Employees should be provided with and required to use impervious clothing, gloves, face shields and other appropriate protecting clothing necessary to prevent repeated or prolonged skin contact with solid or liquids containing DBDMH.”
- Causes irreversible eye damage
- Causes burns. May be absorbed through the skin in harmful amounts.
- “May be harmful if inhaled. Material is extremely destructive to the tissue of the mucous membranes and upper respiratory tract.”
- “Causes severe burns and eye damage”
- “Toxic if swallowed.” “May be fatal if swallowed.”

***DBDMH does not have GRAS status with the FDA (205.600(b)(5))***

DBDMH does not have GRAS status with the FDA. It is regulated as a “food contact substance” by the FDA and as a pesticide by the EPA.

***Alternatives exist (205.600(b)(1)) and DBDMH is not essential (205.600(b)(6))***

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<sup>83</sup> Van Leeuwen FXR, den Tonkelaar EM, van Logten MJ (1983) Toxicity of sodium bromide in rats: effects on endocrine system and reproduction. *Food and Chemical Toxicology* 21(4): 383-389.

<sup>84</sup> <http://www.cdc.gov/niosh/docs/81-123/pdfs/0193.pdf>

Alternatives to DBDMH exist, including hot water sprays and other antimicrobials already on the National List, including lactic acid, peracetic acid and ozone. These appear to be working fine, as the FDA outbreaks database shows that there have been no outbreaks of illnesses traced to the consumption of organic meat.<sup>85</sup>

### ***Grass-finishing ruminants reduces potential E. coli contamination***

Studies show that *E. coli* contamination of beef carcasses may be preventable when ruminants are given their natural diet of pasture and hay prior to slaughter.

Early studies from the 1960s and 1970s showed that a decrease in hay intake and overfeeding with grains causes an increase in total fecal coliform counts.<sup>86</sup> The groundbreaking study that defined this debate was by Cornell researchers in 1998.<sup>87</sup> They found that cattle fed a 90% corn/soy ration (typical of feedlot diets) contained generic *E. coli* populations that were 1000-fold higher than cattle fed a 100% good-quality hay diet. The researchers also found that the *E. coli* recovered from the feces were 1,000-fold more resistant to the “acid shock” test (simulating whether it would survive the ‘acid shock’ of entering the human stomach) than the *E. coli* recovered from cattle fed 100% hay. The scientists found that switching cattle from a grain-diet to a hay-diet five days prior to slaughter could reduce the prevalence of *E. coli*. One limitation of this study is that no O157:H7 *e. coli*, a particularly dangerous strain, were detected.

Numerous studies have been conducted, and a 2009 review of these studies concludes that “comparing grain-fed to forage-fed cattle still indicates that more *E. coli* (including O157:H7) is present in the feces of grain-fed cattle.”<sup>88</sup>

### ***Additional human health concerns***

Since DBDMH is an antimicrobial, it raises the question of whether residues on meat would impact beneficial intestinal flora of the consumer.

There appears to be no scientific studies conducted to ensure that foods treated with this antimicrobial chemical do not negatively impact beneficial intestinal flora.

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<sup>85</sup> Food and Drug Administration, based on a search of the Recalls, Market Withdrawals and Safety Alerts Database. Available: <http://www.fda.gov/Safety/Recalls/default.htm>

<sup>86</sup> Brownlie, L.E. and F.H. Grau (1967) Effect of food intake on growth and survival of salmonellas and *Escherichia coli* in the bovine rumen. *Journal of General Microbiology* 46: 125; see also Allison, M. J., Robinson, I. M., Dougherty, R. W and J. A. Bucklin (1975) Grain overload in cattle and sheep: changes in microbial populations in the cecum and rumen. *American Journal of Veterinary Research* 36: 181–185

<sup>87</sup> Diez-Gonzalez, T., Calloway, T.R., Kizoulis, M.G. and J.B. Russell (1998) Grain feeding and the dissemination of acid-resistant *Escherichia coli* from cattle. *Science* 281:1666-8

<sup>88</sup> Callaway et al. (2009) “Diet, *E. Coli* O157:H7, and Cattle: A Review after 10 Years.” *Current Issues in Molecular Biology* 11:67-80

## CONCLUSION

The Handling Subcommittee voted unanimously to reject DBDMH from addition to the National List. We agree that the petition for DBDMH should be rejected.

The lack of publicly available safety testing data, combined with strong indications that human health and environmental concerns exist, renders this material a “poster child” of why US consumers are switching to the organic label, which mandates greater scrutiny of chemical inputs in food production.

Moreover, some of the answers on the decision tree should be corrected. We do not agree that the answer to “Are there adverse effects on environment from manufacture, use and disposal?” should be “no.” It appears that DBDMH and its breakdown product, HBrO, are both toxic to aquatic life. The only information regarding the environmental impacts of DBDMH comes from the petitioner. If anything, the environmental impacts are unknown, and we do not believe the Handling Subcommittee has enough information to confidently state that no negative environmental effects exist.

The Handling Subcommittee answered “no” to the question, “Is there any harmful effect on human health?” The entire section titled “Effects on Human Health” was redacted from the petition, as “Confidential Business Information.” This causes suspicion. If the content of this section revealed that test results affirmed DBDMH’s safety, would it be considered Confidential Business Information? Multiple animal studies on DBDMH and its breakdown product, HBrO, have shown effects on reproductive and endocrine function. Again, the fact that the Handling Subcommittee does not know the answer to this question does not justify the assumption that the material is perfectly safe for human health.

Serious concerns exist about this chemical antimicrobial, which is regulated as a pesticide by the EPA. Operating under the Precautionary Principle, the NOSB should reject the petition to add DBDMH to the National List.