factor similar to those in proposed § 106.97(b)(2) and allow manufacturers to assure the agency that their products meet that requirement without requiring redundant testing.

c. *Iron status.* If FDA were to adopt a quality factor for iron, manufacturers would be required to collect and maintain data that establish that the iron in an infant formula is bioavailable and maintains the iron status of infants that consume the formula. These data would be necessary to demonstrate that an infant formula provides enough iron to prevent iron deficiency and anemia.

Alterations in a number of biochemical measurements are useful signs associated with inadequate iron intake or the development of iron deficiency. Early signs of inadequate iron intake, which reflect the depletion of iron storage sites, are reductions in serum ferritin concentration and transferrin saturation (Ref. 86). If the dietary intake of iron remains inadequate, impaired erythropoiesis (i.e., the process whereby the body produces new red blood cells) may be reflected in alterations in erythrocyte maturation and increases in erythrocyte size, erythrocyte protoporphyrin concentration, or serum transferrin receptor levels. If the period of inadequate iron intake continues, erythropoiesis is further impaired, and hemoglobin concentration, hematocrit, and mean corpuscular volume decrease.

Iron deficiency without anemia should be considered to be a risk factor for iron-deficiency anemia, which may be associated with long-lasting, adverse effects in infants (Ref. 86). Therefore, FDA is considering requiring one measurement of iron status that is sensitive to each of the three stages of inadequate iron intake (stage 1, decreased stores, normal erythropoiesis; stage 2, decreased stores and early stage impaired erythropoiesis; and stage 3, decreased stores and late stage impaired erythropoiesis). For example, FDA is considering requiring that manufacturers measure: (1) Serum ferritin concentration, because such a measurement is sensitive to decreased iron stores and normal erythropoiesis; (2) transferrin saturation or erythrocyte protoporphyrin concentration, because such measures are sensitive to decreased iron stores and early stage impaired erythropoiesis; and (3) hematocrit percentage, hemoglobin concentration, or mean corpuscular volume, because such measurements are sensitive to decreased iron stores and late stage impaired erythropoiesis. This approach would be consistent with the recommendations of the CON/AAP Task Force (Ref. 6). It would also provide reasonable assurance that low iron availability in an infant formula would be detected, and that an infant formula that does not provide sufficient iron to meet the infant's requirement, and thereby does not meet the quality factor requirement for iron, will not be marketed.

FDA also is considering whether circumstances exist that would justify establishing an exemption from the requirements to determine iron status. FDA has tentatively concluded that the reasons and justification for such an exemption are essentially those set forth above in the discussion of proposed § 106.97(b)(2). FDA requests comment on whether, if it adopts a quality factor for iron, it should provide for exemptions from testing similar to those set forth in proposed § 106.97(b)(2) to show that the formula meets that factor and allow manufacturers to assure the agency that their products meet that quality factor requirement without requiring redundant testing.

F. Records and Reports

1. Introduction

Under subpart C of part 106, FDA is proposing to revise the requirements on the records that must be made and retained. FDA is proposing requirements on batch records; records on CGMP and quality control procedures; maintenance of distribution records on formulas for export only; audits; and notifications to FDA. These proposed changes to current § 106.100 are outlined in Table III below:

TABLE III

Current Regulation	Proposed Regulation
§ 106.100(a)	No Change.
§ 106.100(b)	No Change.
§ 106.100(c)	No Change.
§ 106.100(d)	No Change.
§ 106.100(e), (f), and (h).	Current § 106.100(e), (f), and (h) will be incorporated into proposed § 106.100(e). New § 106.100(f) will codify the records required for the CGMP regulations found in proposed subpart B.
§ 106.100(g)	Current § 106.100(g) with modification.
§ 106.100(h)	Current § 106.100(h) is incorporated into § 106.100(e). § 106.100(h) Reserved.
§ 106.100(i)	No Change.
§ 106.100(j)	Current § 106.100(j) with modification.
§ 106.100(k)	Current § 106.100(k) with modification.
§ 106.100(l)	No Change.
§ 106.100(m)	No Change.
§ 106.100(n)	No Change.
§ 106.100(o)	No Change.

2. Batch Production and Control Records

Proposed § 106.100(e) requires that manufacturers make and retain records (hereafter referred to as "batch records") that include complete information relating to the production and control of each batch of infant formula. Section 412(b)(4)(A)(i) of the act requires the establishment, by regulation, of requirements for the retention of all records, including records containing the results of all testing required under section 412(b)(2)(B) of the act, necessary to demonstrate compliance with the CGMP requirements and quality control procedures prescribed under section 412(b)(2). In proposed § 106.100(e) FDA is proposing to require that manufacturers prepare and maintain records that include complete information relating to the production and control of the batch to ensure that the complete history of each batch of infant formula is available for review in the event that a problem arises with a particular batch.

Proposed § 106.100(e)(1) requires that the batch records include the appropriate master manufacturing order. As discussed above, proposed § 106.50(a) requires that manufacturers produce each infant formula in accordance with a master manufacturing order that has been approved by a responsible official of the company. The master manufacturing order thus provides fundamental information about the batch. Having all the information concerning the production of a batch of infant formula, including the master manufacturing order, in one place as a part of a batch record will ensure that there is a document available that makes readily apparent whether a batch was properly produced. It will also ensure that all the information needed to evaluate the cause of any problem that may develop with a batch of infant formula is readily available. Thus, FDA has tentatively concluded that the master manufacturing order is an essential part of the batch record.

Proposed § 106.100(e)(1)(i) requires that the master manufacturing order include the significant steps in the production of the batch of infant formula and the date on which each

significant step occurred. Thus, the master manufacturing order will include a list of the significant steps for the production of each infant formula and a space to write in the date the step was performed. Thus, it will provide both a check that the step was performed and a record of when it was performed. FDA has tentatively concluded that this information is necessary because all production activities for a specific batch of infant formula may not be accomplished in one day but may occur over a number of days, and people who begin work the second day will know what work has been completed, and what has not been. Moreover, each date is needed so that a batch of formula can be traced if, at a later date, a problem that may adversely affect an infant formula is identified at a specific production stage. Having the date available will allow the manufacturer to identify all batches that may have been affected by the problem.

Proposed § 106.100(e)(1)(ii) requires that, if the manufacturer has more than one line or set of equipment in the plant in which the formula is made, the master manufacturing order include the identity of equipment and processing lines used in producing the batch of infant formula. This information will allow the manufacturer to ensure that the equipment on which the formula was produced met the requirements of § 106.30. This information also will facilitate the identification of all batches of formula that may be affected by equipment malfunctions or that were produced on the same equipment as a batch that is discovered to be microbiologically contaminated.

Proposed § 106.100(e)(1)(iii) requires that the master manufacturing order include the identity of each batch or lot of ingredients, containers, and closures used in producing the batch of infant formula. All materials used in infant formula will have to meet the specifications of proposed § 106.40(d) and be identified by a batch or lot number as specified in proposed § 106.40(c). FDA has tentatively concluded that it is necessary to propose that the identity of each batch or lot of ingredients, containers, and closures used in producing the batch of infant formula be recorded in the master manufacturing order to enable the manufacturer to ensure that all of those materials met the requirements of § 106.40, particularly the standards for acceptance or rejection of the materials. Recording this information also will allow the manufacturer to evaluate the contribution of specific ingredients, containers, and closures to any problem with a batch of infant formula that may develop.

FDA is not proposing to require that the batch records contain the results of any tests conducted on ingredients, containers, and closures in accordance with proposed § 106.40(d) because the same lot of raw materials may be used in multiple batches. The identification of the batch or lot of all ingredients, containers, and closures in the master manufacturing order should be sufficient to allow the manufacturer to locate and review relevant test results if problems arise with a particular batch of infant formula.

Proposed § 106.100(e)(1)(iv) requires that the master manufacturing order include the amount of each ingredient to be added to the batch of infant formula and a check (verification) that the correct amount was added. As discussed above, proposed § 106.50(b) requires that the manufacturer establish controls to ensure that raw and in-process ingredients required by the master manufacturing order are examined by one person and checked by a second person or system to ensure that the correct weight or measure of the ingredient is added to the batch. The agency has tentatively concluded that recording in the master manufacturing order the amount of each ingredient added to the batch of formula, and a check (verification) that the correct amount was added, are appropriate controls to ensure that the correct weight or measure of the ingredient is added to the batch. This proposed requirement is necessary to ensure that there is compliance with proposed § 106.50(b), to provide a record that the batch of infant formula includes all of the ingredients in the amounts specified in the master manufacturing order, and to provide assurance that the product contains all of the required nutrients.

Proposed § 106.100(e)(1)(v) requires that the master manufacturing order include copies of all labeling used and the results of the examinations conducted during the finishing operations to ensure that containers and packages in the batch are correctly labeled. (The importance of ensuring that containers are correctly labeled was discussed in conjunction with proposed § 106.60(b).) The inclusion in the batch records of copies of the labeling used on each batch of infant formula will provide a record of such labeling and will document that the finishing operation examinations, required by proposed § 106.60(b), are conducted.

Proposed § 106.100(e)(2) requires that the batch record include any deviations from the master manufacturing order and any corrective actions taken. While the manufacturer's goal should be to produce the infant formula in accordance with the master manufacturing order, on occasion deviations may occur. On these occasions, the deviations, and any corrective actions taken because of the deviations, should become a part of the batch record. For example, if a batch of liquid infant formula was thermally processed at a different temperature than the temperature specified in the master manufacturing order, the batch record would state the actual processing temperature. The record would also state any corrective actions taken because of this processing temperature, such as a change in processing time. A record of deviations from the master manufacturing order and of the corrective actions taken by the manufacturer will allow the manufacturer to quickly determine whether all deviations have been appropriately addressed, and if they have not been, whether the actions needed to correct the deviations have been identified. It will also provide relevant information if a problem arises with that batch of infant formula.

Proposed § 106.100(e)(3) requires that the batch records include documentation of the monitoring at any production and in-process control point, step, or stage where control is deemed necessary to prevent adulteration. As discussed above, proposed § 106.6(c)(2) requires this monitoring. FDA is proposing that the documentation that the monitoring required by proposed § 106.6(c)(2) is occurring be included in the batch records to ensure that a measurement or observation made at one particular point in time can be related to a particular batch. The linkage of the record to the batch is especially important when a standard or specification is not met. It will enable the manufacturer to determine what batches may have been affected by a deviation and to take appropriate action, such as withholding a batch from distribution.

Proposed § 106.100(e)(3)(i) requires that the batch records include a list of the standards or specifications established at each point, step, or stage in the production process where control is deemed necessary to prevent adulteration, and that it include documentation of the scientific basis for each standard or specification. As discussed above, proposed § 106.6(c)(1) requires the establishment of such standards or specifications. The agency has tentatively concluded that a list of these standards or specifications must be a part of the batch record so that the manufacturer will have them readily

available to compare to the actual values obtained during the monitoring operation of the production and in-process control system. Also, the documentation of the scientific basis for each standard or specification will verify that each was established by trained and experienced sources. Such documentation will summarize the work performed to establish the standard or specification and will establish the source used. If changes to the standard or specification become necessary, this documentation of the scientific basis for each standard or specification will assist the manufacturer in making such changes.

Proposed § 106.100(e)(3)(ii) requires that the batch records include the actual values obtained during the monitoring (such as the actual temperatures and actual times that the measurements were taken), any deviations from the established standards or specifications, and any corrective actions taken. For example, notations that refrigeration temperatures are satisfactory or unsatisfactory, without a record of the actual temperatures, are subject to varying interpretation and thus will not ensure that preventive controls are working. It is important that the actual values be recorded. In addition, actual values are necessary to discern trends or to pinpoint the onset of a problem. The record of any corrective actions taken will show what the manufacturer did when a standard or specification was violated, and how the manufacturer is ensuring that the infant formula is not adulterated. Entry of information on the records at the time of the monitoring ensures that the record does not rely on the memory of the observer and thus is as accurate and valid as possible.

Proposed § 106.100(e)(3)(iii) requires that the batch records identify the person monitoring each point where control is deemed necessary to prevent adulteration. FDA has tentatively concluded that it is important that the responsible individuals be identified in the batch record so that the manufacturer can check that a qualified person is actually monitoring the point, step, or stage where control is deemed necessary to prevent adulteration, and so that such individual can be contacted if a problem with a batch of infant formula is identified at a later date. These individuals are in the best position to know of any other information that may not have seemed pertinent at the time but, in retrospect, could be important in identifying the cause of the problem and initiating actions to prevent it from recurring.

Proposed § 106.100(e)(4) requires that the batch records include the conclusions and followup, along with the identity, of the qualified individual who investigated any deviations, or failures to meet specifications, that occurred during the production of the batch. Under these proposed regulations, individuals qualified by training or experience must conduct an investigation of any deviation from the master manufacturing order and of the corrective actions taken (§ 106.50(a)(2)); conduct an investigation of a finding that a batch or any of its ingredients failed to meet any manufacturer's specifications (§§ 106.40(d) and 106.70(c)); and conduct an investigation of a failure to meet any specification or standard at any point where control is deemed necessary to prevent adulteration (§ 106.6(c)(4)).

FDA has tentatively concluded that the record of the conclusions and followup of these investigations is necessary to enable the manufacturer to ensure that it has complied with proposed §§ 106.6(c)(4), 106.40(d), 106.50(a)(2), and 106.70(c). Such records will provide information on how the production of the batch of infant formula deviated from established standards or specifications and on the cause of any problem with the formula, if infants are reported to have been adversely affected by the product at a later date. Identification of the qualified individual who conducted the investigations will ensure that there is responsibility and accountability for the investigation and will allow the responsible individuals to be contacted, if necessary. These individuals will be in the best position to provide information if additional details about the record are needed.

Proposed § 106.100(e)(5) requires that the batch records include the results of all testing performed on the batch of infant formula, including testing on the in-process batch, at the final-product stage, and on finished product throughout the shelf life of the product. Section 412(b)(2)(B) of the act requires that manufacturers conduct such testing. FDA has tentatively concluded that the assembly of such records in one place will enable the manufacturer to ensure that the batch of infant formula complies with proposed §§ 106.55 and 106.91 and will facilitate the review of the test results in the event that a problem arises with the batch.

Proposed § 106.100(e)(5)(i) states that the batch records are to include the results of any quality control testing conducted, in accordance with proposed § 106.91(a) and (b), to verify that each nutrient required by § 107.100 is present at the required level, and that any nutrient added by the manufacturer is present at the appropriate level. Including the results of this testing in the batch records will provide data needed to evaluate compliance of the batch of infant formula with proposed § 106.91, and provide data needed to evaluate a batch of infant formula if problems, such as adverse events in infants, occur later with that particular batch. These records will show the levels of nutrients in the formula and will provide information to help the manufacturer determine whether any problems associated with the formula are attributable to the nutrient levels in the product.

Proposed § 106.100(e)(5)(i)(A) requires that manufacturers maintain a summary table in the batch record that identifies the stages of the manufacturing process at which the nutrient analysis is conducted for each nutrient, in accordance with proposed § 106.91(a). As discussed above, proposed § 106.91(a) provides flexibility in the stage at which many of the nutrients are tested. A summary table will facilitate the manufacturer's compliance with quality control procedures because it will allow a manufacturer to quickly verify that it has tested for all the nutrients required by § 107.100 during the production of the infant formula.

Proposed § 106.100(e)(5)(i)(B) requires that the quality control records in the batch record include a summary table on the stability testing program, conducted in accordance with proposed § 106.91(b), including the nutrients tested and the frequency of testing of nutrients throughout the shelf life of the product. As discussed above, proposed § 106.91(b) requires that manufacturers test infant formula at the beginning, midpoint, and end of the shelf life, and with sufficient frequency to ensure that the manufacturer is aware if there is a significant deterioration in the required level of a nutrient. Therefore, proposed § 106.91(b) provides flexibility in the testing frequency, depending on the shelf life and the characteristics of the product. A summary table will facilitate the manufacturer's compliance with quality control procedures because it will allow a manufacturer to quickly determine whether it has tested for all the nutrients required by § 107.100 with sufficient frequency to verify that the "use by" date on the formula is appropriate.

Proposed § 106.100(e)(5)(ii) requires that the batch records for powdered infant formula include the results of any testing conducted in accordance with proposed § 106.55(b) to document that the tests were done and to verify compliance with the microbiological

quality standards in proposed § 106.55(c). As discussed above, proposed § 106.55(b) requires that manufacturers test representative samples of each batch of powdered infant formula to ensure that the batch meets the microbiological quality standards in proposed § 106.55(c) and therefore is not adulterated. This record will also provide the manufacturer with data to evaluate adverse events that infants may have experienced after consuming this batch of infant formula by showing whether microbiological contamination could have contributed to the adverse event.

3. CGMP Records

Proposed § 106.100(f) identifies the records that manufacturers must make and retain pertaining to CGMP described in proposed subpart B of part 106. Section 412(b)(4)(A)(i) of the act requires the establishment by regulation of requirements for the retention of all records necessary to demonstrate compliance with the CGMP, including testing designed to prevent the adulteration of infant formula. FDA has already discussed proposed regulations (proposed § 106.100(e)) respecting the retention of records relating to each batch of infant formula. FDA also is proposing regulations respecting the retention of records relating to the overall operation of the plant and the maintenance of equipment, because these records are necessary to demonstrate that the infant formula was manufactured in a manner designed to prevent adulteration. Maintenance of these records will help manufacturers identify trends in the processing of the infant formula, in particular trends that show when the process is breaking down in a way that will lead to the production of adulterated product. These records also will provide information to assist the manufacturer in tracking the cause of adverse events to a formula, if such events are reported.

Proposed § 106.100(f)(1) requires that manufacturers make and retain records of the frequency and results of the testing of water used in the production of infant formula. These records will show if problems are starting to develop with the water supply so that manufacturers can take corrective actions before the water is inappropriate for use in infant formula.

Proposed § 106.100(f)(2) requires that manufacturers make and retain records, in accordance with § 106.30(d), of accuracy checks on instruments and controls. Under this proposal, these records must include a certification of the accuracy of any known reference standard used and a history of its recertification. As discussed previously, the accuracy of the reference standard must be ensured before it can be used to ensure that the production instruments are properly calibrated. These records also will provide information to assist the manufacturer in tracing the source of a problem, if one arises, with a batch of infant formula. For example, if infants have adverse events to a batch of infant formula, records containing a certification of accuracy of the reference standards used and a history of their recertification would assist the manufacturer in determining whether the problem was created because a production instrument was calibrated with an inaccurate reference instrument.

FDA is proposing to require that, at a minimum, the records specify the instrument or control being checked, the date of the accuracy check, the standard used, the calibration method used, the results found, any actions taken if the instrument is found to be out of calibration, and the initials or name of the individual performing the test. These records will enable the manufacturer to determine, based on the performance of the instrument, whether the calibration schedule is sufficient to ensure the accuracy of the instrument. These records also will provide information on when and how the instruments were calibrated to assist the manufacturer in identifying the cause of a problem, if one arises, with a batch of infant formula.

Including the date of the accuracy check in the record will permit a determination of the accuracy of the instrument or control over time; including the standard used will allow the manufacturer to verify that the standard was properly calibrated; and including the calibration method used will ensure that the instrument is being calibrated free from the variability that can occur when different laboratory personnel perform the same calibration. The results of the accuracy check in the record will show whether the instrument or control is accurate, or whether a correction was necessary. Documenting the actions taken if the instrument is found to be out of calibration will enable the manufacturer to ensure that a correction was made. Requiring that the individual performing the test note his or her initials or name in the record will document who was last responsible for ensuring the accuracy of the instrument or control and will allow the manufacturer to discuss questions that may arise about the record with the person in the best position to know additional, but unrecorded, details about the record.

If calibration of an instrument shows that a specification or standard, at a point, step, or stage in the production process where control is deemed necessary to prevent adulteration, has not been met, a written evaluation of all affected product, and of any actions that need to be taken with respect to that product, needs to be made. For example, if the manufacturer is monitoring temperature to ensure that a specification or standard of 250 °F is maintained as a minimum temperature, and calibration of the temperature indicating instruments against a reference standard reveals that it was reading a true temperature of 248 °F, an evaluation of the health hazard significance of this temperature deviation must be made. This proposed requirement is necessary because, if an instrument is found to have been giving inaccurate readings, all infant formula produced subject to such inaccuracies must be identified and evaluated for the possibility that the inaccuracies caused the formula to be adulterated. In identifying the affected product to ensure that the health of potentially affected infants is fully protected, in the absence of evidence to the contrary, such evaluation would cover all product manufactured since the last time the instrument was calibrated and found to be accurate.

Proposed § 106.100(f)(3) requires that manufacturers make and retain records, in accordance with proposed § 106.30(e)(3)(ii), of the temperatures monitored for cold storage compartments and thermal processing equipment. These records are needed to show that the thermal processing equipment or cold storage compartments are being maintained at the correct temperatures to prevent adulteration of the product. The records of these temperatures will enable the manufacturer to identify trends in temperature fluctuations that can signal the need to perform nonscheduled maintenance.

FDA is proposing in § 106.100(f)(4) that equipment cleaning, sanitizing, and maintenance records, showing the date and time of maintenance, as well as the lot number of each batch of infant formula processed between equipment startup and shutdown for cleaning, sanitizing, and maintenance, be made and maintained. These records will allow the manufacturer to ensure that equipment and utensils are being cleaned and maintained regularly and to check that the frequency of such cleaning, sanitizing, and maintenance is appropriate in light of the actual, as

opposed to planned, use of the equipment. For example, a manufacturer may need to increase the frequency of cleaning, sanitizing, and maintenance if actual rate of production consistently exceeds the predicted rate of production. These records also will allow the manufacturer to trace all formula that may be affected if evidence becomes available that a particular cleaning, sanitizing, or maintenance was improperly performed.

Proposed § 106.100(f)(4) also requires that the person performing and checking the cleaning, sanitizing, or maintenance date and sign or initial the record indicating that the work was performed. Identification of the person performing and checking the cleaning, sanitizing, or maintenance will allow the manufacturer to ensure that a qualified person is doing these tasks and to discuss questions that may arise about the record with the person in the best position to know additional, but unrecorded, details about the record.

Proposed § 106.100(f)(5) requires that manufacturers make and retain records, in accordance with § 106.35(c), on all automatic (mechanical or electronic) equipment used in the production or quality control of infant formula. Proposed § 106.100(f)(5)(i) requires that the automatic equipment records include a list of all systems used, with a description of computer files and of the inherent limitations of each system. The manufacturer cannot effectively operate the system, and correct problems that arise, if it does not understand the system. It is not always possible for the individuals who developed and best understand the system to be present when the system is operating. Therefore, these records will enable the manufacturer to operate and troubleshoot the systems even when the individuals who best know the system are not available.

Proposed § 106.100(f)(5)(ii) requires that the automatic equipment records include a copy of all software used. Having a copy of all software used will minimize the manufacturer's down time if problems occur, and parts of the software are lost from the system. For example, if a computer virus is found in the software used to run the processing lines, having a copy of the software to reload into the hardware will minimize the time lost. Likewise, if there is a problem with the software used to perform quality control testing, having copies of this software will ensure that the testing can continue with a minimum amount of time lost.

Proposed § 106.100(f)(5)(iii) further requires that the automatic equipment records document installation, calibration, testing or validation, and maintenance of the systems used. These requirements are necessary for compliance with section 412(b)(4)(A)(i) of the act. As discussed more fully above with respect to proposed § 106.35 (b)(1), (b)(2), and (b)(4) CGMP requires that all systems be installed, calibrated, and maintained in a manner necessary to ensure that they are capable of performing their intended function and of producing or analyzing infant formula as intended, and that all systems be validated before their first use to manufacture commercial product. In addition to documenting that the manufacturer is complying with CGMP, records documenting installation, calibration, testing or validation, and maintenance of systems are necessary to provide information if the manufacturer later tries to determine why a problem with the system is occurring or tries to determine why the system is not producing an infant formula that complies with the manufacturer's specifications for the product.

Proposed § 106.100(f)(5)(iv) requires that the automatic equipment records include a list of all persons authorized to create or modify software. This record will help to minimize delays when the name of a person with those skills is needed quickly.

Proposed § 106.100(f)(5)(v) requires that the automatic equipment records document modifications to software, including the identity of the person who modified it. This documentation will ensure that the manufacturer is aware of any changes made to the software, and that it has a record of how the changed system works, so that it can continue to operate the system even in the absence of the responsible individual who made the modification to the system. A record of the identity of the person who modified the software will show who was responsible for modifying the software if problems arise with the operation of the system and will identify the person in the best position to know additional, but unrecorded, details about the software modification to help in troubleshooting the software problems.

Proposed § 106.100(f)(5)(vi) requires that the automatic equipment records include documentation of retesting or revalidation of modified systems. This proposed requirement is necessary for compliance with section 412(b)(4)(A)(i) of the act. As discussed more fully above in the section on proposed § 106.35(b)(5), CGMP requires that all modifications to software be made by a designated individual, and that all systems be revalidated after any modification to ensure that infant formula produced or analyzed using the modified software complies with subparts B and C. FDA has tentatively concluded that records on retesting or revalidation of the modified systems, just like records on the initial testing or validation of the system (§ 106.100(f)(5)(iii)), are necessary to document that the work has been done properly and to provide information if the manufacturer later tries to determine why a problem with the system is occurring or tries to determine why the system isnot producing an infant formula that complies with the manufacturer's specifications for the product.

Proposed § 106.100(f)(5)(vii) requires that the manufacturer make and retain a backup file of data entered into a computer or related system. It also requires that this backup file consist of a hard copy or alternative system, such as duplicate diskettes, tapes, or microfilm, designed to ensure that backup data are exact and complete, and that they are secure from alteration, inadvertent erasures, or loss. This proposed requirement is necessary to ensure compliance with CGMP because computer files can be easily altered or erased. Backup files of data will allow the manufacturer to readily reload the files of data if problems occur in the operation of the computer or related system, so that the manufacturer's down time is minimized, and so that the data entered into the system will be an exact copy of the data previously used in the system.

Proposed § 106.100(f)(6) requires that manufacturers make and retain records on ingredients, containers, and closures, including the identity and quantity of each lot, the name of the supplier, the supplier's lot number, the name and location of the manufacturer (if different from the supplier), the date of receipt, and the receiving code as specified (proposed § 106.100(f)(6) (i) through (vi)). These records will enable the manufacturer to document that it is complying with proposed § 106.40(g). Moreover, this information is needed to enable the manufacturer to track the source of each ingredient, container, or closure used in infant formula if a problem arises. If an ingredient, container, or closure is found to cause adulteration of the formula, it is important to be able to determine the source of the material, so that use of such materials can be halted and prevented in the future.

Proposed § 106.100(f)(6)(vii) requires that the records on ingredients, containers, and closures include the results and conclusions of any test or examination, including retesting and