single infant formula product bearing the same code.

11. Controls on the Release of Finished Infant Formula

Proposed § 106.70(a) requires that the manufacturer determine that each batch of formula meets all of the manufacturer's specifications before releasing the batch for distribution. Specifically, each batch must meet the requirements of § 106.55 on microbiological contamination to ensure that the infant formula does not contain microorganisms at levels that may be injurious to the health of infants and render the formula adulterated and must meet the requirements of § 106.91(a) on quality control procedures to ensure that the infant formula provides the required nutrients at the required levels, and that it provides any nutrient added by the manufacturer. Proposed § 106.70(a) is designed to ensure that any infant formula that fails to meet the manufacturer's specifications, or that is adulterated for any reason, will not be introduced into interstate commerce.

Proposed § 106.70(b) requires that each batch of infant formula that fails to meet the manufacturer's specifications be rejected. Although proposed § 106.70(b) recognizes that the formula may be reprocessed, it requires that the reprocessed product be shown to meet the requirements of § 106.70(a) before the product is released. FDA has tentatively concluded that this proposed requirement is necessary to ensure that any defect that caused a batch of infant formula to be rejected is corrected before the formula is released into commerce.

Proposed § 106.70(c) requires that an individual qualified by training or experience conduct an investigation of a finding that a batch of infant formula fails to meet any manufacturer's specifications. This investigation is necessary to determine why such a failure occurred and to assist the manufacturer in developing controls to ensure that such a failure does not reoccur. FDA has proposed to require that the individual who conducts the investigation be qualified to ensure that the investigation is properly conducted.

12. Traceability

Section 412(g)(1) of the act requires that each manufacturer make and retain such distribution records as may be necessary to effect and monitor recalls of the formula, and section 412(b)(4)(A)(vi) requires that each manufacturer retain all complaints concerning infant formulas that may reveal the possible existence of a hazard to health. Therefore, infant formulas must be traceable to permit identification of the product that is the subject of a complaint and to make it possible to determine whether that batch of infant formula presents a possible hazard to health. Traceability of an infant formula is also necessary so that the recall requirements of the act can be met.

The agency's view, based on its experience, is that coding is the most effective method for ensuring traceability. It provides a uniform system that is able to identify large numbers of batches of infant formula with a distinctive code that is easily understood and that can be used by manufacturers, retailers, and consumers. A code also allows a large amount of information to be presented on the container of infant formula in a very small space. Therefore, the agency is proposing, under sections 412 (b)(4)(A)(vi) and (g)(1) and 701(a) of the act that batches of infant formula be identified with a distinctive code that will allow the traceability of an infant formula.

Current § 106.90 requires that manufacturers ensure traceability by coding all infant formulas in conformity with the coding requirements in § 113.60(c) for thermally processed low-acid foods packaged in hermetically sealed containers. Section 113.60(c) requires that the code identify the establishment where the product is packed, the product contained therein, the year packed, the day packed, and the period during which packed, and that the packing period code be changed with sufficient frequency to permit ready identification of lots during their sale and distribution. FDA is proposing to carry the requirement that manufacturers code their product in accordance with § 113.60(c) forward in proposed § 106.80(a).

FDA has tentatively determined that it is appropriate to code liquid infant formulas in this manner because they are thermally processed low-acid foods, and a batch is produced in a relatively short period of time, usually a day. It also may be appropriate for coding some powdered infant formulas in this manner if they are processed in a short enough time to make the day packed and the period during which packed meaningful information.

Proposed § 106.80(b) allows for alternative coding of batches of powdered infant formula. Powdered infant formula is usually manufactured in stages over a longer period of time than liquid infant formula. Some powdered infant formulas are dry mixed in a number of stages over an extended period of time. In other cases, powdered infant formula is mixed in liquid form at one manufacturing facility and shipped to a second site for spray drying and packaging. Powdered infant formula manufacturing is often not completed in a short enough period of time for coding based on the date packed or the period of time in which it was packed to be meaningful information. Therefore, under the alternate method that FDA is proposing, a sequential code would be assigned so that all the essential information needed to track any problems with the infant formula could be determined.

13. Audits of CGMP

Proposed § 106.90 requires that manufacturers (or their agents) conduct regularly scheduled audits to determine whether they are complying with CGMP. This provision derives from section 412(b)(2)(B)(iv) of the act, which requires that the CGMP include "the conduct by the manufacturer of an infant formula or an agent of such manufacturer of regularly scheduled audits to determine that such manufacturer has complied with the regulations prescribed under" section 412(b)(2)(A) of the act. Section 412(b)(2)(A) requires that the Secretary (and by delegation FDA) establish CGMP's by regulation.

FDA is proposing to require that regularly scheduled audits be part of CGMP because such audits are the best way to ensure overall compliance with CGMP and to identify recurring problems that may dictate an alteration in the master manufacturing order. For example, regularly scheduled audits of all deviations from the manufacturer's specifications or procedures will accentuate deviations that occur repeatedly and will enable the manufacturer to identify specifications or procedures that should be reassessed.

Section 412(b)(2)(B)(iv) of the act also specifies that such audits are to "be conducted by appropriately trained individuals who do not have any direct responsibility for the manufacture or production of infant formula." FDA is therefore proposing that an individual be knowledgeable in all aspects of infant formula production perform the audit. Without such broad knowledge, the individual conducting the audit will not be able to adequately evaluate the manufacturer's production and in-process control procedures. In addition, because the purpose of the audit is to determine whether the manufacturer is complying with the CGMP regulations issued under section 412(b)(2)(A) of the act, the agency has tentatively concluded that the person conducting the audit needs to be knowledgeable in

these regulations. Without such knowledge, the person would be unable to make the determinations that are the very purpose of the audit.

The requirement that the audit be performed by an individual who has no direct responsibility for the matters being audited is one way to ensure the objectiveness of the audit process. The person should be free of any past involvement in the activities being audited because the audit is intended to uncover any problems or shortcomings in the manufacturer's procedures. A person who has been involved may feel that finding problems will reflect poorly on his or her work. Therefore, FDA has tentatively concluded that the audit must be conducted by someone who has no direct interest in the outcome of the audit.

C. Quality Control Procedures

1. Introduction

FDA is proposing to redesignate and revise subpart B of part 106 as subpart C of part 106. Under this proposal, several sections of the current regulations will be revoked, and several sections will be redesignated without change. The latter sections are being recodified, however, to fit the organization of the proposed regulations. Table II describes the current and proposed regulations as follows:

TABLE II

Current regulation	Proposed regulation
INGREDIENT CONTROL	
§ 106.20(a), § 106.20(b)(1), § 106.20(b)(2).	Changed by §§ 106.91(a)(1) and 106.40(d).
IN-PROCESS CONTROL	
§ 106.25(a)	§ 106.50(a)(1).
§ 106.25(b)(1)	Omitted.
§ 106.25(b)(2)	§ 106.91(a)(4).
§ 106.25(b)(3)	§ 106.91(a)(2).
§ 106.25(b)(4)	§ 106.91(a)(4) with modification.
§ 106.25(b)(5)	§ 106.91(a)(3) with modification.
FINISHED PRODUCT EVALUATION	
§ 106.30(a)	§ 106.91(a).
§ 106.30(b)(1)(i)	§ 106.91(a)(3).
§ 106.30(b)(1)(ii)	§ 106.91(a) with modification.
§ 106.30(b)(2), § 106.30(b)(3).	§ 106.91(b) with modification.
§ 106.30(c)(1)	Omitted.
§ 106.30(c)(2)	§ 106.3(i) §§ 106.91(b)(1) and 106.97(b)(1) with elimination of the osmolality and vitamin D assay.
§ 106.30(d)	Omitted.

FDA is proposing quality control procedures under the authority granted by section 412(b)(2), (b)(3), and (b)(4) of the act, which direct the Secretary (and by delegation, FDA) to establish by regulation the quality control procedures that he or she determines are necessary to ensure that an infant formula provides the required nutrients at the required levels. In the Congressional Record of September 27, 1986, Senator Metzenbaum stated: "The most important provision of this amendment is the simple requirement that each batch of formula must be tested for each essential nutrient that must be contained in the formula" (Ref. 1). The quality control procedures in proposed subpart C of part 106 are the minimum practices that manufacturers must implement to ensure that the infant formula that they produce contains the required nutrients at the required levels throughout the shelf life of the product. Under section 412(a)(3) of the act, an infant formula is deemed to be adulterated if the processing of the formula does not comply with quality control procedures prescribed by the Secretary.

2. Nutrient Testing

Proposed § 106.91(a) describes the testing that FDA has tentatively concluded each manufacturer must conduct on each batch of infant formula to ensure that it provides the required nutrients at the required levels and provides any nutrient added by the manufacturer. FDA is proposing these requirements under the authority of two sections of the act. Section 412(b)(2)(B)(i) of the act provides that the quality control procedures shall include requirements for testing, in accordance with section 412(b)(3), of each batch of infant formula for each required nutrient, before distribution of such batch. Section 412(b)(3)(D) of the act states that if the Secretary adds a required nutrient, the Secretary must require that the manufacturer of the infant formula test each batch of such formula for that nutrient in accordance with section 412(b)(3)(A), (b)(3)(B), and (b)(3)(C) of the act.

Current § 106.20(a) and (b)(2), which FDA is proposing to replace with § 106.91(a)(1), do not require that manufacturers analyze nutrient premixes if the premixes come with a supplier's guarantee or certification. Proposed § 106.91(a)(1), however, requires that each nutrient premix used in the manufacture of an infant formula be tested by the formula manufacturer for each nutrient that the manufacturer is relying on the premix to provide to ensure that the premix complies with the manufacturer's specification. This change is required by section 412(b)(3)(B) of the act. Section 412(b)(3)(B) was included in the 1986 amendments because infant formula manufacturers were increasingly relying on the use of formula premixes, and Congress felt that relying on a premix supplier's written assurance that its premix product was properly tested was inadequate (Ref. 1). In 1985, the Department of Justice sought an injunction against a premix supplier because, "as a result of inadequate quality control, numerous * * * vitamin and mineral mixes—used in infant formula—have been misbranded and adulterated" (Ref. 3). The premix supplier entered into a consent decree of permanent injunction that enjoined it from shipping any of its vitamin/mineral premixes for use in infant formulas until it completed a number of specific acts that were designed to improve its quality control (Ref. 50).

FDA is proposing to redesignate current § 106.25(b)(3) as § 106.91(a)(2), which requires that after the addition of the premix, or at the final-product stage but before distribution, each batch of infant formula be tested to confirm that the nutrients contained in any nutrient premix used in such infant formula are present in each batch of infant formula in the proper concentration. This requirement implements section 412(b)(3)(C)(ii) of the act, which requires that infant formula be tested to ensure that any nutrient premixes used by the manufacturer are actually included in the batch of infant formula in the proper amount. Without this check, inadvertent failure to include the premix could go undetected, and infant formula that is deficient in the nutrients that were to be provided by the premix would be introduced into the market.

Current § 106.30(b)(1)(i) requires that the manufacturer analyze representative samples of each batch of finished infant formula for specific nutrients to assess process degradation. FDA is carrying forward a modified version of this requirement in proposed § 106.91(a)(3), which requires that each batch of infant formula be tested for vitamins A, C, and

E and thiamin at the final-product stage, before distribution. This regulation is proposed under section 412(b)(3)(A) of the act, which states: "At the final product stage, each batch of infant formula shall be tested for vitamin A, vitamin B1, vitamin C, and vitamin E * * *." In the Congressional Record, Senator Metzenbaum stated that testing for these vitamins is required at the final-product stage because they are vulnerable to degradation (Ref. 1). Testing at the final-product stage will ensure that these nutrients are present in the infant formula at the end of all the processing steps that may destroy them.

Proposed § 106.91(a)(4) requires that, before distribution, each batch of infant formula be tested for all nutrients required to be included, and any others that have been included, but for which testing to comply with § 106.91(a)(1) or (a)(3) was not conducted. This proposed provision takes a markedly different tack than current § 106.30(b)(1)(ii), which states that no analyses are needed for linoleic acid, vitamin D, vitamin K, choline, inositol, and biotin before release of a batch of infant formula for commercial or charitable distribution. This change in approach is necessary because section 412(b)(3)(C) of the act, which was added by the 1986 amendments, states that each batch of formula must be tested for each nutrient required by the law to be present in an infant formula. Also, manufacturers are adding nutrients not required by § 107.100, such as selenium, to infant formulas. These nutrients meet the definition for "nutrient" in proposed § 106.3(m) because they have been identified as essential for infants by NAS through its development of a Recommended Dietary Allowance or an Estimated Safe and Adequate Daily Dietary Intake range. The agency has not objected to the addition of nutrients not required by § 107.100 to infant formulas. However, it is important that the level of these added nutrients be controlled, and that the level of the added nutrient be consistent from batch to batch and be uniform throughout the batch of infant formula.

The level of a nutrient needs to be controlled because some nutrients can be toxic to an infant if given at too high a level. Controlling the level of the added nutrient for consistency from batch to batch and in a particular batch of infant formula will ensure that the infant receives the essential nutrient on a consistent basis and will also ensure that the infant does not receive too high, or too low, a level of the nutrient because the nutrient was not uniform throughout the batch of infant formula.

3. Stability Testing

Current § 106.30(c) requires that the manufacturer, using representative samples collected from finished product batches, conduct stability analysis for selected nutrients with sufficient frequency to substantiate the maintenance of nutrient content throughout the shelf life of the product. The 1986 amendments added subsection 412(b)(2)(B)(ii) to the act, which requires "regularly scheduled testing, by the manufacturer of an infant formula or an agent of such manufacturer, of samples of infant formula during the shelf life of such formula to ensure that such formulas are in compliance with" section 412 of the act. To implement this section of the act, the agency is redesignating and revising current § 106.30(b)(3) as proposed § 106.91(b), which requires quarterly collection of samples of infant formula for stability testing to provide a check on nutrient stability. This periodic check will alert the manufacturer if nutrient stability has changed in some unpredicted way so that the formula no longer complies with section 412 of the act. Quarterly testing of infant formulas for nutrient stability is currently conducted by the industry (Refs. 51 and 52), and the agency is not aware of any problems that have resulted from this frequency of testing. The agency requests comment on whether this proposed frequency of sample collection for stability testing is appropriate.

The agency has tentatively concluded that this periodic sample collection to check on nutrient stability must be performed on a batch of each physical form (powder, ready-to-feed, or concentrate) of each infant formula, at each different manufacturing facility, because different forms of the product may contain different ingredients, and different forms of infant formula are subjected to different processing procedures. Therefore, ensuring the nutrient stability of one form of the product, such as the powder, will not answer questions about the nutrient stability of other forms of the product. Thus, the agency has tentatively concluded that each form of the infant formula must be sampled on a periodic basis for nutrient stability. Also, the agency has tentatively concluded that the sampling of one batch of each physical form of each infant formula must be conducted at each manufacturing facility. This proposed requirement is necessary because manufacturers may produce the same infant formula at more than one facility, and the manufacturing conditions at one facility may not be the same as the conditions at another facility. The differences in conditions cannot be allowed to affect the quality of the formula.

Proposed § 106.91(b) further requires testing at the beginning, midpoint, and end of the shelf life of the infant formula. Testing at the beginning of the shelf life shows that the formula is in compliance with the nutrient requirements of the act when it is released for distribution. Testing at the midpoint of the shelf life will alert the manufacturer if any nutrient is deteriorating at a rate different from that predicted, so that the nutrient may not be in the formula at a level to comply with the act throughout the formula's shelf life. Testing at the end of shelf life will ensure that the formula contained all the nutrients needed to comply with the act throughout its shelf life and will provide continued justification for the predicted shelf life.

Additional testing may be necessary to ensure that a formula complies with section 412 of the act throughout its shelf life. Such testing is likely to focus on a particular nutrient and its stability within the matrix of the formulation. This additional testing will ensure that, if there is a significant deterioration in the level of the nutrient in the formula, the manufacturer will be aware of this fact and will be able to take steps promptly to have the product removed from the market, before a significant number of infants are exposed to a deficient product.

The agency is not proposing to specify what frequency is required because manufacturers have experience with the nutrient stability of the infant formula matrices that they produce and are thus in a position to determine how frequently testing is necessary. For example, the manufacturer is in a position to know whether the nutrient levels of a milk-based infant formula need to be tested on a different basis than that of a soy-based product, or whether the nutrient levels of an infant formula that contains hydrolyzed protein needs to be tested more frequently than that of an infant formula that contains non-hydrolyzed protein. Manufacturers will be able to comply with section 412(b)(2)(B)(ii) of the act by testing different nutrients at different frequencies. For example, unstable nutrients, such as vitamins, may require testing on a more frequent basis than more stable nutrients, such as minerals. Proposed § 106.91(b) allows the manufacturers the discretion to determine the necessary frequency of testing to ensure that their infant formula complies with the nutrient

requirements of the act, as long as the minimum testing (i.e., at the beginning, middle, and end of the shelf life) required by proposed § 106.91(b) is accomplished.

Proposed § 106.91(b)(1) provides for an addition to the stability testing required under § 106.91(b). FDA is proposing that the first batch of each form of a new infant formula be subjected to such testing to ensure that the product complies with the nutrient requirements of section 412 of the act throughout its shelf life.

Proposed § 106.91(b)(2) requires the sampling of the first batch of an infant formula in which there has been a change in formulation or in processing that could affect whether the formula is adulterated under section 412(a) of the act and requires testing of these samples for each nutrient that has been, or may have been, affected by the change. The change in formulation or processing referred to here would not be a "major change" because a "major change" would mean that the formula is a "new infant formula." Examples of the types of changes that are subject to proposed § 106.91(b)(2) are: (1) Reducing a "required nutrient" in a minor way or increasing a "required nutrient" that is subject to maximum limits in § 107.100 in a minor way; (2) replacing one nutrient form with another form, such as replacing vitamin A acetate with vitamin A palmitate or replacing calcium carbonate with tricalcium phosphate; (3) changing a time-temperature condition of preheating, handling, mixing, or sterilizing an in-process product; or (4) changing the oxygen content of a packaged product that might have a minimal effect on the level of nutrients. Requiring sample collection for stability testing when a manufacturer makes changes such as these in the manufacture of the product will ensure that the manufacturer can verify the predicted shelf life of the changed formula.

Proposed § 106.91(b)(2) requires that the manufacturer ensure that the infant formula meets all the nutrient requirements of section 412 of the act. This provision is proposed under the authority of section 412(b)(2)(A) of the act, which provides for the establishment of CGMP's for infant formulas, including quality control procedures that are necessary to assure that the infant formula provides nutrients in accordance with section 412 (b) and (i) of the act, as well as section 412(b)(2)(B)(ii). If the formulation or processing of the infant formula has been changed, the manufacturer must consider what nutrients may have been affected by the change and test for each of these nutrients in the final-product stage of the first batch of the changed formula. For example, if the manufacturer makes a change in the amount of a protein source used in the infant formula, the firm must test the formula for protein content and for any nutrients provided endogenously to the formula by the protein, such as minerals like calcium and phosphorus. The manufacturer is aware of how much of each mineral it is relying on the protein source to provide to the formula. When the amount of the protein source used in the formula is changed, the manufacturer must test for the level of all nutrients it relies on the protein source to provide to the formula to ensure that all nutrients in the formula meet the requirement of § 107.100.

4. Quality Control Records

Proposed § 106.91(c) requires that manufacturers make and retain records of the results of all testing performed on the batch of infant formula in accordance with proposed § 106.100(e)(5)(i) and a full description of the methodology used in accordance with proposed § 106.100(f)(7). As discussed in the description of the proposed revisions to subpart F of part 106, FDA has authority to require these records under section 412(b)(4)(A)(i) of the act. Providing a record of the results of quality control testing will verify that each nutrient required by § 107.100 is present in each batch of infant formula at the required level, and that any nutrients added by the manufacturer are present at the appropriate level. These records will show the levels of nutrients in the formula and will provide data needed to evaluate a batch of infant formula if problems, such as adverse events in infants, occur later with that particular batch. Records that describe the full methodology used to conduct the quality control testing will provide consistency in the procedure that the manufacturer is using to test for the nutrients in each batch of infant formula, even when different laboratory personnel are conducting the testing. The accuracy and reproducibility of quality control testing depend on the procedure used to conduct the test.

5. Audits of Quality Control Procedures

Proposed § 106.92 requires that the manufacturer of an infant formula, or an agent of such a manufacturer, conduct regularly scheduled quality control audits to ensure that an infant formula provides required nutrients and has been manufactured in a manner designed to prevent adulteration. Proposed § 106.92 derives from section 412(b)(2)(B)(iv) of the act, which requires that the quality control procedures prescribed by the Secretary include "the conduct by the manufacturer of an infant formula or an agent of such manufacturer of regularly scheduled audits to determine that such manufacturer has complied with the regulations prescribed under" section 412(b)(2)(A) of the act (stating that the Secretary (and FDA by delegation) establish by regulation "quality control procedures that the Secretary determines are necessary to assure that an infant formula provides nutrients in accordance with" section 412 (b) and (i) and "is manufactured in a manner designed to prevent adulteration of the formula". FDA is proposing to require that regularly scheduled audits be part of quality control procedures because such audits will document compliance with the quality control procedures and will identify recurring problems that may dictate an alteration in the master manufacturing order. For example, regularly scheduled audits of the results of tests of nutrient levels in infant formulas and of any deviations from the manufacturer's specifications or procedures for acceptable nutrient levels will reveal deviations that occur on a repeated basis and will enable the manufacturer to identify specifications or procedures that should be reassessed.

Proposed § 106.92 further requires that the audits be performed by an individual who, as a result of education, training, and experience, is knowledgeable in all aspects of infant formula production and of the agency's regulations concerning quality control procedures, but who has no direct responsibilities for the matters being audited. The legal authority for this provision, the importance of the responsible individual's knowledge in all aspects of infant formula production and the agency's regulations, and the need for the audit to be performed by an individual who has no direct responsibility for the matters being audited were discussed previously under the proposed CGMP regulations in § 106.90.

By proposing different regulations (proposed §§ 106.90 and 106.92) that require audits of CGMP and of quality control procedures, the agency is not suggesting that it will require that separate audits be conducted. These regulations are being proposed separately to make clear that the regularly scheduled audits required by section 412(b)(2)(B)(iv) of the act are an aspect both of CGMP and of quality control procedures. The agency would have no objection to a combined audit

of CGMP and of quality control procedures.

6. Revocation of the Requirement for Determination of Vitamin D by the Rat Bioassay Method

FDA is proposing to revoke the requirement in current § 106.30(c)(2) for the determination of vitamin D by a rat bioassay method. This rat bioassay for vitamin D is no longer a viable assay because appropriate animals for conducting this test are difficult to acquire (Ref. 53), and an alternate analytical method for the determination of vitamin D in infant formulas has been approved by the Association of Official Analytical Chemists (Ref. 54).

D. Conduct of Audits

Section 412(b)(2)(B)(iv) of the act provides that CGMP and quality control procedures include regularly scheduled audits to determine whether the manufacturer is complying with CGMP, including following the quality control procedures that are necessary to ensure that an infant formula provides the required nutrients at the required levels, and whether it is operating in a manner designed to prevent adulteration of the formula. FDA is proposing to require in § 106.94(a) that manufacturers develop and follow a written audit plan that is available at the manufacturing facility for FDA inspection. A written audit plan is necessary to provide consistency in how audits are conducted and to ensure that the auditor can determine whether the facility is operating in compliance with the applicable procedures.

Proposed § 106.94(b) requires that the audit plan include the procedures that the manufacturer uses to determine whether the facility is operating in accordance with CGMP, with the applicable quality control procedures, and in a manner designed to prevent adulteration of the infant formula it produces. This proposed requirement derives from current § 106.100(j), which defines audit procedures as the methods used to review the manufacturing and quality control procedures and is intended to direct the manufacturer's attention to the fundamental goals of the manufacturing process in formulating its audit plan.

Proposed § 106.94(c) sets out the minimum requirements for the audit procedures that are to be employed by manufacturers. Under proposed § 106.94(c)(1) these procedures are to include a review of how the production and in-process control system established under § 106.6(b) is operating. In particular, proposed § 106.94(c)(1)(i) specifies that the evaluation of the production and in-process control system include observation of the production of infant formula and a comparison of the observed process to the written production and in-process control plan required under proposed § 106.6(b). FDA has tentatively concluded that such observations will show whether the production and in-process control system is being followed appropriately, and, if not, they will identify any deviations from the production and in-process control system, so that the manufacturer can take corrective actions to ensure that infant formula is produced in compliance with the production and in-process control system.

Proposed § 106.94(c)(1)(ii) requires that the evaluation of the production and in-process control system include a review of records of the monitoring of points, steps, or stages where control is deemed necessary to prevent adulteration. As discussed below, proposed § 106.100(e)(3) requires that the batch production and control records document the monitoring of all points where control is deemed necessary to prevent adulteration in the manufacturing of the batch. FDA has tentatively concluded that proposed § 106.94(c)(1)(ii) is necessary because the auditor can observe the production of only a limited number of batches of infant formula. A review of the production and in-process control records of all batches produced in a given period of time will ensure that the production and in-process control system is working appropriately on a continuous basis, will identify any point that monitoring reveals is out of control on a recurring basis, and will identify where the production and in-process control system needs improvement.

Proposed § 106.94(c)(1)(iii) requires that the evaluation of the production and in-process control system include a review of records of how deviations from any standard or specification at points, steps, or stages where control is deemed necessary to prevent adulteration were handled. As discussed below, proposed § 106.100(e)(4)(iii) requires that the batch records include the conclusions and followup of an investigation of the failure to meet any specification or standard at any point where control is deemed necessary to prevent adulteration. A review of these records as a part of the audit will identify failures that occur on a repeated basis and will show how these failures are handled by the manufacturer. The auditor will be able to evaluate whether the conclusions and followup of these investigations are appropriate for each failure to meet the specification or standard.

Proposed § 106.94(c)(2) requires that the audit procedures include a review of a representative sample of all records maintained in accordance with proposed § 106.100 (e) and (f). As discussed below, proposed § 106.100(e) sets out the requirements for the batch production and control records, and proposed § 106.100(f) sets out the requirements for records related to observance of CGMP. A review of a representative sample of these records will show the auditor whether there has been compliance with the appropriate regulations in producing the batches of product so that the formula is not adulterated. Section 412(b)(2)(B)(iv) of the act states that the audit is conducted to determine whether the manufacturer has complied with the regulations establishing CGMP for infant formulas, including quality control procedures. FDA has tentatively concluded that review of a representative sample of the records maintained in accordance with § 106.100 (e) and (f) is necessary to determine whether the manufacturer is complying with these regulations.

E. Quality Factors for Infant Formulas

1. What Are Quality Factors?

The agency is proposing to create a new subpart E to implement the quality factor requirements of sections 412 (a)(2) and (b)(1) of the act. Section 412(a)(2) of the act states that an infant formula is adulterated unless it meets the quality factor requirements that are established under section 412(b)(1). Section 412(b)(1) of the act states that the Secretary shall by regulation establish requirements for quality factors, including quality factor requirements for required nutrients for infant formulas to the extent possible consistent with current scientific knowledge. Therefore, it is incumbent on manufacturers to establish that the infant formula that they produce meets the minimum quality factor requirements that FDA adopts.

What Congress meant by "quality factors" is discussed in the report of the House Committee on Interstate and Foreign Commerce that accompanied the 1980 act. The report states that quality factors "pertain to the bioavailability of a nutrient and the maintenance of levels or potency of nutrients during the expected shelf life of the product" (Ref. 5). FDA, in proposed § 106.3(o), has defined "quality factors" in a manner that encompasses several basic concepts, including the concepts of