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RTI Project Number
6673-6

Survey of Manufacturing Practices in the Dietary Supplement Industry

Final Report

May 17, 2000

Prepared for

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Introduction

In November 1995, representatives of the dietary supplement industry submitted to the Food and Drug Administration (FDA) a suggested outline for developing good manufacturing practice (GMP) regulations to ensure that dietary supplements are safe for consumers for their intended use. Through regulation, the Secretary may prescribe GMP regulations for dietary supplements. If such regulations were to be prescribed, they would be modeled after current GMPs for food.

FDA contracted with the Research Triangle Institute (RTI) to conduct a survey of the dietary supplement industry to learn about the existing manufacturing practices in the industry and what constitutes GMPs. This effort is part of the process of considering whether to institute rule making to develop GMP regulations.

The objectives of the survey were to

- learn about the existing manufacturing practices in the industry and
- 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.

We selected a sample of 966 dietary supplement establishments from the Dietary Supplement Enhanced Establishment Database (DS-EED) using a stratified systematic sample design. A telephone-mail-telephone survey approach was used for data collection. We conducted telephone interviews to screen establishments for eligibility and to recruit eligible establishments for the mail survey. Nonrespondents to the mail survey were contacted by telephone to

remind them to complete and return the mail survey. We received a total of 238 completed surveys.

This report describes the sample design and survey administration procedures and presents summary statistics for the survey questions. The report is organized as follows: Section 2 describes the sample design, Section 3 discusses the survey instrument design and our survey administration procedures, and Section 4 describes our weighting and analysis procedures and presents selected survey results.

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Sample Design

In this section, we present the sample design for the survey. We describe the universe for the survey, the sample stratification, and the sample allocation.

2.1 SURVEY UNIVERSE

The universe for this survey is defined as the 1,973¹ dietary supplement establishments in the DS-EED that manufacture, repackage, supply ingredients, distribute, import, or export dietary supplement products. 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 (Muth and Wendling, 1999).

2.2 SAMPLE STRATIFICATION

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

¹Version 1 of the DS-EED contained 2,004 records. Thirty-one duplicates were found in the data cleaning process and were removed from the sampling frame, resulting in 1,973 records.

The DS-EED includes nine product type codes: vitamins and minerals,² 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 type. For stratification and reporting results, we defined four *mutually exclusive* superstrata:

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; 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 dietary supplements (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/relabeler, distributor, other). Establishments that manufacture and are also input suppliers, repackers, or distributors are classified as manufacturers.

2.2.1 Product Type Stratification

Using the product type 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, and (4) other dietary supplements.

2.2.2 Size Stratification

The Small Business Administration (SBA) classifies companies as small based on the size of the entire company or firm. Because the DS-EED data on size are only for a specific establishment, we had to obtain parent company information on employment and/or

²Vitamins and minerals are grouped together because most plants that manufacture either of these also manufacture the other.

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 *infoUSA* the DS-EED data records (N=2,004) 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. *InfoUSA* matched 1,219 of the 2,004 records in the DS-EED to their U.S. database of 10.3 million businesses.

Of the 1,219 matched records, 31 records were found to be duplicates of other records and were removed, giving a total of 1,188 matched records and 1,973 total records in the sampling frame. The non-matched records (785 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 employment or revenue size were not available for the non-matched records, we created an “unknown” size stratum for these establishments. In reporting results, we used the survey responses on number of employees to correctly classify these establishments.

Of the 1,188 matched records, 180 were linked to ultimate parents. The parent company data for these 180 establishments were merged with the survey universe. The remaining 1,008 records did not link to an ultimate 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 1,973 establishments in the survey universe was classified as part of a small or large business 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 matched record in the DS-EED survey universe did not link with an ultimate parent in the *infoUSA* database), the employment size or annual revenues of the establishment were used to categorize the establishment. If an establishment’s parent company had 500 or fewer employees or sales less than \$20 million (if data on

employment were not available), then the establishment was classified as small

Because the dietary supplement industry is characterized by small establishments, we further divided small establishments into two categories 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 2-1 shows the number of establishments in the survey universe or population by the 16 sampling strata

Table 2-1. Survey Universe, by Sampling Strata

	Very Small		Small		Large		Unknown		Total
	Number	Percent (%)							
1. Vitamins and Minerals	317	29.8	281	26.5	98	9.2	366	34.5	1,062
2. Amino Acids/Proteins/ Animal Extracts	27	31.0	20	23.0	6	6.9	34	39.1	87
3. Herbals and Botanicals	187	42.6	58	13.2	5	1.1	189	43.1	439
4. Other	117	30.4	83	21.6	25	6.5	160	41.6	385
Total	648	32.8	442	22.4	134	6.8	749	38.0	1,973

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; 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.

^aTotals may not add to 100 percent due to rounding.

2.3 SAMPLE ALLOCATION

Our sample allocation approach was designed to produce valid and reliable results that can be generalized to the subpopulations of interest—product type and establishment size. The sample allocation used was designed to yield 400 completed surveys. Table 2-2 presents the sample allocation for the initial sample size of 941 establishments.

Table 2-2. Initial Sample Sizes, by Sampling Strata

Product Type	Size				Total
	Very Small	Small	Large	Unknown	
1. Vitamins and Minerals					
Initial Sample Size	68	105	59	34	266
Expected Number of Respondents	28	43	34	14	119
2. Amino Acids/Proteins/Animal Extracts					
Initial Sample Size	27	20	6	34	87
Expected Number of Respondents	11	8	3	14	36
3. Herbals and Botanicals					
Initial Sample Size	187	58	5	164	414
Expected Number of Respondents	76	24	3	67	170
4. Other					
Initial Sample Size	64	61	25	24	174
Expected Number of Respondents	26	25	14	10	75
Total					
Initial Sample Size	346	244	95	256	941
Expected Number of Respondents	141	100	54	105	400

The initial sample sizes were based on the following assumptions:

- 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 (overall contact rate of 85 percent).
- The eligibility rate (dietary supplement establishment) will be at least 90 percent for all strata.
- The recruiting rate for the initial telephone interview (Part 1) will be at least 74 percent for the very small, small, and unknown size strata and 82 percent for the large stratum (overall Part 1 response rate of 75 percent).
- The response rate for the mail survey (Part 2) will be at least 74 percent for the very small, small, and unknown size strata and 82 percent for the large stratum (overall Part 2 response rate of 75 percent).

To achieve the desired number of completes by strata, we oversampled some strata, undersampled some strata, and took a

census (i.e., selected all sample points) for some strata. If we took a proportionate sample, then all strata would have a sampling rate of approximately $941/1,973=48$ percent (sample size/population). When we do not take a census but the sampling rate is greater than 48 percent, then it is an oversample; likewise, if the sampling rate is less than 48 percent, then it is an undersample.

We allocated the sample across the 16 product type and size strata as follows:

- For the vitamins and minerals product type, we undersampled the very small, small, and unknown size strata and oversampled the large size stratum.
- For the amino acids/proteins/animal extracts product type, we selected all sample points (i.e., took a census) in each of the four size stratum.
- For the herbals and botanicals product type, we took a census of the very small, small, and large size strata and oversampled the unknowns.
- For the "other" product type, we took a census of the large size stratum, oversampled the very small and small size strata, and undersampled the unknowns.

Prior to selecting the sample, we sorted by facility type within each of the 16 sampling stratum. Then we selected a stratified systematic sample so that the facility types were proportionally represented in each product type/size stratum.

Because the actual eligibility rates were lower than anticipated, we drew additional sample for the herbals and botanicals/unknown stratum, which resulted in taking a census of this stratum. Time constraints prevented us from drawing additional sample from the other strata. The final sample size was 966 establishments.

Table 2-3 shows the final sample sizes, by the 16 sampling strata.

Table 2-3. Final Sample Sizes, by Sampling Strata

Product Type	Size				Total
	Very Small	Small	Large	Unknown	
1. Vitamins and Minerals	68	105	59	34	266
2. Amino Acids/Proteins/Animal Extracts	27	20	6	34	87
3. Herbals and Botanicals	187	58	5	189	439
4. Other	64	61	25	24	174
Total	346	244	95	281	966

3

Survey Design and Administration

In this section, we describe the design of the mail survey instrument and our survey administration procedures, and present the survey response rates. We also discuss how we used the survey results to update the DS-EED.

3.1 SURVEY INSTRUMENT DESIGN

A telephone-mail-telephone survey approach was used for data collection. We initially contacted establishments in the sample by telephone and screened them for eligibility. Eligible respondents were recruited for the mail survey. For nonrespondents to the mail survey, we made follow-up telephone calls to remind them to complete and return the mail survey. Appendix A provides a copy of the final mail survey instrument.

The survey was designed to determine the extent to which establishments use written procedures and maintain records for specific manufacturing practices. We developed the survey based on the current GMPs for food (21 CFR Part 110), the Advance Notice of Proposed Rulemaking for Current GMPs in Manufacturing, Packing, or Holding Dietary Supplements (vol. 62, no. 25, February 6, 1997), and input from FDA staff.

The survey is organized as follows:

1. Products and Markets
2. Good Manufacturing Practices (GMPs)
3. Personnel
4. Buildings and Facilities

5. Equipment
6. Quality Control and Laboratory Operations
7. Production and Process Controls
8. Warehousing
9. Consumer Complaints
10. Plant Information

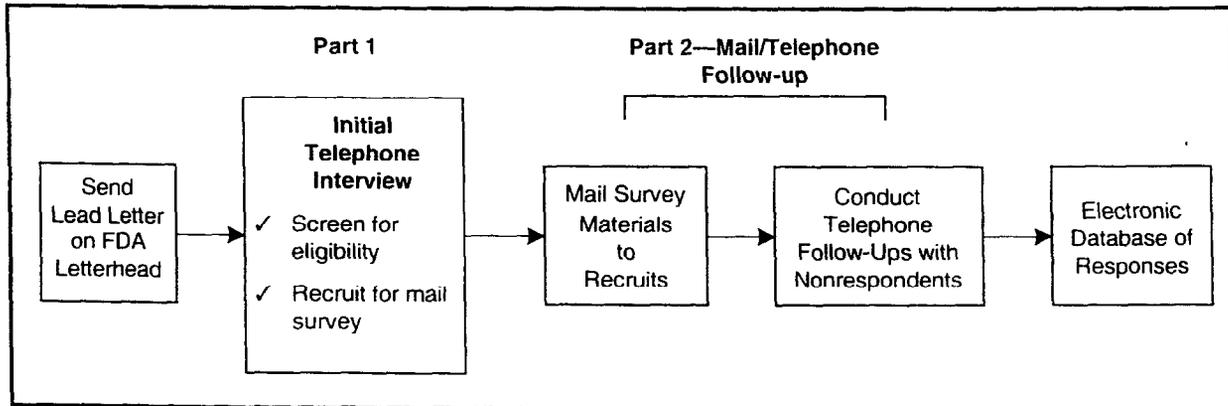
To pretest the survey instrument, we conducted telephone interviews with four dietary supplement establishments. FDA had previously visited these establishments as part of this project. We sent the survey to the selected establishments and asked them to complete the survey; then we conducted a telephone interview to obtain their feedback on the survey instrument. Based on the comments provided by the pretest respondents, we revised the survey instrument. Because we made only minor revisions to the survey instrument, we were able to include the pretest responses in the full-scale analysis.

The Information Collection Request Supporting Statement was submitted to the Office of Management and Budget (OMB) on September 29, 1999. The information collection request received emergency processing. OMB approval was received on November 22, 1999.

3.2 PROCEDURES

Figure 3-1 illustrates our survey approach. First, we sent each establishment in the sample a lead letter on FDA letterhead and a 1-page brochure to explain the purpose of the survey, the value of the establishments' participation, and our confidentiality procedures. Appendix B provides a copy of the lead letter and brochure.

We followed this mailing with a telephone call to each establishment to screen them for eligibility and to recruit eligible establishments for the mail survey. To be eligible for the survey, establishments had to currently manufacture, repackage, supply ingredients, distribute, import, or export dietary supplement products for human consumption. Establishments that were brokers only or were a headquarters site with no manufacturing operations were not eligible. We found that about 50 percent of the establishments sampled were not eligible for the survey because

Figure 3-1. Telephone-Mail-Telephone Survey Approach

they were no longer in operation or did not have any dietary supplement operations (e.g., made dietary supplements for pets, herbs/spices used for food, homeopathic remedies, or herbal beauty products).

We sent recruited establishments the survey via Federal Express to expedite the delivery and to signify the importance of the survey. The mailing included a postage-paid envelope for returning the mail survey.

We conducted follow-up telephone calls with nonrespondents to the mail survey to remind them to complete and return the survey; if such attempts were unsuccessful, on the third callback we attempted to complete the interview over the telephone. We found that most establishments were not willing to complete the survey over the telephone.

We used a variety of procedures to maximize our response rate. As previously mentioned, we sent prospective respondents a lead letter on FDA letterhead and a 1-page brochure describing the research study (see Appendix B). This letter included a contact name and phone number at FDA and assured respondents that all results would be kept confidential. Also, the letter offered to send respondents an aggregated summary of the survey results as an incentive to participate.

We also operated a toll-free survey help line during the full-scale survey administration. Respondents could call the survey help line to request assistance when completing the mail survey.

For the initial and follow-up telephone interviews, we attempted to contact each sample point (i.e., talk with an employee at the establishment) up to 8 times before assigning a disposition of nonresponse. For nonrespondents to the initial and follow-up telephone interviews, we attempted up to two refusal conversions. Finally, as previously mentioned, we used Federal Express to mail the survey materials.

Our subcontractor, Harris Interactive, administered the survey using computer-assisted telephone interviewing (CATI). We conducted the full-scale data collection over a 10-week period from November 29, 1999 to February 4, 2000. Limited telephone interviewing took place between Christmas and New Years Day.

3.3 SURVEY RESPONSE

We received a total of 238 completed mail surveys. Table 3-1 shows the number of completed surveys by sampling strata.

Table 3-1. Number of Completed Surveys, by Sampling Strata

Product Type	Size				Total
	Very Small	Small	Large	Unknown	
1. Vitamins and Minerals	19	39	13	1 ^a	72
2. Amino Acids/Proteins/Animal Extracts	8	7	0	5	20
3. Herbals and Botanicals	58	25	0	30	113
4. Other	14	13	2	4	33
Total	99	84	15	40	238

^aFor weighting purposes, we moved this respondent to the small stratum. See Appendix C for a description of the weighting procedures.

Tables 3-2 and 3-3 present the final disposition of the sample and the response rates by product type and size, respectively. We present this information separately for the initial telephone interview and the mail survey. For the initial telephone interview (Part 1), we assigned each sample point a disposition of *recruit*, *refusal*, or *ineligible*. In the following cases, eligibility status could not be determined:

Table 3-2. Final Disposition of Sample and Response Rates, by Product Type

	Vitamins and Minerals	Amino Acids/ Proteins/ Animal Extracts	Herbals and Botanicals	Other	Total
Initial Telephone Interview (Part 1)					
Recruits	132	39	219	54	444
Refusals	33	9	32	9	83
Ineligibles	101	39	188	111	439
Total Sample	266	87	439	174	966
Eligibility Rate (%)	62.03	55.17	57.18	36.21	54.55
Recruiting Response Rate (%)	80.00	81.25	87.25	85.71	84.25
Mail Survey (Part 2)					
Respondents	72	20	113	33	238
Nonrespondents	51	17	80	15	163
Ineligibles	9	2	26	6	43
Total Recruits	132	39	219	54	444
Eligibility Rate (%)	93.18	94.87	88.13	88.89	90.32
Mail Survey Response Rate (%)	58.54	54.05	58.55	68.75	59.35
Overall Eligibility Rate (%)	58.65	52.87	51.25	32.76	50.10
Overall Response Rate (%)	46.83	43.92	51.08	58.93	50.00

- The sample point was contacted but did not complete the screening questions (e.g., the individual identified as the contact person was not available or asked to be called back).
- The sample point was contacted but refused to participate prior to answering the screening questions.
- The sample point was contacted but there was a language barrier.

For sample points where the eligibility status was unknown, we estimated the proportion of eligibles among known eligibles and ineligibles and used this proportion to distribute the unknowns between eligibles (i.e., refusals) and ineligibles.

Table 3-3. Final Disposition of Sample and Response Rates, by Establishment Size

	Very Small	Small	Large	Unknown	Total
Initial Telephone Interview (Part 1)					
Recruits	186	133	33	92	444
Refusals	33	26	7	17	83
Ineligibles	127	85	55	172	439
Total Sample	346	244	95	281	966
Eligibility Rate (%)	63.29	65.16	42.11	38.79	54.55
Recruiting Response Rate (%)	84.93	83.65	82.50	84.40	84.25
Mail Survey (Part 2)					
Respondents	99	84	15	40	238
Nonrespondents	74	40	13	36	163
Ineligibles	13	9	5	16	43
Total Recruits	186	133	33	92	444
Eligibility Rate (%)	93.01	93.23	84.85	82.61	90.32
Mail Survey Response Rate (%)	57.23	67.74	53.57	52.63	59.35
Overall Eligibility Rate (%)	59.54	61.48	36.84	33.10	50.10
Overall Response Rate (%)	48.60	56.66	44.20	44.42	50.00

The “ineligibles” disposition includes the following:

- sample points that do not currently manufacture, repackage, supply ingredients, distribute, import, or export dietary supplement products for human consumption;
- sample points for which the telephone number was disconnected;
- sample points that are out of business; and
- a percentage of the sample points for which the eligibility status was unknown.

Recruits are those sample points that completed the initial telephone interview and agreed to be sent the mail survey. Refusals are those sample points that were eligible for the survey but declined to participate (includes a percentage of the sample points that refused to participate and the eligibility status was unknown)

The eligibility rate for the initial telephone interview—the proportion of the total sample that was eligible for the survey—is calculated as follows:

$$\text{Eligibility Rate} = \frac{\text{Recruits}_{\text{part 1}} + \text{Refusals}_{\text{part 1}}}{\text{Total Sample}} \quad (3.1)$$

The eligibility rate for all establishments sampled was 55 percent. This means that 55 percent, or 527 of the 966 sample points, met the eligibility criteria for participating in the survey. The majority of ineligibles were sample points that had no dietary supplement operations or had disconnected phone numbers.

The recruiting response rate for the initial telephone interview—the proportion of the total number of eligible sample points that agreed to be sent a mail survey—is calculated as follows:

$$\text{Recruiting Response Rate} = \frac{\text{Recruits}_{\text{part 1}}}{\text{Recruits}_{\text{part 1}} + \text{Refusals}_{\text{part 1}}} \quad (3.2)$$

The recruiting response rate for all establishments was 84 percent. The recruiting response rate did not vary much by size of establishment. Among the product type categories, the recruiting response rate was highest for the herbals and botanicals and the other product type category.

For the mail survey (Part 2), we assigned each sample point recruited for the mail survey a disposition of *respondent*, *nonrespondent*, or *ineligible*. Respondents are sample points that completed the mail survey. Nonrespondents are sample points that were recruited for the mail survey but did not complete it. Ineligibles are sample points that were recruited for the mail survey but were determined to be ineligible once they received the mail survey.

Since we found that some recruits were actually ineligible during the mail survey phase, we cannot assume that all nonrespondents to the mail survey are eligible. We prorated the nonrespondents between eligible nonrespondents and ineligibles using the proportion of eligibles among known eligibles and ineligibles for Part 2. The eligibility rate for Part 2 was calculated as shown in Equation 3.1. The Part 2 eligibility rate for all establishments was 90 percent.

The survey response rate for the mail survey—the proportion of the recruits that actually completed the mail survey—is calculated as follows:

$$\text{Mail Survey Response Rate} = \frac{\text{Respondents}_{\text{part 2}}}{\text{Respondents}_{\text{part 2}} + \text{Nonrespondents}_{\text{part 2}}} \quad (3.3)$$

The mail survey response rate for all establishments was 59 percent. The mail survey response rate was highest for the small size category and the herbals and botanicals and vitamins and minerals product type categories.

The overall eligibility rate for Parts 1 and 2 is calculated as follows:

$$\frac{\text{Recruits}_{\text{part 1}} + \text{Refusals}_{\text{part 1}} - \text{Ineligibles}_{\text{part 2}}}{\text{Total Sample}} \quad (3.4)$$

The overall eligibility rate for all establishments was 50 percent. The eligibility rate was lowest among establishments in the large and unknown size categories and the other product type category.

The overall response rate for Parts 1 and 2 is calculated as follows:

$$\text{Overall Response Rate} = \text{Recruiting Response Rate}_{\text{part 1}} \cdot \text{Mail Survey Response Rate}_{\text{part 2}} \quad (3.5)$$

The overall response rate for all establishments was 50 percent. Among the product type categories, the overall response rate ranged from a low of 44 percent for amino acids/proteins/animal extracts to a high of 59 percent for the other category. Among the size categories, the overall response rate ranged from a low of 44 percent for the large and unknowns to a high of 57 percent for small establishments.

The shortfall in the number of respondents was caused by a combination of lower-than-expected eligibility rates and response rates for the mail survey.

Our estimated contact/eligibility rate was 76.5 percent. Our actual overall eligibility rates were much lower—33 to 61 percent for very small, small, and unknown establishments and 37 percent for large establishments. Many of the establishments in the DS-EED are no longer in business or do not have dietary supplement operations.

Our estimated recruiting rates for the initial telephone interview were 74 percent for very small, small, and unknown establishments

and 82 percent for large establishments. Our actual recruiting rates were higher—84 to 85 percent for very small, small, and unknown establishments and 83 percent for large establishments. However, many of the establishments recruited for the mail survey did not complete and return the survey.

Our estimated response rates for the mail survey were 74 percent for very small, small, and unknown establishments and 82 percent for large establishments. Our actual response rates were much lower—53 to 68 percent for very small, small, and unknown establishments and 54 percent for large establishments.

The poor response rates for the mail survey result from the following factors:

- ▶ The most common reason given for not participating was the amount of time required to complete the survey, particularly the need to refer to records to complete some of the questions.
- ▶ Concerns about confidentiality and a general mistrust of FDA kept some plants from responding.
- ▶ For some plants, concerns about legality issues kept companies from responding to the survey.
- ▶ Data collection took place during the month of December, a difficult time for conducting surveys.
- ▶ The data collection period was shorter (10 weeks) than generally recommended for a mail survey due to FDA's reporting deadline. This prevented us from releasing additional sample and making extensive follow-ups to nonrespondents.

3.4 UPDATING THE DS-EED

We used the data from the survey to update the DS-EED. We deleted records that were found to be ineligible for the survey and updated location information.

Table 3-4 shows the types and number of plant or establishment records deleted from the DS-EED. We deleted a total of 438 plant records. Version 1 of the DS-EED (used to draw the survey sample) contained 2,004 records (Muth and Wendling, 1999). Version 2 of the DS-EED contains 1,566 plant records (Muth, Karns, and Cates, 2000). The number of establishments in the DS-EED, Version 2 (1,566 establishments) is different from the estimated eligible population of 906 establishments (see Appendix C for a

Table 3-4. Records Deleted from the DS-EED

	Number of Records
DS-EED, Version 1	2,004
Records deleted	
Duplicates	52 ^a
No dietary supplement operations	234
Nonworking phone number	130
Out of business	22
Total	438
DS-EED, Version 2	1,566

^aIn preparing the DS-EED for drawing the sample, we found 31 duplicates. We found 21 additional duplicates when we prepared Version 2, for a total of 52 duplicates. Records were considered duplicate entries when their information matched in all the following fields: address, city, state, and phone.

discussion of how we estimated the eligible population). Although we can estimate the number of ineligible establishments using the weighted survey data, we can only delete records for ineligible establishments that we actually contacted during survey administration. The difference in the number of records in Version 2 of the DS-EED and the estimated eligible population has no impact on the survey results.

We also used the survey data to update the plant name, phone number, and location information when this information was available. Updated information was available for 271 records.

4

Survey Results

In this section, we briefly discuss our weighting and analysis procedures and present selected survey results.

4.1 WEIGHTING PROCEDURES

We generated survey estimates by applying survey weights to the respondent record data. A brief summary of our weighting procedures is provided below. Appendix C describes our weighting procedures in greater detail.

Survey weights were computed in several steps:

1. Initial sampling weights were computed to reflect the different probabilities of selection induced by the sampling design (i.e., by using different sampling rates in the various strata).
2. We then used weighting classes to adjust these weights for nonresponse to the initial telephone interview.
3. Because our population included Canadian establishments that were not eligible for the survey, we post-stratified to adjust to the population size excluding Canadian establishments.
4. We made a second nonresponse adjustment for nonresponse to the mail survey.

Nonresponse adjustments ensure that, within each weighting 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, also tend to reduce the biases of nonresponse to the extent that weighting classes are homogeneous.

4:2 ANALYSIS PROCEDURES

As discussed in Section 2, for stratification purposes we used information in the DS-EED to classify establishments by product type and size. To report the survey results, we classified respondents by product type and by establishment size based on their answers to the survey. We defined the product type categories using the responses to Question 1.2 (primary product type) and Question 1.3 (all other product types). Using the responses to these two questions, we defined four *mutually exclusive* categories:

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; 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 dietary supplements (all other product types)

Using the responses to the question in the initial telephone interview on total number of employees for the company that owns the plant, we classified respondents into one of three size categories:

1. Very small (less than 20 employees)
2. Small (20 to 500 employees)
3. Large (more than 500 employees)

Table 4-1 provides the number of respondents by the product type and establishment size reporting domains. The number of respondents for the amino acids/proteins/animal extracts and other product type category and the large size category is small for making inferences to the population. This can be seen by the large confidence intervals associated with these analysis domains.

Some respondents (about 10 percent) found that some sections of the survey were not applicable. This was particularly true for establishments that import or export only, or distribute only. In some cases, these respondents would skip entire sections or only answer a few questions in the section. A survey was not considered complete if the respondent only completed sections 1, 2, and 10.

Table 4-1. Number of Respondents by Reporting Domains

	Number of Respondents
Product Type	
Vitamins and Minerals	118
Amino Acids/Proteins/Animal Extracts	16
Herbals and Botanicals	97
Other	7
Total	238
Establishment Size	
Very Small	110
Small	114
Large	14
Total	238

For survey sections 3, 4, 5, 8, and 9, we excluded from our analysis respondents that did not answer *any* questions in that section. In Appendices D and E, a x.0 question is included at the beginning of the table (with the exception of Section 9) in which to report the percentage of respondents that did not complete any questions in that section. The x.0 questions were not included in the mail survey but are added for reporting purposes. For example, in Table D-3, we report that 9.10 percent of respondents answered Question 3.0 as no. This means that 9.10 percent of respondents did not complete this section of the survey (i.e., no personnel at that site handle raw materials, in-process materials, or finished product).

Most statistical software packages assume simple random sampling from an infinite population and are not appropriate for variance estimation of sample survey estimates. That is, they do not compensate for survey design features such as stratification. Therefore, they would produce biased variance estimates for the survey data. We used Stata,¹ a statistical analysis software tool, to compute the weighted proportions and means and the 95 percent

¹StataCorp. 1999. *Stata Statistical Software: Release 6.0*. College Station, TX: Stata Corporation.

confidence intervals for the point estimates. Stata takes into account the stratified sample design when computing the variances.

For some analyses, we only had one respondent or observation in a cell or strata and therefore could not compute variances. For variance estimation, we collapsed some strata so that for most analyses we had at least two observations per stratum and could compute variances.

4.3 SELECTED RESULTS

Tables 4-2 through 4-10 present summary statistics for selected questions by establishment size. Appendix D provides the weighted responses for all survey questions by establishment size, and Appendix E provides the weighted responses by product type.

In addition to the estimated proportions and means, we provide the 95 percent confidence intervals for the point estimates. The confidence interval is the range of the estimate. For example, in Table 4-3 we report that the 95 percent confidence interval for the percentage of dietary supplement establishments that have standard operating procedures (SOPs) is between 71.54 and 86.02 percent. This means that we are 95 percent confident that the percentage of dietary supplement establishments that have SOPs is between 71.54 and 86.02 percent.

Table 4-2. Plant Characteristics

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
<i>Type of operations^a</i>																
Manufacturer	62	53.49	39.87	66.62	75	68.51	56.62	78.39	9	62.59	34.80	83.98	146	61.68	53.00	69.67
Repackager/relabeler/ encapsulator	23	26.64	15.96	40.99	41	41.51	30.25	53.74	3	23.50	7.35	54.33	67	34.11	26.27	42.93
Ingredient or input supplier	30	21.92	13.28	33.98	45	38.63	27.75	50.79	4	30.48	11.81	58.95	79	30.94	23.54	39.48
Distributor	59	56.64	43.09	69.27	70	57.07	44.96	68.39	6	42.14	19.45	68.73	135	56.10	47.35	64.49
Importer	28	23.47	14.06	36.50	40	35.00	24.42	47.31	5	37.66	16.18	65.40	73	30.13	22.72	38.75
Exporter	31	29.14	18.23	43.13	43	37.47	26.69	49.66	6	42.83	20.02	69.17	80	34.13	26.42	42.79
Other	7	3.64	1.73	7.51	3	4.58	1.15	16.52	0	0.00	0.00	0.00	10	3.93	1.62	9.21
<i>Primary line of business^b</i>																
Vitamins and minerals	15	24.13	13.49	39.36	36	42.35	31.35	54.16	9	68.59	40.88	87.34	60	35.81	28.19	44.22
Herbals and botanicals, not including extracts	32	25.98	16.02	39.22	24	17.81	10.51	28.56	2	17.68	4.31	50.61	58	21.35	15.21	29.12
Herbals and botanicals extracts	39	26.98	18.12	38.17	24	17.27	10.46	27.17	1	4.49	0.61	26.47	64	20.82	15.40	27.52
Amino acids	1	0.57	0.08	4.01	2	0.95	0.23	3.77	1	4.73	0.64	27.56	4	0.98	0.38	2.51
Protein products	5	5.96	1.73	18.57	5	2.33	0.96	5.52	1	4.51	0.61	26.58	11	4.02	1.73	9.06
Animal extracts	0	0.00	0.00	0.00	0	0.00	0.00	0.00	0	0.00	0.00	0.00	0	0.00	0.00	0.00
Concentrates, metabolites, and constituents	3	1.71	0.51	5.56	1	2.95	0.41	18.36	0	0.00	0.00	0.00	4	2.26	0.56	8.65
Other	6	9.59	3.42	24.13	5	4.87	1.38	15.76	0	0.00	0.00	0.00	11	6.66	3.05	13.95
Multiple responses	7	3.96	1.84	8.29	16	11.02	6.34	18.47	0	0.00	0.00	0.00	23	7.37	4.71	11.35
Non-dietary supplement product	1	0.57	0.08	4.01	1	0.46	0.06	3.26	0	0.00	0.00	0.00	2	0.48	0.12	1.94

(continued)

Table 4-2. Plant Characteristics (continued)

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
Produce other food products	12	6.81	3.77	11.99	39	32.28	22.26	44.25	1	7.62	1.03	39.47	52	19.92	14.19	27.22
Produce drugs																
OTC drugs	9	6.12	3.01	12.03	17	11.42	6.75	18.67	4	29.40	11.26	57.76	30	10.06	6.94	14.36
Rx drugs	0	0.00	0.00	0.00	0	0.00	0.00	0.00	0	0.00	0.00	0.00	0	0.00	0.00	0.00
OTC and Rx drugs	3	4.58	0.97	19.03	12	8.75	4.73	15.64	4	34.01	13.51	62.97	19	8.26	4.84	13.75
Own plants at other locations	15	21.49	11.45	36.68	33	24.54	16.47	34.91	10	75.76	48.32	91.26	58	25.91	19.12	34.08

(continued)

Table 4-2. Plant Characteristics (continued)

	Very Small (n = 110)				Small (n = 114)			
	n	Mean	95% CI		n	Mean	95% CI	
			Low	High			Low	High
Average square footage of facility	91	24,675	355	48,994	102	71,355	52,980	89,730
Average number of full-time employees	102	7.63	6.06	9.20	103	95.51	73.20	117.81
Average number of full-time QC employees	79	3.01	0.18	5.85	99	7.24	5.31	9.17
Average number of batches per year	87	222.95	134.52	311.38	76	554.07	407.25	700.89
Average annual gross sales revenue (\$)	102	13,803,005	0.00 ^c	34,900,000	101	27,954,987	13,000,000	42,900,000
	Large (n = 14)				Overall (n = 238)			
	n	Mean	95% CI		n	Mean	95% CI	
			Low	High			Low	High
Average square footage of facility	11	595,734	3,771	1,187,696	204	75,733	42,203	109,263
Average number of full-time employees	13	1,005.23	300.43	1,710.03	218	105.47	58.66	152.27
Average number of full-time QC employees	12	88.24	25.65	150.83	190	10.27	5.51	15.03
Average number of batches per year	12	308.96	181.59	436.33	175	380.80	292.64	468.95
Average annual gross sales revenue (\$)	13	73,330,263	14,700,000	132,000,000	216	23,971,303	11,600,000	36,400,000

^aRespondents could select more than one response.

^bThe primary line of business is the line of business that contributes to the majority of revenues—either greater than 50 percent of revenues or the greatest of several lines such as 35 percent if all other lines contribute less.

^cEstimated confidence interval for lower bound was less than zero so we truncated the interval

Table 4-3. Good Manufacturing Practices (GMPs)

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
Follow a published GMP model	61	51.76	38.26	65.02	86	72.97	60.63	82.55	12	88.98	63.97	97.35	159	64.60	56.09	72.27
For plants following GMPs, the GMP model used ^a																
FDA Food GMPs	41	68.55	49.65	82.81	52	63.99	51.66	74.72	6	51.86	24.92	77.75	99	64.70	55.38	73.03
Advance Notice of Proposed Rulemaking	14	25.99	12.46	46.42	23	33.09	21.21	47.61	4	38.22	15.16	68.19	41	30.99	21.92	41.81
National Nutritional Foods Association (NNFA) GMPs	13	27.73	13.66	48.21	25	30.16	19.33	43.77	1	8.57	1.14	43.12	39	27.75	19.09	38.47
FDA Drug CGMPs	10	16.66	6.72	35.71	29	33.57	22.18	47.26	9	73.84	41.22	91.91	48	30.59	22.09	40.67
U.S. Pharmacopeia GMPs	10	16.56	6.64	35.65	25	36.72	24.92	50.37	7	56.71	28.31	81.29	42	31.15	22.39	41.50
For plants <i>not</i> following GMPs, how plants verify identity, purity, and composition of ingredients and products ^a																
Sanitation standard operating procedures (SSOPs)	8	22.56	—	— ^b	6	14.18	—	— ^b	0	0.00	—	— ^b	14	19.09	—	— ^b
Other QA program	11	20.18	—	— ^b	9	33.99	—	— ^b	0	0.00	—	— ^b	20	25.29	—	— ^b
Certificate of Analysis	27	64.55	—	— ^b	19	85.73	—	— ^b	0	0.00	—	— ^b	46	72.02	—	— ^b
Certificate of Identity	10	11.96	—	— ^b	6	23.66	—	— ^b	0	0.00	—	— ^b	16	16.34	—	— ^b
Other	17	45.57	—	— ^b	7	24.70	—	— ^b	0	0.00	—	— ^b	24	37.05	—	— ^b
Have standard operating procedures (SOPs)	79	65.17	50.98	77.10	104	91.11	81.08	96.08	12	88.98	63.97	97.35	195	79.73	71.54	86.02

^aRespondents could select more than one response.

^bConfidence interval could not be estimated because there was only one observation (respondent) in a stratum for that question.

Table 4-4. Personnel

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
Have written procedures on disease control	47	55.74	41.51	69.09	74	71.17	58.99	80.90	13	100.00	100.00	100.00	134	66.62	57.96	74.29
Have written procedures on maintaining personal cleanliness	67	69.80	55.01	81.38	95	84.99	72.39	92.44	13	100.00	100.00	100.00	175	79.78	71.44	86.16
Have written procedures on education, training, or experience requirements	53	53.95	39.41	67.84	82	70.98	58.20	81.12	12	93.15	63.84	99.06	147	65.43	56.37	73.49
Maintain records of personnel education, training, or experience	54	54.22	39.63	68.12	84	73.66	61.31	83.15	12	93.15	63.84	99.06	150	67.00	57.99	74.92

Table 4-5. Buildings and Facilities

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
Facility Ownership ^a																
Owned	39	36.10	24.01	50.27	68	59.80	47.47	71.00	11	85.17	55.41	96.37	118	51.19	42.43	59.88
Leased	62	63.90	49.73	75.99	43	40.20	29.00	52.53	2	14.83	3.63	44.59	107	48.81	40.12	57.57
Owned Facilities																
Have written procedures on maintenance of the grounds about the plant	9	24.33	9.49	49.63	38	60.35	45.34	73.64	10	90.63	53.87	98.77	57	52.35	40.65	63.79
Have written procedures on general maintenance and sanitation of the buildings, fixtures, and other physical facilities of the plant	20	61.22	41.95	77.52	54	79.35	63.66	89.39	10	94.46	68.48	99.26	84	75.31	64.74	83.51
Have written procedures on the storage and use of cleaning and sanitizing materials	16	52.82	31.31	73.33	47	69.33	52.88	81.99	11	100.00	100.00	100.00	74	67.13	55.17	77.22
Have written procedures on pest control	20	59.40	37.16	78.36	52	77.27	61.84	87.69	10	94.46	68.48	99.26	82	73.48	62.04	82.45

(continued)

Table 4-5. Buildings and Facilities (continued)

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
<i>Leased Facilities</i>																
Have written procedures on maintenance of the grounds about the plant or verify and keep records that facility owner is taking proper measures	10	19.79	8.65	39.13	18	32.98	17.93	52.56	1	46.18	4.93	93.42	29	25.95	16.11	39.00
Have written procedures on general maintenance and sanitation of the buildings, fixtures, and other physical facilities of the plant or verify and keep records that facility owner is taking proper measures	26	39.91	23.93	58.38	25	58.88	38.90	76.31	2	100.00	100.00	100.00	53	49.12	36.72	61.64
Have written procedures on the storage and use of cleaning and sanitizing materials or verify and keep records that facility owner is taking proper measures	24	36.89	21.47	55.55	26	57.32	37.19	75.28	2	100.00	100.00	100.00	52	46.78	34.42	59.55
Have written procedures on pest control or verify and keep records that facility owner is taking proper measures	18	33.16	18.28	52.39	32	79.57	59.45	91.19	2	100.00	100.00	100.00	52	54.41	42.00	66.29

^aPlants were classified as owning their facility if 50 percent or more of the plant's facilities are owned.

Table 4-6. Equipment

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
Have written procedures on the cleaning, sanitizing, and maintaining of equipment and utensils	57	60.50	45.22	73.98	95	81.04	68.32	89.44	13	100.00	100.00	100.00	165	73.89	64.92	81.23
Validate that equipment, instruments, and controls are installed correctly	63	67.71	52.41	79.96	70	56.25	44.36	67.47	11	85.17	55.40	96.37	144	62.40	53.62	70.44
Validate that equipment, instruments, and controls are used correctly	68	67.42	51.84	79.90	80	66.19	53.65	76.80	11	85.17	55.40	96.37	159	67.72	59.01	75.35
Validate equipment used in quality control	55	62.98	47.92	75.88	82	67.11	54.22	77.86	10	77.20	47.55	92.67	147	66.02	56.77	74.18

Table 4-7. Quality Control and Laboratory Operations

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
Have unit or person responsible for quality control (QC)	85	74.45	60.20	84.87	108	92.39	79.86	97.38	12	91.00	69.49	97.82	205	84.52	76.64	90.08
Have written procedures on the responsibilities and procedures of the QC person/unit	48	64.53	49.77	76.96	91	86.03	75.54	92.47	12	100.00	100.00	100.00	151	78.59	70.70	84.81
For plants that receive ingredients, require some or all suppliers to provide a Certificate of Analysis (CoA)	81	87.66	75.54	94.23	105	98.82	96.31	99.63	12	100.00	100.00	100.00	198	94.26	88.95	97.10
For plants that require a CoA, verify reliability of supplier's CoA	46	66.65	51.67	78.88	85	80.62	68.80	88.70	10	87.43	60.01	96.99	141	75.62	67.14	82.48
Conduct tests on raw materials	75	65.92	51.79	77.68	99	88.08	78.30	93.80	11	79.86	49.47	94.14	185	78.02	69.92	84.42
For plants that test raw materials, use tests to confirm identity of ingredients	74	94.71	70.07	99.28	97	99.11	96.35	99.79	11	100.00	100.00	100.00	182	97.54	88.63	99.51
For plants that test raw materials, use tests to detect contamination of raw materials	74	94.71	70.07	99.28	96	97.79	92.13	99.40	10	90.46	53.91	98.71	180	96.27	88.65	98.84

(continued)

Table 4-7. Quality Control and Laboratory Operations (continued)

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
For plants that test raw materials, use tests to determine potency	28	38.38	24.01	55.11	71	75.86	63.93	84.78	10	91.81	58.94	98.87	109	62.96	53.58	71.46
Conduct tests on in-process materials and/or finished products	61	55.81	42.08	68.71	91	79.94	68.05	88.17	10	73.32	44.42	90.43	162	69.11	60.65	76.45
For plants that test in-process materials and/or finished products, use tests to confirm identity of ingredients	59	98.14	92.76	99.54	85	95.04	88.14	98.01	10	100.00	100.00	100.00	154	96.40	92.34	98.35
For plants that test in-process materials and/or finished products, use tests to detect contamination of raw materials	58	97.17	91.34	99.11	83	91.96	83.70	96.22	9	89.61	51.20	98.61	150	93.65	88.62	96.55
For plants that test in-process materials and/or finished products, use tests to determine potency	25	49.56	32.38	66.85	70	82.44	73.10	89.03	10	100.00	100.00	100.00	105	71.88	62.85	79.44
Hold representative reserve samples of each batch	73	64.98	50.98	76.80	96	83.67	72.25	90.97	10	72.24	42.95	89.99	179	74.95	66.64	81.75
For plants that have laboratory operations, have written procedures for laboratory operations	39	74.17	61.73	83.63	74	81.45	66.45	90.68	9	93.58	64.78	99.14	122	80.10	70.05	87.38

Table 4-8. Production and Process Controls

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
For plants that receive dietary supplement ingredients, have written procedures for receipt of dietary supplement ingredients	56	71.08	54.46	83.48	86	92.71	87.00	96.03	10	94.38	68.16	99.25	152	84.23	76.20	89.92
For plants that have production processes, have written procedures for production processes	65	88.43	80.99	93.21	94	90.88	79.65	96.21	12	95.28	72.35	99.36	171	90.30	83.95	94.31
For plants that have production processes, use production and process controls that identify the points, steps, or stages in the manufacturing process to prevent adulteration	48	56.99	41.78	70.99	83	77.88	65.77	86.58	10	76.84	50.25	91.60	141	70.09	61.27	77.64

Table 4-9. Warehousing

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
Warehouse has temperature controls	72	74.04	61.19	83.77	72	67.90	56.20	77.72	8	66.39	38.36	86.25	152	70.40	62.28	77.41
Warehouse has humidity controls	13	19.27	9.56	35.03	23	23.54	14.53	35.79	3	27.63	9.17	59.07	39	21.95	15.15	30.71
Have written procedures for storage procedures to control against adulteration as well as deterioration of the product and the container	47	49.70	36.07	63.37	77	66.71	54.77	76.83	11	87.30	58.83	97.06	135	60.62	51.85	68.74
Have written procedures on proper precautions to reduce the potential for mix-ups or adulteration or contamination	50	40.31	28.51	53.35	86	76.04	64.43	84.75	11	87.30	58.83	97.06	147	61.59	52.92	69.58

Table 4-10. Consumer Complaints

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
Have written procedures for handling consumer complaints	52	55.44	42.10	68.03	85	77.68	67.24	85.52	13	95.49	73.42	99.39	150	68.95	60.93	75.98
Procedures for handling adverse events associated with consumer complaints ^a																
Incident is reported to FDA	15	19.37	9.90	34.43	17	17.24	9.69	28.79	5	32.10	13.20	59.52	37	18.94	12.70	27.30
Product is tested for identity and composition	66	62.40	48.41	74.58	83	73.98	62.49	82.91	8	56.99	30.46	80.04	157	68.08	59.55	75.55
Product is reformulated	19	19.23	10.64	32.23	34	34.49	23.93	46.84	5	34.13	14.36	61.56	58	27.88	20.79	36.28
Product is recalled	59	60.13	46.51	72.35	75	62.60	50.43	73.36	6	41.75	19.33	68.20	140	60.43	51.80	68.47
Other	34	25.62	16.25	37.93	22	22.15	13.42	34.29	4	34.01	13.51	62.97	60	24.27	17.67	32.37

^aRespondents could select more than one response.

References

- Muth, M.K., and B. Wendling. 1999. "Dietary Supplement Enhanced Establishment Database, Version 1." Research Triangle Park, NC: Research Triangle Institute.
- Muth, M.K., S.A. Karns, and S.C. Cates. 2000. "Dietary Supplement Enhanced Establishment Database, Version 2." Research Triangle Park, NC: Research Triangle Institute.

**Appendix A:
Mail Survey**

FRONT COVER



U.S. Food and Drug Administration

Form Approved: OMB No. 0910-0422

Expiration Date: 4-30-00

See OMB Statement on inside cover

Survey of Manufacturing Practices in the Dietary Supplement Industry

(Harris will place
label here)

**This survey applies only to
the plant listed on this label.
Refer to this label as instructed
in the survey.**

INSIDE COVER

Public reporting burden for this collection of information is estimated to average 1.13 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspects of this collection of information, including suggestions for reducing this burden to:

Peter Vardon
U.S. Department of Health and Human Services
Food and Drug Administration
330 C Street, SW
Washington, DC 20204

An agency may not conduct or sponsor and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number.

Introduction

The Research Triangle Institute (RTI) is conducting a survey of the dietary supplement industry as part of a research study for the U.S. Food and Drug Administration (FDA). The purpose of this survey is to learn about the existing manufacturing practices in the industry. This effort is part of the process of considering whether to institute rulemaking to require good manufacturing practice (GMP) regulations for the dietary supplement industry.

This plant was randomly selected to participate in this survey. Please answer all questions as they pertain to the plant named on the mailing label attached to the front of this survey booklet. ***Plant is defined as all of the buildings and facilities, including warehouses, used in your dietary supplement operations and within the general area of the address shown on the mailing label.***

Your participation is voluntary, and your responses will be kept strictly ***confidential***. Only anonymous data (no identifying information on your plant) will be provided to the FDA. The name of your establishment will not be linked to your responses. Only aggregate results will be reported to the public.

The survey will take about an hour to complete. Please answer each question by circling the appropriate answer(s) or writing your answer in the space provided. For the purposes of this survey, RTI has defined many of the terms used in the survey. These definitions are provided in the left margin. ***Please return the completed survey in the enclosed postage-paid return envelope within five business days.***

If you have any questions on this research study, please contact:

Peter Vardon
U.S. Department of Health and
Human Services
Food and Drug Administration
330 C Street, SW
Washington, DC 20204
Phone: 202-205-5329
e-mail: PVardon@bangate.fda.gov

or **Heather Carter-Young**
Center for Economics Research
Research Triangle Institute
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Phone: 1-800-334-8571 (ext. 8331)
e-mail: cyoung@rti.org

If you have questions regarding your rights as a research participant, you may contact Dr. Steven Garfinkel at RTI (1-800-334-8571 ext. 6382).

Questions?

Call the Survey Helpline (1-800-866-7655, ext. 548)

If you have any questions as you complete the survey, please call the Survey Helpline at 1-800-866-7655 and ask for Michele LaPrade, extension 548. The Helpline is operated by Harris Interactive, on behalf of RTI, and operates on weekdays from 8:00 a.m. to 5:00 p.m. EST.

1

Products and Markets

1.1 Which of the following describes the dietary supplement operations at this plant? (*Circle all that apply.*)

1. Manufacturer—manufacture dietary supplements from ingredients, may package and label the product itself or transfer it to a repackager/relabeler/encapsulator or distributor
2. Repackager/relabeler/encapsulator—repackage, relabel, or encapsulate dietary supplements manufactured by another firm
3. Ingredient or input supplier—supply ingredients or bulk finished products used to manufacture dietary supplements at this plant or another firm
4. Distributor—distribute products manufactured by this plant or another firm
5. Importer—import either ingredients for further processing or finished products for distribution
6. Exporter—export either ingredients for further processing or finished products for distribution
7. Other (*Specify*): _____

1.2 For your dietary supplement operations at this plant, what is the product type for your **primary line of business**? (*Circle only one.*)

(Your plant's primary line of business for your dietary supplement operations is defined as the one that contributes the majority of revenues—either greater than 50% of revenues or the greatest of several lines such as 35% if all other lines contribute less.)

1. Vitamins and minerals
2. Herbals and botanicals, not including extracts
3. Herbal and botanical extracts
4. Amino acids
5. Protein products
6. Animal extracts
7. Concentrates, metabolites, and constituents
8. Other (*Specify*): _____

1.3 What *other* product types, not including your primary line of business, **do you produce** at this plant? By produce we mean, manufacture, repack/relabel/encapsulate, supply ingredients, distribute, import, or export. (*Circle all that apply.*)

1. Vitamins and minerals
2. Herbals and botanicals, not including extracts
3. Herbal and botanical extracts
4. Amino acids
5. Protein products
6. Animal extracts
7. Concentrates, metabolites, and constituents
8. Other (*Specify*): _____

1.4 Does this plant produce any food products other than dietary supplements?

1. Yes
2. No

1.5 Does this plant produce any over-the-counter (OTC) or prescription (Rx) drugs? (*Circle only one.*)

1. Yes, OTC drugs
2. Yes, Rx drugs
3. Yes, OTC and Rx drugs
4. No

1.6 Is this plant a member of any of the following trade organizations? (*Circle all that apply.*)

1. American Herbal Products Association (AHPA)
2. Consumer Health Products Association (CHPA) (formerly known as Nonprescription Drug Manufacturers Association)
3. Council for Responsible Nutrition (CRN)
4. National Nutritional Foods Association (NNFA)
5. Utah Natural Products Alliance (UNPA)
6. Other (*Specify*): _____

2

Good Manufacturing Practices (GMPs)

For the purposes of this survey, **Good Manufacturing Practices (GMPs)** are the minimum sanitary and processing procedures that a company may have written, adopted, or may follow in practice to ensure that dietary supplements are of consistent quality and contain no unintended components (for example, contaminants) that may pose a safety concern or are otherwise necessary to ensure that a product is not adulterated.

2.1 Does this plant follow a published **Good Manufacturing Practices (GMPs)** model for the dietary supplement products produced at this plant?

1. Yes
2. No Skip to question 2.3

2.2 Which of the following are your GMPs for dietary supplement operations patterned after? (*Circle all that apply.*)

1. FDA Food CGMPs (21 CFR Part 110)
2. Advance Notice of Proposed Rulemaking for Dietary Supplements
3. National Nutritional Foods Association (NNFA) GMPs
4. FDA Drug CGMPs (21 CFR Parts 210 and 211)
5. U.S. Pharmacopeia (USP) GMPs
6. Other (*Specify*): _____

Skip to question 2.5

2.3 If **not** following published GMPs, how does this plant verify the identity, purity, and composition of dietary supplement products and ingredients? (*Circle all that apply.*)

1. Sanitation standard operating procedures (SSOPs)
2. Other quality assurance (QA) program
3. Certificate of Analysis
4. Certificate of Identity
5. Other (*Specify*): _____

2.4 Why does this plant **not** follow published GMPs?

Standard operating procedures (SOPs) detail a specific sequence of events to perform a task. SOPs may include sanitation or operation procedures.

2.5 Does this plant have standard operating procedures (SOPs)?

1. Yes
2. No **Skip to the STOP box below**

2.6 Is there written documentation of the SOPs?

1. Yes
2. No



Please Read Before Continuing!

In Sections 3 through 9, we ask about the procedures for personnel, buildings and facilities, equipment, quality control and laboratory operations, production and process controls, warehousing, and consumer complaints to protect against adulteration and contamination. For the purposes of this survey, **adulteration** includes the presence in a product of any poisonous or harmful substance that may make the product injurious to health, the presence of filth or any other contaminate in the product, less or more of an ingredient than the product label claims, and the manufacture of a product in insanitary conditions in which the product may have become contaminated or injurious to health.

For each specific procedure (e.g., procedures for personnel on disease control, personal cleanliness, and training), we ask about the following:

- **Are there written procedures?** Written procedures can include posted signs, policy and procedure (P&P) manuals, and information posted on the company's internal website.
- **Does plant management verify and keep records that these procedures are being followed?** **Verification** is the confirmation by examination and provision of objective evidence that specified requirements have been fulfilled. Verification may include direct observation of monitoring procedures, internal audits, calibration of equipment at specified intervals, and records review. Records can include written and electronic documentation.
- **Are records made of any corrective actions taken if the procedures are not followed?** Corrective actions are the procedures to be followed when a deviation is discovered during the monitoring process. Records can include written and electronic documentation.

3

Personnel

Written procedures for **disease control** specify the conditions under which employees (including contract/temporary personnel) may not work in a dietary supplement plant. This includes but is not limited to illness; open lesions, including boils, sores, or infected wounds; or any other abnormal source of microbial contamination.

Written procedures for **personal cleanliness** specify the hygienic practices employees (including contract/temporary personnel) shall follow to protect against adulteration and contamination. This includes but is not limited to wearing outer garments, gloves, and hairnets; washing hands thoroughly; and refraining from eating, drinking, chewing gum, and using tobacco.

Written procedures for **education, training, or experience** specify the training requirements for employees (including contract/temporary personnel) and how written records of training are maintained.

- 3.1** Are there written procedures for personnel on **disease control**?
1. Yes
 2. No
- 3.2** Are there written procedures for personnel on maintaining **personal cleanliness**?
1. Yes
 2. No
- 3.3** Are there written procedures ensuring that all personnel employed in the manufacturing process have the proper **education, training, or experience** needed to perform the assigned functions?
1. Yes
 2. No
- 3.4** Does plant management verify and keep records that the procedures for personnel on disease control, personal cleanliness, and training are being followed?
1. Yes
 2. No Skip to question 3.6
- 3.5** Are records made of any corrective actions taken if procedures are **not** followed?
1. Yes, for some procedures
 2. Yes, for all procedures
 3. No
- 3.6** Are records maintained of personnel education, training, or experience?
1. Yes
 2. No Skip to Section 4 on page 7

3.7 How long are records of personnel education, training, or experience maintained? (*Circle one and enter number of years if necessary.*)

1. Term of employment
2. ____ year(s) after expiration date
3. ____ year(s) from date of manufacture
4. Other (*Specify*): _____

4 Buildings and Facilities

Written procedures for ***maintenance of the grounds*** specify how the grounds about the plant shall be maintained to protect against adulteration. This includes but is not limited to properly storing equipment; maintaining roads, yards, and parking lots; and maintaining adequate drainage and operating systems for waste treatment and disposal.

Written procedures for ***general maintenance and sanitation of the buildings, fixtures, and other physical facilities*** specify how the plant shall be maintained in a sanitary condition and kept in repair to prevent adulteration.

Written procedures for ***cleaning and sanitizing materials*** specify that they be safe and adequate under the conditions of use and how they shall be used, held, and stored in a manner that protects against adulteration.

4.1 What percentage of this plant's facilities are owned vs. leased? (*Include warehouse facilities located at this plant. Total should sum to 100%.*)

- a. Owned _____ % square feet
 b. Leased _____ % square feet
 Total 100% square feet

If 50% or more of this plant's facilities are ***owned***, complete ***questions 4.2 – 4.7.***

If 50% or more of this plant's facilities are ***leased***, complete ***questions 4.8 – 4.21.***

Owned Facilities

4.2 Are there written procedures on ***maintenance of the grounds*** about the plant?

1. Yes
2. No

4.3 Are there written procedures on ***general maintenance and sanitation of the buildings, fixtures, and other physical facilities*** of the plant?

1. Yes
2. No

4.4 Are there written procedures on the storage and use of ***cleaning and sanitizing materials***?

1. Yes
2. No

Written procedures for **pest control** specify what measures shall be taken to exclude pests from processing areas and to protect against adulteration by pests.

4.5 Are there written procedures on **pest control**?

1. Yes
2. No

4.6 Does plant management verify and keep records that procedures for buildings and facilities maintenance are being followed?

1. Yes

2. No **Skip to Section 5 on page 11**

4.7 Are records made of any corrective actions taken if procedures are **not** followed?

1. Yes, for some procedures

2. Yes, for all procedures

3. No

Skip to Section 5 on page 11

Leased Facilities

Written procedures for **maintenance of the grounds** specify how the grounds about the plant shall be maintained to protect against adulteration. This includes but is not limited to properly storing equipment; maintaining roads, yards, and parking lots; and maintaining adequate drainage and operating systems for waste treatment and disposal.

4.8 What is the **remaining** term of the lease? (*Enter number of years or months.*)

a. _____ years

b. _____ months

4.9 For leased facilities, who is primarily responsible for **maintaining the grounds** about the plant?

1. Plant management (lessee)

2. Facility owner (lessor) **Skip to question 4.11**

4.10 For leased facilities, are there written procedures on **maintenance of the grounds** about the plant?

1. Yes **Skip to question 4.12**

2. No **Skip to question 4.12**

4.11 Does plant management verify and keep records that the facility owner is properly **maintaining the grounds**?

1. Yes

2. No

Written procedures for **general maintenance and sanitation of the buildings, fixtures, and other physical facilities** specify how the plant shall be maintained in a sanitary condition and kept in repair to prevent adulteration.

4.12 For leased facilities, who is primarily responsible for **general maintenance and sanitation of the buildings, fixtures, and other physical facilities** of the plant?

1. Plant management (lessee)
2. Facility owner (lessor) Skip to question 4.15

4.13 For leased facilities, are there written procedures on **general maintenance and sanitation of the buildings, fixtures, and other physical facilities** of the plant?

1. Yes
2. No

Written procedures for **cleaning and sanitizing materials** specify that they be safe and adequate under the conditions of use and how they shall be used, held, and stored in a manner that protects against adulteration.

4.14 For leased facilities, are there written procedures on the storage and use of **cleaning and sanitizing materials**?

1. Yes Skip to question 4.17
2. No Skip to question 4.17

4.15 Does plant management verify and keep records that the facility owner is properly **maintaining the buildings, fixtures, and other physical facilities** of the plant?

1. Yes
2. No

4.16 Does plant management verify and keep records that the **cleaning and sanitizing materials** used by the facility owner are being properly stored and used?

1. Yes
2. No

Written procedures for **pest control** specify what measures shall be taken to exclude pests from processing areas and to protect against adulteration by pests.

4.17 For leased facilities, who is primarily responsible for **pest control**?

1. Plant management (lessee)
2. Facility owner (lessor) Skip to question 4.19

4.18 For leased facilities, are there written procedures on **pest control**?

1. Yes Skip to question 4.20
2. No Skip to question 4.20

4.19 Does plant management verify and keep records that the facility owner is taking proper **pest control** measures?

1. Yes
2. No

4.20 Does plant management verify and keep records that procedures for buildings and facilities maintenance are being followed?

1. Yes

2. No **Skip to Section 5 on page 11**

4.21 Are records made of any corrective actions taken if procedures are *not* followed?

1. Yes, for some procedures

2. Yes, for all procedures

3. No

5 Equipment

Written procedures for *cleaning, sanitizing, and maintaining equipment and utensils* specify how equipment and utensils shall be cleaned, sanitized, and maintained in a manner that protects against adulteration.

Validation is the examination and provision of objective evidence that equipment, instruments, and controls are accurate, adequately maintained, and adequate in number for the intended uses to measure, regulate, or record temperature, pH, water activity, or other condition.

- 5.1** Are there written procedures on the *cleaning, sanitizing, and maintaining of equipment and utensils*?
1. Yes
 2. No **Skip to question 5.4**
- 5.2** Does plant management verify and keep records that these procedures are being followed?
1. Yes
 2. No **Skip to question 5.4**
- 5.3** Are records made of any corrective actions taken if procedures are *not* followed?
1. Yes, for some procedures
 2. Yes, for all procedures
 3. No
- 5.4** Does this plant *validate* that equipment, instruments, and controls are *installed* correctly?
1. Yes
 2. No
- 5.5** Does this plant *validate* that equipment, instruments, and controls are *used* correctly?
1. Yes
 2. No
- 5.6** Does this plant *validate* the equipment used in quality control? Quality control equipment includes automatic, mechanical, electronic, and computer equipment, including hardware and software.
1. Yes
 2. No

6 Quality Control and Laboratory Operations

6.1 Is there a unit or person responsible for quality control?

1. Yes
2. No **Skip to question 6.4**

6.2 Are there written procedures on the responsibilities and procedures required of the quality control unit/person?

1. Yes
2. No

6.3 For which of the following does the quality control unit/person have responsibility and authority? (*Circle all that apply.*)

1. Approval/rejection of cleaning and maintenance procedures
2. Approval/rejection of procedures, specifications, controls, tests, and examinations for purity, quality, and composition
3. Approval/rejection of raw materials
4. Approval/rejection of packaging materials
5. Approval/rejection of labeling
6. Approval/rejection of finished dietary products
7. Other (*Specify*): _____

A **Certificate of Analysis** is a statement from the supplier about the identity, strength, quality, and purity of a dietary supplement raw material, ingredient, or finished product.

6.4 Does this plant require suppliers to provide a **Certificate of Analysis**? (*Circle only one.*)

1. Yes, from some suppliers
2. Yes, from all suppliers
3. No, do not require CofA from any suppliers **Skip to question 6.7**
4. Do not receive ingredients **Skip to question 6.7**

6.5 Does this plant verify the reliability of the suppliers' **Certificate of Analysis**?

1. Yes
2. No **Skip to question 6.7**

Raw materials are any ingredients intended for use in the manufacture of a dietary ingredient or dietary supplement, including those that may not appear in such finished product.

6.6 How is reliability of the suppliers' **Certificate of Analysis** verified? (Circle all that apply.)

1. Conduct on-site review of suppliers' operations
2. Perform tests in-house to confirm results
3. Use off-site laboratory to confirm results
4. Require suppliers to conduct tests as part of supply specifications
5. Standard reference materials
6. Other (Specify): _____

6.7 Does this plant conduct tests on any **raw materials**? (Circle all that apply.)

1. Yes, in-house
2. Yes, off-site
3. No **Skip to question 6.14**

6.8 What percentage of raw materials are sampled and tested? (Provide average for all raw materials.)

_____ % of lots

6.9 Which of the following testing techniques are used to confirm **identity of ingredients** for raw materials? (Circle all that apply.)

1. Physical
2. Chemical
3. Microbiological
4. Visual (macroscopic or microscopic)
5. Organoleptic
6. No tests are conducted to confirm identity of ingredients
7. Other (Specify): _____

6.10 Which of the following testing techniques are used for detecting **contamination** of raw materials? (Circle all that apply.)

1. Physical
2. Chemical
3. Microbiological
4. Visual (macroscopic or microscopic)
5. Organoleptic
6. No tests are conducted to detect contamination
7. Other (Specify): _____

6.11 Does this plant conduct chemical tests to determine **potency** of raw materials?

1. Yes
2. No

6.12 For the most recent fiscal year, approximately what percentage of raw materials was rejected because of the wrong identity, contamination, or potency? (If none, enter zero.)

_____ % of lots **If zero, skip to question 6.14**

6.13 What was the reason(s) for the rejection? (Circle all that apply. For each item circled, enter the percentage of raw materials rejected for this reason. The total should sum to 100%.)

- | | |
|--|---------|
| 1. Microbial contamination | _____ % |
| 2. Pesticide, herbicide, fungicide contamination | _____ % |
| 3. Other chemical contamination | _____ % |
| 4. Wrong ingredient | _____ % |
| 5. Subpotency | _____ % |
| 6. Superpotency | _____ % |
| 7. Aflatoxin or other toxin | _____ % |
| 8. Other | _____ % |
| Total | 100% |

In-process materials and/or finished products are any materials fabricated, compounded, blended, ground, extracted, sifted, sterilized, derived by chemical reaction, or processed in any other way that is produced for and used in the preparation of a dietary supplement.

6.14 Does this plant conduct tests on any ***in-process materials and/or finished products***?

1. Yes
2. No **Skip to question 6.21**

6.15 What percentage of in-process materials and/or finished products are sampled and tested? (Provide an average for *in-process materials* and for *finished products*; if none, enter zero. Include continuous monitoring.)

- a In-process materials: _____ % of batches
- b Finished products: _____ % of batches

6.16 Which of the following testing techniques are used to confirm **identity of ingredients** for in-process materials and/or finished products? (Circle all that apply.)

1. Physical
2. Chemical
3. Microbiological
4. Visual (macroscopic or microscopic)
5. Organoleptic
6. No tests are conducted to confirm identity of ingredients
7. Other (Specify): _____

6.17 Which of the following testing techniques are used for detecting **contamination** of in-process materials and/or finished products? (Circle all that apply.)

1. Physical
2. Chemical
3. Microbiological
4. Visual (macroscopic or microscopic)
5. Organoleptic
6. No tests are conducted to detect contamination
7. Other (Specify): _____

6.18 Does this plant conduct chemical tests to determine **potency** of in-process materials and/or finished products?

1. Yes
2. No

6.19 For the most recent fiscal year, approximately what percentage of in-process materials and/or finished products was rejected because of the wrong identity, contamination, or potency? (If none, enter zero.)

- a. In-process materials: _____ % of batches
- b. Finished products: _____ % of batches

If zero, skip to question 6.21

6.20 What was the reason(s) for the rejection? (Circle all that apply. For each item circled, enter the percentage of in-process materials and/or finished products rejected for this reason. The total for each column should sum to 100%.)

	In-Process Materials	Finished Products
1. Microbial contamination	_____ %	_____ %
2. Pesticide, herbicide, fungicide contamination	_____ %	_____ %
3. Other chemical contamination	_____ %	_____ %
4. Wrong ingredient	_____ %	_____ %
5. Subpotency	_____ %	_____ %
6. Superpotency	_____ %	_____ %
7. Formulation with missing ingredient	_____ %	_____ %
8. Aflatoxin or other toxin	_____ %	_____ %
9. Other	_____ %	_____ %
Total	100%	100%

6.21 Which of the following testing methods are generally used for testing of raw materials, in-process materials, or finished products? (Circle all that apply.)

1. Association of Analytical Chemists (AOAC)
2. U.S. Pharmacopeia (USP)
3. Food Chemical CODEX (FCC)
4. American Chemical Society (ACS)
5. In-house methods
6. Other (Specify): _____
7. No testing conducted **Skip to question 6.24**

6.22 Does your testing policy specify the use of standard reference materials?

1. Yes
2. No **Skip to question 6.24**

6.23 What is the source of the standard reference materials? (Circle all that apply.)

1. Compendial reference standard
2. In-house **primary** reference materials
3. In-house **working** reference materials
4. Other (Specify): _____

6.24 Does your plant hold representative reserve samples of each batch manufactured?

1. Yes
2. No **Skip to question 6.26**

Written procedures for **laboratory operations** specify the procedures that shall be used to assure that dietary supplement products conform to appropriate standards of purity, quality, and composition and that packaging materials are safe and suitable for their intended purpose.

6.25 How long do you hold representative reserve samples?
(Circle one and enter number of years.)

1. ____ year(s) after expiration date
2. ____ year(s) from date of manufacture
3. Other (Specify): _____

6.26 Are there written procedures for **laboratory operations**?

1. Yes
2. No **Skip to question 6.31**
3. Do not have laboratory operations
Skip to Section 7 on page 18

6.27 Does plant management verify and keep records that these procedures are being followed?

1. Yes
2. No **Skip to question 6.29**

6.28 Are records made of any corrective actions taken if procedures are **not** followed?

1. Yes, for some procedures
2. Yes, for all procedures
3. No

6.29 Do your written procedures for laboratory operations include any of the following? (Circle all that apply.)

1. Sample selection, method description, validation of methodology and results, acceptance/rejection criteria, and use of test results
2. Methods for determining ingredient identity and for detecting adulteration
3. Tests to assess the stability characteristics of products in determining appropriate storage conditions and expiration dating (include testing conducted at corporate headquarters)
4. Procedures for handling and filing test records

6.30 How long are records for laboratory operations retained?
(Circle one and enter number of years.)

1. ____ year(s) after expiration date
2. ____ year(s) from date of manufacture
3. Other (Specify): _____

6.31 Does this plant verify and keep records that laboratory equipment is calibrated correctly?

1. Yes
2. No

7 Production and Process Controls

Written procedures for **receipt of dietary supplement ingredients** specify the criteria for accepting dietary supplement ingredients.

7.1 Are there written procedures for **receipt of dietary supplement ingredients**?

1. Yes
2. No **Skip to question 7.6**
3. Do not receive dietary supplement ingredients
Skip to question 7.6

7.2 Does plant management verify and keep records that these procedures are being followed?

1. Yes
2. No **Skip to question 7.4**

7.3 Are records made of any corrective actions taken if procedures are **not** followed?

1. Yes, for some procedures
2. Yes, for all procedures
3. No

7.4 Do your written procedures for receipt of dietary supplement ingredients include any of the following?
(Circle all that apply.)

1. Written acceptance criteria for dietary supplement ingredients developed by a competent individual
2. Certificate of Analysis specifications
3. Representative sample and authenticated plant reference held in an environmentally appropriate repository for each receiving and production lot/batch
4. Records linking the Certificate of Analysis to the identity of the unprocessed raw material and to the finished product
5. Records to trace and verify compliance with laws on harvest of wildcrafted botanicals
6. Audit records concerning the reliability of supplier Certificate of Analysis
7. Records for source of animal derived materials or products
8. Records for fish and fishery demonstrating that FDA fish and fishery products HACCP regulations are followed
9. Records for raw materials to assure segregation of raw, in-process, and finished product and protection against adulteration

Written procedures for **production processes** specify the requirements of master and batch production and control records.

7.5 How long are records on receipt of dietary supplement ingredients retained? (*Circle one and enter number of years.*)

1. ____ year(s) after expiration date
2. ____ year(s) from date of manufacture
3. Other (*Specify*): _____

7.6 Are there written procedures for **production processes**?

1. Yes
2. No **Skip to question 7.11**
3. No production processes conducted
Skip to Section 8 on page 21

7.7 Does plant management verify and keep records that these procedures are being followed?

1. Yes
2. No **Skip to question 7.9**

7.8 Are records made of any corrective actions taken if procedures are **not** followed?

1. Yes, for some procedures
2. Yes, for all procedures
3. No

7.9 Do your written procedures for production processes include any of the following? (*Circle all that apply.*)

1. Master production and control records
2. Batch production and control records
3. Equipment use and cleaning records, including dates of use and product and lot number of each batch processed
4. Records that demonstrate that automatic equipment, including mechanical and electronic equipment (computers), used in the manufacturing process is designed, installed, tested, calibrated, validated, maintained, and checked to ensure that they are capable of and are performing the intended functions
5. Records for reprocessing of a product
6. Records to assure that correct labels and labeling and safe packaging materials are used
7. Records to permit tracking the history of the manufacturing process
8. Reserve samples of each batch of dietary supplement product are retained and stored under conditions consistent with the product labeling

7.10 How long are records on production processes retained?
(Circle one and enter number of years.)

1. ____ year(s) after expiration date
2. ____ year(s) from date of manufacture
3. Other (Specify): _____

7.11 Does this plant use production and process controls that identify the points, steps, or stages in the manufacturing process to prevent adulteration?

1. Yes
2. No **Skip to Section 8 on page 21**

7.12 Does this plant's production and process controls have specifications that must be met for identity, purity, quality, strength, and composition of components, ingredients, or dietary supplements and packing and labeling materials?
(Circle all that apply.)

1. Yes, for components
2. Yes, for ingredients
3. Yes, for dietary supplements
4. Yes, for packing and labeling materials
5. No, none of the above

7.13 Does this plant conduct tests to monitor the production and in-process control points, steps, or stages to ensure the identity, purity, quality, strength, and composition of components, ingredients, or dietary supplements? (Circle all that apply.)

1. Yes, for components
2. Yes, for ingredients
3. Yes, for dietary supplements
4. No, none of the above

8 Warehousing

Written procedures for **storage procedures** specify how finished products shall be stored to protect against adulteration and deterioration.

- 8.1** Does your warehouse have temperature or humidity controls? (*Circle all that apply.*)
1. Temperature controls
 2. Humidity controls
 3. No temperature or humidity controls
- 8.2** Are there written procedures for **storage procedures** to control against physical, chemical, and microbial adulteration as well as deterioration of the product and container?
1. Yes
 2. No **Skip to question 8.7**
- 8.3** Does plant management verify and keep records that these procedures are being followed?
1. Yes
 2. No **Skip to question 8.5**
- 8.4** Are records made of any corrective actions taken if procedures are **not** followed?
1. Yes, for some procedures
 2. Yes, for all procedures
 3. No
- 8.5** Do your written procedures for warehousing include any of the following? (*Circle all that apply.*)
1. Procedures and records for forward and backward tracing of product
 2. Procedures and records for salvaged products that include product examination and reprocessing as appropriate

- 8.6** How long are records on warehousing retained? (*Circle one and enter number of years.*)
1. ____ year(s) after expiration date
 2. ____ year(s) from date of manufacture
 3. Other (*Specify*): _____

- 8.7** Are there written procedures on proper precautions to **reduce the potential for mix-ups or adulteration or contamination** of ingredients, raw materials, or in-process formulations (e.g., safety controls and operating practices or separation of ingredients)?
1. Yes
 2. No **Skip to Section 9 on page 23**

- 8.8** Does plant management verify and keep records that these procedures are being followed?
1. Yes
 2. No **Skip to Section 9 on page 23**

- 8.9** Are records made of any corrective actions taken if procedures are **not** followed?
1. Yes, for some procedures
 2. Yes, for all procedures
 3. No

9 Consumer Complaints

Written procedures for **consumer complaints** specify how all written and oral complaints regarding products are handled.

9.1 Are there written procedures at the plant or corporate level for handling **consumer complaints**?

1. Yes
2. No **Skip to question 9.6**

9.2 Does management verify and keep records that these procedures are being followed?

1. Yes
2. No **Skip to question 9.4**

9.3 Are records made of any corrective actions taken if procedures are **not** followed?

1. Yes, for some procedures
2. Yes, for all procedures
3. No

9.4 Do your written procedures for handling consumer complaints include any of the following? (*Circle all that apply.*)

1. Procedures for handling all written and oral complaints
2. Records concerning the handling of complaints including any investigations, investigation findings, and follow-up action taken
3. Procedures for requiring reporting of serious adverse events to FDA MEDWATCH

9.5 How long are records on consumer complaints retained at the plant or corporate headquarters? (*Circle one and enter number of years.*)

1. ____ year(s) after expiration date
2. ____ year(s) from date of manufacture
3. Other (*Specify*): _____

9.6 What are your procedures for handling adverse events associated with consumer complaints? *(Circle all that apply.)*

1. Incident is reported to FDA
2. Product is tested for identity and composition
3. Product is reformulated
4. Product is recalled
5. Other *(Specify)*: _____

9.7 Does this plant have a recall procedure in place?

1. Yes
2. No

9.8 Who evaluates reports on consumer complaints? *(Circle all that apply.)*

1. In-house medical personnel
2. In-house scientific personnel
3. In-house quality control personnel
4. In-house regulatory affairs personnel
5. Outside contractor
6. Other *(Specify)*: _____

10 Your Plant

10.1 What was the calendar year during which this plant was built? *(If multiple buildings, use date of oldest building.)*

10.2 What was the calendar year during which the **dietary supplement operations** began at this plant? *(If multiple buildings, use date of earliest operation.)*

10.3 What is the total square footage of this plant? *(Include warehouse facilities.)*

_____ square feet

10.4 Are this plant's facilities connected to a city water supply?

1. Yes **Skip to question 10.6**
2. No

10.5 Is the water supply at this plant potable?

1. Yes
2. No

10.6 Does your company own plants at other locations?

1. Yes
2. No

10.7 How many employees are currently employed at this plant? *(Include contract/temporary employees.)*

- a. Full-time _____
- b. Part-time _____

10.8 How many employees employed at this plant are working in **quality control**? *(Include contract/temporary employees.)*

- a. Full-time _____
- b. Part-time _____

10.9 For the most recent fiscal year, provide the number of batches of **dietary supplement** product by product form. (Enter the number of batches for each form; if none, enter zero.)

- a. Powder _____ batches
- b. Liquid _____ batches
- c. Paste _____ batches
- d. Capsule _____ batches
- e. Tablet or caplet _____ batches
- f. Gelcap _____ batches
- g. Other (Specify): _____ batches
- h. Other (Specify): _____ batches
- Total _____ batches

10.10 What were the gross sales revenue for the **dietary supplement operations only** at this plant for the most recent fiscal year? (Your responses will be kept completely confidential; that is, information identifying your plant will not be linked to your responses. Do not include nonsales revenue such as interest income.)

- 1. Less than \$500,000
- 2. \$500,000 to just under \$1 million
- 3. \$1 to just under \$2.5 million
- 4. \$2.5 to just under \$5 million
- 5. \$5 to just under \$10 million
- 6. \$10 to just under \$20 million
- 7. \$20 to just under \$50 million
- 8. \$50 to just under \$100 million
- 9. \$100 to just under \$500 million
- 10. \$500 million or more

**Appendix B:
Lead Letter
and Brochure**

**LEAD LETTER**Food and Drug Administration
Washington DC 20204

November 24, 1999

Quality Assurance Manager
[Company]
[Street Address]
[City, State ZIP]

Dear Sir/Madam:

I am writing to ask your participation in a very important study. The Food and Drug Administration (FDA) has contracted with the Research Triangle Institute (RTI) to conduct a nationwide survey of establishments that manufacture, pack, and/or hold dietary supplements. The purpose of the survey is to learn about the existing manufacturing practices in the dietary supplement industry. Results of the survey will add to the agency's understanding of the economic impact that any proposal to establish current Good Manufacturing Practice (cGMP) regulations may have on both large and small firms in the dietary supplement industry. Your establishment is among 400 dietary supplement establishments randomly selected to participate in the survey. Your participation is crucial for its success.

RTI is a not-for-profit contract research organization located in North Carolina with an established history of conducting economic research for FDA and other government agencies. A representative from RTI will soon be calling you to ask for your cooperation. RTI will then send you a copy of the survey to complete at your convenience. The survey includes questions about your establishment and its manufacturing practices. After completing the survey, please return it in the postpaid envelope provided within five business days of receipt. Individual data collected by RTI for this study will be kept strictly confidential. Only anonymous data (no identifying information on your firm) will be provided to the FDA. The name of your establishment will not be linked to your responses. All study participants will receive a copy of the report summarizing the survey findings.

If you have any questions about the survey, please do not hesitate to contact Peter J. Vardon with FDA, or Heather Carter-Young with RTI, both listed on the enclosed brochure, or me at (202) 205-5657. We thank you in advance for your cooperation.

Sincerely,

Richard A. Williams, Ph.D.
Director, Division of Market Studies
Office of Scientific Analysis and Support
Center for Food Safety and Applied Nutrition

**How can I find out more
about the study?**

*For further information on this study,
please contact one of the following indi-
viduals:*

Mr. Peter Vardon

US Department of Health and Human
Services

Food and Drug Administration

330 C Street, SW

Washington, DC 20204

Phone: 202-205-5329

E-mail: pvardon@bangate.fda.gov

Ms. Heather Carter-Young

Center for Economics Research

Research Triangle Institute

3040 Cornwallis Road

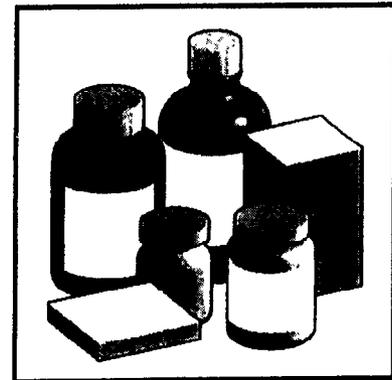
PO Box 12194

Research Triangle Park, NC 27709

Phone: 800-334-8571 x8331

E-mail: cyoung@rti.org

**Survey of
Manufacturing
Practices in
the Dietary
Supplement
Industry**



FDA

U.S. Food and Drug Administration

BROCHURE

BROCHURE (CONTINUED)

B-4

What's this study about?

The Survey of Manufacturing Practices in the Dietary Supplement Industry is being conducted by the Food and Drug Administration (FDA). The purpose of the survey is to learn about the existing manufacturing practices in the dietary supplement industry. The survey results will add to the agency's understanding of the economic impact that any proposal to establish current Good Manufacturing Practice (cGMP) regulations may have on both large and small firms in the dietary supplement industry.

The survey asks about manufacturing practices for the following:

- Personnel
- Buildings and Facilities
- Equipment
- Quality Control and Laboratory Operations
- Production and Process Controls
- Warehousing
- Consumer Complaints

Who is conducting the survey?

The survey was commissioned by FDA and is being conducted by the Research Triangle Institute (RTI). RTI is a not-for-profit contract research organization located in North Carolina with an established history of conducting economic research for FDA and other government agencies. RTI will collect the individual survey data, summarize the information, and provide results to FDA.

How was I selected to participate?

Your plant is one of 400 dietary supplement plants randomly selected from a nationwide sample to participate in the survey.

Is the survey confidential?

Absolutely! Individual data collected by RTI for this study will be kept *strictly confidential*. Only anonymous data (no identifying information on your firm) will be provided to the FDA. The name of your establishment will not be linked to your responses.

How long does it take?

A representative from RTI will contact you by telephone to identify the most appropriate person at your plant to complete the survey and to get the correct mailing address. This call will take about 5 minutes. RTI will then send you the mail survey to complete at your convenience. The mail survey will take about an hour to complete.

Why should I participate?

The Survey of Manufacturing Practices in the Dietary Supplement Industry is important for the FDA, your plant, and the dietary supplement industry.

Participation is voluntary, but we cannot substitute another plant if you decide not to participate. Information on this plant is important to the analysis being conducted by FDA.

All study participants will receive a copy of the report summarizing the survey findings.

**Appendix C:
Weighting
Procedures**

Survey weights were computed in several steps:

1. Initial sampling weights were computed to reflect the different probabilities of selection induced by the sampling design (i.e., by using different sampling rates in the various strata).
2. We then used weighting classes to adjust these weights for nonresponse to the initial telephone interview.
3. Because our population included Canadian establishments that were not eligible for the survey, we post-stratified to adjust to the population size excluding Canadian establishments.
4. We made a second nonresponse adjustment for nonresponse to the mail survey.

Nonresponse adjustments ensure that, within each weighting 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, also tend to reduce the biases of nonresponse to the extent that weighting classes are homogeneous.

We describe each step in more detail below.

C.1 INITIAL SAMPLING WEIGHTS

We first assigned each selected establishment (i.e., sample point) an initial sampling weight. The initial sampling weight is equal to the inverse of the selection probability where the selection probability is equal to the stratum sample size (n) divided by the stratum population (N). Thus, for each of the 16 product type and size sampling stratum we calculated the initial sampling weights as follows:

$$W_0 = \frac{\text{population size (N) for stratum}}{\text{sample size (n) for stratum}} \quad (\text{C.1})$$

The sum of the initial sampling weights across all sampled establishments in a stratum is equal to the population for that stratum.

C.2 NONRESPONSE ADJUSTMENT FOR INITIAL TELEPHONE INTERVIEW (PART 1)

Next, we adjusted the initial sampling weights for nonresponse to the initial telephone interview (Part 1). To reduce the potential bias caused by nonresponse, we divided the population into mutually exclusive groups or weighting classes. We then adjusted the sampling weights of responding establishments in each weighting class so that the sum of the weights equals the number of eligible establishments in the weighting class.

We defined the weighting classes by collapsing the 16 sampling strata into 9 weighting classes. We collapsed strata or cells if there were less than 20 Part 1 respondents in a cell. Because of the unique characteristics of large establishments and the small number of large respondents, we defined one weighting class for large respondents. For the vitamins and minerals and the other product type categories, we collapsed the very smalls and unknowns into one weighting class. For the amino acids/proteins/animal extracts product type, we collapsed the very smalls, smalls, and unknowns into one weighting class.

We calculated adjustment factors (F_1) within each of the nine weighting classes as follows:

$$F_1 = \frac{\text{sum of weights } (W_0) \text{ for eligibles in class}}{\text{sum of weights } (W_0) \text{ for respondents}_{\text{part 1}} \text{ in class}} \quad (\text{C.2})$$

The adjusted weight for each responding establishment in a weighting class is equal to

$$W_1 = W_0 \cdot F_1 \quad (\text{C.3})$$

C.3 POST-STRATIFICATION ADJUSTMENT

Because our population included Canadian establishments that were not eligible for the survey, we post-stratified to adjust to the population size excluding Canadian establishments. We used the same weighting classes for this adjustment as described above. The post-stratification adjustment factor for each weighting class is equal to

$$F_2 = \frac{\text{revised population size in class} \\ \text{(excludes Canadian establishments)}}{\text{sum of weights for non-Canadian} \\ \text{respondents and ineligibles in class}^1} \quad (\text{C.4})$$

The adjusted weight for each responding establishment in a weighting class is equal to

$$W_2 = W_1 \cdot F_2 \quad (\text{C.5})$$

C.4 NONRESPONSE ADJUSTMENT FOR MAIL SURVEY (PART 2)

We adjusted the sampling weights for nonresponse to the mail survey using the same approach described for Part 1. Because of the small number of respondents in the other product type category, we collapsed the two weighting classes into one, for a total of eight weighting classes for the Part 2 nonresponse adjustment.

We calculated adjustment factors (F_3) within each weighting class as follows:

$$F_3 = \frac{\text{sum of } W_2 \text{ weights for} \\ \text{eligible respondents}_{\text{part 1}} \text{ in class}}{\text{sum of } W_2 \text{ weights for} \\ \text{respondents}_{\text{part 2}} \text{ in class}} \quad (\text{C.6})$$

The final adjusted weight (W_3) for each responding establishment in a weighting class is equal to

$$W_3 = W_2 \cdot F_3 \quad (\text{C.7})$$

After computing the weights, we found that one respondent had a relatively large weight. This company was the only respondent in the vitamin and minerals/unknown stratum, and it was in the vitamin and minerals and small analysis domains. We computed unequal weighting design effects with and without this observation included in the analysis domains to determine the impact of the unequal weights. We found that the difference in design effects was significant. To correct for this, for weighting purposes we moved this respondent from the vitamin and minerals/unknown stratum to the vitamin and mineral/small stratum (to match the

¹For the post-stratification adjustment we included ineligibles since the population we are adjusting to includes ineligibles.

respondent's reporting domain) and assigned the corresponding initial weight. We then re-computed the weights for the vitamin and minerals stratum. The weights for the other product types did not change.

We weighted all results using the final adjusted weights (W_3). The sum of the final adjusted weights across all respondents to the mail survey is equal to the population of eligible establishments.

Table C-1 shows the estimated eligible population by the product type and establishment size reporting domains (as defined in Section 4).

Table C-1. Estimated Eligible Population

	Number of Respondents	Estimated Eligible Population
<i>Product Type</i>		
Vitamins and Minerals	118	610
Amino Acids/Proteins/Animal Extracts	16	36
Herbals and Botanicals	97	243
Other	7	17
Total	238	906
<i>Establishment Size</i>		
Very Small	110	394
Small	114	465
Large	14	47
Total	238	906

**Appendix D:
Weighted Results by
Establishment Size**

The results for each section of the survey are reported in a separate table (e.g., Table D-1 corresponds to Section 1 of the survey). For each question response item, we provide the number of respondents who circled that answer (n), the proportion of respondents who circled that answer (%), and the 95 percent confidence interval for the point estimate (Low and High values). Where appropriate, we report the mean response.

The totals for a question may not always sum to 100 percent due to rounding. We have indicated with an (*) when respondents could select more than one response.

Because of the skip patterns, the number of respondents varies by question. We excluded from the analysis respondents who appropriately skipped questions. For example, respondents who answered 2 (No) to Question 2.5 were not included in the frequency for Question 2.6.

Table D-1. Weighted Responses for Section 1: Products and Markets

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
1.1* Which of the following describes the dietary supplement operations at this plant?																
1. Manufacturer—manufacture dietary supplements from ingredients, may label the product it to a repackager/encapsulator or distributor	62	53.49	39.87	66.62	75	68.51	56.62	78.39	9	62.59	34.80	83.98	146	61.68	53.00	69.67
2. Repackager/relabeler/encapsulator—relabel, or encapsulate dietary supplements manufactured by another firm	23	26.64	15.96	40.99	41	41.51	30.25	53.74	3	23.50	7.35	54.33	67	34.11	26.27	42.93
3. Ingredient or ingredient supplier—supply ingredients or bulk finished products to manufacture dietary supplements at this plant or another firm	30	21.92	13.28	33.98	45	38.63	27.75	50.79	4	30.48	11.81	58.95	79	30.94	23.54	39.48
4. Distributor—distribute products manufactured by this plant or another firm	59	56.64	43.09	69.27	70	57.07	44.96	68.39	6	42.14	19.45	68.73	135	56.10	47.35	64.49
5. Importer—import ingredients for further processing or finished products for distribution	28	23.47	14.06	36.50	40	35.00	24.42	47.31	5	37.66	16.18	65.40	73	30.13	22.72	38.75
6. Exporter—export ingredients for further processing or finished products for distribution	31	29.14	18.23	43.13	43	37.47	26.69	49.66	6	42.83	20.02	69.17	80	34.13	26.42	42.79
7. Other	7	3.64	1.73	7.51	3	4.58	1.15	16.52	0	0.00	0.00	0.00	10	3.93	1.62	9.21
No answer	1	0.54	0.07	3.82	1	1.14	0.16	7.81	0	0.00	0.00	0.00	2	0.82	0.18	3.67

(continued)

Table D-1. Weighted Responses for Section 1: Products and Markets (continued)

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
1.2 For your dietary supplement operations at this plant, what is the product type for your primary line of business? ^a																
1. Vitamins and minerals	15	24.13	13.49	39.36	36	42.35	31.35	54.16	9	68.59	40.88	87.34	60	35.81	28.19	44.22
2. Herbals and botanicals, not including extracts	32	25.98	16.02	39.22	24	17.81	10.51	28.56	2	17.68	4.31	50.61	58	21.35	15.21	29.12
3. Herbal and botanical extracts	39	26.98	18.12	38.17	24	17.27	10.46	27.17	1	4.49	0.61	26.47	64	20.82	15.40	27.52
4. Amino acids	1	0.57	0.08	4.01	2	0.95	0.23	3.77	1	4.73	0.64	27.56	4	0.98	0.38	2.51
5. Protein products	5	5.96	1.73	18.57	5	2.33	0.96	5.52	1	4.51	0.61	26.58	11	4.02	1.73	9.06
6. Animal extracts	0	0.00	0.00	0.00	0	0.00	0.00	0.00	0	0.00	0.00	0.00	0	0.00	0.00	0.00
7. Concentrates, metabolites, and constituents	3	1.71	0.51	5.56	1	2.95	0.41	18.36	0	0.00	0.00	0.00	4	2.26	0.56	8.65
8. Other	6	9.59	3.42	24.13	5	4.87	1.38	15.76	0	0.00	0.00	0.00	11	6.66	3.05	13.95
Respondent selected multiple responses	7	3.96	1.84	8.29	16	11.02	6.34	18.47	0	0.00	0.00	0.00	23	7.37	4.71	11.35
Non-dietary supplement product	1	0.57	0.08	4.01	1	0.46	0.06	3.26	0	0.00	0.00	0.00	2	0.48	0.12	1.94
No answer	1	0.54	0.07	3.82	0	0.00	0.00	0.00	0	0.00	0.00	0.00	1	0.24	0.03	1.67

(continued)

Table D-1. Weighted Responses for Section 1: Products and Markets (continued)

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
1.3* What other product types, not including your primary line of business, do you produce at this plant? By product, on average, do you manufacture, repack, relabel/encapsulate, supply ingredients, distribute, import, or export?																
1. Vitamins and minerals	23	30.40	18.75	45.27	34	34.43	23.78	46.91	1	11.15	1.56	49.74	58	31.46	23.74	40.36
2. Herbals and botanicals, not including extracts	32	38.86	26.24	53.17	61	62.42	51.01	72.59	4	30.48	11.81	58.95	97	50.50	42.18	58.80
3. Herbal and botanical extracts	28	24.48	14.91	37.48	54	49.23	37.54	61.01	3	22.86	7.46	52.17	85	37.09	29.19	45.76
4. Amino acids	13	16.30	8.28	29.59	40	46.13	34.85	57.83	2	15.24	3.77	45.23	55	31.55	24.05	40.16
5. Protein products	10	12.11	5.20	25.69	30	35.59	24.94	47.89	1	7.62	1.03	39.47	41	23.92	17.18	32.28
6. Animal extracts	10	10.68	4.45	23.48	17	22.76	13.65	35.45	0	0.00	0.00	0.00	27	16.31	10.33	24.80
7. Concentrates, metabolites, and constituents	9	9.11	3.74	20.53	19	25.56	15.98	38.27	1	7.62	1.03	39.47	29	17.47	11.49	25.67
8. Other	3	1.47	0.46	4.59	4	1.89	0.71	4.95	1	6.54	0.90	34.91	8	1.95	0.97	3.90
Non-dietary supplement product	8	4.30	2.13	8.49	11	7.95	4.13	14.74	4	27.37	10.18	55.61	23	7.38	4.81	11.18
No other product types	32	20.62	13.11	30.88	13	10.05	4.85	19.68	3	19.73	6.12	48.07	48	15.15	10.51	21.34
1.4 Does this plant produce any food products other than dietary supplements?																
1. Yes	12	6.81	3.77	11.99	39	32.28	22.26	44.25	1	7.62	1.03	39.47	52	19.92	14.19	27.22
2. No	96	91.86	86.32	95.28	74	66.58	54.59	76.75	13	92.38	60.53	98.97	183	78.92	71.57	84.77
Don't know	1	0.54	0.07	3.82	0	0.00	0.00	0.00	0	0.00	0.00	0.00	1	0.24	0.03	1.67
No answer	1	0.79	0.11	5.53	1	1.14	0.16	7.81	0	0.00	0.00	0.00	2	0.93	0.22	3.86

(continued)

Table D-1. Weighted Responses for Section 1: Products and Markets (continued)

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
1.5 Does this plant produce any over-the-counter (OTC) or prescription (Rx) drugs?																
1. Yes, OTC drugs	9	6.12	3.01	12.03	17	11.42	6.75	18.67	4	29.40	11.26	57.76	30	10.06	6.94	14.36
2. Yes, Rx drugs	0	0.00	0.00	0.00	0	0.00	0.00	0.00	0	0.00	0.00	0.00	0	0.00	0.00	0.00
3. Yes, OTC and Rx drugs	3	4.58	0.97	19.03	12	8.75	4.73	15.64	4	34.01	13.51	62.97	19	8.26	4.84	13.75
4. No	95	85.10	73.01	92.34	84	78.69	69.95	85.42	6	36.59	16.18	63.29	185	79.26	72.90	84.45
Don't know	1	0.54	0.07	3.82	0	0.00	0.00	0.00	0	0.00	0.00	0.00	1	0.24	0.03	1.67
No answer	2	3.67	0.76	15.94	1	1.14	0.16	7.81	0	0.00	0.00	0.00	3	2.18	0.61	7.47
1.6* Is this plant a member of any of the following trade organizations?																
1. American Herbal Products Association (AHPA)	40	23.69	16.74	32.40	41	25.29	18.03	34.24	2	11.02	2.65	36.03	83	23.85	19.26	29.13
2. Consumer Health Products Association (CHPA) (formerly known as Nonprescription Drug Manufacturers Association)	3	4.79	1.07	19.01	9	6.84	3.33	13.54	4	27.35	10.17	55.59	16	7.03	3.85	12.51
3. Council for Responsible Nutrition (CRN)	7	10.39	3.95	24.66	20	20.82	12.57	32.47	5	34.97	14.78	62.52	32	17.03	11.33	24.80
4. National Nutritional Foods Association (NNFA)	44	40.02	27.69	53.76	65	60.88	49.32	71.34	4	26.27	9.73	54.09	113	50.00	41.46	58.54
5. Utah Natural Products Alliance (UNPA)	1	0.52	0.07	3.66	5	3.48	1.34	8.77	0	0.00	0.00	0.00	6	2.01	0.84	4.72
6. Other	13	13.02	6.25	25.14	21	16.53	9.76	26.63	2	12.35	2.89	40.02	36	14.79	9.77	21.76
Not applicable	35	32.11	20.80	45.98	26	19.78	12.45	29.95	5	38.52	16.69	66.21	66	26.12	19.38	34.21
Don't know	1	0.54	0.07	3.82	0	0.00	0.00	0.00	0	0.00	0.00	0.00	1	0.24	0.03	1.67

^aThe primary line of business is the line of business that contributes to the majority of revenues—either greater than 50 percent of revenues or the greatest of several lines such as 35 percent if all other lines contribute less.

*Total may sum to greater than 100% because respondents could select more than one answer.

Table D-2. Weighted Responses for Section 2: Good Manufacturing Practices (GMPs)

	Very Small (n = 110)				Small (n = 114)				Large (n = 14)				Overall (n = 238)			
	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
			Low	High			Low	High			Low	High			Low	High
2.1 Does this plant follow a published <i>Good Manufacturing Practices (GMPs)</i> model for the dietary supplement products produced at this plant?																
1. Yes	61	51.76	38.26	65.02	86	72.97	60.63	82.55	12	88.98	63.97	97.35	159	64.60	56.09	72.27
2. No (Skip to question 2.3)	39	41.82	29.05	55.79	24	23.83	14.72	36.19	0	0.00	0.00	0.00	63	30.39	23.11	38.82
Not applicable (Skip to question 2.3)	6	3.22	1.44	7.03	1	0.48	0.07	3.41	1	6.54	0.90	34.91	8	1.99	1.00	3.93
No answer	4	3.20	1.09	9.00	3	2.72	0.81	8.77	1	4.49	0.61	26.47	8	3.02	1.42	6.31
2.2* (If 2.1 is Yes) Which of the following are your GMPs for dietary supplement operations patterned after?																
1. FDA Food CGMPs (21 CFR Part 110)	41	68.55	49.65	82.81	52	63.99	51.66	74.72	6	51.86	24.92	77.75	99	64.70	55.38	73.03
2. Advance Notice of Proposed Rulemaking for Dietary Supplements	14	25.99	12.46	46.42	23	33.09	21.21	47.61	4	38.22	15.16	68.19	41	30.99	21.92	41.81
3. National Nutritional Foods Association (NNFA) GMPs	13	27.73	13.66	48.21	25	30.16	19.33	43.77	1	8.57	1.14	43.12	39	27.75	19.09	38.47
4. FDA Drug CGMPs (21 CFR Parts 210 and 211)	10	16.66	6.72	35.71	29	33.57	22.18	47.26	9	73.84	41.22	91.91	48	30.59	22.09	40.67
5. U.S. Pharmacopeia (USP) GMPs	10	16.56	6.64	35.65	25	36.72	24.92	50.37	7	56.71	28.31	81.29	42	31.15	22.39	41.50
6. Other	10	20.46	8.52	41.54	7	4.76	2.01	10.83	1	8.57	1.14	43.12	18	10.50	5.45	19.27
Don't know	1	1.05	0.14	7.30	0	0.00	0.00	0.00	0	0.00	0.00	0.00	1	0.36	0.05	2.59
No answer	1	1.00	0.14	7.01	0	0.00	0.00	0.00	0	0.00	0.00	0.00	1	0.35	0.05	2.48
(Skip to question 2.3)																

(continued)