reviewed by at least one responsible official, and that this official will need to evaluate how the change will affect the nutrient content and the suitability of the product for infants, to ensure that the infant formula is not adulterated.

A significant change in the master manufacturing order without proper approval may result in the production of an infant formula that lacks a required nutrient or that is not manufactured in an appropriate way. For example, homogenization of an infant formula is done to ensure a uniform dispersion throughout the formula of the lipid ingredients as well as the fat-soluble nutrients. If the master manufacturing order were changed, and the homogenization process done before the fat source was added, the fat-soluble nutrients would not be uniformly dispersed in the formula, and the formula would be adulterated. The system of review and approval required by proposed § 106.50(a)(3) will minimize the possibility that a significant change could result in an adulterated product.

In order to ensure that the appropriate ingredients are added during the manufacturing process, and that the formula contains all of the nutrients required by § 107.100 and therefore is not adulterated, FDA is proposing in § 106.50(b) that each raw or in-process ingredient required by the master manufacturing order be examined by one person and checked by a second person or system. This requirement will ensure that there will be a check to prevent mixups in the use of ingredients and to prevent the use of unapproved ingredients. Confirmation that the master manufacturing order is being followed, and that ingredients are being properly added, is particularly important because these matters are fundamental to ensuring that the formula is manufactured correctly, and that it contains the nutrients required by § 107.100 but not unapproved ingredients that might adulterate the formula.

In proposed § 106.50(c), FDA is requiring the identification of all compounding and storage containers, processing lines, and major equipment used during the production of a batch of infant formula. Identification of these items will enable the manufacturer to accurately determine the status of all batches of infant formula during all stages of the manufacturing process, will help to prevent mixups in the addition of ingredients to the formula, and will facilitate prompt action by the manufacturer if any problems in processing are identified. For example, identifying that a particular storage container contains a batch of formula that has not yet had all ingredients added to it will prevent a manufacturer from inadvertently final-stage packaging the product and thus will help to ensure that adulterated product is not introduced into interstate commerce. The presence of the lot or batch number will help to identify the product if a problem does occur.

Proposed § 106.50(d) requires that manufacturers establish controls to ensure that required nutrient levels are maintained in the formula, and that the formula is not contaminated with microorganisms or other contaminants and thereby adulterated. In addition, the agency is proposing to require establishment of controls for mixing time, speed, temperature, and flow rate of product and other critical parameters necessary to ensure the addition of required ingredients to, and the homogeneity of, the formula. These parameters are determined by the manufacturer according to its experience and knowledge of what will result in a homogeneous, safe, and uniform product. It is essential that controls be established for each of these parameters, or the likelihood that there will be inconsistencies in production from batch to batch will be greatly increased. For example, if processing temperatures are not specified, the formula could be processed at high temperatures that can destroy vitamins or other essential nutrients, resulting in a product that is adulterated because it does not meet the nutrient requirements specified in section 412(i) of the act. Similarly, without established procedures for mixing time and speed, the product may be produced using processing parameters that will not result in formula that is uniformly mixed and thus does not contain all nutrients at the required levels.

FDA is proposing to require that manufacturers establish controls for the spray-drying process for powdered infant formula to prevent microbial and other contamination (§ 106.50(d)(2)). Although spray drying involves a heat treatment, the temperature is not sufficient to sterilize the formula. Consequently, powdered infant formulas are vulnerable to microbial contamination during the spray-drying process. Even if the equipment and the formula are free of microbial and other forms of contamination initially, the spray-drying process may permit contamination of the product as a result of dust or other air-borne gross particulates in the intake air. Thus, FDA has tentatively concluded that it is important that the manufacturer establish controls for the spray-drying process that will ensure that the powdered formula does not become contaminated with microorganisms or other contaminants.

The controls that manufacturers should consider include: (1) Using equipment constructed to ensure that static accumulation of particulate matter is controlled; (2) using and maintaining equipment constructed to protect the product from dust and environmental contamination; (3) controlling condensation, moisture, and temperature conditions throughout the plant to prevent *Salmonella* and *Listeria* growth in static materials; (4) controlling condenser cooling water to prevent potential *Salmonella* and other bacterial contamination; (5) controlling sampling and cleanout ports on the evaporator for buildup of static material and avenues for airborne contaminants; and (6) controlling product flow through the plant to prevent unnecessary product movement between areas that may increase the likelihood of cross-contamination.

As stated above, contaminants may enter the product in the air introduced into the spray-drying equipment during the spray- drying process. Air can contain free microorganisms or particulate material that is contaminated with microorganisms. Controls to prevent microbial contamination of the formula by airborne sources must address not only the presence of microorganisms themselves but also the sources of dust, moisture, and other airborne contaminants that may be sources of microbial contamination. Therefore, proposed § 106.50(d)(2) requires that manufacturers filter the intake air before heating to remove dust or other air-borne gross particulates that can result in the production of adulterated formula.

FDA is proposing to require that manufacturers control the removal of air from finished product containers (proposed § 106.50(d)(3)) and ensure that containers of finished products are properly sealed (proposed § 106.50(d)(4)), that visible closure and seal defects are detected (proposed § 106.50(d)(4)(i)), and that destructive tests are performed to determine closure strength (proposed § 106.50(d)(4)(ii)). These requirements are necessary to prevent oxidation and deterioration of nutrients in the formula caused by air or contaminants during the product's shelf life. FDA is also proposing that equipment that is used to prevent adulteration be monitored, either by personnel or monitoring equipment, to alert the manufacturer to malfunctions (see § 106.50(e)). As a result of such monitoring, the manufacturer will be

able to minimize the amount of product produced subject to a malfunction that may develop and to take prompt corrective actions.

In order to prevent rejected in-process materials from being inadvertently commingled with acceptable materials, FDA is proposing that manufacturers establish controls that ensure that the rejected materials are clearly identified and quarantined, and that reprocessed materials will not produce adulterated formula (see § 106.50(f)).

9. Controls to Prevent Adulteration from Microorganisms

An infant formula that is contaminated with microorganisms may, depending on the characteristics of the microorganisms, raise a safety concern that would cause the infant formula to be adulterated under section 402(a)(1) of the act. For example, all serotypes of the genus *Salmonella* can cause illness (often gastrointestinal) in infants and adults (Refs. 33 and 34) and the infectious dose is low (Ref. 35). Moreover, microorganisms that are generally harmless in older children and adults can cause serious bacterial infections in infants because the immune systems of infants are still developing (Ref. 36). For example, newborns and infants are susceptible to infection with *Listeria monocytogenes* that may cause severe illness or death (Ref. 37) and, as in the case of *Salmonella*, the infectious dose is believed to be low (Ref. 38).

Likewise, *Staphylococcus aureus* is harmful to infants because some strains of this microorganism produce an enterotoxin that causes acute gastrointestinal illness (nausea, vomiting, cramps) soon after the food is ingested (Ref. 39). *Bacillus cereus* can produce diarrhea and vomiting in adult humans (Ref. 40) when food contaminated with at least $10^5$ *B. cereus* cells is consumed. The infectious dose of *B. cereus* for infants is not known; however, as already noted, infants are more susceptible to bacterial infections than are healthy adults and older children because the immune systems of infants are not fully developed.

FDA has long held that health concerns may arise due to the presence of any detectable *Salmonella*, *Listeria*, or *S. aureus* bacteria in infant formula or due to levels of *B. cereus* that exceed 1,000 "colony forming units" (CFU's) per gram (g) of a powdered infant formula. Such health concerns would cause the agency to consider an infant formula that is so contaminated to be adulterated under section 402(a)(1) of the act (see 54 FR 3783, Jan. 26, 1989, and 56 FR 66566, Dec. 24, 1991).

Moreover, the presence of microorganisms in an infant formula reflects that the formula was prepared, packed, or held under insanitary conditions whereby it may have been rendered injurious to health and therefore is adulterated under sections 402(a)(4) and 412 of the act. For example, the presence of *Escherichia coli* in a sample of infant formula is an indicator of fecal contamination, implying that the infant formula has been contaminated by manufacturing practices conducted under insanitary conditions and therefore is adulterated under sections 402(a)(4) and 412 of the act. In addition, consistent with the standard adopted by the International Commission on Microbiological Specifications for Foods (ICMSF) of the Food and Agricultural Organization of the United Nations and the World Health Organization (WHO) and based on the results from FDA and Canadian Surveys (Refs. 41, 42, and 43), an aerobic plate count (APC) (i.e., the number of microorganisms that will grow under certain specified conditions) that is greater than 10,000 CFU's per g of a powdered infant formula evidences that the formula has been prepared, packed, or held under insanitary conditions.

Illnesses from the use of microbiologically contaminated infant formulas have occurred (Ref. 33). Moreover, as recently as May 1993, infant formula contaminated with *Salmonella* bacteria was the subject of a recall (Ref. 44). Thus, contamination of infant formula with microorganisms of public health significance is more than a theoretical possibility. Therefore, FDA has tentatively concluded that manufacturers need to have in place controls to ensure that formulas are not microbiologically contaminated at levels of public health significance, and that, if they are, those formulas do not enter interstate commerce. Proposed § 106.55 requires manufacturers to establish such controls.

Proposed § 106.55(a) requires that manufacturers of liquid infant formula comply with the procedures specified in part 113. These products are thermally-processed low-acid foods that are packaged in hermetically sealed containers that are heated to achieve commercial sterility. Therefore, they are appropriately subject to the requirements of part 113.

Proposed § 106.55(b) requires that manufacturers of powdered infant formula test representative samples of every batch of the formula at the final product stage, before distribution, to ensure that the infant formula meets the microbiological quality standards specified in proposed § 106.55(c). This proposed requirement is necessary because although powdered infant formulas are heat treated during processing, they are not thermally processed to achieve commercial sterility. Proposed § 106.55(b) requires testing at the final product stage because microbiological contamination can be inadvertently introduced by ingredients at any time during production or through improper processing or holding procedures (Ref. 45).

Proposed § 106.55(c) establishes that any powdered infant formula that contains any microorganism at levels that exceed the microbiological quality standards for that microorganism as listed in this section will be deemed to be adulterated under sections 402 and 412 of the act. Proposed § 106.55(c) defines microbiological quality standards as the maximum allowable number of microorganisms present in 1 g of dry formula, expressed as CFU/g or "most probable number" (MPN)/g, and herein designated the "M value" for the specific microorganism.

The microorganisms for which FDA is proposing M values are those that are of known public health significance or that are indicators that the formula have been prepared, packed, or held under insanitary conditions. The microorganisms and each proposed M value listed in proposed § 106.55(c) are adapted from guidelines previously published and discussed in the proposed and final rules on infant formula record and record retention requirements (see 54 FR 3783, Jan. 26, 1989, and 56 FR 66566, Dec. 24, 1991, respectively). The agency notes, however, that microorganisms that must be tested for in infant formula and the proposed M values for each microorganism listed in this proposed rule represent minimum requirements for the microbiological quality of an infant formula based on standards and methods currently available.

a. *Aerobic plate count (APC).* Proposed § 106.55(c) establishes an APC M value of 10,000 CFU/g as the maximum level that is consistent with sanitary conditions in the facility in which a powdered infant formula is produced. An APC M value greater than the proposed standard indicates that the formula was produced under insanitary conditions whereby it may have been rendered injurious to health and thus is adulterated under sections 402(a)(4) and 412 of the act.

The APC is the number of microorganisms that will grow on the APC nutrient medium, incubated at 35 °C for 24 hours in air (Ref. 46). "Microorganisms" (as defined in

proposed § 106.3(k)) include yeasts, molds, bacteria, and viruses. The APC medium supports the growth of most microorganisms, including yeasts, molds, and all bacteria required to be tested for under proposed § 106.55(c); however, the APC medium does not support the growth of viruses. The APC count is expressed in CFU's because multiple microorganisms may adhere together or attach to the same location on an agar plate, and microbiologists cannot determine whether one or several individual microorganisms initiated the colony that they detect growing on the plate.

This M value for the APC proposed in § 106.55(c) is consistent with the standard adopted by the ICMSF and the WHO and the results from FDA and Canadian Surveys (Refs. 41, 42, and 43). The ICMSF based its standards on the degree of health hazard the microorganisms present and conditions of use of the product (Ref. 41).

FDA has tentatively arrived at this APC M value because the microbial quality of products consumed by infants is of primary concern (Ref. 43). When infant formulas are produced under good commercial processing, the available evidence shows that the APC will be below this M value (Refs. 42 and 43). The agency is notaware of adverse events occurring in infants who consumed products with an APC below this M value.

b. *Coliforms, fecal coliforms, and E. coli. E. colli* are bacteria, including some strains that are pathogenic for infants, that thrive in the human intestinal tract. The presence of *E. coli* in a sample of powdered infant formula is an indicator that the infant formula has been contaminated by manufacturing practices conducted under insanitary conditions and therefore is adulterated under sections 402(a)(4) and 412 of the act.

*E. coli* bacteria are a subset of a more diverse group of bacteria known collectively as fecal coliforms, which also thrive in the human intestinal tract and therefore are also indicators of fecal contamination. Fecal coliforms are destroyed by pasteurization, and the presence of these microorganisms in a pasteurized product evidences that there has been post-process contamination of the formula (Ref. 47). Fecal coliforms in turn are a subset of a still further diverse group of bacteria known as coliforms, which include bacteria that may or may not be indicators of fecal contamination. However, contamination with coliforms is a reliable indicator of post-process contamination of the formula, even if the source of the contamination is not fecal.

In previously issued guidelines, the agency recommended that powdered infant formulas be tested for the presence of *E. coli* (54 FR 3783); however, one comment on this recommendation suggested that, to allow greater flexibility and reduce the cost for manufacturers, the manufacturer should be given the option of testing for coliforms, fecal coliforms, or *E. coli*. Specific tests for contamination with *E. coli* provide the most definitive evidence of fecal contamination, but tests for specific bacteria are more cumbersome than general tests for a group of bacteria such as fecal coliforms. Similarly, general tests for fecal coliforms are more cumbersome than universal tests for an even more diverse group of bacteria such as coliforms.

The agency is proposing in § 106.55(c) that manufacturers screen their samples of powdered infant formula for evidence of contamination with *E. coli* using sequential tests for detecting and enumerating coliforms and fecal coliforms. Under the proposal, manufacturers ordinarily would only perform the simplest test (i.e., the test for coliforms) using a test sample of the infant formula. The results of the coliform test determine whether the manufacturer needs to followup with a more specific test for fecal coliforms using as the test sample cultured bacteria prepared during the coliform test. As discussed below, the agency is not proposing that manufacturers followup a positive result in the fecal coliform test with a more specific test for *E. coli* but rather is proposing that a violative sample in the fecal coliforms test will represent conclusive evidence that the infant formula is adulterated.

The general test for coliforms is an example of an MPN test. MPN counts are estimates of the number of organisms present in a sample. Methods resulting in an MPN require inoculation of multiple tubes of liquid culture medium with multiple dilutions of the sample. The method specified in FDA's Bacteriological Analytical Manual (BAM) (Ref. 46) requires inoculation of 3 replicate tubes of culture medium with each of 3 sample dilutions, for a total of 9 tubes. The tubes contain culture medium selective for the microorganism of interest. After appropriate incubation (time, temperature, and atmosphere), each tube is scored as positive or negative for the presence of the organism. Examples of a positive result include the presence of growth, a biochemical color change, and the production of gas.

A mathematical formula is used to calculate the MPN of microorganisms present based on the number of positive tubes in each of the three separate dilutions. Since the calculation in question involves a repetitious process, the mathematical formula used to calculate the MPN has been employed to create easy-to-use tables that are available in the BAM and in other books of statistical tables. Most tables present both a value for the MPN and confidence limits for that value. The calculated table values for the MPN, using BAM methods, are dependent on the level of the dilution in which a positive result is found. The following table values are based on an inoculation series of 0.1, 0.01 g, and 0.001 g (or mL) of the infant formula. When no tubes in any dilution produce a positive result, the calculated MPN value is zero.[3] When a single tube in the greatest dilution (least concentrated) produces a positive result, the calculated MPN value is equal to 3.01.[4] When a single tube in the middle dilution produces a positive result, the calculated MPN value is equal to 3.05.[5] In all other situations in which there is a positive result in at least one tube (including a single positive tube in the lowest dilution (greatest concentration)), the calculated MPN value is greater than 3.05.

If no tubes in any dilution produce a positive result in a test for bacterial contamination of a powdered infant formula (i.e., if the MPN is zero), such contamination is unlikely. If a single tube in any dilution produces a positive result in a test for bacterial contamination of the product, such contamination is a possibility. However, there are two situations in which a single positive tube is generally considered to reflect a false positive test result: (1) When no tube in the lowest dilution (greatest concentration) produces a positive result, but a single tube in the middle dilution produces a

[3] The calculated MPN value of zero when no tubes in any dilution produce a positive result is a recent change that appears in the MPN tables of the 8th ed. of the BAM. In previous editions of the BAM, the calculated MPN value when no tubes in any dilution produce a positive result was "less than 3."

[4] The calculated MPN value of 3.01 when a single tube in the greatest dilution produces a positive result is a recent change that appears in the MPN tables of the 8th ed. of the BAM. In previous editions of the BAM, the calculated MPN value when a single tube in the greatest dilution produces a positive result was 3.

[5] The calculated MPN value of 3.05 when a single tube in the middle dilution produces a positive result is a recent change that appears in the MPN tables of the 8th ed. of the BAM. In previous editions of the BAM, the calculated MPN value when a single tube in the middle dilution produces a positive result was 3.

positive result (i.e., the calculated MPN value is equal to 3.01); or (2) when no tube in the lowest dilution produces a positive result, but a single tube in the greatest dilution (least concentration) produces a positive result (i.e., the calculated MPN value is equal to 3.05). FDA considers that if a sample of a powdered infant formula produces positive test results that reflect one of these two situations, bacterial contamination also is unlikely.

However, in all other situations (e.g., if a single tube in the lowest dilution (greatest concentration) produces a positive result, or if two or more tubes in any dilution produce a positive result), bacterial contamination of a powdered infant formula is likely. Therefore, when the calculated MPN value in a test for bacterial contamination is greater than 3.05, that is if a sample of powdered infant formula produces positive test results in which a single tube in the lowest dilution produces a positive result or in which two or more tubes in any dilution produce a positive result, the powdered infant formula likely is contaminated with bacteria.

FDA is proposing to use the calculated MPN values in the BAM as a means of setting a numerical specification because these tables are generally available, represent standard practice in the industry, and provide a simple way to classify samples as violative or nonviolative. Based on the above discussion of calculated MPN values, FDA is proposing in § 106.55(c) that powdered infant formula be classified as nonviolative for coliforms in all situations in which the calculated MPN value is less than or equal to 3.05 and classified as presumptively violative for coliforms in all situations in which the calculated MPN value is greater than 3.05. In other words, FDA is proposing that an MPN value of 3.05 represents the maximum allowable number of coliforms present in 1 g of dry infant formula. This proposal is consistent with current FDA infant formula microbiological guidelines. The agency requests comment on the specification of 3.05 MPN/g as the maximum allowable number of coliforms in dry infant formula.

FDA has stated that infant formula with a calculated MPN value of greater than 3.05 in the coliform test is presumptively violative because, under proposed § 106.55(c), the manufacturer may either consider the sample violative without further testing or may conduct an additional test, the fecal coliform test. Although an MPN value of greater than 3.05 MPN/g is a valid quality indicator of microbial contamination, coliform contamination may not be fecal in origin, and it may not reflect the presence of infant pathogenic microorganisms. Therefore, FDA has tentatively concluded that an infant formula for which an MPN value of greater than 3.05 MPN/g is found in the coliform test need not be considered violative if a negative result is found in a more specific test for fecal coliforms.

If the coliform test using powdered infant formula samples results in an M value greater than 3.05 MPN/g, the manufacturer may use the cultured bacteria from one or more of the tubes producing the positive result as a sample inoculum for the fecal coliform test. A sample inoculum producing an MPN value in the fecal coliform test of less than or equal to 3.05 would indicate that the coliform contamination is not fecal in origin, because under incubation conditions that are specific for fecal coliforms, the bacteria were not detected. The testing would effectively screen out coliforms that are not of concern, which is not possible with the more general test. Therefore, FDA has tentatively concluded that an MPN value less than or equal to 3.05 in the fecal coliform test be classified as nonviolative. FDA also has tentatively concluded that an MPN value greater than 3.05 in the fecal coliform test is a valid quality indicator demonstrating that the formula contains fecal coliforms such as *E. coli* and, therefore, is adulterated under sections 402(a)(4) and 412 of the act. The agency is proposing that powdered infant formula that results in an MPN value greater than 3.05 in the fecal coliform test be classified as violative.

If the *E. coli* test was performed, the sample inoculum would be the cultured bacteria from positive tubes in the fecal coliforms test. However, the agency is not proposing to require specific testing for the presence of *E. coli*, or to set a specification for an M value for *E. coli*, because the specification of less than or equal to 3.05 MPN/g in the fecal coliforms test is sufficient to ensure that nonviolative samples do not contain *E. coli* since *E. coli* is a type of fecal coliform. Moreover, FDA has tentatively concluded that an MPN value greater than 3.05 in the fecal coliform test is a sufficient quality indicator of fecal contamination that the agency need not propose, as an option, that a manufacturer may conduct an additional specific test for the presence of *E. coli*. The agency requests comments on the proposed requirements for sequential testing for coliforms and fecal coliforms, with no testing for *E. coli*.

c. *Salmonella.* Tests for the presence of *Salmonella* involve the enrichment in a broth of the entire analytical unit followed by plating onto culture plates rather than the culture of a series of dilutions that is performed in tests for coliforms. A positive result in a test for *Salmonella* is based on the detectable presence of the microorganism on the culture plate rather than on the mathematical calculations that result in a MPN.

Proposed § 106.55(c) requires that powdered infant formula be tested for *Salmonella* and provides that the formula is adulterated if any *Salmonella* is found. All serotypes of this genus of bacteria can cause illness (often gastrointestinal) in infants and adults (Refs. 33 and 34). The presence of any *Salmonella* in infant formula could render it injurious to an infant who consumes it because the infectious dose of these bacteria is low (Ref. 35). Therefore, FDA has tentatively concluded that the risk from *Salmonella* is of such significance that an M value of zero (i.e., none detectable) for *Salmonella* in infant formula is necessary to protect the health of infants.

d. *Listeria monocytogenes.* Tests for the presence of *L. monocytogenes* are similar to those for *Salmonella* and a positive result is based on the detectable presence of the microorganism on the culture plate rather than on the mathematical calculations that result in a MPN.

Proposed § 106.55(c) requires that powdered infant formula be tested for *L. monocytogenes* and provides that the formula is adulterated if any *L. monocytogenes* is found. Individuals with immune systems that make them susceptible to infections, such as newborns and infants with incompletely developed immune systems, are susceptible to infection with *L. monocytogenes* which may cause severe illness or death (Ref. 37). The infectious dose of this bacterium is believed to be low (Ref. 38). Because the specific dose of this bacterium that may cause illness is not known but is believed to be low, FDA has tentatively concluded that the risk from *L. moncytogenes* is of such significance that an M value of zero (i.e., none detectable) for *L. monocytogenes* in powdered infant formula is necessary to protect the health of infants. The agency requests comment on this proposed specification for *L. monocytogenes*.

e. *Staphylococcus aureus. S. aureus* is harmful to infants because some strains of this microorganism produce an enterotoxin that causes acute gastrointestinal illness (nausea,

vomiting, cramps) soon after the food is ingested (Ref. 39). Tests for *S. aureus* involve liquid culture of series of dilutions as was discussed previously in reference to coliform and fecal coliform testing and results are calculated as MPN based on tables in the BAM. Proposed § 106.55(c) requires that powdered infant formula be tested for *S. aureus* and establishes an M value of 3.05 for this microorganism. FDA has tentatively concluded that the risk from *S. aureus* is of such significance that an M value of 3.05 is necessary to protect the health of infants.

f. *Bacillus cereus.* Tests for *B. cereus* involve liquid culture of a series of dilutions as was discussed previously in reference to coliform and fecal coliform testing and results are calculated as MPN based on tables in the BAM. Proposed § 106.55(c) requires that powdered infant formula be tested for *B. cereus* when the APC exceeds 100 CFU/g and establishes an M value for *B. cereus* of 100 MPN/g or 100 CFU/g. This proposed M value for *B. cereus* is lower than the M value of 1,000 MPN/g or 1,000 CFU/g in the current recommended infant formula microbiological guidelines (54 FR 3783). *B. cereus* can produce diarrhea and vomiting in adult humans (Ref. 40) when food contaminated with at least $10^5$ *B. cereus* cells is consumed. The infectious dose of *B. cereus* for infants is not known; however, because the immune systems of infants are not fully developed, infants are more susceptible to bacterial infections than are healthy adults and older children. In the absence of data on the dose of *B. cereus* capable of causing disease in infants, the agency is concerned that a safety standard of 1,000 MPN/g or 1,000 CFU/g poses a potential risk to infants who consume rehydrated formula because *B. cereus* in rehydrated powdered infant formula is capable of rapid growth and can reach $4.9 \times 10^6$ cells/g within 24 hours at 26 °C (Ref. 48), a level sufficient to cause disease. Therefore, FDA has tentatively concluded that the risk from *B. cereus* is of such significance that an M valve that is lower than the current standard of 1,000 MPN/g or 1,000 CFU/g is necessary to protect the health of infants.

Powdered infant formulas and similar products (e.g., powdered milk) produced under CGMP contain less than 100 MPN/g or 100 CFU/g of *B. cereus* (Refs. 43 and 48). Additionally, an FDA survey of different production lots of milk-, soy-, and protein hydrolysate-based powdered infant formulas (Ref. 49) showed that the maximum APC was 103 CFU/g, and that the proportion of *B. cereus* in the samples ranged from 1.2 to 63.9 percent of the APC. Therefore, FDA has tentatively concluded that an M value of 100 MPN/g or 100 CFU/g for *B. cereus* will adequately protect the health of infants. Moreover, because this M value is higher than the *B. cereus* levels typically found in infant formula currently being produced (Refs. 43, 48, and 49), the proposed M value of 100 MPN/g or 100 CFU/g will not be overly burdensome.

g. *Methods.* Proposed § 106.55(c) states that the agency intends to determine compliance with the proposed M values using the methods in the BAM. These methods provide reproducible, consistent, and accurate results at different laboratories. The agency proposes to incorporate the BAM by reference in § 106.55(c) in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. While manufacturers may use other equivalent methods, a manufacturer who uses methods that do not provide results that are consistent with the results obtained by methods approved by FDA will bear the risk that the firm's product is not in compliance with the law.

The agency intends to test for *Salmonella* using the method described in Chapter 5, BAM, including the sample preparation procedures described in section C, paragraph 1 and the sampling plan described in Chapter 1, BAM; for *L. monocytogenes* using the method described in Chapter 10, BAM and the sampling plan described in Chapter 1, BAM; for coliforms, fecal coliforms, and *E. coli* using the MPN method described in Chapter 4, BAM; for *S. aureus* using the MPN method described in Chapter 12, BAM; for *B. cereus* using the MPN or plate count method described in Chapter 14, BAM. The agency intends to determine the APC using the method described in Chapter 3, BAM. All chapter references are to the 8th ed. BAM. FDA intends to update the reference to reflect the most recent edition of the BAM at the time the final rule based on this proposed rule is issued.

h. *Records.* Proposed § 106.55(d) requires that manufacturers make and retain records, in accordance with proposed § 106.100 (e)(5)(ii) and (f)(7) on the testing of infant formula for microorganisms. As discussed in the description of the revisions to proposed subpart F of part 106, FDA has the authority to require such records under section 412(b)(4)(A)(i) of the act. These records will document whether the batch of powdered infant formula meets the microbiological quality standards of proposed § 106.55(c) and is therefore not adulterated. Records that describe the full methodology for testing powdered infant formula for microbiological quality will provide consistency in the testing of the microbiological quality of the formula, even if different laboratory personnel conduct the tests. The accuracy and reproducibility of microbiological quality testing depend on the procedure used to conduct the test. In addition, the records will provide the manufacturer with data to evaluate any complaints received associated with a particular batch of infant formula by showing whether microbiological contamination could have contributed to the adverse event.

10. Controls to Prevent Adulteration During Packaging and Labeling of Infant Formula

Because consumers rely on correct labels to select a formula to meet their childrens' individual needs and to have proper instructions for the use of the formula, FDA is proposing § 106.60(a) which requires manufacturers examine packaged and labeled infant formula to ensure that containers and packages bear the correct labels, use-by dates, and traceability codes. The proposal also requires that labels be designed, printed, and applied so that they remain attached and legible during processing, handling, storage, and use (proposed § 106.60(b)), and that all formula held in a single package be the same product bearing the same traceability code, and that the package carry the product name, name of the manufacturer, and the code (proposed § 106.60(c)).

These proposed requirements will ensure that infants who have allergies will not be placed at risk by consuming formula containing ingredients to which they are allergic, and that consumers will be aware of the date when the product may no longer be appropriate for use. In addition, the traceability codes will show the origin of the product if there were a recall, and the packaging requirements will make it more difficult for counterfeit formula, or formula with counterfeit labels, to be shipped in interstate commerce. There have been cases of counterfeit shipments in which a single package held more than one product, or held a single product which bore more than one code. The proposed regulations are not only intended to reduce the incidence of counterfeit activities, but to ensure that firms that receive the formula are aware that only one product should be in the packaging, and that all containers should be identified with the code shown on the package. This requirement will not impose an additional burden on industry because manufacturers routinely package a