

Guidance for FDA Staff

Compliance Policy Guide

Sec. 527.300 Dairy Products - Microbial Contaminants and Alkaline Phosphatase Activity

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**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Food Safety and Applied Nutrition
Office of Regulatory Affairs**

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I. Introduction:

*The purpose of this document is to provide guidance for FDA staff regarding its enforcement policies for pathogens and indicators of inadequate pasteurization or post-pasteurization contamination of dairy products.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. Background:

Significant outbreaks of illness associated with dairy products include salmonellosis (including infections with some multi-drug resistant *Salmonella*), enterohemorrhagic *Escherichia coli* (EHEC) O157:H7 infections, listeriosis, staphylococcal food poisoning, botulism, and *Yersinia enterocolitica* infection. (A *Federal Register* notice of availability for draft CPG Sec. 555.320 *Listeria monocytogenes* was published on February 7, 2008 (73 FR 7293)). Symptoms of illnesses from pathogens may include anything from mild discomfort to headaches, nausea, vomiting, watery or bloody diarrhea, cramps, and hemolytic uremic syndrome. In some cases, death may result.

A. Pathogens

The presence of pathogens in dairy products is an indicator of poor sanitation, temperature abuse, inadequate pasteurization (21 CFR 133.3(d)), fermentation failure, or obtaining milk from diseased animals. Many pathogens originate from the feces of the

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dairy animals themselves. Contamination of the udder and teats by the feces may in turn contaminate raw milk. Insanitary practices by milk handlers may contribute to the contamination. Insanitary or inadequate processing conditions also may contaminate the raw milk dairy product. Pasteurization of raw milk is lethal to pathogens. Thus, the presence of pathogens in a dairy product made from milk that was subjected to a pasteurization process indicates inadequate pasteurization or post-pasteurization contamination.

Salmonella - *Salmonella* is a pathogen that, when consumed, can cause an infection. A dose of as little as 15-20 organisms can cause illness. The symptoms of infection include gastroenteritis. *Salmonella* is shed in the feces of infected animals and can contaminate pasture land and milking parlors.

EHEC O157:H7 and other enterohemorrhagic *Escherichia coli* - The infectious dose of EHEC O157:H7 is estimated to be between 10-100 organisms. When food contaminated with the EHEC O157:H7 is consumed, the pathogen colonizes the intestinal tract where it produces a toxin and causes haemorrhagic colitis that can progress to more serious complications such as haemolytic uraemic syndrome or thrombotic thrombocytopenic purpura. EHEC O157:H7 is the predominant EHEC strain that has caused illness worldwide. However, other EHEC serotypes have also been implicated in illness and are of public health concern.

Campylobacter jejuni - A dose of 400-500 organisms of *Campylobacter jejuni* can cause infection. Symptoms of infection include abdominal pain, fever, diarrhea, and vomiting. *Campylobacter jejuni* can either be shed in feces or in milk from an infected udder of a dairy animal. Most human outbreaks of infection of *Campylobacter jejuni* that are associated with dairy products have been linked to raw milk or inadequately pasteurized milk.

Yersinia enterocolitica - *Yersinia enterocolitica* is a pathogen which causes infection. Symptoms of infection include gastroenteritis, fever, diarrhea, bloody stools, rash, joint pain, nausea, vomiting, headache, and malaise. Infection by *Yersinia enterocolitica* is also considered a cause of reactive arthritis. *Yersinia enterocolitica* has been found in many different animals and is shed in feces.

Clostridium botulinum - *Clostridium botulinum* produces a neurotoxin. A few nanograms (ng) of the neurotoxin can cause illness. Symptoms include lassitude, weakness, vertigo, double-vision, difficulty speaking, and difficulty swallowing. Symptoms can progress to difficulty of breathing, weakness of other muscles, abdominal distention, and constipation. The incidence of this disease is low, but the mortality rate is high if not treated immediately and properly. Although the neurotoxin is heat labile and can be destroyed when exposed to a minimum of 80 °C for 10 minutes, the time and temperature reached in pasteurization do not destroy the neurotoxin.

Enterotoxigenic *Staphylococcus* – Some species of *Staphylococcus* produce an enterotoxin that is extremely heat stable and is not inactivated at pasteurization

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temperatures. When ingested, the enterotoxin may rapidly produce symptoms including nausea, vomiting, retching, abdominal cramps, muscle cramping, headache, and transient changes in blood pressure and pulse rate. The presence of any *Staphylococcus* enterotoxin in a dairy product is of public health concern.

A dairy cow with mastitis may be the source of enterotoxigenic *Staphylococcus* in raw milk, which may subsequently be commingled with other milk. Also, at any point from the milk collection process to the packaging of the finished product, enterotoxigenic *Staphylococcus* species can be introduced by an infected human, inadequate employee hygienic practices, such as inadequate hand washing, equipment and utensils that are not cleaned and sanitized, or contaminated raw material.

Staphylococcus aureus has traditionally been used as a microbiological indicator of insanitation during processing. Because of environmental factors, low levels of *Staphylococcus aureus* may be found in raw milk, even when produced using good manufacturing practices (GMPs). However, excessive numbers of *Staphylococcus aureus* organisms in raw milk or other dairy products, i.e., greater than or equal to 10^4 cfu/g, indicate that the product was produced under insanitary conditions.

Bacillus cereus - *Bacillus cereus* can cause illness when 10^6 cfu/g or more are consumed in food. There have been two enterotoxins produced by *Bacillus cereus* identified as causing foodborne illness. Illness is characterized by abdominal pain and diarrhea or nausea and vomiting. *Bacillus cereus* is commonly found in soil, on vegetables, and in many raw and processed foods, including milk and cheese.

Additional information about foodborne pathogens and associated diseases can be found in the Bad Bug Book.

B. Nontoxigenic *Escherichia coli*

Escherichia coli has traditionally been used as a microbiological indicator of insanitation during processing. *Escherichia coli* are not inherently present in the milk of a dairy animal. *Escherichia coli* in milk and dairy products generally originate from animal or human feces. Thus, the presence of *Escherichia coli* in milk or other dairy product means that the milk or dairy product was exposed either directly or indirectly to feces.

Because of the close association of raw milk with the animal environment, low levels of *Escherichia coli* may be present in raw milk or products made from raw milk, even when properly produced using GMPs. Insanitary conditions, including poor employee hygiene practices, improperly sanitized utensils and equipment, or contaminated raw materials, may also be a source of *Escherichia coli* in milk and other dairy products.

C. Alkaline phosphatase

Alkaline phosphatase is an enzyme that is naturally found in milk. Although the alkaline phosphatase in milk is more thermal resistant than nonsporeforming microorganisms, it is denatured by pasteurization temperatures. Therefore, the presence of alkaline phosphatase indicates the milk was not properly pasteurized. The alkaline phosphatase

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level should be negligible in dairy products, other than certain cheese and cheese products.

For some dairy products such as certain cheeses, microorganisms used during production produce alkaline phosphatase. For some cheeses, the maximum level of alkaline is established in the standard of identity for the cheese (21 CFR part 133). For other cheese and related cheese products required to be made from pasteurized milk, the alkaline phosphatase level should not be greater than 3 µg/0.25 g (12 micrograms phenol equivalents per gram).

III. Policy:

FDA will review the available evidence on a case-by-case basis to determine whether a dairy product is adulterated and, in doing so, will be guided but not bound by the following general statements of policy relating to the presence in those products of pathogens, nontoxicogenic *Escherichia coli*, or alkaline phosphatase.

A. Pathogens

***Salmonella* species, EHEC O157:H7 and other enterohemorrhagic *Escherichia coli*, *Campylobacter jejuni*, *Yersinia enterocolitica*, vegetative cells of *Clostridium botulinum*, *Clostridium botulinum* toxin, *Staphylococcus enterotoxin*, or *Bacillus cereus* enterotoxin**

Dairy products may be considered adulterated within the meaning of section 402(a)(1) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 342 (a)(1)) in that they bear or contain a poisonous or deleterious substance which may render them injurious to health when *Salmonella* species, EHEC O157:H7 and other enterohemorrhagic *Escherichia coli*, *Campylobacter jejuni*, *Yersinia enterocolitica*, vegetative cells of *Clostridium botulinum*, *Clostridium botulinum* toxin, *Staphylococcus enterotoxin*, or *Bacillus cereus* enterotoxin are present.

Staphylococcus aureus

Dairy products may be considered adulterated within the meaning of section 402(a)(4) of the Act (21 U.S.C. 342(a)(4)), in that they have been prepared, packed, or held under insanitary conditions whereby they may have been rendered injurious to health when *Staphylococcus aureus* are present at levels greater than or equal to 10⁴ cfu/g.

Bacillus cereus

Dairy products may be considered adulterated within the meaning of section 402(a)(4) of the Act (21 U.S.C. 342(a)(4)), in that they have been prepared, packed, or held under insanitary conditions whereby they may have been rendered injurious to health when *Bacillus cereus* are present at levels greater than or equal to 10⁴ cfu/g.

B. Nontoxicogenic *Escherichia coli*

Dairy products may be considered adulterated within the meaning of section 402(a)(4) of the Act (21 U.S.C. 342(a)(4)), in that they have been prepared, packed, or held under insanitary conditions whereby they may have become contaminated with filth when

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Escherichia coli is found at levels greater than 10 MPN per gram in two or more subsamples or greater than 100 MPN per gram in one or more subsamples.

C. Alkaline phosphatase

Dairy products made from bovine milk may be considered adulterated within the meaning of section 402(a)(4) of the Act (21 U.S.C. 342 (a)(4)) when:

- For cheese and related cheese products required to be made from pasteurized milk (21 CFR part 133), alkaline phosphatase levels are:
 - Greater than 5 µg/0.25 g (20 micrograms phenol equivalents per gram) in one or more subsamples for brick (21 CFR 133.108), semisoft (21 CFR 133.187), and semisoft part-skim cheeses (21 CFR 133.188);
 - Greater than 4 µg/0.25g (16 micrograms phenol equivalents per gram) in one or more subsamples for Limburger cheese (21 CFR 133.152); or
 - Greater than 3 µg/0.25 g (12 micrograms phenol equivalents per gram) in one or more subsamples for all other cheese and related cheese products.
- For dairy products other than cheese and related cheese products, alkaline phosphatase level is greater than or equal to 2.0 micrograms phenol equivalents per gram in one or more subsamples.

IV. Regulatory Action Guidance:

Interstate Milk Shippers

Dairy products produced in an Interstate Milk Shippers (IMS) listed plant that may be considered adulterated under the Act should first be referred to the appropriate State regulatory agency for follow-up. This includes a non-IMS product manufactured in an IMS-listed plant for which the State is providing a regulatory program to address these issues. If the State is unable to take appropriate action, the district should proceed to initiate FDA action as indicated below.

Direct Reference

The following represent criteria for direct reference seizure submission to the Division of Compliance Management and Operations (HFC-210), for direct reference import detention by the district and for direct reference submission of detention without physical examination (DWPE) to ORA, Office of Regional Operations, Division of Import Operations and Policy (HFC-170):

Analysis of the dairy product demonstrates that one or more subsamples is positive for *Salmonella* species, *Campylobacter jejuni*, *Yersinia enterocolitica*, *Staphylococcus enterotoxin*, or *Bacillus cereus* enterotoxin.

Recommendations

The following represent criteria for recommending seizure, import detention, or DWPE to CFSAN/Office of Compliance/Division of Enforcement (HFS-605):

1. For all dairy products:

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- EHEC O157:H7 or other enterohemorrhagic *Escherichia coli*, or vegetative cells of *Clostridium botulinum*, or *Clostridium botulinum* toxin found in one or more subsamples; or
 - *Escherichia coli* found at levels greater than 10 MPN per gram in two or more subsamples or greater than 100 MPN per gram in one or more subsamples; or
 - *Staphylococcus aureus* found at levels greater than or equal to 10^4 cfu/g in one or more subsamples; or
 - *Bacillus cereus* found at levels greater than or equal to 10^4 cfu/g in one or more subsamples.
2. For cheese and related cheese products made from pasteurized bovine milk:
- Alkaline phosphatase level in:
 - Brick, semisoft, and semisoft part-skim cheeses - greater than 5 µg/0.25 g (20 micrograms phenol equivalent per gram) in one or more subsamples;
 - Limburger cheese - greater than 4 µg/0.25g (16 micrograms phenol equivalent per gram) in one or more subsamples for Limburger cheese;
 - All other cheese and related cheese products - greater than 3 µg/0.25g (12 micrograms phenol equivalent per gram) in one or more subsamples.
3. For all other dairy products made from bovine milk, except cheese and related cheese products:
- Alkaline phosphatase level is greater than or equal to 2.0 micrograms phenol equivalents per gram in one or more subsamples.

Other Considerations

This guidance does not establish acceptable levels of pathogens, nontoxigenic *Escherichia coli*, or alkaline phosphatase in dairy products. FDA may choose to take action against adulterated food that does not meet the criteria under this Section.

V. Specimen Charges:

Domestic Seizure

A. Pathogens

***Salmonella* species, EHEC O157:H7 or other enterohemorrhagic *Escherichia coli*, *Campylobacter jejuni*, *Yersinia enterocolitica*, vegetative cells of *Clostridium botulinum*, *Clostridium botulinum* toxin, *Staphylococcus enterotoxin*, *Bacillus cereus* enterotoxin**

The article of food was adulterated when introduced into and while in interstate commerce and is adulterated while held for sale after shipment in interstate commerce, within the meaning of the Act, 21 U.S.C. 342(a)(1), in that it bears and contains a poisonous or deleterious substance, namely _____, which may render it injurious to health.

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Staphylococcus aureus

The article of food was adulterated when introduced into and while in interstate commerce and is adulterated while held for sale after shipment in interstate commerce, within the meaning of the Act, 21 U.S.C. 342(a)(4), in that it has been prepared, packed, and held under insanitary conditions whereby it may have been rendered injurious to health.

Bacillus cereus

The article of food was adulterated when introduced into and while in interstate commerce and is adulterated while held for sale after shipment in interstate commerce, within the meaning of the Act, 21 U.S.C. 342(a)(4), in that it has been prepared, packed, and held under insanitary conditions whereby it may have been rendered injurious to health.

B. Nontoxigenic *Escherichia coli*

The article of food was adulterated when introduced into and while in interstate commerce and is adulterated while held for sale after shipment in interstate commerce, within the meaning of the Act, 21 U.S.C. 342(a)(4), in that it has been prepared, packed, and held under insanitary conditions whereby it may have become contaminated with filth.

C. Alkaline phosphatase

The article of food was adulterated when introduced into and while in interstate commerce and is adulterated while held for sale after shipment in interstate commerce, within the meaning of the Act, 21 U.S.C. 342(a)(4), in that it has been prepared, packed, and held under insanitary conditions whereby it may have been rendered injurious to health.

Import Detention

A. Pathogens

***Salmonella* species, EHEC O157:H7 or other enterohemorrhagic *Escherichia coli*, *Campylobacter jejuni*, *Yersinia enterocolitica*, vegetative cells of *Clostridium botulinum*, *Clostridium botulinum* toxin, *Staphylococcus enterotoxin*, *Bacillus cereus* enterotoxin**

The article of food is subject to refusal of admission pursuant to section 801(a)(3) of the FD&C Act in that it appears to be adulterated within the meaning of section 402(a)(1) of the FD&C Act in that it bears and contains a poisonous and deleterious substance, namely _____, which may render it injurious to health.

Staphylococcus aureus

The article of food is subject to refusal of admission pursuant to section 801(a)(3) of the FD&C Act in that it appears to be adulterated within the meaning of section 402(a)(4) of the FD&C Act in that it has been prepared, packed, and held under insanitary conditions whereby it may have been rendered injurious to health.

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Bacillus cereus

The article of food is subject to refusal of admission pursuant to section 801(a)(3) of the FD&C Act in that it appears to be adulterated within the meaning of section 402(a)(4) of the FD&C Act in that it has been prepared, packed, and held under insanitary conditions whereby it may have been rendered injurious to health.

B. Nontoxigenic *Escherichia coli*

The article of food is subject to refusal of admission pursuant to section 801(a)(3) of the FD&C Act in that it appears to be adulterated within the meaning of section 402(a)(4) of the FD&C Act in that it has been prepared, packed, and held under insanitary conditions whereby it may have become contaminated with filth.

C. Alkaline phosphatase

The article of food is subject to refusal of admission pursuant to section 801(a)(3) of the FD&C Act in that it appears to be adulterated within the meaning of section 402(a)(4) of the FD&C Act in that it has been prepared, packed, and held under insanitary conditions whereby it may have been rendered injurious to health.*

Material between asterisks is new or revised.

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