*B. Benefits*

1. Option 1—Adopt Regulations More Stringent Than the Proposed Regulations

More stringent regulations for infant formula would cause infant formula manufacturers to undertake further activity to ensure the safety of infant formula. If there were identifiable risks from infant formula that were not addressed by this proposal, then this additional activity might decrease those health risks. However, FDA is not aware of identifiable health risks from infant formula that are not addressed by this proposal.

2. Option 2—Adopt the Proposed Regulations

The proposed regulation has two primary benefits: A potential direct reduction in the health risks posed by infant formula, and a potential reduction in the cost of entering the infant formula industry. The latter effect could lead to an increase in the competitiveness of the infant formula industry, resulting in lower infant formula prices and a reduction in the incidence of risky infant feeding practices linked to high infant formula prices.

One example of a current activity that can be linked to a direct reduction in health risks but that is not explicitly required by current law or regulation is the performance of growth studies for new infant formulas. FDA currently requests and receives these studies to demonstrate that the infant formula meets the quality factor requirements of section 412(b)(1) of the act. However, because section 412(b)(1) of the act does not list specific quality factors that infant formulas must meet, a quality factor for healthy growth currently is not expressly stipulated. In the absence of this proposed rule, manufacturers could decline to perform these growth studies in the future with a potential consequence that products that do not support normal growth would be marketed. Low growth rates would not be detected by existing regulatory and legal requirements that measure only the levels of required nutrients because the required nutrients may be present but not be bioavailable, and there is no mechanism for testing bioavailability other than the proposed studies.

An example of a formula associated with low growth rates that would not have been detected in the absence of growth studies was an experimental formula that contained a source of fatty acids not previously used in infant formula. Because only a small amount of the new fat source was added to a commercial formula, it is reasonable to assume that all required nutrients were present within legal specifications. Consequently, it would likely have met all current regulations. Nonetheless, this formula was found to result in low infant growth rates (Ref. 87). In this case, the manufacturer undertook the necessary growth studies and detected the problem on its own. However, manufacturers might not undertake these studies on their own in the future. In addition, even if manufacturers continue to undertake these studies in the absence of this regulation, they may not do these studies correctly.

In general, low rates of infant growth are associated with higher than normal levels of infant morbidity. If a problem of this type were to occur, a large number of infants could potentially be affected.

Other types of current activity can also be linked to a direct reduction in health risks and also are not explicitly required by current law or regulation. In the absence of this regulation, incumbent or new manufacturers may not undertake this activity in the future. However, as explained earlier, because of reputation effects and legal liability, such a refusal seems unlikely.

An example of a health risk from infant formula is the 1978 incident, discussed elsewhere in this document, in which a required nutrient was missing from an infant formula. Recurrence of this particular problem is unlikely because section 412(d)(1)(A) of the act already explicitly requires the submission of the quantitative formulation of an infant formula as part of the mandatory FDA notification of a new infant formula. Recurrence of this problem is also made unlikely because section 412(b)(2) of the act already explicitly requires the testing of infant formula for all required nutrients. However, the risk of a formula being sold without a required nutrient is minimized to the extent possible by specifically clarifying this part of the infant formula law in the regulation.

Another example of a health risk associated with infant formula is an incident in which infant formula was found to contain *Salmonella*. It appears that the manufacturer was testing for *Salmonella* in a manner consistent with the testing requirements of this proposed rule, and therefore it is not clear that this particular incident would have been avoided if the proposed rule had been in effect. This proposed rule will reduce the risk of microbiological contamination, however, because it requires manufactures to institute a production and in-process control system. The production and in-process control system establishes standards or specifications to be met throughout the production of their product. Other provisions of the proposed regulation that will also help to prevent microbiological contamination of infant formulas are controls to prevent adulteration by workers (proposed § 106.10), controls on the required temperature of cold storage compartments used for storing ingredients and uncanned infant formula (proposed § 106.30(e)(2)), controls on the monitoring of the temperature of both cold storage and thermal processing equipment (proposed § 106.30(e)), controls on the spray-drying process for powdered infant formula including the filtering of the intake air before heating to prevent microbial growth (proposed § 106.50(d)(2)), and controls to ensure that each container of finished product is properly sealed (proposed § 106.50(d)(4)).

The incident in which infant formula was found to contain *Salmonella* resulted in two reported cases of salmonellosis in infants. The average value of preventing a single case of salmonellosis is estimated to be about $2,000 (Ref. 88). If an incident like this is avoided in the future because of this proposed rule, the value of the adverse health effects avoided would be a benefit of this proposed rule.

This incident also resulted in two recalls. FDA estimates a combined cost, including costs that accrued to both the manufacturer and FDA of approximately $0.7 million per recall. If an incident like this is avoided in the future because of this proposed rule, the recall costs that would otherwise have been associated with this incident would also be a benefit of this proposed rule.

Another benefit of the proposed regulations is a potential reduction in the administrative and time costs of entering the infant formula industry. Currently, infant formula manufacturers must analyze and interpret the relevant laws to determine the legal requirements involved in the manufacture of infant formula. Incumbent firms have tended to accept FDA's interpretations of these laws and have received information on this interpretation incrementally over time, chiefly through direct contact with FDA on various issues.

It is reasonable to expect that potential entrants into the infant formula industry would also prefer to rely on FDA's interpretations of the relevant laws. However, considerable time and administrative costs are involved in obtaining this information because there is no established

mechanism by which manufacturers can obtain this information other than direct communication with FDA on various particular issues. By providing an explicit specification of the activities that are required by the relevant laws, the proposed regulations, if adopted, will reduce the time and administrative costs involved in entering this industry.

In order to determine the net effect of the proposed rule on the cost of entering the infant formula industry, the reduction in time and administrative costs must be weighed against the additional compliance costs imposed by this proposed rule on new firms. These countervailing compliance costs are probably low because new firms will probably undertake voluntarily the same activity that is currently undertaken voluntarily by incumbent manufacturers. Therefore, the net effect of this proposed rule is likely to be the reduction in the cost of entering the infant formula industry. Publication of the proposed and final regulations will provide a means of expedited entry for new firms into the infant formula market.

A reduction in the cost of entering the infant formula industry will promote both price competition and innovation in this industry. Increased price competition may lead to health benefits because, as stated above, high infant formula prices may encourage some consumers to: (1) Improperly dilute infant formula to reduce the cost per serving; (2) prematurely switch from infant formula to cow's milk; or (3) use inappropriate substitutes for breast milk and infant formula.

A final benefit of this proposed rule is the cost savings generated by the elimination of the current FDA requirement that a vitamin D rat bioassay be performed for all major changes in infant formula. In 1992, there were approximately 50 major changes. The cost of a rat bioassay for vitamin D for infant formula at a private lab is about $1,070 (Ref. 89). Infant formula manufacturers should therefore save approximately $54,000 in testing costs per year.

3. Option 3—Adopt Regulations Less Stringent than the Proposed Regulations

Except for the value of the risk reductions resulting from requirements that go beyond activity currently undertaken by infant formula manufacturers the benefits of this option are identical to those of Option 2.

*C. Conclusions*

In accordance with Executive Order 12286, FDA has analyzed the economic effects of this proposed rule and has determined that this rule, if issued, will not be a significant rule as defined by that order. In accordance with the Regulatory Flexibility Act, FDA certifies that the proposed rule will not have a significant impact on a substantial number of small businesses.

The primary compliance costs of Option 2 include both direct costs of new requirements and precluded production cost reductions which may occur without this regulation. FDA has estimated direct costs to incumbent manufacturers to be approximately $0.7 million in the first year and $0.6 million each additional year. An additional cost to incumbent manufacturers is the cost of repairing or replacing instruments and controls when those instruments and controls cannot be adjusted to agreement with the reference standard. FDA has insufficient information to estimate this cost. FDA does not expect compliance with the proposed regulations to cause any significant increase in the price of infant formula products. However, the agency requests comments about any potential effects of the proposed regulations on the price of infant formula products.

The primary benefit of Option 2 is the reduction in the risk that defective infant formula will be produced, go undetected, and reach the market. FDA has insufficient information to estimate this potential benefit. In addition, this proposed rule is also expected to reduce the time and administrative costs of entering the infant formula industry. This benefit may increase price competition in the infant formula industry and reduce the health risks associated with high infant formula prices. FDA also has insufficient information to estimate these benefits.

Except for the costs and benefits associated with activity required by this proposed rule that some incumbent manufacturers do not currently undertake, the costs and benefits of Option 3 are identical to those of Option 2. FDA has insufficient information to estimate either the costs or benefits of this option.

Option 1 is expected to have higher costs and lower benefits than either Option 2 or Option 3.

VII. Paperwork Reduction Act of 1995

This proposed rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The title, description, and respondent description for the proposed collection of information are shown below, along with an estimate of the annual recordkeeping and periodic reporting burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary information, and completing and submitting the registrations, notifications, and other submissions that would be required under the proposed regulations.

FDA solicits public comment in order to: (1) Evaluate whether the proposed collection of information is necessary for the proper performance of the functions of the agency, including whether the information will have practical utility; (2) evaluate the accuracy of the agency's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) enhance the quality, utility, and clarity of the information to be collected; and (4) minimize the burden of the collection of information on those who are to respond, including through the use of automated collection techniques, where appropriate or other forms of information technology.

*Title:* Current Good Manufacturing Practice, Quality Control Procedures, Quality Factors, Notification Requirements, and Records and Reports, for the Production of Infant Formula.

*Description:* FDA is proposing regulations on recordkeeping requirements that include: (1) Records pertaining to batch production and control; (2) records pertaining to current good manufacturing practice and quality control; (3) records pertaining to distribution of the infant formula; and (4) records pertaining to regularly scheduled audits. FDA is also proposing regulations on reporting requirements pertaining to: (1) Registration of a new infant formula; (2) submission requirements for a new infant formula; (3) submission requirements to provide assurance that an infant formula meets the quality factor requirements; (4) submission requirements when there is a change in the formulation or processing of the formula that may affect whether the formula is adulterated; and (5) submission requirements to provide assurance that the infant formula complies with the requirements of the Federal Food, Drug, and Cosmetic Act and is not adulterated.

*Description of Respondents:* Infant Formula Manufacturers.

ESTIMATED ANNUAL RECORDKEEPING BURDEN

| 21 CFR | No. of recordkeepers | Annual frequency of recordkeeping | Total annual records | Hours per recordkeeping | Total hours |
|---|---|---|---|---|---|
| 106.6 | 5 | 1 | 5 | 200 | 1,000 |
| 106.20(f)(4) and 106.100(f)(1) | 5 | 52 | 260 | 3 | 780 |
| 106.30(d) and 106.100(f)(2) | 5 | 25 | 125 | 4 | 500 |
| 106.30(e)(3)(ii) and 106.100(f)(3) | 5 | 365 | 1,825 | 2 | 3,650 |
| 106.30(f) and 106.100(f)(4) | 5 | 365 | 1,825 | 3 | 5,475 |
| 106.35(c) and 106.100(f)(5) | 5 | 2 | 10 | 500 | 5,000 |
| 106.40(d) | 5 | 20 | 100 | 30 | 3,000 |
| 106.40(g) and 106.100(f)(6) | 5 | 122 | 610 | 4 | 2,440 |
| 106.50 | 5 | 1 | 5 | 200 | 1,000 |
| 106.55(d) 106.100(e)(5)(ii), and 106.100(f)(7) | 5 | 182 | 910 | 3 | 2,730 |
| 106.60(c) | 5 | 1 | 5 | 40 | 200 |
| 106.91(c), 106.100(e)(5)(i), and 106.100(f)(7) | 5 | 365 | 1,825 | 4 | 7,300 |
| 106.94 | 5 | 1 | 5 | 88 | 440 |
| 106.97 | 5 | 0.6 | 3 | 225 | 675 |
| 106.100(e) | 5 | 365 | 1,825 | 9 | 16,425 |
| Total | | | | | 50,615 |

ESTIMATED ANNUAL REPORTING BURDEN

| 21 CFR | No of respondents | Annual frequency per response | Total annual responses | Hours per response | Total hours |
|---|---|---|---|---|---|
| 106.110 | 3 | NA | 20 | 1 | 20 |
| 106.120 | 3 | NA | 20 | 49 | 980 |
| 106.121 | 3 | NA | 10 | 50 | 500 |
| 106.130 | 3 | NA | 20 | 2 | 40 |
| 106.140 | 3 | NA | 25 | 5–10 | 125–250 |
| Total | | | | | 1,790 |
| Total Recordkeeping and Reporting Burden | 52,405 | | | | |

FDA tentatively concludes that there are no capital costs or operating and maintenance costs associated with the reporting and recordkeeping provisions of this proposed rule. However, the agency welcomes comments on any such anticipated costs.

As required by section 3507(d) of the Paperwork Reduction Act of 1995, FDA has submitted a copy of this proposed rule to OMB for its review of the information collection requirements. Other organizations and individuals interested in submitting comments regarding this burden estimate or any aspect of these information collection requirements, including suggestions for reducing the burden, should direct them to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, ATTN: Desk Officer for FDA. Written comments on the information collection should be submitted by August 8, 1996.

## VIII. Requests for Comments

Interested persons may, on or before October 7, 1996, submit to the Dockets Management Branch (address above) written comments regarding this proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

## IX. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.


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87. Carlson, S. E., R. J. Cooke, S. H. Werkman, and E. A. Tolley, "First Year Growth of Preterm Infants Fed Standard Compared to Marine Oil n-3 Supplemented Formulas," *Lipids*, 27:901–907, 1992.
88. Memorandum of telephone conversation between Marty Hudtloff, FDA, and Ed Puro, FDA, March 15, 1994; cost of Maple Island recalls note, memorandum from Robert Fish, March 7, 1994; memorandum from Martin Hudtloff, February 28, 1994; Establishment History Report on B2110076.
89. Memorandum of telephone conversation between Hazleton Labs and Ed Puro, FDA, March 17, 1993.

List of Subjects

*21 CFR Part 106*

Food grades and standards, Infants and children, Nutrition, Reporting and recordkeeping requirements, Incorporation by reference.

*21 CFR Part 107*

Food labeling, Infants and children, Nutrition, Reporting and recordkeeping requirements, Signs and symbols.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to Commissioner of Food and Drugs, it is proposed that 21 CFR parts 106 and 107 be amended as follows:

## PART 106—INFANT FORMULA—REQUIREMENTS PERTAINING TO CURRENT GOOD MANUFACTURING PRACTICE, QUALITY CONTROL PROCEDURES, QUALITY FACTORS, RECORDS AND REPORTS, AND NOTIFICATIONS

1. The authority citation for 21 CFR part 106 continues to read as follows:

Authority: Secs. 201, 412, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 350a, 371).

2. The heading for part 106 is revised to read as set forth above.

3. Section 106.1 is revised to read as follows:

### § 106.1 Status and applicability of the regulations in part 106.

(a) The criteria set forth in subparts B, C, and D of this part prescribe the steps that manufacturers must take under section 412(b)(2) and (b)(3) of the Federal Food, Drug, and Cosmetic Act (the act) in processing infant formula. If the processing of the formula does not comply with any regulation in subparts B, C, or D of this part, the formula will be deemed to be adulterated under section 412(a)(3) of the act.

(b) The criteria set forth in subpart E of this part prescribe the quality factor requirements that infant formula must