



International Dairy Foods Association

Milk Industry Foundation

National Cheese Institute

International Ice Cream Association

January 29, 2010

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852
Electronic Comments: <http://www.regulations.gov>

Re: Section 527.300 Dairy Products: Microbial Contaminants and Alkaline Phosphatase Activity Compliance Policy Guide (CPG 7106.08)

Dear Center for Food Safety and Nutrition (CFSAN) Staff:

The International Dairy Foods Association (IDFA), Washington, DC, represents the nation's dairy manufacturing and marketing industries and their suppliers, with a membership of 550 companies representing a \$110-billion a year industry. IDFA is composed of three constituent organizations: the Milk Industry Foundation (MIF), the National Cheese Institute (NCI) and the International Ice Cream Association (IICA). IDFA's 220 dairy processing members run more than 600 plant operations, and range from large multi-national organizations to single-plant companies. Together they represent more than 85% of the milk, cultured products, cheese and frozen desserts produced and marketed in the United States. IDFA can be found online at www.idfa.org.

We appreciate this opportunity to comment on Section 527.300 Dairy Products: Microbial Contaminants and Alkaline Phosphatase Activity Compliance Policy Guide (CPG 7106.08). The information in this document appears to be an accumulation of older FDA positions and reference values for identifying the need for regulatory action on specific human pathogens and alkaline phosphatase values in foods. We believe that reliance on this information, without documenting, referencing or taking into account more recent microbiological and alkaline phosphatase information has led to incorrect and sometimes overly stringent levels in the "Recommendations" section that trigger seizure, import detention or DWPE by FDA or Customs officials. While this CPG appears to be targeted at imported foods, it is likely to be used for domestically produced foods as well.

Below are specific concerns provided to assist FDA CFSAN staff in utilizing the most recent science and expert opinion to arrive at more substantiated microbiological and alkaline phosphatase levels.

1. *Staphylococcus aureus* levels of concern where toxin production can be confirmed as a threat to human health are recognized in most dairy scientific circles as 10^5 - 10^6 cfu/g. We believe that a level of no less than 10^5 cfu/g be considered as the point at which adulteration and seizure might be appropriate, depending on other related circumstances. We are recommending that FDA CFSAN scientific staff make additional efforts to identify supporting scientific articles and consult with nationally recognized dairy microbiologists such as Dr. Kathy Glass (University of Wisconsin) and Dr. Kathryn Boor (Cornell University) to ensure the proposed level reflects the most current science, research and thinking.
2. *Bacillus cereus* levels of concern in most scientific articles related to dairy products range from 10^5 - 10^6 and there is some debate, yet unresolved, as to what is the level where *B. cereus* becomes a threat to human health. We are recommending that FDA CFSAN scientific staff make additional efforts to identify supporting scientific articles and consult with nationally recognized dairy microbiologists such as Dr. Kathy Glass (University of Wisconsin) and Dr. Kathryn Boor (Cornell University) to ensure the proposed level reflects the most current science, research and thinking.
3. Significant problems occur when using alkaline phosphatase to determine whether milk used in cheesemaking was adequately pasteurized. Microbial alkaline phosphatase production from still-active starter cultures in the cheese and reactivated phosphatase create false readings that cannot always be segregated. While the CPG refers to this screening test, there is no confirmatory test indicated. A positive phosphatase result derived from the phenol screening test must be confirmed to determine whether the activity is from residual, microbial, or reactivated phosphatase. Also, this proposal also does not provide recognition that many cheeses are made from types of concentrated milks.

We consulted with two manufacturers of the predominant instruments for analyzing for alkaline phosphatase in the U.S. It is clear from these consultations that using alkaline phosphatase to identify adulteration in cheese is questionable. Some of their comments specific to the Federal Register notice are captured below.

a. Alkaline Phosphatase (ALP) (pg 6): “.the presence of alkaline phosphatase indicates the milk was not properly pasteurized.” A much more correct statement would be the following, "The presence of alkaline phosphatase (ALP) activity above the current regulatory levels (350 mU/L or 1.0 ug phenol/mL) indicates possible improper pasteurization of the milk or incursion of raw milk into the finished product during post-pasteurization processing."

b. Alkaline Phosphatase (pg 7): In this section on the ALP values in cheese there are two concerns.

- (1) The ALP values provided for the 5 different cheeses (brick, semisoft, semisoft part skim, Limburger and “all other”) should be provided in both ug phenol/g and mU/g or mU/Kg. The reasons for this are (a) Both the phenol method and the mU methods have been shown to be equivalent. (b) The vast majority of processing plants are using the mU methods first approved by the FDA in 1991 and are no longer using the phenol method introduced and little changed since 1938. (c) As a general rule of thumb $1.0 \text{ ug phenol/mL} = 350 \text{ mU/L}$. Simple conversion of

the included numbers with the equivalent mU/g numbers would make the document more up-to-date relevant to workers in the field who are being investigated or whose products are being examined.

(2) The statement that 2.0 ug phenol for “other” products lacks such specificity such as to make it useless within the context of this document. For example, does this refer to yogurt or goat milk or to both. This statement should be removed or greatly clarified.

c. For all dairy products, except cheese and cheese products: (a) Any ALP value should be provided in both mU/L and ug phenol/mL for reasons stated as above. (b) It is not clear why the ug phenol values has been increased for fluid dairy products from 1.0 ug phenol to 2.0 ug.

d. Alkaline phosphatase: This section states that ALP determines “adulteration.” There are only four specific types of information that ALP assays on dairy products can provide (a) Improper pasteurization (time and/or temperature variation from the regulatory requirements for that product labeling). (b) The presence of raw unpasteurized milk incursion into the finished product. (c) The presence of ALP derived from bacteria or other microorganisms. (d) The presence of a “reactivated” ALP that resulted from the improper storage of a pasteurized finished product at elevated temperatures for an extended period of time. Efforts are underway to differentiate the four different types of ALP and newer methods are in development, but at this time, are not validated.

Approaching this issue from a more technical view, as a rule of thumb one can expect that the concentration of ALP in a finished cheese product made from pasteurized milk will increase in value by a factor of 10 or more. In other words, in-coming pasteurized milk with an ALP value of 150 mU/L will produce a cheese with a value of about 1500 mU/Kg. FDA, for example, has published data on many different cheese types. (<http://vm.cfsan.fda.gov/~ebam/bam-27.html>).

The claim is that cheese made from milk with a 1 ug phenol/mL ALP value will produce a perfectly good product with values up to 10 to 20 ug phenol/g depending on the cheese type. For most cheeses, FDA's BAM states a value of up to 20 ug phenol/g as acceptable. By extrapolation, a 1 ug phenol/mL milk is equivalent to about 300 to 500 mU/L using the Fluorophos ALP procedure. Unfortunately, there is still a problem with the usage of these levels for cheeses. When a regulatory agency pulls a finished product from the store shelves, the variability in the characteristics of the cheese, even from the same manufacturer, require that for regulatory purposes, FDA should establish a bench mark for all cheeses in the marketplace and use that for comparison purposes. By merging all cheeses in the marketplace into three arbitrary categories, it is likely that unnecessary regulatory action will be taken against cheeses made from pasteurized milk.

Example: A cheese manufacturer can measure ALP levels on all in-coming batches of pasteurized milk and measure ALP levels in each lot of cheese made from that milk. These two numbers for each product will provide a paired set. If product "Z" has 150 mU/L on the milk and 1500 mU/Kg on the cheese after the lot has been made then this will become the profile for that product. The second test which can be done is re-pasteurization of the cheese product. For product "Z" for example, make an extraction of the cheese following the standard procedure followed by lab pasteurization of the extract (63 deg C for 30 min). The re-test of the extract after pasteurization will result in a product with an ALP value of less than or equal to 150 mU/Kg. The reason for this is that the original 1500 mU/Kg was due to concentration of the residual (acceptable) bovine milk ALP during the cheese manufacturing. Historical records by lot which show this to be true for product "Z" can help to provide very powerful evidence of the quality of this product. A

manufacturer may find that lot "Z" which normally produces the paired results 150 and 1500 mU/Kg has on this one occasion produced a finished product of say 3000 mU/Kg. The lab re-pasteurization may help to sort this out. Lab re-pasteurization will reduce the 3500 mU/Kg by a percentage which reflects the bovine ALP concentration and the remaining ALP results are most likely due to microbial heat resistant ALP. For example, for product "Z"

At release Lab Pasteurized Results

Product "Z" 1500 mU/Kg ~ 150 mU/Kg Bovine residual

Current lot 3000 mU/Kg ~ 150 mU/Kg Bovine residual

Bad in-coming milk: Current lot 3000* mU/Kg ~ 1500 mU/Kg

1500 mU/Kg from Bovine residual, no problem.

*1500 mU/Kg remains due to high initial microbial levels in the incoming raw milk. This is not a problem related to use of unpasteurized milk, since the incoming milk used to make the cheese met regulatory requirements. The assumption here is that lab re-pasteurization will always reduce the ALP value by a number which reflects the in-coming residual bovine milk. Bovine residual ALP will concentrate during manufacturing but it will never increase beyond what was found when the product was shipped. A product after six months which has 1500 mU/Kg will drop to it's pre-shipment 150 mU/Kg after re-pasteurization. The percentage which it does not drop will reflect the percentage of microbial ALP which is in the product.

Additionally, there is an ISO/IDF standard for testing alkaline phosphatase in cheese: ISO 11816-2. It is the fluorimetric method and includes an alkaline phosphatase extraction method. This may be the only internationally recognized standard for alkaline phosphatase. It is understood that the EU representatives are still attempting to determine how to interpret the data with cutoffs and optimize its application properly with respect to cheese. Noting this and other previous points, we recommend that FDA CFSAN scientific advisors consult with industry experts and academia on this issue and for the present, drop the use of alkaline phosphatase as a determining factor for the use of unpasteurized milk in cheeses.

4. Esherichia coli levels for cheese products may or may not be appropriate as identified in the recommendations. However, we have two questions. Did FDA CFSAN scientists analyze whether any cheese cultures today exhibit E. coli characteristics and thereby might be counted as part of the E. coli contaminant load, when in fact some of this might be from cheese culture? The second question is the significant variation in E coli. levels depending on the number of samples and whether the cheese was made from raw milk. The CPG and accompanying information does not provide supporting information to justify these differences.
5. The use of alkaline phosphatase to determine whether milk used in making non-cheese dairy products has not been solidly validated for many of these products. We consulted with two manufacturers of the predominant instruments for analyzing for alkaline phosphatase in the U.S. It is clear from these consultations that using alkaline phosphatase to identify adulteration in some non-cheese dairy products is inappropriate. Similar to our comments in # 3 above, we believe that FDA CFSAN scientific advisors should consider conducting a wider scientific

literature search as well as consult with alkaline phosphatase experts in the industry and academia, before finalizing this part of the CPG.

In summary, IDFA and its members appreciate the opportunity to provide comments on the Microbial Contaminants and Alkaline Phosphatase Activity Compliance Policy Guide (CPG 7106.08). We encourage FDA CFSAN staff to conduct a more thorough review of the current scientific literature and consult with known experts from academia and the instrument testing industry in order to provide more substantive support for the proposed microbiological levels and the use of alkaline phosphatase for triggering regulatory action and seizures of dairy products. If you have any questions, please feel free to contact me at 202-220-3544 or asayler@idfa.org.

Sincerely,

Allen R. Sayler, Vice President, Regulatory Affairs & International Standards
International Dairy Foods Association

Cc: Clay Hough
Cary Frye