reexamination, performed on them and their disposition. These records will document that appropriate testing is being conducted to ensure that the ingredients will not adulterate the infant formula, and that the containers and closures will protect the infant formula against adulteration. Further, these records will show the basis on which each ingredient, container, and closure was released for use in infant formula production if questions about such release later arise. Individual lots of ingredients, containers, and closures are likely to be used in a number of different batches of infant formula; therefore, the agency is proposing that the records on ingredients, containers, and closures be a part of the records pertaining to CGMP. Retaining such records in the CGMP records, rather than in each batch record, will eliminate the duplication of records and simplify the recordkeeping. The disposition of the ingredients, containers, and closures will show which materials were destroyed because they did not meet the manufacturers specifications (and not used in manufacture in compliance with § 106.40(d)), and which batches of infant formula were made using each lot of ingredients, containers, or closures. Thus, the manufacturer will know which lots of ingredients, containers, or closures were used in making infant formula and will be able to confirm that those lots complied with proposed § 106.40(d). Moreover, if a batch of formula is shown to be adulterated, these records will help the manufacturer to identify the source of the adulteration.

Proposed § 106.100(f)(7) requires that manufacturers make and retain records that include a full description of the methodology used to test powdered infant formulas to verify compliance with proposed § 106.55(c) and the methodology used to conduct quality control testing in accordance with § 106.91 (a) and (b). The agency has not specified in these regulations the methodologies that must be used to conduct microbiological and quality control testing. Thus, FDA has tentatively concluded that a manufacturer needs to maintain a record that fully describes the methodology that it has decided to use to test powdered infant formula for microorganisms and for quality control testing. Such a record is necessary if there is to be consistency in the procedure that the manufacturer follows in testing each batch of infant formula, particularly in light of the fact that the laboratory personnel conducting the testing are likely to vary. The accuracy and reproducibility of microbiological and quality control testing depend on the procedure used to conduct the test.

FDA is proposing that the full description of the methodology be retained as part of the CGMP records, rather than in the batch record provided for in proposed § 106.100(e)(5), because these methods will be used to test multiple batches of infant formula. Retaining such records in the CGMP records, rather than in each batch record, will mean that the manufacturer has to maintain only one document, rather than having to reproduce it each time that it runs a batch of formula. Thus, the proposed approach will eliminate duplication of records and simplify recordkeeping.

4. Records on Distribution of Infant Formulas

Proposed § 106.100(g) adds to current § 106.100(g) a requirement that records pertaining to distribution of the infant formula show that products intended for export only are in fact exported. It has recently come to the attention of the agency that infant formulas produced for export have been diverted and sold in the United States. All persons introducing any new infant formula into interstate commerce, which includes persons exporting an infant formula to a foreign country, are required by section 412(c) of the act to register and make a submission to the agency 90 days before marketing the formula. (See discussion of proposed §§ 106.110 and 106.120.)

As discussed in the section of this preamble on proposed § 106.120(c), the agency has tentatively concluded that it will not require manufacturers who produce infant formula for export only to submit the same information that would be required for products intended or offered for sale in the United States. In lieu of the information required by § 106.120(b), FDA is proposing to allow manufacturers of products for export only to give assurances that the infant formula will not be sold or offered for sale in domestic commerce. This provision is based, in part, on section 801(e) of the act, which states that a food will not be deemed to be adulterated or misbranded under the act if, among other things, it is not sold or offered for sale in domestic commerce. Thus, the agency has tentatively concluded that the additional recordkeeping requirement on distribution of infant formulas for export only in proposed § 106.100(g) is necessary so that verification that the infant formula was not in fact sold or offered for sale in domestic commerce will be readily available in the manufacturer's records.

5. Audit Records

Proposed § 106.100(j) carries forward the requirement in current § 106.100(j) that the manufacturer make and retain records, which include the audit plans and procedures, that pertain to regularly scheduled audits. As discussed above, the written audit plan, which includes audit procedures, is required under proposed § 106.94(a) and (b). The proposed section further requires that records of audits include the findings of the audit and a listing of any changes made in response to these findings. This requirement is proposed under the authority of section 412(b)(4)(A)(v) of the act, which requires that manufacturers retain all records of the results of regularly scheduled audits conducted under the requirements prescribed by the Secretary (and by delegation, FDA) under the authority of section 412(b)(2)(B)(iv).

Proposed § 106.100(j) also requires that the manufacturer make readily available for authorized inspection the audit plans and procedures and a statement of assurance that the regularly scheduled audits are being conducted. This provision implements section 412(b)(4)(B)(ii) of the act, which requires that the manufacturer provide written assurance that the regularly scheduled audits are being conducted by the manufacturer. However, proposed § 106.100(j) also provides that the findings of the audit and any changes made in response to these findings need not be made available to FDA. This provision is brought forward from current § 106.100(j) and reflects section 412(b)(4)(B)(ii) of the act, which states that a "manufacturer need only provide written assurances to the Secretary that the regularly scheduled audits required by" section 412(b)(2)(B)(iv) of the act "are being conducted by the manufacturer, and need not make available to the Secretary the actual written reports of such audits."

6. Modification of Current § 106.100(k)(3)

The agency also is revising current § 106.100(k)(3) to reflect the numbering changes in the regulations on notifying the agency of a causal relationship between the consumption of an infant formula and an infant's death. The agency is moving the requirements of current § 106.120(b) to § 106.150 to reflect the changes it is proposing in subpart G. Thus, the reference to § 106.120 in § 106.100 (k)(3) will be changed to read "§ 106.150," if the

agency adopts the relevant proposed changes.

G. Registration, Submission, and Notification Requirements

1. Introduction

The act provides for three types of notices that manufacturers of infant formula must provide to FDA and sets forth the general information that must be included in each type of notice. First, manufacturers of a new infant formula must register with FDA, in accordance with section 412(c)(1)(A) of the act, providing the name and address of the firm and all establishments that will manufacture the new infant formula. Second, manufacturers must submit to FDA, in accordance with section 412(d) of the act, certain information concerning a new infant formula or an infant formula in which there is a change in formulation or processing that may affect whether the formula is adulterated under section 412(a) of the act. Third, manufacturers must notify FDA, in accordance with section 412(e) of the act, of any adulterated or misbranded infant formula that has left their control.

The agency has not specified the information that must be included in an infant formula registration, submission, or notification. While firms have been able to function under these requirements since the 1986 amendments were enacted with respect to the notice that manufacturers must provide to the agency under section 412(c) and (d) of the act, inquiries from industry suggest that manufacturers are uncertain about the information that they must provide. Some manufacturers have needed to make multiple submissions for a new infant formula because of deficiencies in the initial submission. For example, some submissions have contained information concerning more than one formula without clearly identifying which information applied to which formula. Some submissions have not contained the information required by section 412(d)(1) of the act. Therefore, FDA recognizes that it will be useful both to manufacturers and to the agency to issue regulations to ensure that registrations and submissions required by the act follow a consistent format and contain the necessary information for the agency to determine whether there is a basis to object to the marketing of a new infant formula. Such regulations will facilitate the manufacturer's preparation of the notice and also will facilitate the agency's review of the notice once FDA receives it.

These proposed regulations also will make clear when a registration, notification, or submission to the agency is needed. For example, as stated above, it has recently come to the attention of the agency that some firms that manufacture infant formula intended only for export are not aware of their registration and submission responsibilities. Section 412(c)(1) of the act requires that a person introducing a new infant formula into interstate commerce (which includes export to a foreign country) must register the infant formula and make the proper submission 90 days before marketing it. These proposed regulations make clear that registration and submission requirements apply to infant formulas intended only for export as well as to infant formula intended for the domestic market.

Finally, for completeness, FDA has decided that it would be useful to both manufacturers and the agency, to carry forward current § 106.240, concerning notification of a violative infant formula, as § 106.150. Doing so will consolidate in one place in the agency's regulations all requirements concerning notice to the agency to meet the requirements of section 412(c), (d), and (e) of the act.

2. New Infant Formula Registration

Proposed § 106.110(a) requires that a manufacturer of a new infant formula register with FDA before introducing the formula, or delivering it for introduction, into interstate commerce. Because "interstate commerce" is defined in section 201(b) of the act as "(1) commerce between any State or Territory and any place outside thereof, and (2) commerce within the District of Columbia or within any other Territory not organized with a legislative body," under this provision, a manufacturer is required to register with FDA before introducing a new infant formula into the United States market or before beginning exporting the formula. Proposed § 106.110(a) sets out how to comply with section 412(c)(1)(A) of the act. Failure to provide the notice required by section 412(c)(1)(A) of the act is a prohibited act under section 301(s).

Under section 412(c)(1)(A) of the act, proposed § 106.110(b) sets out the information required in a new infant formula registration. While manufacturers may register at any time before introducing a new formula into interstate commerce, FDA urges that they do so at the same time that they submit notice of their intent to market a new infant formula in accordance with section 412(c)(1)(B) and (d)(1) of the act. Receiving registration and the 90 day submission at the same time will facilitate the agency's review.

3. New Infant Formula Submission

Section 412(c)(1)(B) of the act requires that manufacturers of a new infant formula submit to FDA a notice of their intent to market the new formula that complies with section 412(d)(1) of the act. The notice must be submitted at least 90 days before the infant formula is introduced or delivered for introduction into interstate commerce[6]. Proposed § 106.120 implements this requirement.

Proposed § 106.120(a) sets out the requirement that a manufacturer submit a notice of its intent to market a new infant formula and provides the address to which such notices are to be submitted.

Proposed § 106.120(b) sets forth the information that manufacturers must include in their new infant formula submission. This proposed regulation implements and specifies the information called for in section 412(d)(1) of the act.

a. *General information required in a 90-day submission.* Because the registration of a new infant formula (proposed § 106.110) need not accompany the new infant formula submission (proposed § 106.120), and because a third submission on a newinfant formula that verifies that the new infant formula, as produced, contains all required nutrients (see proposed § 106.130) will be submitted separately, FDA has tentatively concluded that the name of the infant formula is needed to ensure that all information on a particular infant formula is filed together and is available to determine whether the agency should object to the marketing of the formula. Information on the form of the product is necessary for an accurate evaluation of the product because different

[6] While section 412(c)(1) and (c)(1)(B) of the act state "No person shall introduce or deliver for introduction into interstate commerce any new infant formula unless—such person has at least 90 days before marketing such new infant formula, made the submission to the Secretary required by" section 412(c)(1) of the act, FDA has recognized since 1986 that this citation is in error (see "Requirements for Infant Formulas" published by FDA's Industry Programs Branch, CFSAN), and that the correct citation is section 412(d)(1). This correction agrees with the language of section 412(d)(1) of the act, which states what a submission about any infant formula subject to section 412(c) of the act should include. It is also consistent with the rules of statutory construction. See *Colonial Life & Accident Insurance Co.* v. *American Family Life Assurance Co.*, 846 F. Supp. 454, 463 n. 14(D.S.C. 1994) (where the legislature has made a mistake in reference, and its intent is manifest, the statute may be read as corrected in order to give effect to the legislative intent).

requirements may apply to different forms of a formula. For example, powdered infant formula must meet the microbiological quality requirements in proposed § 106.55, whereas liquid forms of a formula do not. Therefore, FDA is proposing to require this information in § 106.120(b)(1), under the authority of sections 412(d)(1) and 701(a) of the act, even though it is not explicitly required in section 412(d)(1).

Proposed § 106.120(b)(2) requires that the submission include an explanation of why the formula is a new infant formula to facilitate a determination by the agency as to the type of evaluation the new infant formula requires. For example, if the formula is a new infant formula because a new manufacturing plant will be used to produce it, but the formulation of the product is not changed, FDA will evaluate the processing and arrange to inspect the new facility but may conclude that testing to provide assurance that quality factor requirements have been met is not necessary. Thus, FDA is proposing to require the submission of this information, even though, like the information required under proposed § 106.120(b)(1), submission of this information is not specifically provided for in the act. The agency tentatively concludes that this information is necessary for the efficient enforcement of sections 412(c)(1)(B) and (d)(1) of the act.

b. *Formulation and processing information required in a 90-day submission.* Pursuant to section 412(d)(1)(A) of the act, proposed § 106.120(b)(3) requires that the submission include the quantitative formulation of the infant formula. The agency is proposing that, if the notice concerns more than one form of the formula, the submission include quantitative information on each form of the formula that is the subject of the notice. FDA is proposing to require that manufacturers submit the formulation in units per volume (for liquid formulas) or units per dry weight (for powdered formulas) because formulations expressed in these units will facilitate agency understanding of the formula. Manufacturers already will have the formulation available in these units as a part of the master manufacturing order, and submitting the formulations in these units should not require additional calculations by the manufacturer.

Proposed § 106.120(b)(3) also requires, under section 412(d)(1)(B) of the act, that the submission include a description of any reformulation of the infant formula, including a listing of each new or changed ingredient and a discussion of the effect of such changes on the nutrient levels in the formulation. For example, if the protein source in an infant formula is replaced with a protein source that contains a different amount of protein (e.g., from casein to a mixture of casein and whey), it is important to ensure that the amount of the new protein source used will provide the amount of protein required by § 107.100. As another example, if an ingredient such as sodium selenite is added to the formula for the first time, it is important to ensure that the level of the ingredient provides selenium (in the form of selenite) at a level that is consistent with the infant's needs and yet within the safe range of selenium intake.

Proposed § 106.120(b)(4) requires that the submission include a description, when applicable, of any change in processing of the infant formula, and that such description identify the specific change in processing, including side-by-side, detailed schematic diagrams comparing the new processing to the previous processing (including processing times and temperatures). This proposed requirement implements section 412(d)(1)(B) of the act, which states that the submission must include a description of any change in the processing of an infant formula. FDA is proposing that the description of the change in processing include detailed schematic diagrams comparing the new processing to the previous processing because schematic diagrams are efficient tools for identifying the nature and significance of changes in processing.

c. *Assurance that the infant formula will not be marketed unless it meets quality factor and nutrient requirements of the act.* Pursuant to section 412(d)(1)(C) of the act, proposed § 106.120(b)(5) requires that the submission include an assurance that the infant formula will not be marketed unless it meets the quality factor requirements of section 412(b)(1) of the act and the nutrient content requirements of section 412(i) of the act.

Proposed § 106.120(b)(5)(i) requires that the assurance that the formula meets the quality factor requirements, which are set forth in subpart E of part 106, be provided by a submission that complies with § 106.121. Section 412(d)(1)(C) of the act requires that, 90 days before marketing a new infant formula, a manufacturer submit assurances that the infant formula will not be marketed unless it meets the quality factor requirements established by regulations under section 412(b)(1). Section 412(d)(2) of the act requires that, after the first production of a new infant formula and before introduction into interstate commerce of such formula, the manufacturer submit a written verification that summarizes test results and records demonstrating that such formula complies with the quality factor requirements. However, FDA has tentatively concluded that to implement sections 412 (d)(1) and (d)(2) of the act in a way that ensures that the statutory goals are achieved—that is, to ensure that the agency has all the relevant information for a sufficient period of time to conduct a meaningful review of the nutritional adequacy of the formula while enabling the infant formula manufacturer to market its product as expeditiously as possible—it is appropriate to require that the assurances that the quality factors will be met be provided by means of data that would otherwise be required as part of the verification submission. FDA notes that such a requirement would only codify current practice. Since passage of the 1986 amendments, infant formula manufacturers have been providing data demonstrating that a new infant formula meets the quality factor requirements as a part of the submission made 90 days before marketing.

Proposed § 106.120(b)(5)(ii) requires that the assurance that the formula complies with the nutrient content requirements, which are set forth in § 107.100, be provided by a statement assuring that the formula will not be marketed unless it meets the nutrient requirements of § 107.100, as demonstrated by testing required under subpart C of part 106.

The agency acknowledges that there is an apparent inconsistency in how it interprets the word "assurance" in section 412(d)(1)(C) of the act as it relates to assurance that the infant formula meets the quality factor requirements and assurance that the infant formula meets nutrient content requirements. FDA has tentatively concluded, however, that assurance that the formula will meet the quality factor requirements is a threshold question that must be answered affirmatively before the effort in setting up the line for first production of the infant formula would be justified. Therefore, the agency is proposing to require that the assurance that the infant formula will meet the quality factor requirements be provided by data submitted 90 days before marketing the formula.

On the other hand, the agency is proposing that the assurance that the formula will not be marketed unless it meets the nutrient requirements of § 107.100 can be provided by a statement to that effect (as opposed to data) submitted 90 days before marketing of the formula because the

data and records demonstrating that the formula complies with the nutrient requirements of § 107.100 will not be available until the production line is set up, and the first production of the infant formula has occurred. FDA will receive verification that the formula meets the nutrient requirements as a part of the submission required by section 412(d)(2) of the act (see proposed § 106.130(b)(3), below). Therefore, FDA has tentatively concluded that it is adequate to receive a commitment from the manufacturer, 90 days before marketing, that the infant formula will not be marketed unless it meets the nutrient requirements of § 107.100.

d. *Assurance that the processing of the infant formula complies with the CGMP and quality control procedures of the act.* Under section 412(d)(1)(D) of the act, proposed § 106.120(b)(6) requires that the submission include assurance that the processing of the infant formula complies with section 412(b)(2) of the act (CGMP, including quality control procedures).

Proposed § 106.120(b)(6)(i) requires that the assurance that the processing of the infant formula complies with section 412(b)(2) of the act include a statement that the formula will be produced in accordance with subparts B and C of part 106. This proposed requirement is a necessary element of the assurance required by section 412(d)(1)(D) of the act because the requirements for CGMP are set forth in subpart B and the requirements for quality control procedures are set forth in subpart C. In the Congressional Record (Ref. 1), Senator Metzenbaum stated that the amendments to the Infant Formula Act set up requirements "which will prevent our Nation's Children from ever again being threatened by defective baby formula. 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).

Proposed § 106.120(b)(6)(ii) requires that the assurance that the processing of the infant formula complies with section 412(b)(2) of the act include the basis on which the manufacturer has concluded that each ingredient meets the requirement of proposed § 106.40(a), i.e., that the ingredient is an approved food additive, is authorized by a prior sanction issued by the agency, or is GRAS for its intended use. The statute provides that the manufacturer submit, 90 days before marketing a new infant formula, assurance that the processing of the formula complies with the CGMP regulations, and that the formula is manufactured in a way that is designed to prevent its adulteration. FDA has tentatively concluded that, to implement the act in a way that will ensure that the statutory goals are achieved, that is, to ensure that the agency has all the relevant information for a sufficient period of time to conduct a meaningful review of the formula while enabling the manufacturer to market its product as expeditiously as possible, it is appropriate to require that the assurance that none of the ingredients will adulterate the formula be provided by an explanation of how each ingredient meets proposed § 106.40(a). FDA has tentatively concluded that this approach is appropriate because, like the evidence that the formula meets the quality factors, evidence that all the ingredients in the infant formula are safe goes to a threshold question that must be answered affirmatively before the effort in setting up the production line for the first production of the infant formula would be justified. Moreover, an infant formula manufacturer would want to have information demonstrating that each of the ingredients in the formula is safe before marketing the formula, because without such information, a responsible manufacturer would not include the ingredient in its product.

FDA will review the new infant formula submission to ensure that a safe product will be produced (sections 201(s), 402(a)(1) and (a)(2), and 409 of the act). If the agency is not presented with basis on which it can be satisfied that the use of an ingredient in an infant formula will be safe, FDA will not be able to acquiesce in the marketing of the formula. The legislative history of the 1986 amendments supports that Congress anticipated that FDA would provide this type of review. In the Congressional Record of September 27, 1986, Senator Metzenbaum stated:

> I continue to be concerned, however, that our food and drug laws do not differentiate between foods and infant formulas. But they are fundamentally different. An infant formula is designed as the sole source of nutrition for a baby. An infant formula is used daily. A baby must thrive from its content for the first and most formative months of his or her life. I expect the Secretary to look closely at whether or not our standards in this area for foods are adequate standards for infant formula. I have no reason at this time to suspect that there is a problem here. But I continue to urge the Secretary to give thorough consideration to the important distinctions between infant formula and other foods, as well as food additives which may be used with infant formulas. (Ref. 1)

One way for a manufacturer to satisfy the agency that proposed § 106.40(a) is met would be for the manufacturer to use only ingredients that are: (1) Listed as GRAS for such use in 21 CFR part 182 or affirmed as GRAS for such use in 21 CFR part 184 or otherwise GRAS for such use under the regulations included in those parts; (2) approved for such use by a food additive regulation; or (3) authorized by a prior sanction issued by FDA.

Alternatively, the requirements of proposed § 106.40(a) can be met by a showing that the substance is GRAS within the meaning of § 170.30 (21 CFR 170.30), which states that "general recognition of safety may be based only on the view of experts qualified by scientific training and experience to evaluate the safety of substances directly or indirectly added to foods" (§ 170.30(a)). To clarify this point, § 170.30(a) states that "[g]eneral recognition of safety requires common knowledge about the substance throughout the scientific community knowledgeable about the safety of substances directly or indirectly added to food." The qualified experts can base their views on either: (1) Scientific procedures, or (2) in the case of a substance used in food prior to January 1, 1958, through experience based on common use in food (section 201(s) of the act).

Under § 170.30(b), general recognition of safety based upon scientific procedures requires the same quantity and quality of scientific evidence as is required to obtain approval of the ingredient as a food additive, and it must ordinarily be based on published studies, which may be corroborated by unpublished studies and other data and information. If the manufacturer of an infant formula wishes to use an ingredient because there is general recognition of safety based upon scientific procedures, FDA is proposing to require in § 106.120(b)(6)(ii) that the manufacturer include as a part of its new infant formula 90-day submission the rationale for why the ingredient is GRAS and the evidence that demonstrates that there is common knowledge about the safety of the substance throughout the scientific community knowledgeable about the safety of such substance. FDA is proposing that this evidence include a bibliography of published studies, copies of those scientific publications about the substance, and an explanation as to why, based on the published studies, the use of the substance in infant formula is GRAS.

Under § 170.30(c)(1), if a substance is GRAS based on common use in food prior to January 1, 1958, this determination must be based solely on

food use of the substance before January 1, 1958, and must ordinarily be based upon generally available data and information. Thus, GRAS based on common use in food prior to January 1, 1958, may be determined without the quantity or quality of scientific procedures required for approval of a food additive regulation. If the manufacturer of an infant formula wishes to use an ingredient based solely on food use of the substance prior to January 1, 1958, it should provide as a part of the new infant formula 90-day submission the evidence supporting that the ingredient was in common use in infant formula prior to January 1, 1958, and an explanation of why that use provides the basis for general recognition of the safety of the substance.

FDA has recognized that it is impractical to list all substances that are GRAS for their intended use based on their common use in food prior to 1958 (see 21 CFR 182.1(a)). The agency regards such common food ingredients as salt, pepper, vinegar, and baking powder as safe for their intended use. Also, current § 170.30(d) provides that a "food ingredient of natural biological origin that has been widely consumed for its nutrient properties in the United States prior to January 1, 1958, without known detrimental effects, which is subject only to conventional processing as practiced prior to January 1, 1958, and for which no known safety hazard exists, will ordinarily be regarded as GRAS * * *." Some ingredients are used in infant formulas even though they are not listed or affirmed as GRAS by the agency for their intended use. Vitamin K, for example, is required to be a part of an infant formula under section 412(i) of the act and, in the form of phylloquinone, is considered to be safe and suitable for infant formulas when used in accordance with prescribed levels in § 107.100, although no source of vitamin K, such as phytonadione or phylloquinone, has been listed or affirmed as GRAS by the agency. Likewise, sodium selenite has been added to infant formulas to provide the amount of selenium that has been determined to be essential for infants by NAS (Ref. 19). Published experimental and clinical data provide a basis upon which experts qualified by scientific training and experience could evaluate the safety of sodium selenite as a source of selenium for use in infant formula and could conclude that it is safe. The agency anticipates that other ingredients may be shown to be GRAS because they are generally accepted sources of substances that are established as essential for infants by an authoritative body such as NAS. However, manufacturers should not take this acknowledgment to mean that they are free to declare that the use of any ingredient they want to use is GRAS. Any ingredient that cannot meet the standard of § 170.30 for a GRAS determination will be viewed by the agency as a food additive, and any infant formula that contains a food additive that the agency has not approved for use in infant formula is subject to being acted against by the agency.

If the safety of an ingredient is not expressly recognized in an FDA regulation, the burden will rest on the manufacturer of the infant formula to include in its new infant formula submission an explanation of why the substance is GRAS under § 170.30, along with the published and other information that provides the basis for that explanation, in accordance with proposed § 106.120(b)(6)(ii). If the agency adopts this approach, a failure of the agency to object to a manufacturer's determination that an ingredient is GRAS in a new infant formula submission will not constitute a GRAS affirmation by the agency. However, if FDA knows of no reason to question the safety of an ingredient to be used in infant formula, the agency will not object to the manufacturer's relying on its own determination that use of the substance is GRAS.

e. *Submission 90 days before marketing a new infant formula intended only for export.* When a new infant formula is intended only for export, proposed § 106.120(c) provides that manufacturers may submit, in lieu of the information required under proposed § 106.120(b), a statement that the infant formula meets the specifications of the foreign purchaser, does not conflict with the laws of the country to which it is to be exported, is labeled on the outside of the shipping package to indicate that it is intended for export only, and will not be sold or offered for sale in domestic commerce. This proposed requirement recognizes that under section 801(e) of the act, in certain limited circumstances, manufacturers may lawfully export products that are adulterated or misbranded. The information required under proposed § 106.120(c) will demonstrate that those limited circumstances exist. FDA has tentatively concluded that proposed § 106.120(c) will provide manufacturers with the flexibility allowed under section 801(e) of the act while meeting the requirements of sections 412(c) and (d) of the act.

f. *Submission 90 days before marketing—administrative procedures.* Proposed § 106.120(d) states that the submission will not constitute notice under section 412 of the act unless it complies fully with § 106.120(b), and the information that it contains is set forth in a manner that is readily understandable, so that FDA can complete its review in a timely manner and advise the manufacturer if it has any concerns about the marketing of the formula before the 90 days is up. Proposed § 106.120(d) makes clear that the agency will notify the submitter if the notice is not adequate because it does not meet the requirements of sections 412(c) and (d) of the act.

Proposed § 106.120(e) provides that if a new infant formula submission contains all the information required by proposed § 106.120(b), FDA will acknowledge its receipt and notify the manufacturer of the date of receipt, which will be the filing date for the submission (and the manufacturer will be able to plan those actions necessary to begin marketing the new formula in reliance on that date). Further, pursuant to section 412(c)(1)(B) of the act, proposed § 106.120(e) also requires that the manufacturer not market the new infant formula until 90 days after the filing date. Congress provided for 90-day notice so that the agency would have sufficient time to examine all of the material submitted and decide whether there is any basis for concern about the marketing of the formula.

Proposed § 106.120(f) makes clear that if the manufacturer provides additional information in support of a new infant formula submission, FDA will determine whether it represents a substantive amendment to the submission, and that, if it does, FDA will assign the new infant formula submission a new filing date. FDA is proposing to adopt § 106.120(f) to clarify how it will treat amendments to infant formula notifications. In the 9 years since the passage of the 1986 amendments, the treatment of additional submissions has been the source of some confusion. FDA has tentatively concluded that it is necessary to give a new filing date to a new infant formula submission when a substantive amendment is made to it so that the agency has time to examine all of the material submitted and to determine whether there is any basis for concern about the marketing of the formula.

4. Quality Factor Submission

Proposed § 106.121 sets forth the requirements for specific information that a manufacturer must submit to