Information Collection Request Supporting Statement

for

Survey of Good Manufacturing Practices
in the Dietary Supplement Industry

Revised Draft

September 27, 1999

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INFORMATION COLLECTION REQUEST SUPPORTING STATEMENT

The purpose of this supporting statement is to verify that the collection of information encompassed by this request complies with the Paperwork Reduction Act of 1995. The supporting statement shows that this information collection is necessary to determine if there is a need for good manufacturing practice (GMP) regulations in the dietary supplement industry. Through regulation, the Secretary may prescribe GMP regulations. In order to make a determination if these regulations are required, FDA must know more about existing manufacturing practices. Because of several recent illnesses and deaths that may have resulted from contaminated dietary supplements, a public health risk may exist from the absence of GMPs and therefore emergency processing of this information collection request is required.

A telephone-mail-telephone survey approach, using computer-assisted telephone interviewing (CATI), will be used for data collection. A sample of 717 establishments will be selected using stratified systematic sampling. The sample allocation is designed to yield 400 completed surveys. The purposes of this information collection are to (1) learn about the existing manufacturing practices in the dietary supplements industry and (2) help the agency formulate a policy to ensure that dietary supplement products are produced under conditions that will result in a safe and properly labeled product without unnecessary costs to the industry. The survey data will be used to estimate the percentage of establishments, by product type (e.g., herbals and botanicals, vitamins and minerals, etc.) and size, that are currently practicing GMPs. The survey will provide an understanding of the economic impact that any proposal to establish GMP regulations will have on both large and small establishments in the dietary supplement industry.

A telephone-mail-telephone survey approach will be used to collect the data. In Phase 1, establishments will be contacted by telephone and screened for eligibility. Eligible establishments will be recruited for the mail survey. In Phase 2, establishments will be contacted by telephone if they do not return the mail survey in the specified timeframe. On the third follow-up call, the interviewer will attempt to collect the responses to the mail survey over the telephone.

As required by the Office of Management and Budget, Section A of this supporting statement provides a justification for this information collection, while Section B provides information about the statistical methods employed by this information collection. As required, Appendix 1 contains the text of a notice to the public to be published in the *Federal Register*. Appendix 2 contains the CATI script for the initial telephone interview. Appendix 3 contains the mail survey instrument.

A. JUSTIFICATION

A.1 Circumstances

On October 25, 1994, the Dietary Supplement Health and Education Act (the DSHEA) (Pub. L. 103-417) was signed into law. The DSHEA, among other things, amended the act by adding section 402 (g) (21 U.S.C. 342 (g)) which provides, in part, that:

> The Secretary may by regulation prescribe good manufacturing practices for dietary supplements. Such regulations shall be modeled after current good manufacturing practices for food and may not impose standards for which there is no current and generally available analytical methodology. No standard of current good manufacturing practice may be imposed unless such standard is included in a regulation promulgated after notice and opportunity for comment in accordance with chapter 5 of title 5, United States Code.

Although section 402 (g) of the act does not require that the Secretary (and by delegation, FDA) adopt regulations that prescribe good manufacturing practices (GMPs), a significant segment of the dietary supplement industry has told FDA that such regulations would be helpful for ensuring that dietary supplements are safe for their intended use.

On November 20, 1995, representatives of the dietary supplement industry submitted to FDA a suggested outline for the development of GMP regulations for dietary supplements. FDA evaluated the outline and determined that it provided an extremely useful starting point should FDA decide to proceed to rulemaking to adopt GMP regulations for dietary supplements. However, the agency recognizes that the first question that must be addressed is whether there is the need for such regulations or whether part 110 (21 CFR part 110) continues to be adequate. Therefore, the agency issued an advance notice of proposed rulemaking on February 6, 1997 (*Federal Register*, Vol. 62, No. 25). The advance notice of proposed rulemaking includes the industry submission and asks for public comment on the framework that the submission presents.

As part of the process of considering whether to institute rulemaking to require GMP regulations, the agency would like to conduct a survey of firms that manufacture, pack, or hold dietary supplements to learn about existing manufacturing practices.

A.2 Use of Information

The Economics Branch of the Center for Food Safety and Applied Nutrition will primarily use the information gathered in the study. The purposes of this information collection are to (1) learn about

the existing manufacturing practices in the dietary supplements industry and (2) help the agency formulate a policy to ensure that dietary supplement products are produced under conditions that will result in a safe and properly labeled product without unnecessary costs to the industry. The survey data will be used to estimate the percentage of establishments, by product type (e.g., herbals and botanicals, vitamins and minerals, etc.) and size, that are currently practicing GMPs. The survey will provide an understanding of the economic impact that any proposal to establish GMP regulations will have on both large and small establishments in the dietary supplement industry.

The survey is organized to determine the extent to which establishments use written procedures and maintain records for the following: (1) personnel to ensure they have proper education, training, and experience and are knowledgeable in disease control; (2) buildings and facilities are maintained against adulteration; (3) equipment is cleaned and sanitized; (4) quality control and laboratory operations check that certificates of analysis are reliable and that identity and adulteration tests are conducted on raw materials and in-process formulations; (5) production and process controls use master and batch records as well as other records; (6) warehousing and distribution operations maintain records for forward and backward tracing of product; and (7) consumer complaints are handled and documented.

Research Triangle Institute (RTI) will develop and administer the survey in conjunction with its survey subcontractor, Harris Interactive. RTI will conduct a telephone-mail-telephone survey that will be administered to 717 establishments with approximately 400 survey completions. The sample will be stratified by size and product type and will be representative of the subpopulations of interest.

A.3 Use of Information Technology

RTI will use CATI for the initial and follow-up telephone interviews. CATI will enable RTI to efficiently record the responses and identify and correct reporting inconsistencies during the interview. CATI reduces the occurrence of missing responses to specific questions because interviewers can press respondents for answers, define any terms that are unclear, and answer any other questions the respondents may have. Harris Interactive, RTI's subcontractor for the data collection, has extensive experience recruiting for and conducting CATI surveys with business establishments.

A.4 Duplication Identification

A search of published literature and FDA archives by the Economics Branch of FDA's Center for Food Safety and Applied Nutrition failed to identify any data that statistically estimate the prevalence of specific GMPs among dietary supplement establishments.

A.5 Minimize Burden to Small Entities

Because the survey will be administered to a sample of dietary supplement establishments representative of the subpopulations of interest, small entities will certainly be respondents. However, FDA does not feel that alternative collection procedures for small entities are necessary. The entities will not be required to collect or record information, since their survey responses will be derived from their standard procedures and existing records. Also, because a mail survey is being used, the survey can be completed at the convenience of respondents.

A.6 Consequences of Not Conducting Collection

FDA will collect data only once to conduct an economic analysis to determine if GMP regulations are required for dietary supplements. This is not a periodic data collection. Without this data collection, the existing manufacturing practices of dietary supplement establishments is not known, and the economic analysis may be incomplete or misleading. If small entities are not included in the information collection, the information on GMPs used in the analysis may not accurately represent the impact of requiring regulations for small entities. Furthermore, because of several recent illnesses and deaths that may have resulted from contaminated dietary supplements, a public health risk may exist from the absence of GMP regulations, thereby making the need for this information collection urgent. The hazards associated with poor manufacturing practices include chemical and biological contamination, unlabeled ingredients, and highly variable amounts of active ingredients.

A.7 Special Circumstances Explanation

No special circumstances require additional explanations.

A.8 Public Comments and Consultation Outside the Agency

The emergency *Federal Register* notice will provide an opportunity for comment.

During the comment period for the *Federal Register* notice, RTI will conduct a pretest of the mail survey instrument with up to nine dietary supplement establishments. RTI will conduct two or three of the pretest interviews in person at the establishment site; the remaining pretest interviews will be conducted by telephone. The site visits will include a tour of the plant production processes. Once RTI has completed the pretest, we will revise the survey instrument based on any comments provided by the pretest respondents.

A.9 Payment or Gift to Respondents

Respondents will be provided a summary of the survey results in return for their participation. No payment or gift will be offered to respondents.

A.10 Assurance of Confidentiality

The confidentiality of respondents will be assured by using an independent contractor to collect the information, by enacting procedures to prevent unauthorized access to respondent data, and by preventing the public disclosure of the responses of individual participants. FDA will not have access to the survey responses of individual establishments. FDA has contracted with RTI to develop the sampling frame, draw the sample, contact the participants, collect the data, and record and analyze the data.

RTI has standard procedures for assuring the confidentiality of survey respondents. RTI manages the data collected from human subjects in ways that prevent unauthorized access at any point during the study. RTI's confidentiality guidelines specifically restrict the release of personally identifying information about respondents to anyone outside the project team. These procedures improve the response rate and ensure the confidentiality of all interview data.

RTI will not disclose the responses of individual establishments. RTI will only report survey results in aggregate, pooling the responses from establishments within a stratum. No survey results will be reported for strata with fewer than eight observations.

A.11 Sensitive Sexual, Religious, or Private Information

Not applicable. The survey instrument does not contain any questions that might be considered sensitive.

A.12 Hour Burden Estimates

Based on previous establishment surveys, FDA estimates that the burden of this collection of information will average 1.13 hours per respondent (see Table 1). This estimate covers the entire survey process, including making the initial telephone contact, gathering the data needed, and completing the survey by mail or telephone.

Table 1. Estimated Annual Reporting Burden[a]

Number of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
400	1	400	1.13	452

[a]There are no capital costs or operating and maintenance costs associated with this collection of information.

A.13 Total Annual Cost Burden to Respondents or Recordkeepers Excluding Hours Burden Shown in Items 12 and 14

Not applicable. Respondents will have no additional burden beyond the hours burden shown in item A.12. Respondents will not need capital equipment, ongoing recordkeeping operations, or services to complete the information collection.

A.14 Annual Cost to the Federal Government

RTI estimates the total cost to the Federal Government for this information collection to be $177,820, which represents 2,665 labor hours and incidental costs such as mailing, communications, and supplies. As shown in Table 2, this estimate includes FDA's activities, as well as RTI's. FDA will spend time refining the survey instruments, reviewing sampling design and data collection methods, and conducting an economic analysis using the collected data. RTI will develop and pretest the survey instrument, design and draw the sample, collect the data, analyze the data, and produce a final report.

A.15 Explanation of Program Changes or Adjustments

This is a new collection.

Table 2. Agency and Contractor Annual Burden/Cost Estimates

	Burden Hours				
Collection Activity	**Management***	**Technical****	**Clerical**	**Total Hours**	**Cost*****
Agency					
Refine Survey Instrument	15	0	0	15	$720
Review Sample Design and Sampling Methods	10	0	0	10	$480

Review and Monitor Data Collection Methods and Products	30	0	0	30	$1,440
Economic Analysis	70	0	0	70	$3,360
Contractor Services (RTI)					
Develop Survey Instrument	100	170	34	304	$23,521
Pretest Survey Instrument	100	150	8	258	$19,962
Design and Draw Sample	68	210	42	320	$24,238
Conduct Phase 1 and Phase 2 Data Collection	60	1,100	50	1,210	$74,278
Analyze Data	80	238	10	328	$21,833
Produce Final Report	40	40	40	120	$7,988
Total Burden and Cost	573	1,908	184	2,665	$177,820

*Includes administrative and senior professional staff.
**Includes junior professional and technical staff and telephone interviewers.
***Agency rates for management were calculated using midpoint of pay-level range for GS13 for 1999. This rate was multiplied by 1.6 to cover fringe benefits, overhead, other direct costs, and fees and then divided by 2,080 hrs/year. Contractor services were calculated using weighted averages of hourly rates that include salary, fringe, overhead, and fees. Other direct costs (e.g., communication, services, and supplies) are included in the totals.

A.16 Publication of Results

RTI will use the data to prepare a report that discusses the prevalence of GMPs by product type and size for the dietary supplements industry. Tables 3 and 4 show how RTI will organize this information by GMP procedure for each product type and size stratum.

Table 3. Example: Percentage of Dietary Supplement Establishments with Written Procedures for Personnel, by Product Type

	Percentage of Establishments (%)				
	Vitamins and Minerals	**Herbals and Botanicals, Including Extracts**	**Amino Acids/ Proteins/ Animal Extracts**	**Other Dietary Supplements**	**Overall**
Disease control					
Personal cleanliness					

Education, training, and experience	

Table 4. Example: Percentage of Dietary Supplement Establishments with Written Procedures for Personnel, by Size

	Percentage of Establishments (%)			
	Very Small	**Small**	**Large**	**Overall**
Disease control				
Personal cleanliness				
Education, training, and experience				

This survey is a one-time collection of information to determine the prevalence of GMP procedures among dietary supplement establishments. Target dates are listed in Table 5.

A.17 Explanation of Inappropriateness of Displaying OMB Approval Expiration Date

No exemption is requested.

A.18 Exceptions to the Certification Statement of OMB Form 83.I

No exceptions requested.

Table 5. Survey Schedule

Activity	Start Date	End Date
Instrument pretest (up to 9 establishments)	9/15/99	10/15/99
Federal Register notice published	10/1/99	10/31/99
OMB approval	10/31/99	11/5/99
Data collection	11/15/99	1/21/00
Data analysis	1/24/00	2/11/00
Final report production	2/11/00	2/28/00

B. COLLECTIONS OF INFORMATION EMPLOYING STATISTICAL METHODS

B.1 Describe Universe

The universe for this survey is defined as the 2,004 dietary supplement establishments in the DS-EED database that manufacture, repackage, supply ingredients, or distribute dietary supplement products in the United States. RTI developed the DS-EED using FDA's Official Establishment Inventory (OEI) and supplemented the information in the OEI with information from trade organizations, trade shows, and electronic databases that cover various aspects of the industry. Table 6 lists the SIC codes and descriptions of the industries included in the DS-EED. The primary SIC code for a dietary supplement establishment may be a SIC code for a non-dietary supplement industry.

The anticipated overall response rate is 72 percent for the very small, small, and unknown size strata and 79 percent for the large stratum. This response rate is calculated as the product of the response rates for Phases 1 and 2. This response rate takes into consideration that data will be collected over the Thanksgiving and Christmas holidays. The data collection cannot be postponed until after the holidays because of reporting requirements required by FDA.

B.2 Procedures

(i) Stratification

The primary purpose of stratification in our data analysis is to ensure that estimates for population subdivisions are precise. In this case, subdivisions of the population of particular interest are establishment size and product type because these characteristics will be important factors influencing the prevalence of GMP procedures.

The DS-EED includes nine product type codes: vitamins and minerals,[1] herbals and botanicals, herbal and botanical extracts, amino acids, proteins, animal extracts, tea-like products, concentrates/metabolites/constituents, and other dietary supplements. Establishments may be classified by one or more product types. For the proposed survey, we defined four *mutually exclusive* superstrata:

[1] Vitamins and minerals are grouped together because most plants that manufacture either of these also manufactures the other.

Table 6. Industries Included in the DS-EED

SIC Code	SIC Description
2032	Canned Specialties
2047	Dog and Cat Food
2048	Prepared Feeds and Feed Ingredients for Animals and Fowls, Except Dogs and Cats
2052	Cookies and Crackers
2064	Candy and Other Confectionery Products
2075	Soybean Oil Mills
2077	Animal and Marine Fats and Oils
2086	Bottled and Canned Soft Drinks and Carbonated Waters
2087	Flavoring Extracts and Flavoring Syrups, Not Elsewhere Classified
2099	Food Preparations, Not Elsewhere Classified
2721	Periodicals: Publishing, or Publishing and Printing
2819	Industrial Inorganic Chemicals, Not Elsewhere Classified
2821	Plastics Materials, Synthetic Resins, and Nonvulcanizable Elastomers
2833	Medicinal Chemicals and Botanical Products
2834	Pharmaceutical Preparations
2835	In-Vitro/In-Vivo Diagnostic Substance
2836	Biological Products—Except Diagnostic
2841	Specialty Cleaning, Polishing, and Sanitation Preparations
2843	Surface Active Agents, Finishing Agents, Sulfonated Oils, and Assistants
2844	Perfumes, Cosmetics, and Other Toilet Preparations
2851	Paints, Varnishes, Lacquers, Enamels, and Allied Products
2869	Industrial Organic Chemicals, NEC
2879	Pesticides and Agricultural Chemicals, Not Elsewhere Classified
2899	Chemicals and Chemical Preparations, Not Elsewhere Classified
3089	Plastics Products, Not Elsewhere Classified
3295	Minerals and Earths, Ground or Otherwise Treated
3341	Secondary Smelting and Refining of Nonferrous Metals
3679	Electronic Components, Not Elsewhere Classified
3841	Surgical Instrument/Apparatus
3842	Orthopedic, Prosthetic, and Surgical Appliances and Supplies
3843	Dental Equipment and Supplies
5087	Chiropractic Equipment and Supply
5122	Drugs, Drug Proprietaries, and Druggists' Sundries
5149	Groceries and Related Products, Not Elsewhere Classified
5499	Miscellaneous Food Stores
7389	Business Services, Not Elsewhere Classified
8731	Commercial Physical Research
8734	Testing Laboratories

1. Vitamins and minerals (includes establishments also classified as herbals and botanicals or amino acids/proteins/animal extracts)

2. Amino acids/proteins/animal extracts (includes establishments also classified as herbals and botanicals, including extracts; excludes establishments also classified as vitamins and minerals)

3. Herbals and botanicals, including extracts (excludes establishments also classified as vitamins and minerals or amino acids/proteins/animal extracts)

4. Other (all other product types)

We further stratified each of the four superstrata into four size categories—very small, small, large, and unknown—resulting in 16 sampling strata.

We also classified each establishment into one mutually exclusive facility type category (manufacturer, input supplier, repacker, distributor, other). Establishments that manufacture and are also input suppliers, repackers, or distributors are classified as manufacturers.

Product Type Stratification

Using the product codes in the DS-EED, we classified each establishment into one of the four superstrata: (1) vitamins and minerals; (2) amino acids/proteins/animal extracts; (3) herbals and botanicals, including extracts; and (4) other dietary supplements.

Size Stratification

The SBA classifies companies as small based on the size of the entire company. Because the DS-EED data on size are only for a specific establishment, we had to obtain parent company information on employment and/or revenue to correctly classify each establishment as part of a small or large company.

To obtain parent company data for establishments in the survey universe, we sent *info*USA the DS-EED data records and requested (among other variables) the name, address, primary SIC code, employment size (in ranges), and revenue (in ranges) of parent company firms with establishments in the survey universe. *Info*USA matched 1,219 of the 2,004 records to their U.S. database of 10.3 million businesses. The non-matched records (786 establishments) did not match because they are recently established businesses, they are out of business, or because there has been a name or address change. Because data on revenue or employment size were not available for the non-matched records, we

created an "unknown" stratum for these establishments. The survey will collect information on revenue and employment so we can correctly classify these establishments for the analysis.

Of the 1,219 matched records, 187 were linked to ultimate parents. The parent company data for these 187 establishments were merged with the survey universe. Of the remaining records, 1,032 establishments were matched but did not have a larger parent company. For these records, the establishment and parent company were the same entity, so we used establishment-level data to define the establishment's size.

Using SBA size standards, each of the 2,004 establishments in the survey universe was classified as parts of small or large businesses based on the employment size or annual revenues of each establishment's parent company. The SBA size standards represent the largest size a firm may be, in terms of either the number of employees or annual receipts, and still remain eligible as a small business for various types of federal assistance. When an establishment did not have a parent company (i.e., when a record in the DS-EED survey universe did not link with an ultimate parent in the *info*USA database), the employment size or annual revenues of the establishment was used to categorize the establishment. If an establishment's parent company had a sales volume or employment size that exceeded the SBA size standard for the parent company's primary four-digit SIC code, the establishment was categorized as large. Conversely, an establishment whose parent company had an employment size or sales volume less than or equal to the SBA size standard for the parent company's primary four-digit SIC code was classified as small. Table 7 provides a listing of SBA size standards for the four-digit SIC codes found in the survey universe. In such cases where the SBA size standard did not precisely coincide with an employment or sales range, we categorized the establishment as small.

Because the dietary supplement industry is characterized by small establishments, we further divided small establishments based on employment size—very small and small. An establishment was classified as very small if the number of employees is less than 20. Table 8 presents the size of establishments by the four product type superstrata.

Sampling Allocation

The sample is designed to produce valid and reliable results that can be generalized to the subpopulations of interest. The proposed sample allocation is designed to yield 400 completed surveys. Table 9 presents the sample allocation for the initial sample size of 717 establishments. To allocate the sample across the 16 product type and size strata, we oversampled the amino acids/proteins/animal extracts and herbals and botanical product types.

Table 7. Size Definitions by SIC Code

SIC Codes	SBA Size Standard
0139, 0273	$500,000 in sales
1382, 4725, 5421, 5499, 5719, 5912, 5941, 5963, 5995, 5999, 6162, 6282, 6719, 7231, 7299, 7319, 7389, 7997, 8049, 8111, 8231, 8322, 8399, 8733-8742, 8999, 9999	$5,000,000 in sales
1521	$17,000,000 in sales
7377	$18,000,000 in sales
5961	$18,500,000 in sales
5047-5199,	100 employees
1422, 1459, 1499, 2023, 2026, 2033-2041, 2047-2051, 2064, 2075, 2077, 2086-2099, 2721, 2759, 2835, 2836, 2844, 2879, 2891, 2899, 3295, 3341, 3565, 3599, 3672, 3841-3861, 3949, 8731	500 employees
2062, 2821, 2833, 3834, 2841	750 employees
2032, 2819, 2869, 3315	1,000 employees

Table 8. Size of Establishments, by Product Type [a]

	Very Small	Percent Very Small (%)	Small	Percent Small (%)	Large	Percent Large (%)	Unknown	Percent Unknown (%)	Total
1. Vitamins and minerals	323	30.0	287	26.7	77	7.2	388	36.1	1,075
2. Amino acids/proteins/ animal extracts	27	31.0	20	23.0	5	5.7	35	40.2	87
3. Herbals and botanicals, including extracts	188	42.2	61	13.7	4	0.9	193	43.3	446
4. Other dietary supplements	113	28.5	79	19.9	34	8.6	170	42.9	396
Total	**651**	**32.5**	**447**	**22.3**	**120**	**6.0**	**786**	**39.2**	**2,004**

Note: 1: Vitamins and minerals—Includes establishments also classified as herbals and botanicals or amino acids/proteins/animal extracts.
2: Amino acids/proteins/animal extracts—Includes establishments also classified as herbals and botanicals, including extracts; excludes establishments also classified as vitamins and minerals.
3: Herbals and botanicals, including extracts—Excludes establishments also classified as vitamins and minerals or amino acids/proteins/animal extracts.
4: Other—all other product types.

[a]Totals may not add to 100 percent due to rounding.

Table 9. Sample Allocation

Product Type	Size				
	Very Small	Small	Large	Unknown	Total
1. Vitamins and Minerals					
Initial Sample Size	56	67	49	30	202
Expected Number of Respondents	30	36	33	16	115
2. Amino Acids/Proteins/Animal Extracts					
Initial Sample Size	27	20	5	35	87
Expected Number of Respondents	15	11	3	19	48
3. Herbals and Botanicals, Including Extracts					
Initial Sample Size	170	61	4	70	305
Expected Number of Respondents	92	33	3	38	166
4. Other Dietary Supplements					
Initial Sample Size	33	37	31	22	123
Expected Number of Respondents	18	20	21	12	71
Total					
Initial Sample Size	286	185	89	157	717
Expected Number of Respondents	155	100	60	85	400

Note: 1: Vitamins and minerals—Includes establishments also classified as herbals and botanicals or amino acids/proteins/animal extracts.
2: Amino acids/proteins/animal extracts—Includes establishments also classified as herbals and botanicals, including extracts; excludes establishments also classified as vitamins and minerals.
3: Herbals and botanicals, including extracts—Excludes establishments also classified as vitamins and minerals or amino acids/proteins/animal extracts.
4: Other—all other product types.

We undersampled the vitamins and minerals and other dietary supplements product types. Regarding the size strata, we undersampled the unknowns and oversampled the very small, small, and large strata. Prior to selecting the sample we will sort by facility type within each sampling stratum. Then we will select a stratified systematic sample so that facility types are proportionally represented in each product type/size strata.

The initial sample sizes shown in Table 9 are based on the assumptions shown below. These assumptions are based on previous experience with establishment surveys.

- The contact rate (reachable phone number) will be at least 83 percent for the very small, small, and unknown size strata and 95 percent for the large stratum.

- The eligibility rate (dietary supplement establishment) will be at least 90 percent for all strata.

- The response rate for the initial recruitment telephone interview (Phase 1) will be at least 85 percent for the very small, small, and unknown size strata and 89 percent for the large stratum.

- The cooperation rate with the mail survey/follow-up telephone interview (Phase 2) will be at least 85 percent for the very small, small, and unknown size strata and 89 percent for the large stratum.

(ii) Estimation

RTI will generate survey estimates by applying survey weights to the respondent record data. Survey weights will be computed in several steps. Initially, sampling weights will be computed to reflect the different probabilities of selection induced by the sampling design (i.e., by using different sampling rates in the various strata). These weights will be assigned to the (n=717) selected establishment records in the sample files.

Next, RTI will adjust these weights for nonresponse to minimize the potential bias due to survey nonresponse. RTI plans to use weighting class adjustments. One possible approach would be to consider the 16 strata as weighting classes.

Weighting class adjustments will ensure that, within each class, respondent weights sum to the population counts of eligible establishments. These adjustments, implemented with the computation and application of adjustment factors in each class, will also tend to reduce the biases of nonresponse to the extent that weighting classes are homogeneous.

Weighted estimates will be calculated for subpopulations of interest (i.e., by product type and by size). RTI will also compute estimated variances and standard errors for these estimates.

An indication of the expected precision of survey estimates are the widths of 95 percent confidence intervals (CIs) for percentage estimates of important reporting domains. Table 10 provides estimates of confidence intervals for the reporting domains of interest. For estimates for the herbals and botanicals product type, we expect 95 percent CIs of +/- 0.68 percent when the estimate is about 30 percent. The CI width will be slightly larger for an estimate of 50 percent (+/- 0.71 percent) and smaller for a percentage estimate of 10 percent (+/- 0.55 percent). For estimates for very small establishments, we expect 95 percent CIs of +/- 1.59 percent when the estimate is about 30 percent.

The CI width will be larger for an estimate of 50 percent (+/- 1.71 percent) and smaller for a percentage estimate of 10 percent (+/- 1.15 percent). The

Table 10. Expected Precision of Survey Estimates

Domain	N	n	Prevalence 10%	20%	25%	30%	35%	40%	50%
Product Type									
Vitamins and minerals	1,075	115	2.80	3.59	3.85	4.05	4.20	4.30	4.38
Amino acids, proteins, and animal extracts	87	48	1.05	1.06	1.06	1.06	1.06	1.06	1.06
Herbals and botanicals, including extracts	446	166	0.55	0.63	0.66	0.68	0.69	0.71	0.71
Other	396	71	1.12	1.27	1.31	1.35	1.37	1.39	1.41
Size									
Very Small	651	155	1.15	1.43	1.52	1.59	1.64	1.68	1.71
Small	447	100	0.88	1.01	1.05	1.08	1.11	1.12	1.14
Large	120	60	0.85	0.86	0.86	0.87	0.87	0.87	0.87
Unknown	786	85	2.31	2.88	3.07	3.22	3.33	3.40	3.46

Note: 1: Vitamins and minerals—Includes establishments also classified as herbals and botanicals or amino acids/proteins/animal extracts.
2: Amino acids/proteins/animal extracts—Includes establishments also classified as herbals and botanicals, including extracts; excludes establishments also classified as vitamins and minerals.
3: Herbals and botanicals, including extracts—Excludes establishments also classified as vitamins and minerals or amino acids/proteins/animal extracts.
4: Other—all other product types.

confidence intervals above include the design effects that are induced by over- and under-sampling establishments in the various product type and size strata. Because we are sampling a large proportion of the population of dietary supplement establishments, the finite population correction factor was used in the computation of precision. For the actual analysis, the precision estimates should improve when

establishments in the unknown size stratum are categorized into the appropriate size strata, thus increasing the number of observations for analysis.

The proposed information collection does not have any specialized problems, unusual sampling procedures, or periodic data collection cycles.

B.3 Methods to Maximize Response Rate

The anticipated overall response rate is 72 percent for the very small, small, and unknown size strata and 79 percent for the large stratum. This response rate is calculated as the product of the response rates for Phases 1 and 2. This response rate takes into consideration that data will be collected over the Thanksgiving and Christmas holidays. The data collection cannot be postponed until after the holidays because of reporting requirements required by FDA.

RTI expects to keep nonresponse biases to a minimum by achieving good response rates. Nonresponse bias depends on two factors: the amount of nonresponse (i.e., the response rate) and the extent to which respondents differ from nonrespondents in the survey characteristics of interest. In fact, the bias can be mathematically expressed as a product of these two factors. The bias can be reduced substantially by maximizing response rates.

RTI proposes a variety of procedures to maximize response rates. Prospective respondents will be sent a lead letter on FDA letterhead and a 1-page brochure describing the research study and the importance of their participation. This letter will include the OMB number and a contact name and phone number at FDA. Also, the letter will offer to send respondents an aggregated summary of the survey results as an incentive to participate.

The mail survey materials will be sent via Federal Express to expedite their delivery and to signify the importance of the survey. Along with the survey materials, respondents will receive a letter on RTI letterhead and another copy of the 1-page brochure. A metered (prepaid) envelope will also be included for returning the mail survey.

Harris Interactive, on behalf of RTI, will operate a toll-free survey help line during the full-scale survey administration. Respondents can call the survey help line to request assistance when completing the mail survey.

For the initial and follow-up telephone interviews, RTI will attempt to contact each sample point up to 8 times (for busy, no answer, and voice mail dispositions) before assigning a disposition of

nonresponse. For refusals to the initial and follow-up telephone interviews, a more experienced interviewer will attempt up to two refusal conversions.

Throughout the data collection process, RTI will maintain procedures to ensure the confidentiality of the survey responses.

RTI will minimize other response errors by providing survey participants with detailed instructions and by making the questions easy to answer, which will also reduce respondents' burden in completing the mail survey.

B.4 Tests of Procedures and Methods

During the comment period for the *Federal Register* notice, RTI will conduct a pretest of the mail survey instrument with up to nine dietary supplement establishments. RTI will conduct two or three of the pretest interviews in person at the establishment site; the remaining pretest interviews will be conducted by telephone. The site visits will include a tour of the plant production processes. Once RTI has completed the pretest, we will revise the survey instrument based on any comments provided by the pretest respondents.

B.5 Statistical Consultant's Name and Telephone Number and Data Collection Contractor Contact

Statistical Consultant's Name and Telephone Number

Mr. Peter Siegel, Statistician
Statistics Research Division, Research Triangle Institute
(919) 541-6348

Data Collection and Analysis Contractor Contact

Ms. Sheryl Cates, Business Analyst
Center for Economics Research, Research Triangle Institute
(919) 541-6810

REFERENCE

Federal Register. February 6, 1997. "Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Dietary Supplements." Vol. 62, No. 25.

APPENDIX 1

FEDERAL REGISTER NOTICE

APPENDIX 2

INITIAL TELEPHONE INTERVIEW SCRIPT

APPENDIX 3

MAIL SURVEY INSTRUMENT