NOTICE

This guideline provides information to dietary supplement[1] ingredient manufacturers who wish to participate in the United States Pharmacopeia's Dietary Ingredient Verification program (USP-DIVP).

The USP-DIVP is designed to assist participants in assuring their customers–dietary supplement manufacturers—that the manufactured ingredient is of good quality. USP considers this a cooperative effort between USP and participants. USP welcomes suggestions for improvements to the program. Success in meeting the requirements of this program will result in a special USP mark for use in a certificate of analysis or similar document. Barring safety concerns (*see Product Recall*), USP maintains the confidentiality of information gained through the verification process. The primary public manifestation of adherence to the program is the certification mark.

This guideline does not constitute a legal and binding contract between USP and the participant. In the event of a conflict between this guideline and the USP-DIVP License Agreement, the terms and conditions of the License Agreement shall have precedence over the terms and conditions of this guideline.

USP does not endorse, guarantee, or warrant the goods and services offered by USP-DIVP participants. USP shall not be liable for any damages whatsoever, including bodily harm and/or property damage that may result from an ingredient of a participant verified in the USP-DIVP. USP reserves the right to change or terminate the USP-DIVP at any time without notice. USP reserves the right to disqualify companies that violate any of the USP-DIVP requirements from participating in the program.

The information in this guideline, including but not limited to text and images herein and their arrangement, is copyrighted.

[1] USP understands that the term *dietary supplement* in the US has different meanings in other countries. Non-US terms include: botanicals, herbals, herbal medicines, and nutraceuticals.

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1. OVERVIEW

The USP's Dietary Ingredient Verification (USP-DIVP) Program is one of several public health programs of the United States Pharmacopeia (USP). Participation is voluntary and open to participants manufacturing dietary supplements ingredients for use in dietary supplement products. USP uses US definitions of dietary supplements to include vitamins, minerals, amino acids, botanical extracts and non-botanicals, and other non-botanical substances that are used in the manufacture of dietary supplement products.

The USP-DIVP includes:

- Evaluation of manufacturers' quality systems through audit for compliance with Good Manufacturing Practices.
- Review of manufacturing and quality control documents for products submitted for certification.
- Laboratory evaluation of ingredient samples from selected lots for compliance with label claim and program requirements.
- Grant of the USP-DIVP certification mark.
- Post-certification surveillance testing of ingredients bearing the USP-DIVP certification mark.

The use of the distinctive USP-DIVP certification mark is granted for ingredients that successfully meet USP-DIVP requirements. The mark indicates the certification of ingredient quality by a trusted and established authority. It provides assurance that:

- The manufacturer's quality system helps to ensure that the ingredient evaluated meets its label or certificate of analysis claim for identity, strength, purity, and quality, and that it is consistent in quality from batch to batch.
- The ingredient is prepared under accepted manufacturing practices.
- The ingredient meets requirements for acceptable limits of contamination.

2. CRITERIA FOR PARTICIPATION

Participants in the USP-DIVP agree to:

- Complete the license agreement.
- Submit requested data and documentation.
- Subject their ingredients and facilities to all reviews, audits, tests, and other requirements specified in the program.
- Abide by the decisions made in accordance with the rules and requirements of the USP-DIVP.
- Operate in accordance with the provisions of relevant national regulations.
- Ensure that ingredients submitted for review meet the requirements specified in *USP–NF* where applicable. In the absence of *USP–NF* standards for such ingredients, ensure that adequate data is submitted for substantiation of the quality of the ingredient(s). Citation for compliance with other recognized pharmacopeias, such as the European Pharmacopoeia, British Pharmacopoeia, Japanese Pharmacopoeia, would be considered adequate quality specifications.
- Provide stability data for the declared shelf-life of the ingredient.
- Pay all fees required by USP agreements or by documents executed between the participant and USP.
- Act in compliance with the USP-DIVP Certification Mark Usage Manual that gives details regarding the placement of the USP ingredient certification mark on ingredient labels and guidelines for advertising.

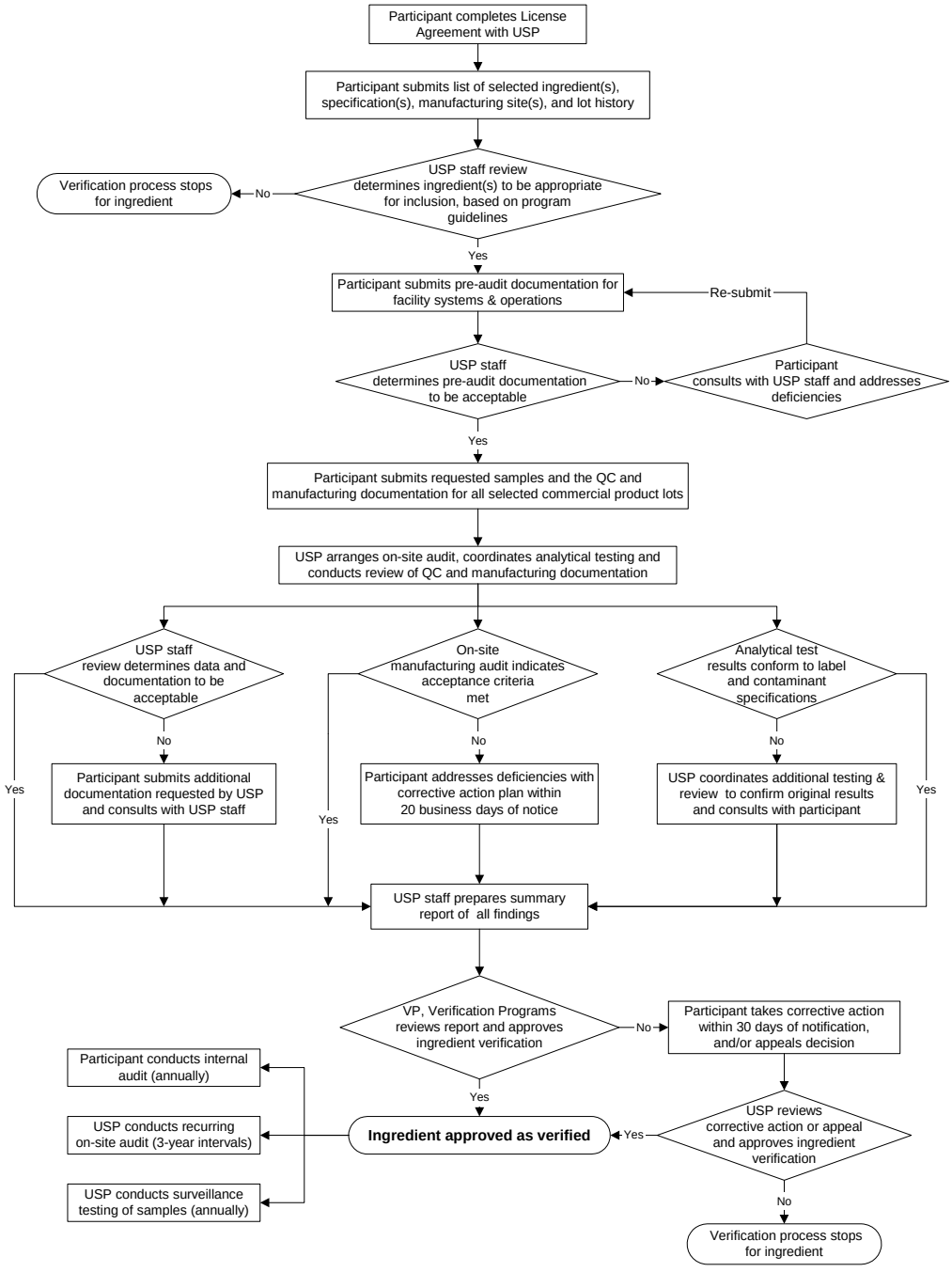
3. REQUIRED PROCESS AND SUBMISSIONS

Participants in the USP-DIVP shall:

- Appoint a duly authorized representative to execute a "License Agreement."
- Provide the list of ingredients for which certification is sought, with lot history (dating back two years) of the ingredients manufactured under the current quality system.
- Enable USP to sample ingredients lots, specified by USP staff.
- Submit the following documentation as described in the guideline (see Forms and Checklists):

    1. Checklist for Pre-Audit Documentation.
    2. Checklist for Quality Control Documentation.
    3. Checklist for Manufacturing Documentation.

4. PROCESS FLOW CHART



5. USP-DIVP INGREDIENT MATRIX

Ingredient	Categorization
Vitamins	Each vitamin will be considered a separate ingredient. Different ester or salt forms of the vitamin will be considered separate ingredients. For example, Vitamin A acetate and Vitamin A palmitate are esters of the same ingredient Vitamin A but will be considered separate ingredients. Similarly, Thiamine hydrochloride and Thiamine mononitrate are salts of the same ingredient Thiamine (Vitamin B1) but are considered separate ingredients. Niacin and Niacinamide are considered different ingredients.
Minerals	Each mineral element will be considered a separate ingredient. Different inorganic salts of the same mineral are considered different ingredients. For example, calcium carbonate, calcium gluconate, calcium citrate are all considered different ingredients. All organometallic compounds are considered different ingredients.
Amino Acids	Each amino acid will be considered a separate ingredient.
Botanical Extracts	Extracts of different species of the same genus will be considered different ingredients. Also, extracts from different plant parts of the same plant species will be considered different ingredients.
Other Dietary Ingredients	This category includes other non botanical dietary ingredients, and other substances that are used as either active or inactive ingredients in the manufacture of dietary supplements, functional foods and other related products.

Note: Participants that manufacture multiple salts, esters, etc. of vitamins and minerals will have special consideration and their ingredients will be categorized based on agreed categories between USP and the participant at the time of submission.

INGREDIENT ACCEPTANCE

Upon completion of the license agreement, the participant submits to USP a list of ingredients for which certification is sought. The USP staff, in consultation with USP's Council of Experts and its appropriate Expert Committees, will review the list of ingredients to confirm that the ingredients are appropriate for inclusion in the program. The participant submits to USP the ingredient lot history (lot number, description of the lot number coding system, date of manufacture, manufacturing facility, and lot size) for all lots of the ingredient (dating back two years) submitted for certification that have been manufactured under the current quality systems.

Ingredients for which there are official or proposed *USP–NF* standards are on the current "Approved" list for inclusion in the USP-DIVP.

All ingredients for which there are no official or proposed *USP-NF* standards will require an evaluation before the ingredients can be included in the USP-DIVP by USP's Dietary Supplements Information Expert Committee (DSI-EC) in accordance with the established criteria for inclusion.

If all ingredients submitted are on the "Approved" list, or meet the inclusion criteria of USP's Expert Committees, USP will accept the ingredients into the USP-DIVP and move forward with the certification process.

If an ingredient is currently on the "Not Approved" list, or does not meet the inclusion criteria of USP's Expert Committees, it will not be considered for the USP-DIVP.

6. EVALUATION OF PRE-AUDIT DOCUMENTATION

The Checklist for Pre-Audit Documentation (see Forms and Checklists) is used by USP-DIVP as a tool to ascertain information about the participating company, its quality systems, and critical manufacturing information.

The participant should complete the Checklist for Pre-Audit Documentation (See Forms and Checklists) and return it to USP. If, on return of the form, the USP staff informs the participant that additional information is required, such information should be submitted within ten business days. The USP-DIVP's Observation(s)/Corrective Action Plan(s)/Supplemental Information Form (See Forms and Checklists) is used.

> Note that the requested information must be submitted in the format indicated on the Checklist for Pre-Audit Documentation. The requested information needs to be submitted in a three-ring binder. Complete documentation needs to be received before the review process can begin.

In evaluating the Checklist for Pre-Audit Documentation, the absence of any of the following will be determined as deficiencies that will exclude the participant's ingredients from consideration for certification until corrected and implemented.

- Flow chart(s) of process(es)
- Site map/layout
- Organizational chart including all key manufacturing and QA/QC personnel
- Qualifications of key personnel
- Training program
- Table of contents from manufacturing, laboratory, QA and QC SOP manuals
- Receiving and material handling SOPs
- Document management system policy and SOPs
- List of process equipment requiring calibration, preventive maintenance, and cleaning
- Program for calibration and preventive maintenance for process equipment
- Change control policy and procedures
- Program for validation of process, cleaning, and analytical methods
- Label management program
- Deviation program
- Laboratory control procedures
- Sample tracking system
- Program for evaluating shelf life of marketed ingredient
- Starting Chemical or Raw Material Supplier Certification Program
- Contract Laboratory Certification Program
- Complaint Program/Recall Program
- Contract Manufacturer Certification Program

In certain cases, the participant may not have a formally established program for some of the quality systems. If so, the participant can provide a description of their informal process along with a proposed plan and schedule to formalize it.

Deficiencies, if any, will be noted on USP-DIVP's Observation(s)/Corrective Action Plan(s)/ Supplemental Information Form (see Forms and Checklists), and provided to the participant. The participant develops corrective action plans within two weeks of receipt of the notification. USP-DIVP will respond to the proposed action plans within two weeks of receipt. If the plan is acceptable, corrective actions must be implemented within three calendar months of receipt of USP-DIVP's decision. If the information on the corrective action is found acceptable by USP-DIVP, it will proceed with the certification process. If the participant fails to develop and implement corrective action, the certification process will be discontinued.

7. SAMPLING AND SUBMISSION OF INGREDIENT DOCUMENTATION

For each ingredient seeking certification, USP-DIVP will select the lot(s) of each ingredient to be used in the certification process. This decision will be based in part on the lot history for the ingredient and the availability of the ingredient for sampling.

USP will select, at minimum, three ingredient lots for each ingredient for which certification is being sought. These lots may be chosen from current production if samples of earlier production are not in stock.

USP will request that the participant sample the ingredient lot(s) and ship them via overnight mail services to USP-DIVP. Alternatively, USP may decide to send a USP-DIVP representative to perform the sampling.

Ingredients submitted to USP-DIVP should be sampled in the commercial packaging, or in a container closure system similar to that of the commercial packaging. The container needs to be labeled, at minimum, with the following information:

- Company Name
- Ingredient Name
- Material Resource Code
- Material Lot Number
- Date Sampled
- Sampler's Initials
- Quantity of Material

After the ingredient lot has been sampled, USP will request that the participant submit the following documentation for the chosen lot(s).

1. Checklist for Quality Control Documentation
2. Checklist for Manufacturing Documentation

Note that the requested information must be submitted in the format indicated on the Checklist for Quality Control Documentation and the Checklist for Manufacturing Documentation (see Forms and Checklists). The requested information needs to be submitted in a three-ring binder. Complete documentation must be received before the review process can begin.

8. EVALUATION OF QUALITY CONTROL DOCUMENTATION

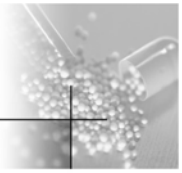
USP will review all quality control documentation submitted (See Checklist for Quality Control Documentation under Forms and Checklists) for ingredients accepted into the USP-DIVP. USP will determine whether the specifications (tests, methods, and acceptance criteria) provided are sufficient to demonstrate consistent and appropriate ingredient quality. USP will review specifications relating to raw materials, in-process and/or intermediate chemicals, final ingredients, packaging and labeling materials, and reference materials as well as validation data, stability data, certificate of analysis, and analytical data from selected lots.

Note that the requested information must be submitted in the format indicated on the Checklist for Quality Control Documentation. The requested information needs to be submitted in a three-ring binder. Complete documentation must be received before the review process can begin.

Raw Materials, Critical/Key Intermediates and Final Ingredients**:** For ingredients for which a *USP–NF,* European Pharmacopoeia (EP), Japanese Pharmacopoeia (JP), or British Pharmacopoeia (BP) monograph exists, USP will verify conformance to the requirements specified in the monograph. If an ingredient does not comply with the monograph, USP will request data supporting the deviation. USP will evaluate the data for acceptance.

For ingredients for which there is no compendial monograph, USP will verify that the specifications provided by the participant are adequate to ensure the identity, strength, purity, and quality, in accordance with the labeling. The specifications will be evaluated, as applicable, for:

- Identification by chemical, spectroscopic, or chromatographic procedures, or by macroscopic/microscopic procedures.
- Content of specific entity or marker(s).
- Heavy metals.
- Residual solvents/organic volatile impurities.
- Known toxic components.
- Insect/foreign matter.
- Pesticide residue.
- Microbial limits.
- Other undesirable components.
- Other quality standards (water, loss on drying, sulfated ash, residue on ignition, organic volatile impurities/residual solvents, pH, etc.).



For critical/key intermediates, the USP will verify that the specifications provided by the participant are adequate to ensure the finished ingredient meets its specifications. Where necessary, either all or some of the key intermediates involved in the manufacture of ingredients under certification will be tested in accordance with compendial specifications or the specifications provided by the participant.

Please refer to the section entitled "Specifications for Raw Material and/or Finished Ingredient" for further details on material specifications.

Packaging and Labeling Materials**:** USP will review descriptions and specifications provided by the participant for packaging materials that are or will be in direct contact with the ingredient (primary packaging materials), as well as samples and specifications provided for labels and labeling materials (i.e., secondary packaging materials).

Reference to the *USP–NF*, other pharmacopeias and standards on labels or labeling must be completely accurate. Other marks or seals generally cannot be used on the label. Labeling must comply completely with all applicable federal labeling regulations.

The American Herbal Products Association's (AHPA's) publication, *Herbs of Commerce* (revised 2000), which was incorporated into federal labeling regulations by the FDA in 1996, should be consulted regarding the proper Latin Binomial and Standardized Common Name for each botanical species.

Method Validation**:** USP will review documentation for each analytical procedure. If the analytical procedure is found in the *USP–NF,* AOAC International Official Method of Analysis (OMA), the Food Chemical Codex, European Pharmacopoeia (EP), British Pharmacopoeia (BP), or Japanese Pharmacopoeia (JP) or is an AOAC International Peer Verified Method (PVM), there is no need for a complete validation report. In this case, the suitability of the procedure for testing the specific ingredient must be supported by analytical data. The data should demonstrate the accuracy and precision of the analyte determination and lack of interference from other components/excipients with the analyte.

If the analytical procedure is not officially recognized, the procedure should, where possible, be validated according to the *USP–NF* General Chapter <1225> *Validation of Compendial Methods*. If a complete validation is not possible, sufficient information and data showing that the analytical procedure is suitable for its intended use and meets proper standards of repeatability, reliability, and specificity must be provided by the participant.

If the validation data provided by the company does not demonstrate that the procedure is suitable for its intended use, USP will provide recommendations.

Reference Materials: USP-DIVP will check the source of reference materials used to support the ingredient specifications. If USP Reference Standards have been used for *USP–NF* tests, no additional information is needed, other than indication of the lot number of the USP Reference Standard used. For non-USP Reference Standards, USP-DIVP will check to ensure that the characterization data submitted supports the suitability of the material for its intended use.

Stability Data: Procedures used in stability studies will be reviewed to determine if they are able to evaluate ingredient quality attributes such as appearance, content, performance characteristics, microbial counts, etc., that are susceptible to change during storage and likely to influence the ingredient's quality. Data for evaluation includes the following:

- Real-time shelf-life studies
- Accelerated stability data 40° C/75% RH for six months
- Historical information may be acceptable based on the data submitted and the time period the data covers.

Drug Master File: If the company has written and/or filed a Drug Master File (DMF) or similar document for submission to regulatory agencies, the DIVP will accept it in lieu of the aforementioned quality control information. This document should address the key elements listed above in this section.

Certificate of Analysis: USP-DIVP will verify that the analytical results on the certificates of analysis, from actual ingredient lots of which USP-DIVP has requested samples, are in compliance with the specification proposed by the participant. In case of non-compliance, USP-DIVP will provide recommendations.

Data for Sample Lots: USP-DIVP will evaluate data collected from ingredient samples on the basis of the criteria described in the quality control documentation.

Request for Supplemental Information: If the quality control documentation is found unacceptable, incomplete, not in the requested format, or inadequate for any reason, USP-DIVP may return it to the participant for revision and resubmission.

If the quality control documentation is considered unacceptable and USP determines, on discussion with the participant, that the evaluation of additional ingredient samples submitted

by the participant will not add useful data, the entire quality control documentation will be deemed unacceptable and the certification process will be discontinued.

If the quality control documentation is considered unacceptable but, on discussion with the participant, there is sufficient cause for USP to confirm any supplied procedures and/or analytical results, the ingredient samples submitted by the participant will be analyzed either in USP laboratories or in USP-approved contracted laboratories. If the laboratory results support the acceptance of the quality control documentation, USP will proceed to the next step in the certification process. If the laboratory results support the acceptance of the quality control documentation, but lead to other issues, a written report will be sent to the participant asking for comments and additional information. If the laboratory results do not support the acceptance of the quality control documentation, the certification process will be discontinued.

9. EVALUATION OF MANUFACTURING DOCUMENTATION

USP will review all manufacturing documentation (submitted per Checklist for Manufacturing Documentation under Forms and Checklists) for ingredients accepted into the USP-DIVP.

Note that the requested information must be submitted in the format indicated on the Checklist for Manufacturing Documentation. The requested information needs to be submitted in a three-ring binder. Complete documentation needs to be received before the review process can begin.

The documentation submitted must include:

- Master formulas/manufacturing directions/manufacturing guide.
- A process diagram of chemical synthesis, extraction, secondary/tertiary recovery, fermentation, grinding, sifting, sizing, cleaning, etc., if applicable.
- Acceptable procedures for reprocessing which have demonstrated that the lot meets label or certificate of analysis declaration and the stability specification. Alternatively, a statement that reprocessing is not performed would suffice.
- Identification of steps requiring a Quality Control check (particularly critical/key intermediate steps involved in synthesis, extractions, sizing, etc.).
- Executed lot records for lots that USP has sampled.

The lot records should include:

- Manufacturing instructions.
- Packaging instructions.
- In-process data related to the quality control for all intermediates involved in the manufacture of the ingredient (fine chemical) under certification.
- Labeling for the subject lot.
- Indication of QA final release approval.

In-process Control: USP will review specifications provided by the participant for in-process control steps defined in their internal manufacturing and process directions.

10. TESTING OF INGREDIENT SAMPLES

Testing of ingredient samples will begin after USP has determined that the quality control documentation and manufacturing documentation for the ingredient is complete according to the initial request for quality control documentation and manufacturing documentation.

Ingredients will be tested for identification, contamination (microbials, heavy metals, pesticides, known toxic components), and assay content of label and/or certificate of analysis claim.

Please refer to the section entitled "Specifications for Raw Material and/or Finished Ingredient" for further details on specifications for testing of ingredient samples.

USP will coordinate testing of ingredient samples either in the USP laboratories or by one or more approved contract laboratories. A single analysis will be performed for each ingredient specification. Test data will then be evaluated for accuracy and to determine if the ingredient conforms to the specification reported by the participant.

If the test data received conform to the ingredient specification and there are no other issues arising from the test results, USP will proceed to the next step in the certification process.

If the test data do not conform to the ingredient specification or if there are other issues arising from the test results, USP will reevaluate the raw data submitted by the laboratory to confirm the accuracy of test results. If specific analytical errors are found, a sample retest will be requested from the laboratory. The laboratory will be requested to reanalyze the original sample, if possible, in duplicate. If the reanalyzed results agree with the initial test result, all results will be averaged and reported. If the reanalyzed results confirm the suspected analytical error, the resample test results will be averaged and reported.

In the case of nonconforming results, in which there is no determinant error, the laboratory will be requested to reanalyze the original sample, if possible, in duplicate, along with a newly submitted sample of the ingredient lot, in duplicate. Testing on each sample set will be performed by different experienced analysts. If the four reanalyzed results disagree with the initial test result, the average of the four reanalyzed test results will be reported. If the four reanalyzed results agree with the initial test result, all results will be averaged and reported.

In all cases, the reported result will be compared to the participant's specification for determining compliance to label and or Certificate of Analysis claim(s). In the event of a question regarding compliance to participant's specification(s), label, and/or Certificate of Analysis claim(s), the decision by USP shall be final.

11. SPECIFICATIONS FOR RAW MATERIAL AND/OR FINISHED INGREDIENT

As previously indicated, for an ingredient for which a compendial monograph exists, USP will verify conformance to the requirements specified in the monograph. If an ingredient does not comply with the monograph, USP will request submission of data supporting the deviation. USP will evaluate the data for acceptance.

For ingredients for which there is no *USP–NF* monograph, USP will verify that the specifications provided by the participant are adequate to ensure the identity, strength, purity, and quality, in accordance with the labeling.

In regards to identification testing for, and to potential adulterants in botanical material, applicants should consult the Food and Drug Administration's Center for Food Safety and Applied Nutrition's (FDA CFSAN) June 25, 1999, Draft Report of the Food Advisory Committee (FAC) Dietary Supplement Working Group on "Ingredient Identity Testing Records and Retention." Participants should take care to eliminate any known toxic components in their ingredients. Two recent issues concerning toxicity involve aristolochic acid and bovine spongiform encephalopathy (BSE). For information regarding aristolochic acid, refer to FDA's document regarding the "Listing of Dietary Ingredients of Concern" (revised 09APR01). In responding to the requirements for material of animal origin, the European Pharmacopoeia (EP) General Chapter 5.2.8 "Minimizing the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Medicinal Products," and FDA's Web site should be consulted.

Pesticides testing should be conducted according to USP <561> *Articles of Botanical Origin* and should comply with the applicable Federal regulations in the United States. In the United States, dietary supplements are subject to the statutory provisions of the Federal Food, Drug, and Cosmetic Act that govern foods but not drugs. Limits for pesticides for foods are determined by the FDA/EPA and where no limit is set, such as is the case for most botanicals, the limit is zero. For practical reasons, the limit that one can establish for the level of a pesticide in a dietary ingredient or supplement is governed by the detection limit of the chosen analytical procedure. In some cases, analytical procedures for pesticides have been specially developed, with guidance from FDA's Pesticide Analytical Manual (PAM), to achieve lower detection limits than that achievable by USP <561> *Articles of Botanical Origin*. For example, the validated analytical procedure developed for the Council for Responsible Nutrition – American Herbal Products Association (CRN-AHPA) Joint Task Force on Pesticides, for detecting quintozene and lindane pesticides in Ginseng raw material,

powders, and/or extracts needs to be employed for any Ginseng ingredient seeking USP-DIVP certification. For pesticides, when feasible, analytical procedures that can achieve lower detection limits should be employed.

Please refer to the following table regarding specifications for raw material and finished ingredients. For questions or clarification please contact the USP-DIVP staff.

Analyte – Contaminant – Test	Reference – Procedure[1]	Acceptance Criteria
Identification of ingredient or marker(s)	*USP–NF,* AOAC-I, EP, BP FCC, JP	As per procedure
Purity or content of specific entity or marker compound(s)	*USP–NF,* AOAC-I, EP, BP FCC, JP	As per procedure
Absence of adulterants	*USP–NF,* AHPA, FAC	As per reference
Known toxic or undesirable components	*USP–NF,* EP, BP, JP, FDA	As per reference
Insects/foreign organic matters	*USP–NF* <561>	As per monograph, or manufacturer criteria
Organic volatile impurities	*USP–NF* <467>	As per monograph, or manufacturer criteria
Pesticides	*USP–NF* <561>, Pesticides Analytical Manual of FDA	Not detected
Quintozene in Ginseng	Council for Responsible Nutrition—American Herbal Products Association (CRN-AHPA)	Not detected, < 10 ppb
Mycotoxins (e.g. Aflatoxins)	*USP–NF,* AOAC[2]	< 20 ppb
Microbial Enumeration Total aerobic microbial count Molds and yeasts Bile-tolerant Gram-negative bacteria	*USP–NF* <2021>, *USP–NF* <2023>, BAM	Upper limit, in units of cfu per g or mL [3]*A*: 10^5; 10^3; 10^3 *B*: 10^4; 10^3 *C*: 10^4; 10^3 *D*: 10^4; 10^3 *E*: 10^2; 10 *F*: 10^3; 10^2
Viable specific microorganisms *Salmonella* species *Escherichia coli* *Staphylococcus aureus* *Clostridium* species (for chondroitin sulfate)	*USP–NF* <2022>	Absent per 10 g or 10 mL Absent per 10 g or 10 mL Absent per 10 g or 10 mL
Heavy Metals	*USP–NF* <231>	As per monograph, or < 10 ppm
Other quality standards Water Loss on Drying Ash (total, acid-insoluble ash) Residue on Ignition pH	 *USP–NF* <921> *USP–NF* <731> *USP–NF* <561> *USP–NF* <281> *USP–NF* <791>	As per monograph, or manufacturer criteria

[1] Refer to glossary for definitions of acronyms, and to section text for more details.
[2] Aflatoxin AOAC-I Official Methods of Analysis include 991.31 and 999.07.
[3] *A*. Dried or powdered botanicals; *B*. Powdered botanical extracts; *C*. Tinctures; *D*. Fluid extracts; *E*. Infusions/Decoctions; *F*. Other raw materials and dietary supplement ingredients.

12. ON-SITE AUDIT CRITERIA

USP staff auditors and/or approved contract auditors perform the on-site audit of the participant's facilities and operations. The on-site audit will be conducted once every three years.

The audit will be performed when both USP and the participant agree upon a date and time. USP-DIVP will communicate the agenda for the audit of a particular area to the management of that area to ensure the availability of required personnel during the audit. Safety procedures for the laboratory or area being audited will be followed.

The auditors will evaluate the findings of the on-site audit, using the following document as guidance:

- ICH Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients published by the United States Food and Drug Administration (August 2001). The Guidance has been subject to consultation by regulatory parties, in accordance with the ICH process. In this Guidance, the term "manufacturing" is defined to include all of the following operations: receipt of materials, production, packaging, repackaging, labeling, relabeling, quality control, release, storage and distribution of fine chemicals, and the related controls.

Auditors will look for the following criteria:

Organization/Personnel

- Dedicated Quality Assurance/Quality Control department.
- Training program for the competency of all employees.

Document Management

- Program for control of Standard Operating Procedures (SOPs), lot records, analytical procedures, and specifications that include required approvals and revision/archival control, where appropriate.

Equipment/Facilities

- Adequate security to prevent access for unauthorized personnel.
- Adequate size and design of facility.
- Maintenance and calibration of equipment to ensure consistent performance for its intended use.
- Documentation of use, calibration, cleaning, and preventive maintenance of equipment.

Sample/Component Control

- Program for receipt, quarantine, disposition, release, and distribution of incoming materials.
- Designation of all raw materials, manufactured intermediates, and finished ingredients as to their status.
- System of material reconciliation.

Deviations

- Maintenance of deviation logs.
- Policy with time frame—for the disposition of deviations.
- SOP for investigating and analyzing non-conforming results and trends.

Laboratory Controls

- Written analytical procedures and specifications.
- Use of compendial procedures where applicable.
- Use of validated/qualified and appropriate methods.
- Review of data and qualifications.
- Monitoring/tracking of media/reagents prior to use.
- Appropriate maintenance and calibration of laboratory equipment/instruments.

Label Control

- Program for controlling label revision.
- Program for monitoring and use of incoming labels.
- Assurance of accountability of labels.
- Monitoring of regulations as required.

Shelf Life Evaluation

- Program to evaluate ingredient shelf life.
- Testing within defined time frames.
- Formal program for resolution of discrepancies in testing.
- Data to support shelf life of ingredients submitted to USP-DIVP for certification.

Quality Assurance Review

- System to ensure ingredient quality prior to release.

Process Performance Evaluation

- Demonstrated for ingredients submitted to USP-DIVP for certification.

Electronic Records/Computerized Systems

- Proof of performance.
- Appropriate security.
- Appropriate backup.

The on-site audit will be conducted according to the Quality Audit Guideline (See Forms and Checklists). Upon completion of the on-site audit, USP will evaluate the on-site audit findings summarized in an audit report, which will include a list of any deficiencies. The audit report will then be forwarded to the participant along with USP-DIVP's report of any actions that the participant needs to take. The participant will have 20 business days to reply to reported deficiencies with a corrective action plan. Failure to do so will result in the discontinuation of the certification process. Proof of corrective action, with the date of completion or progress made, must be submitted to USP with the company's first self-audit report.

13. USP-DIVP REPORT OF FINDINGS

A report will be issued to participants listing the final determination and status of the issues regarding the various elements of the USP-DIVP as it pertains to the participant. The report will be segregated according to the following elements of the program, as applicable:

- Pre-Audit Documentation
- On-Site Audit
- Ingredient(s)
- Quality Control Documentation for all intermediates and finished ingredient
- Manufacturing Documentation
- Analytical Results at all stages of manufacture.

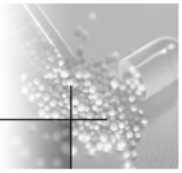
The results for Pre-Audit Documentation and the On-Site Audit apply to the manufacturing site audited and the ingredients manufactured at that site, whereas the results for the ingredient section(s) will be ingredient specific.

The status of the issues or deficiencies within each program element may be divided into three categories: Action Level 1, Action Level 2, and Action Level 3. These three categories differ according to the nature of the issue or deficiency. All Action Levels require some action to be taken by the company.

ACTION LEVEL 1 issues involve a lack of a quality system program element, a lack of essential ingredient criteria, or ingredients identified as having critical deficiencies. Action Level 1 issues may be resolved by supplying essential information or by making major changes to an ingredient/process. Action Level 1 issues involve changes to the current quality system. Action Level 1 issues must be adequately resolved before certification can be given to the ingredient, and may require that the ingredient be resubmitted for certification.

ACTION LEVEL 2 issues involve a lack of information regarding a quality system program element, a lack of significant ingredient criteria, or ingredients identified as having major deficiencies. Action Level 2 issues can be resolved by supplying substantial information or by making minor changes to the ingredient/process. Action Level 2 issues do not involve changes to the current quality system. Action Level 2 issues must be adequately resolved before certification can be given to the ingredient.

ACTION LEVEL 3 issues involve the need for clarifying information or newly requested information regarding a quality system program element, requested improvements to



ingredient criteria, or ingredients identified as having minor deficiencies. Action Level 3 issues can be resolved by supplying additional information or by making requested changes to the ingredient/process. Action Level 3 issues would allow the certification mark to be issued subject to the firm's commitment to address the issues cited within the specified time period.

The status of each category (Pre-Audit Documentation, On-Site Audit, and Ingredients) is indicated by an overall assessment of Pass, Conditional Pass, or Fail, depending on the nature of the issues/deficiencies within each category. The grading system of Pass, Conditional Pass, and Fail is based on the following determination:

PASS indicates that only Action Level 3 issues or deficiencies need to be resolved. Certification would be considered without further qualification, and will be reconsidered based on the company's first self-audit report.

CONDITIONAL PASS indicates that one or more Action Level 2 issues or deficiencies needs to be resolved prior to issuance of the certification mark.

FAIL indicates that one or more Action Level 1 issues or deficiencies need to be resolved. The company would need to make the appropriate change(s) to the ingredient/process and most likely will need to resubmit the ingredient for certification.

The participant understands that compliance with USP-DIVP does not constitute compliance with U.S. federal, state, local, or foreign country requirements. The participant agrees that any sampling, inspections, or tests conducted by USP-DIVP are designed only to verify compliance with USP-DIVP requirements and do not relieve the participant of its responsibility to ensure the quality of its ingredients in the marketplace or to comply with applicable federal, state, local, or foreign country regulations. Compliance with USP-DIVP may not be used as a defense when compliance with legal requirements is an issue. The participant agrees that USP will not be called to testify or otherwise appear on behalf of the participant in any regulatory or other legal proceeding brought by a regulatory agency. USP is not an agent of the participant or acting in capacity thereof.

14. ISSUANCE AND USE OF THE CERTIFICATION MARK

On satisfactory completion of the:

- Evaluation of pre-audit documentation
- Evaluation of on-site audit report
- Evaluation of quality control documentation
- Evaluation of manufacturing documentation
- Testing of ingredient samples

USP will review all labeling that will include the certification mark for the prospective ingredient. USP reserves the right to ask for additional documentation as necessary.

Formal notification of approval to use the certification mark will be made by USP to the participant in writing. The notification will specify which of the participant's ingredient(s) are entitled to the use of the certification mark and other limiting information (such as manufacturing site information) as appropriate.

The certification mark must be used in accordance with the guidelines in the USP-DIVP Certification Mark Usage Manual, which will be provided by USP along with the notification of approval to use the mark. These guidelines relate to:

- Size and color of the certification mark.
- Acceptable format and materials.
- Specifications for reproduction.
- Examples of appropriate and inappropriate use.
- Acceptable and unacceptable usage of the certification mark in advertising and promotional materials, exhibit signage, speaking engagements, presentations, educational materials and events, and on websites.

USP requires submission of artwork for ingredient labels, advertising, promotional, or other materials that include the certification mark for pre-approval. The artwork must be submitted in final mock-up form in color, along with stock (paper) samples and bindery details, if applicable. A specification sheet outlining the strategy/goals of the materials, the target audience, and the number of pieces—if any—to be mailed must be provided along with the artwork. USP may also require actual production copies of artwork using the certification mark to be submitted for evaluation.

Written approval or disapproval of the materials submitted will be provided by USP to the participant within 20 business days. USP may, if necessary, request additional materials from the participant. If the materials are not approved by USP because they are not in accordance with recommended guidelines, USP will notify the participant in writing. The participant will be given an opportunity to correct or adjust deficiencies and resubmit the materials to USP. If requested, USP will work with the participant to bring the materials into compliance.

USP will also periodically survey manufacturing establishments to examine proper usage of the certification mark by licensed users.

News releases and associated references to the USP-DIVP must be submitted to USP for approval prior to release. If desired, USP will also work with the participant on joint news releases. USP will draft, edit, and coordinate approvals of the joint news release and work with the participant to determine the media list for distribution.

A list of licensed participants and licensed ingredients under the USP-DIVP will be made available to the public.

If the certification mark is misused or improperly used, USP will work with the participant licensed to use the certification mark to resolve the problem or any related dispute. USP and the licensed user will agree on a written plan to bring the usage into required compliance. However, if the problem cannot be resolved promptly or to USP's satisfaction, USP will issue a written warning of proposed cancellation of the license to use the certification mark either in its entirety or on an ingredient-specific basis. The warning shall specify the steps required for the participant to come into compliance and avoid cancellation, and a reasonable time period for compliance. In case of continued non-compliance, USP will make a final decision to cancel the participant's license to use the certification mark, either in its entirety or on an ingredient-specific basis. Such a decision may not be appealed by the participant.

Participants are reminded, however, that the terms and conditions set forth in the USP-DIVP License Agreement have precedence over this guideline.

15. NEED FOR RE-EVALUATION AND RENEWAL OF VERIFICATION

After USP has granted approval to use the certification mark, any major changes to an ingredient's specification, process control data, raw material source, equipment, manufacturing site change, testing, or any other criteria deemed by the participant to be essential or significant, must immediately be reported in writing to USP.

A **Major change** is defined as a change that has a substantial potential to have an adverse effect on the identity, strength, quality, and purity of an ingredient as they may relate to the safety or intended use of the ingredient. A major change requires notification to USP and approval by USP prior to implementation. Such notification by the participant must be made in writing with a list of the ingredients that are impacted by such changes, and the rationale for the changes. This type of submission of supplemental information will be classified as PRIOR APPROVAL NOTIFICATION. Such notification shall be clearly marked Prior Approval Notification by the participant. Upon receipt of such notification USP will expedite the review of such notification and communicate its decision within five business days.

A **Moderate change** is a change that has moderate potential to have an adverse effect on the identity, strength, quality and purity of the ingredient as they may relate to the safety or effectiveness of the ingredient. Moderate changes must be communicated by the participant in their Annual Self Audit Report.

A **Minor change** is a change that has minimal potential to have an adverse effect on the identity, strength, quality, and purity as they may relate to the safety and the intended use of the ingredient. Such changes must be communicated by the participant in their Annual Self-Audit Report.

MAJOR CHANGES

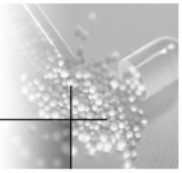
The following are examples of changes that are considered to have a substantial potential to have an adverse effect on the identity, strength, quality, and purity of an ingredient as they may relate to the safety or intended use of the ingredient.

Manufacturing sites:

1. A move to a different manufacturing site, except one used to manufacture or process an intermediate in the manufacture of the ingredient, when the new manufacturing site has never been audited by the USP for the type of operation that is being moved or the move results in a restart at the manufacturing site of a type of operation that has been discontinued for more than two years.
2. A move to a different manufacturing site when the manufacturing site does not have a satisfactory cGMP inspection for the type of operation being moved.
3. A move to a different manufacturing site for the manufacture or processing of an intermediate involved in the manufacture of the ingredient verified by USP or under verification.

Manufacturing process:

1. Change in the route of synthesis of the ingredient.
2. Change from one type of drying process to another (e.g., oven tray, fluid bed dryer, microwave).
3. Changes in solvent used in the manufacturing process.
4. Changes in filtration techniques (e.g., filtration through filter paper to centrifugation or vice versa).
5. Any process change made after the final intermediate processing step in the ingredient manufacture.
6. Changes in the synthesis or manufacture of the ingredient that may affect its impurity profile and/or the physical or chemical or biological properties.
7. For natural products such as botanical extracts or ingredients derived from fermentation processes, changes in source material (e.g., microorganism, plant material) or change in solvent(s).
8. Changes in scale of manufacturing, namely batch size increase or decrease.
9. Change in the production vessel's design and services, such as chill water, hot water, and stirrers, connected to the vessel.
10. Change in the type of vessel used in the production. For example, change from glass-lined reactors to the stainless vessel is considered a major change.
11. Change in the type of antioxidant or preservative used in liquid or semisolid ingredients.



Specifications:

For purposes of defining specifications, *acceptance criteria* are numerical limits, ranges, or other criteria for the tests described. The following are examples of major changes in specifications:

1. Relaxing an acceptance criterion or deleting any part of a specification.
2. Adoption of a new analytical procedure without sufficient rationale for testing raw materials, intermediates, or the final ingredient. An example of this type is a change in the analytical procedure employing high-pressure liquid chromatographic procedure to one employing spectrophotometer or titration.

Package:

1. For liquid and semisolid ingredients, a change to or in polymeric materials (e.g., plastic, rubber) of primary packaging components, when the composition of the components as changed has never been used in a USP-DIVP approved ingredient.
2. For liquid and semisolid ingredients in permeable or semipermeable container closure system, a change to an ink and/or adhesive used on the permeable or semipermeable packaging component to one that has never been used in a USP-DIVP approved ingredient.
3. Deletion of a secondary packaging component intended to provide additional protection to the ingredient (e.g., carton to protect from light, overwrap to limit transmission of moisture or gases).
4. A change to a new container closure system, if the new container closure system does not provide the same or better protective properties than the one used at the time of approval of the ingredient by the USP-DIVP.

Labeling:

1. Change in the labeled storage conditions and expiration dating.
2. Claims of superiority to the same ingredient manufactured by another manufacturer.

Miscellaneous Changes:

An extension or reduction of an expiration period based on data obtained during stability studies.

MODERATE CHANGES

Manufacturing sites:

1. A move to a different manufacturing site for testing, if the new testing facility has the capability to perform the intended testing.

Manufacturing process:

1. Replacement of equipment with that of a similar but not identical design and operating principle that does not affect the process.
2. A change in production control or analytical procedure that provides an increased assurance that the ingredient will have the characteristics of identity, strength, and purity that the ingredient had at the time of certification by USP-DIVP.
3. Any change in the scale of operation of an intermediate (batch size increase or decrease) that involves a different type of equipment for manufacturing.

Specifications:

1. Any change in the analytical procedures for the finished ingredient or raw materials and intermediates, other than editorial, followed by the participant at the time of entering the USP-DIVP.
2. Relaxing an acceptance criterion or deleting a test for raw materials used in the ingredient manufacturing, or in-process materials prior to the penultimate intermediate.
3. Relaxing an in-process acceptance criterion associated with microbiological monitoring of the production environment, materials, and components that are included in the participant's documents submitted to USP-DIVP at the time of entering the program.
4. An addition to a specification that provides increased assurance that the final ingredient submitted for certification will have the characteristics of identity, strength, and purity that it purports or represents to possess.
5. A change in the analytical procedure used for testing components, packaging components, or the penultimate stage intermediate or starting materials that provides the same or increased assurance of the identity, strength, quality, and purity of the material being tested as the analytical procedure described in the submissions of the participant at the time of entering the USP-DIVP.

Package:

1. A change in the dimension of the container closure system such as shape or size.
2. A change in or addition or deletion of a desiccant.
3. A change in the lining material inside the drums.

Labeling:

1. Changes to any cautionary statement on labels such as handling instructions except those as required under local, state, federal, and other applicable regulatory requirements.

MINOR CHANGES

Manufacturing sites:

1. A move to a different manufacturing site, already audited by USP, for secondary packaging.
2. A move to a different manufacturing site, already audited by USP, for labeling.

Manufacturing process:

1. A change in the vessel used for manufacture involving simply replacement of the old vessel with a new one of the same construction material and size.

Specifications:

1. Any change made in the specification made to comply with changes in the official compendium (e.g., *USP–NF*).
2. Tightening of acceptance criteria for the raw materials, intermediates, and final ingredient.

Package:

The following changes in the container closure system are considered minor provided the new package system provides the same or better protective properties (e.g., light, moisture):

1. Changing from metal screw cap to plastic screw cap or vice versa.
2. Changing from one plastic container to another of the same type of plastic (e.g., high-density polyethylene (HDPE) container to another HDPE container).
3. Changes in packaging materials to control odor (e.g., charcoal packets).
4. Changes in bottle filler (e.g., change in weight of cotton or amount used) without changes in the type of filler (e.g., cotton to rayon).
5. A change in or addition of a cap liner.
6. A change in an antioxidant, colorant, stabilizer, or mold-releasing agent for production of the container and/or closure to one that is used at similar levels in the packaging of an ingredient that was submitted to USP-DIVP for certification.

Labeling:

1. Changes in the layout of the package or container label that are consistent with local, state, federal, or other applicable regulations without change in the content of the labeling.
2. Editorial changes such as adding a distributor's name.
3. Labeling changes made to comply with an official compendium.
4. Addition of a foreign language text other than English provided the translation has been approved by a qualified foreign language expert or institution such as embassy or consul general's office.

Miscellaneous changes:

Tightening of acceptance criteria for existing reference standards to provide greater assurance of ingredient purity.

Upon receipt of information of changes, USP will review and determine whether the changes are deemed to be major. The criteria for such determination will be made available, in writing, to the participant. If necessary, USP may require the ingredient or participant to be re-evaluated or the ingredient retested. If re-evaluation is not required, the participant may continue to use the certification mark in accordance with licensed terms.

If re-evaluation is required, USP will immediately notify the participant in writing. USP may also require the participant to cease continued use of the certification mark until the re-evaluation has been completed.

The participant may appeal the decision to require re-evaluation or retesting; however, the participant shall not have the right to appeal the decision requiring them to cease using the certification mark until the final decision is made regarding the status of re-evaluation or retesting.

16. PARTICIPANT'S INTERNAL AUDIT AND ANNUAL REPORTS

Results reported from the participant's internal audit are used to monitor the state of operations within the company after the on-site audit conducted by USP.

The on-site audit will be conducted by USP once every three years. The internal audit must be conducted by the participant annually in the intervening years. To conduct the internal audit, the participant should meet all of the criteria listed in the section ON-SITE AUDIT CRITERIA.

The participant must report the following annually to USP, with the first report due 13 months after initial audit:

- Lot number and date of manufacture of all verified ingredients manufactured.
- Any deviations recorded in these ingredients.
- Audit findings from the internal audit conducted according to the On-site Audit Checklist.

If any compliance issues arise during the review of the annual report, USP reserves the right to conduct an on-site audit.

Companies with multi-national sites will be allowed to submit their corporate audit report for the sites manufacturing the certified ingredient.

17. POST-CERTIFICATION SURVEILLANCE

After the USP-DIVP certification mark is awarded to ingredients, USP will perform at least an annual evaluation of the ingredients to ensure that they continue to meet the criteria to carry the certification mark. Participants will be required to retain samples from their manufacturing to support this surveillance.

USP will contact the participant and request a list of the lots for the certified ingredient(s) produced during the preceding year. From that list, USP will randomly select a minimum of three lots for each ingredient to perform post-certification testing. USP will request samples of the lots from the participant. The samples received by USP will be tested in accordance with the compendial or participant's specification. Consequently, USP will request at a minimum the release specification and analytical procedures used by the participant. USP may also request further documentation based on the ingredient that was certified. USP may do testing beyond the testing specified by the participant's specifications if there is a clear possibility of known contaminants or degradation products.

18. APPEALS

In certain situations USP may suspend, withdraw, or refuse to issue the certification mark to participants in the USP-DIVP. Participants have the opportunity to appeal the following:

- Rejection of pre-audit, quality control, or manufacturing documentation; test results; surveillance results; or audit reports.
- Product recalls.
- Suspension of the certification mark.

Rejection due to documentation, test results, or audit reports

USP may reject as insufficient:

- Documentation that fails to meet the requirements for pre-audit, quality control, or manufacturing documentation.
- Test results that fail to demonstrate that the ingredient meets the labeled amount or other specifications (for initial certification and post-certification surveillance).
- Audit reports that show deficiencies or deviations from good manufacturing practices at the facility.

USP will send written notification of rejection to the participant, along with any relevant findings or reports. The participant will have the opportunity to appeal the rejection or take corrective action(s). Subsequently, if USP rejects the corrective action(s), the participant may appeal that rejection. The participant must send a written notice of appeal, along with any supporting evidence, within 30 days from the date of receiving the written notification from USP.

USP's Appeals Board will review the evidence received with the appeal and decide to accept or reject the participant's data and/or audit reports. In either case, written notification of the decision will be sent to the participant within 20 business days. If the data and/or audit reports are accepted, USP will resume evaluation of the participant and data at the appropriate step in the USP-DIVP process. If the data and/or reports are rejected, the participant can re-enter the program after correcting the deficiencies.

Product recalls

USP is entitled to recommend a product recall if critical ingredient deficiencies are detected. Ingredient deficiencies are considered critical if:

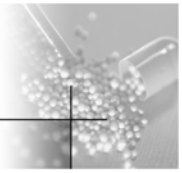
- There is a remote probability that the use of, or exposure to, the ingredient may cause serious adverse health consequences or death when used as intended.
- There is even a reasonable probability that the use of, or exposure to, the ingredient may cause temporary or medically reversible adverse health consequences when used as intended.
- An official from the manufacturing company has submitted fraudulent documents to the USP.
- An official organization, such as the FDA, has recommended a voluntary recall.

Upon recommending a recall, USP will immediately notify the participant. Within 24 hours of such recall recommendation, USP will convene a hearing—by conference call— with the participant's representative(s), who must answer any questions and provide the requested information about the ingredient problem. USP will then affirm or overturn its recommendation to recall the ingredient. If USP decides that a recall is not to be recommended, it will immediately notify the participant. If USP decides that a recall is appropriate, it will immediately contact the appropriate governmental agency, such as the FDA in the USA, and notify the participant to discontinue use of the USP-DIVP certification mark on the ingredient. The participant must take immediate action to do so but may appeal, within five business days, the decision to discontinue use of the certification mark.

Suspension of the certification mark

USP may suspend a participant's right to use the USP-DIVP certification mark due to:

- Violation of any USP-DIVP participation criteria, policies, or procedures by the manufacturing company, its affiliates, or agents.
- Major ingredient deficiencies, which include a major deviation from ingredient standards and/or manufacturing process.
- Major ingredient deficiencies on a new, unreleased ingredient.
- Major changes to an ingredient's specification, process control data, raw material source, equipment, manufacturing site change, testing, or any other change deemed essential by the participant, which must immediately be reported in writing to USP. USP will review the information and determine whether or not to suspend use of the certification mark during re-evaluation or retesting of the ingredient. Such work may include review of analytical data or additional audits at the participant's expense.
- Minor ingredient deficiencies to an ingredient bearing the USP-DIVP certification mark. Minor ingredient deficiencies include deviations from ingredient standards that do not show evidence of manufacturing problems or health risk. The participant must notify USP



of minor ingredient deficiencies. USP will work with the participant to ensure that the minor ingredient deficiencies are resolved. If the participant has repeated minor ingredient deficiencies, USP may suspend use of the certification mark.

The participant may appeal USP's decision to suspend use of the certification mark. The appeal, along with any supporting evidence, must be made within 30 days from the receipt of notification of suspension from USP. If no appeal is made within this period, the suspension becomes a revocation of the use of the certification mark with no further rights of appeal.

When submitting the appeal, the participant may request a review of analytical procedures data, documentation, or an audit. USP will conduct such review or audit at the participant's expense and provide a written report of findings to the participant.

The participant may, on appeal, also request an oral hearing. USP will set a place, time, and date—not more than 60 days after receiving the request for an appeal—for the hearing and notify the participant. USP and the participant may present evidence at the hearing. The participant may be represented by counsel. The participant shall pay all reasonable expenses incurred by USP including, but not limited to, travel expenses.

USP will make a recommendation and provide explanations within 30 days, if in the hearing it is found that the participant:

- Is substantially out of compliance with the USP-DIVP criteria—in which case USP will revoke use of the certification mark.
- Is substantially in compliance with the USP-DIVP criteria—in which case USP will reverse the suspension and reinstate use of the mark.
- Can conduct corrective action within six months to become substantially compliant with USP-DIVP criteria—in which case USP will affirm the suspension until further review. The participant must notify USP within 30 days that it will seek the review. The participant will bear the cost of such review by USP. The participant's failure to notify USP within 30 days, or to be in substantial compliance within six months, will result in revocation of use of the certification mark.

Upon revocation of the certification mark, a participant may re-enter the program one year from such revocation, on payment of full fees.

19. GLOSSARY

Acceptance Criteria: predetermined limits against which sample data are compared to determine compliance with standards of quality.

Adequate: item/area/system/knowledge that meets basic minimum requirements.

AHP: American Herbal Pharmacopeia is a tax-exempt, educational 501 (c) (3) foundation, started in 1995, whose mission is to disseminate authoritative and comprehensive information to the herbal industry, pharmacists, health care practitioners, educational institutions, regulatory agencies, and the general public.

AHPA: American Herbal Products Association is a national trade association of the herbal products industry, which is composed of growers, processors, manufacturers, and marketers of herbs and herbal products.

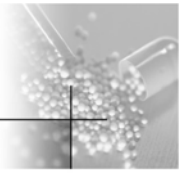
AMB-EC: USP's Analytical Microbiology Expert Committee.

AOAC: AOAC, International, formerly the Association of Official Analytical Chemists, is an independent scientific association of analytical scientists, with members located throughout the world. AOAC publishes Official Methods of Analysis, which contains validated chemical and microbiological analytical methods in the area of foods, beverages, agriculture, and drugs.

Appeals Board: a group consisting of 2 members from the USP Experts Committees; the USP Director of Quality Assurance; the USP Vice President—Information and Standards Development; the Director of Analytical Chemistry, USP-DIVP; and the Director of GMPs, USP-DIVP. The Board will have the authority to review appeals submitted by companies in USP-DIVP regarding: (1) rejection of data, process controls, or audit reports; (2) product recalls; or (3) suspension of the mark.

Auditor: any USP-approved audit firm/consultant or USP-DIVP staff member that performs the on-site audit.

BAM: FDA's Bacteriological Analytical Manual is a collection of procedures preferred by analysts in FDA laboratories for the detection in food and cosmetic products of pathogens (bacterial, viral, parasitic, plus yeast and mold) and of microbial toxins. BAM is published and distributed by AOAC International, and is being placed on FDA's Web site.



Batch (or Lot): a specific quantity of a finished ingredient or other material that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture.

CFSAN: FDA's Center for Food Safety and Applied Nutrition.

Council of Experts (CoE): USP Convention's group of elected scientific experts.

Current Quality System: the quality control system and manufacturing process in place since the last instituted change to the ingredient manufacturing operation.

Dietary Ingredient: as defined in section 201(ff) of the federal Food, Drug, and Cosmetic Act, a dietary ingredient can be a vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total dietary intake, or a concentrate, metabolite, constituent, extract, or combination of the aforementioned ingredients.

Dietary Supplement: as defined in section 201(ff) of the federal Food, Drug, and Cosmetic Act, a dietary supplement is a product that complies with or is intended for ingestion in a form described in section 411(c)(1)(B)(I) of the Federal Food, Drug, and Cosmetic Act; is not represented for use as a conventional food or as a sole item of a meal or the diet; and is labeled as a dietary supplement.

DIVP: Dietary Ingredient Verification Program

DSHEA: Dietary Supplement Health and Education Act of 1994.

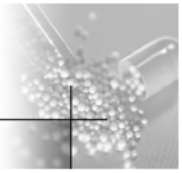
DSI-EC: Dietary Supplement Information Expert Committee.

EP: European Pharmacopoeia.

EC: USP's Expert Committee. One of USP Convention's elected scientific standard-setting bodies.

EPA: U.S. Environmental Protection Agency.

FAC: CFSAN's Food Advisory Committee.



FCC: Food Chemical Codex is a publication under the administrative supervision of the Food and Nutrition Board of the Institution of Medicine/National Academy of Sciences.

FDA: U.S. Food and Drug Administration.

Federal FDC Act: the Federal Food, Drug, and Cosmetic Act.

Fine Chemicals: vitamins, minerals, amino acids, excipients, and other substances that are used in the manufacture of dietary supplements.

IAG: the Industry Advisory Group is a group of representatives from fine chemical manufacturing companies that provide advice for the guidelines and requirements of the USP-DIVP. The number of participating companies, at any particular time, is limited to four. The participating companies are selected by USP on an annual basis.

Ingredient Deficiencies (Major): includes the following: (1) there are major deviations from ingredient standards that are judged would render the ingredient unusable for its intended purpose; or (2) there is a lack of essential ingredient criteria that are judged would render the ingredient unusable for its intended purpose; or (3) the company, affiliates, or agents engage in violation of any USP-DIVP participation criteria, policy, or procedure.

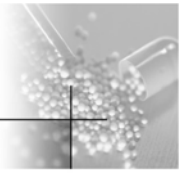
Ingredient Deficiencies (Critical): includes the following: (1) there is a reasonable probability that the use of, or exposure to, the ingredient may cause serious adverse health consequences or death when used as intended; (2) there is even a remote probability that the use of, or exposure to, the ingredient may cause temporary or medically reversible adverse health consequences when used as intended; (3) a company official has submitted fraudulent documents to the USP-DIVP program; or (4) an official organization, such as the FDA, has recommended a voluntary recall.

Ingredient Deficiencies (Minor): deviations from ingredient standards that show evidence of minor manufacturing and/or quality control problems.

LOD: Loss On Drying.

Manufacturing Documentation: the manufacturing directions, master formulation/manufacturing guide, and executed batch records.

Method: a procedure used to generate analytical data.



NF: *National Formulary*, current edition.

Non-standardized Dietary Ingredients: include botanical or "other" dietary ingredient raw material, or traditional-style extracts made according to historical or traditional practices. The dietary ingredient tends to be one whose composition is complex, containing groups of chemical compounds, many of which are not identified and for which no analytical method exists. Naturally occurring botanicals or "other" dietary ingredients for which no label claim is made regarding the chemical constituents (e.g., ground botanicals or ground oyster shells) are considered non-standardized dietary ingredients.

OMA: Official Methods of Analysis is a publication of validated methods under the supervision of the AOAC.

OVI: Organic Volatile Impurities as defined by USP General Chapter <467>.

PAM: FDA's Pesticide Analytical Manual is a repository of the analytical methods used in FDA laboratories to examine food for pesticide residues for regulatory purposes (40 CFR 180.101 (c)). The manual is organized according to the scope of the analytical methods in a two-volume set, available in Adobe Acrobat (pdf) format on the FDA's Web site.

Participant: a company that has qualified to participate in the USP-DIVP.

QA: Quality Assurance.

QC: Quality Control.

Raw Material: any ingredient intended for use in the manufacture of a finished ingredient including those that may not appear in the finished ingredient.

Recall: a company's removal or correction of its marketed ingredient that USP-DIVP, an official organization such as the FDA, or the company initiates due to critical ingredient deficiency.

Reference Standard: characterized chemical substances, used to test for compliance in order to demonstrate identity, strength, quality, and purity for drugs and dietary supplements.

Shall: used to state mandatory requirements.

Shelf-life: the interval of time for which the ingredient must conform to applicable specifications when stored under labeled conditions. The shelf life period should be supported by stability data and be indicated on the ingredient label and exterior commercial packaging.

Should: used to state recommended or advisory procedures or to identify recommended equipment.

Specification: includes the test, test method, and acceptance criteria that define the standard of quality for a material.

SOP: Standard Operating Procedure.

Stability Protocol: documents describing the sample, test specifications, test intervals, conditions, and packaging used to determine the shelf-life.

Standardized Ingredients: For the purposes of this guideline, a limited definition of standardized dietary ingredients is being used. Standardized ingredients are tested to verify that ingredients are truthfully labeled with respect to their contents. For botanicals and "other" ingredients, standardized ingredients contain a defined amount of a particular chemical constituent or group(s) of constituents, known as marker compound(s). Note that a complete definition of standardization includes the information and controls needed to produce a material of predetermined and defined consistency.

USP: United States Pharmacopeia.

USP–NF: the current official volume of the *United States Pharmacopeia-National Formulary* including its supplements.

20. FORMS AND CHECKLISTS

- **Pre-Audit Documentation Checklist**
- **Quality Control Documentation Checklist**
- **Manufacturing Documentation Checklist**
- **On-Site Audit Checklist**
- **Observation(s)/Corrective Action(s)/Supplemental Information Request Form**

Form A DSV-5200

USP Dietary Ingredient Verification

Sec. I. Checklist for Pre-Audit Documents Submitted for Review

COMPANY INFORMATION		
COMPANY NAME	OWNED BY	YEAR ESTABLISHED
ADDRESS		SQ. FOOTAGE OF FACILITY
NAME AND TITLE OF MANUFACTURING CONTACT		PHONE NUMBER
NAME AND TITLE OF QA CONTACT		PHONE NUMBER

EMPLOYEES				
TOTAL NUMBER	MANUFACTURING	QC	QA	OTHER

PRODUCTS

LIST PRODUCTS TO BE CONSIDERED (Attach additional sheet if necessary)

Pre-Audit Documents

Complete documentation, in the requested format, must be received before review begins.

Please include SOPs or descriptions of the following in your pre-audit package.	**SHADED AREA TO BE COMPLETED BY USP-DIVP (If *"NAC"* or *"MI"* Box is checked, USP-DIVP's observation will be provided on Form A DSV-5200 and coded under Section ID as "I.A…, etc" to assign appropriate observation to Form and Section.)** AC = Acceptable NAC = Not Acceptable MI = Missing Information N/A = Not Applicable			
SUBSEC. A. FLOW CHART(S) OF PROCESS(ES) INVOLVED.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
B. Site map/Layout	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
C. Organizational chart including all key manufacturing and QA/QC personnel	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
D. Qualifications of key personnel	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
E. Training program	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
F. Table of contents from manufacturing, laboratory, QA and QC SOP manuals	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
G. Receiving and material handling SOP(s)	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
H. Document management system policy and SOPs	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
I. List of process equipment requiring calibration, preventive maintenance, and cleaning	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
J. Program for calibration and preventive maintenance to maintain suitability of process equipment	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
K. Change control policy and SOPs	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
L. Program for validation of process, cleaning, and analytical methods	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
M. Label control program	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
N. Deviation program	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
O. Laboratory control procedures	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
P. Sample tracking system	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
Q. Program for evaluating shelf life of marketed product	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
R. Program governing electronic data/computerized systems	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**

Form A DSV-5200

USP Dietary Ingredient Verification

Sec. I. Checklist for Pre-Audit Documents Submitted for Review

S. Starting Material Supplier Certification Program	☐ AC	☐ NAC	☐ MI	☐ N/A
T. Contract Laboratory Certification Program	☐ AC	☐ NAC	☐ MI	☐ N/A
U. Complaint Program/Recall Program	☐ AC	☐ NAC	☐ MI	☐ N/A

Form A DSV-5300

USP Dietary Ingredient Verification

Sec. II. Checklist for Quality Control Documents Submitted for Review

COMPANY INFORMATION		
COMPANY NAME		
ADDRESS		
NAME AND TITLE OF MANUFACTURING CONTACT		**PHONE NUMBER**
NAME AND TITLE OF QA CONTACT		**PHONE NUMBER**
INGREDIENT NAME	**MANUFACTURE INGREDIENT CODE**	**USP DIVP BARCODE**

Ingredient Information—Quality Control Methods and Data

Complete documentation, in the requested format, must be received before review begins.

Subsec. A. Specifications for starting chemicals/materials, Critical/Key Intermediates, and packaging/labeling materials.	**SHADED AREA TO BE COMPLETED BY USP-DIVP (If *"NAC"* or *"MI"* Box is checked, USP-DIVP's observation will be provided on Form A DSV-5300 and coded under Section ID as "II.A.1.c. (2)…, etc." to assign appropriate observation to Form and Section.)** AC = Acceptable NAC = Not Acceptable MI = Missing Information N/A = Not Applicable			
1. Raw Material Specification (*USP–NF* standards, BP, EP, or JP or supplier justified specification)				
a. Identification by spectroscopic, organoleptic, chemical and/or chromatographic test. Materials of botanical origin must be labeled with Latin binomial as per Herbs of Commerce and plant part(s) used. If applicable, they must conform to macro/microscopic description in addition to chemical and/or chromatographic identification test.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
b. Content of specific entity/marker compound by chemical and/or biological procedure.	☐ AC	☐ **NAC**	☐ **MI**	☐ **N/A**
c. Undesirable contaminants and components				
(1) Heavy metals (*USP–NF* monograph, or <10ppm)	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
(2) Residual solvents (OVI's or other hazardous solvents when applicable)	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
(3) Known toxic components as mentioned in the specifications (e.g. aristolochic acid, BSE, etc.)	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
(4) Insects/foreign matter (for botanicals or other products as applicable)	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
(5) Pesticides analysis	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
(A) FOR GINSENG, VALIDATED CRN-AHPA QUINTOZENE, DEGREDANTS, AND IMPURITIES GC METHOD	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
(6) Microbial counts and absence of specified microorganisms. Materials of botanical origin may also require a test for Aflatoxins.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
(7) Absence of adulterants (for botanicals in compliance with guidelines set by AHPA and FAC).	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
(8) Other undesirable components.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
d. Other quality standards (water, Loss on Drying, Ash, Residue on Ignition, pH)	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**

Form A DSV-5300

USP Dietary Ingredient Verification

Sec. II. Checklist for Quality Control Documents Submitted for Review

	SHADED AREA TO BE COMPLETED BY USP DIVP AC = Acceptable NAC = Not Acceptable MI = Missing Information N/A = Not Applicable			
2. Critical/Key Intermediates				
a. Supplier physical appearance or characterization, etc.	☐ AC	☐ NAC	☐ MI	☐ N/A
b. Identification per Supplier specifications	☐ AC	☐ NAC	☐ MI	☐ N/A
c. Relevant supplier specifications such as pH, LOD, ROI, etc.	☐ AC	☐ NAC	☐ MI	☐ N/A
d. Assay per supplier specifications, HPLC, GC, TLC, etc.	☐ AC	☐ NAC	☐ MI	☐ N/A
3. Packaging and Labeling Materials				
a. Description and specifications for packaging materials in direct contact with the ingredient.	☐ AC	☐ NAC	☐ MI	☐ N/A
b. Samples and specifications for labels and labeled packaging.	☐ AC	☐ NAC	☐ MI	☐ N/A
Subsec. B. Release and shelf life specifications for the finished ingredient (must be in compliance with official compendia standards, when applicable, otherwise justification needs to be provided)				
1. Physical Examination				
a. Appearance (e.g., dosage form type, shape and size)	☐ AC	☐ NAC	☐ MI	☐ N/A
b. Color	☐ AC	☐ NAC	☐ MI	☐ N/A
2. Identification by spectroscopic, chemical or chromatographic test. Materials of botanical origin must be labeled with Latin binomial and plant part(s) used.	☐ AC	☐ NAC	☐ MI	☐ N/A
3. Content of ingredient by specific entity/marker by chemical and/or biological procedure.	☐ AC	☐ NAC	☐ MI	☐ N/A
4. Undesirable components (not needed if absence is demonstrated through raw materials and process control).				
a. Heavy metals	☐ AC	☐ NAC	☐ MI	☐ N/A
b. Known toxic components	☐ AC	☐ NAC	☐ MI	☐ N/A
c. Microbial count and absence of specified microorganisms	☐ AC	☐ NAC	☐ MI	☐ N/A
5. Other quality standards (Water, pH)	☐ AC	☐ NAC	☐ MI	☐ N/A

Form A DSV-5300

USP Dietary Ingredient Verification

Subsec. C. Testing Method(s) Verification	**SHADED AREA TO BE COMPLETED BY USP DIVP** *AC = Acceptable NAC = Not Acceptable MI = Missing Information N/A = Not Applicable*			
1. Analytical method(s) *from* official compendia, AOAC International's Official Methods of Analysis, a Peer Verified Method, or the Food Chemical Codex should demonstrate suitability for ingredient testing.				
a. Lack of interference of other components and/or excipients with analyte determination.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
b. Accuracy and precision for analyte determination.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
c. Raw data/chromatograms	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
2. Analytical method(s) *not from* official compendia, AOAC International's Official Methods of Analysis, a Peer Verified Method, or the Food Chemical Codex should be verified as per USP <1225> as applicable. Full verification is required for parent member of ingredient family (additional ingredients need only demonstration of suitability). If full verification is not possible, sufficient information must be provided to verify the method(s) suitability for the intended use.				
a. Linearity across suitable range	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
b. Accuracy	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
c. Precision	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
d. Limit of Detection/Limit of Quantitation	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
e. Specificity	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
f. Raw data/chromatograms	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
3. If analytical testing is performed by a contracted laboratory, method validation needs to be submitted by the lab as it pertains to section C1 or C2 above; or lab verification by manufacturer or USP is needed.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
Subsec. D. Reference Materials				
1. A list of all reference standard materials needed for raw material and ingredient testing, indicating the quality and source if not a USP Reference Standard used for a USP test.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
2. For non-USP reference standards or reference standards for non-USP tests, characterization data to support the suitability of the reference material for its intended use.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
Subsec. E. Stability Data				
Data to support the marketed shelf-life period in the commercial package at the storage conditions recommended on the ingredient labeling. Data should be provided for Appearance, Content, Performance characteristics, and Microbial count.				
a. Data from real time shelf life studies and/or	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
b. Data from accelerated stability, 40° C/75% RH and/or	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
c. Data based on historical information covering the time period of the shelf life.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
Subsec. F. Documents for Ingredient Under Review				
1. Certificates of analysis for submitted ingredient.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
2. Copies of raw data, including spectra and chromatograms of samples and standards as applicable.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**

Name and Signature of USP DIVP Reviewer and Date

Reported By: _____ _____ _____

Printed Name Signature Date

Reviewed By: _____ _____ _____

Printed Name Signature Date

Form A DSV-5400

USP Dietary Ingredient Verification

Sec. III. Checklist for Manufacturing Documents Submitted for Review

COMPANY INFORMATION

COMPANY NAME		
ADDRESS		
NAME AND TITLE OF MANUFACTURING CONTACT		PHONE NUMBER
NAME AND TITLE OF QA CONTACT		PHONE NUMBER
INGREDIENT NAME	MANUFACTURING INGREDIENT CODE	USP DIVP BARCODE

Ingredient Information–Manufacturing Records

Complete documentation, in the requested format, must be received before review begins.

Subsec. A. Master formula/Manufacturing Guide for each ingredient containing:	**SHADED AREA TO BE COMPLETED BY USP-DIVP** (If "*NAC*" or "*MI*" Box is checked, USP-DIVP's observation will be provided on Form A of DSV-5400 and coded under ***Section*** ID as "IIIB2…, etc." to assign appropriate observation to Form and Section.) *AC = Acceptable NAC = Not Acceptable MI = Missing Information N/A = Not Applicable*			
1. A diagram for chemical synthesis, extraction, secondary/tertiary recovery fermentation, blending, grinding, etc.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
2. A complete list of starting chemicals/materials (synthesis or extraction) or raw materials, packaging components used in the manufacture of the ingredient, including positive identification of all labeling to be used; designated by names or codes sufficiently specific to indicate any special quality characteristic(s).	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
3. A statement of the weight or measure of each starting chemical or raw material used in the manufacture of a typical batch of the ingredient including ingredients not found in the final ingredient.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
4. The name and weight or measure of each dietary ingredient per unit or per unit of weight or measure, or percentage of the supplement.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
5. A statement of the total weight or measure of the final ingredient.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
6. A statement of theoretical/actual weight or measure of the final ingredient expected at the conclusion of manufacture. Include the maximum and minimum percentages of actual yield beyond which justification to release the batch is required.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
7. Acceptable procedures for reprocessing, re-synthesis, re-extraction, or secondary/tertiary recovery that have demonstrated that the ingredient from a reprocessed batch meets label or C of A declaration and stability or a statement that reprocessing, re-synthesis, re-extraction, or secondary/tertiary recovery is not performed.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
8. A statement of shelf-life print specifications for labeling and any calculations associated with determining the shelf-life dates.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
9. A list of all processes, operations, and process/environmental controls to be performed at each step during the manufacture.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**

Form A DSV-5400

USP Dietary Ingredient Verification

Sec. III. Checklist for Manufacturing Documents Submitted for Review

	SHADED AREA TO BE COMPLETED BY USP DIVP *AC = Acceptable NAC = Not Acceptable* *MI = Missing Information N/A = Not Applicable*			
10. Identification of steps requiring a Quality Control check, particularly with respect to Key/Critical Intermediates.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
11. A description of all equipment and production lines to be used during the manufacture (i.e., storage tanks, intermediate holding tanks, reaction vessels, blending tanks, grinders, mills, homogenization units, piping and chemical transport diagrams).	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
12. List of references for appropriate equipment cleaning procedures, indicating SOP# and description.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
13. Signature(s) of responsible authoring person(s), signature(s) of responsible review/approval person(s) other than author, and effective date.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
Subsec. B Executed lot records for the requested lots of ingredient:				
1. Production order with lot number, manufacturing start date expiration date, and responsible signatures (production operators, supervisor, and final QA review).	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
2. Evidence that the raw materials, starting chemicals/materials, packaging containers, closures and labels, etc., were verified as released and acceptable for use. Copies of the labeling used including labels with lot numbers and shelf-life dates. Evidence that the shelf-life calculation was verified as correct according to the specifications.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
3. Record of all pertinent weights and measures.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
4. All pertinent in-process control data including testing and release of Key/Critical intermediates where applicable.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
5. Identification (by code, lot #, or serial #) of actual raw materials, in-process materials, equipment and lines used.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
6. Environmental control records, as required by manufacturing process directions.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
7. Ingredient yield calculation.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
8. Complete description of any deviation from the written procedures including justification.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
9. Reprocessing information, re-synthesis, re-extraction, or secondary/tertiary recovery if applicable.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**
10. Demonstration that Quality Assurance provides final disposition of ingredient lot.	☐ **AC**	☐ **NAC**	☐ **MI**	☐ **N/A**

Name and Signature of USP-DIVP Reviewer and Date

Reported By: _____ _____ _____

Printed Name Signature Date

Reviewed By: _____ _____ _____

Printed Name Signature Date

FORM A DSV-5201

USP Dietary Ingredient Verification
CHECKLIST FOR ON-SITE AUDIT

COMPANY: _____

DATE: _____

LOCATION: _____

ESCORTS: _____

AUDITORS: _____

NOTE: THIS GUIDELINE IS DESIGNED AS A REMINDER FOR EXPERIENCED AUDITORS TO USE IN CONDUCTING AUDITS. IT IS NOT NECESSARILY INTENDED TO BE ALL-INCLUSIVE OR TO LIMIT THE SCOPE OF THE AUDIT. ONE INGREDIENT MUST BE TRACKED FROM RECEIVING TO FINISHED INGREDIENT RELEASE.

INDEX TO GUIDELINE

RATING:

A - NUMBER OF SATISFACTORY ( )
B - NUMBER OF INADEQUATES ( )
N/A - NUMBER OF NOT APPLICABLE ( )

CALCULATIONS:

C - TOTAL OBSERVATIONS: A + B = C ( )

TOTAL OF A ( ) X 100 = FACILITY RATING ( )

TOTAL OF C ( )

FORM A DSV-5201 ITEM	SATISFACTORY	INADEQUATE	NOT APPLICABLE	COMMENT
A. GENERAL				
Brief company history				
When was the last FDA or other regulatory inspection, What were the results of the inspection?				
Have the inspection issues been resolved?				
Does this company at this site perform all operations?				
If not, what other sites/companies are used and for what functions?				
What type of testing is conducted at this site? ANALYTICAL MICROBIOLOGICAL STERILITY ANIMAL BOTANICAL				
Is there a chemical hygiene plan? Safety program?				
Is there a hazardous waste disposal program?				
Is testing out-sourced?				
Is there a policy of client notification of subcontracting?				
B. ORGANIZATION AND PERSONNEL				
Is there a separate Quality Assurance department?				
Approximately how many employees are in the company? At this site?				
Is there capacity for additional work?				
Are there written job descriptions describing the required qualifications and training needed for each job?				
C. TRAINING				
Is there an SOP for training, addressing both permanent and temporary employees?				
Are training and qualifications documented for each employee, including temporary employees?				
Are there initial and ongoing GMP training and job-specific training for employees?				
Is there a plan to ensure that only authorized personnel (trained personnel) perform the functions they are trained to do?				
Is training performed and documented when SOPs are created or updated?				
Are changes in FDA and regulatory requirements tracked and communicated to employees?				
Do employees have adequate training, experience, and qualifications for their responsibilities?				
Are operator errors tracked, and are "error-prone" employees appropriately retrained? Is this retraining documented and its effectiveness verified?				
D. FACILITIES				
BUILDINGS AND HOUSEKEEPING				
How old are the facilities?				
Is there adequate security to assure there is Inadequate entry by unauthorized persons?				

FORM A DSV-5201 ITEM	SATISFACTORY	INADEQUATE	NOT APPLICABLE	COMMENT
Are size, space, layout, lighting, temperature control, and ventilation adequate for the number of employees and work being performed?				
Are facilities maintained in a clean and orderly manner and in a good state of repair?				
Are there provisions for power backup sources for critical systems if main power should fail, and/or an SOP for recovery from power failure?				
Is there an adequate pest control program?				
Is there an environmental monitoring program that includes qualification and monitoring of all utilities?				
How are temperature and humidity excursions handled?				
PURIFIED WATER SYSTEM				
Describe the type of Purified Water system.				
Is the Purified Water system routinely subjected to analytical and microbiological testing?				
Is the purification system periodically sanitized and adequately maintained?				

E. EQUIPMENT				
CONSTRUCTION, INSTALLATION, AND QUALIFICATION				
Is there an SOP for qualifying new or significantly changed equipment and instruments, including design qualification (DQ), installation qualification (IQ), operational qualification (OQ), and performance qualification (PQ)?				
Has equipment been qualified according to written protocols? Was qualification documented?				
Is equipment of suitable type and size for intended use?				
Is equipment available in sufficient quantity to perform all required operations within the required time frames?				
Are there written procedures for cleaning of equipment, and are use and cleaning logs maintained for major equipment that are not dedicated?				
Are there operational SOPs for all equipment?				
Have software packages for equipment been verified?				
Is there a verification / qualification program for equipment software?				
MAINTENANCE AND CALIBRATION				
Is there a master list of all equipment that specifies those requiring maintenance and/or calibration? Is there a master list of the last calibration of all equipment?				
Are there SOPs for inspection (monitoring the condition), maintenance of equipment, measuring and testing instruments? Do SOPs assign responsibilities; include schedules; describe procedures, equipment, and materials to be used; and require maintenance of records?				
If equipment and instruments malfunction or are determined to be defective, are they immediately taken out of use per an SOP?				
Are there SOPs for calibration of critical equipment, and measuring and testing instruments? Do SOPs assign responsibilities; include schedules; describe procedures, equipment, and materials to be used, including calibration over actual range of use and standards traceable to national standards; and include specifications and tolerances?				
If calibration operations are performed in-house, do SOPs specify proper handling and storage conditions for the traceable standards?				

FORM A DSV-5201 ITEM	SATISFACTORY	INADEQUATE	NOT APPLICABLE	COMMENT
Are the calibration intervals based on the manufacturers' specified frequencies or personal experience?				
Does an SOP specify that equipment cannot be used if it is beyond the calibration due date and describe actions to be taken if equipment is used that is found to have been beyond the due date or is found to be out of calibration limits?				
Is calibrated equipment labeled with date calibrated and date next calibration is due?				
Is equipment in use observed to be within calibration dating?				
Are periodic verifications performed on balances and scales (using a range of weights) to assure that they remain within calibration in the time between full calibrations? Is this documented?				
Are records maintained for maintenance and calibration operations?				
EQUIPMENT CLEANING				
Are there written procedures for cleaning, specifying cleaning agents and procedures?				
Are there data to show that cleaning procedures for non-dedicated instruments are adequate to remove the previous materials?				
Are there data to show that the residues left by the cleaning and/or sanitizing agent are within acceptable limits when cleaning is performed in accordance with the approved method?				
Is there an adequate system to assure that unclean equipment/utensils are not used (e.g., labeling with clean status)?				
Is there proper storage of cleaned equipment so as to prevent contamination?				
F. COMPUTERIZED SYSTEMS				
VERIFICATION OF GMP-RELATED APPLICATIONS				
Are any computerized systems used to perform GMP-related functions? (if not, skip this section)				
Is there a list of all computerized systems and computer applications that defines their uses and identifies which ones perform cGMP-related functions?				
Are there established procedures and policies covering the verification of GMP-related computerized systems and instrumentation? Do these procedures define required verification documentation?				
Have such computerized systems been verified (demonstrated to consistently function as expected)? Are reports available?				
Have any spreadsheets used for performing calculations been verified as being accurate and functioning as expected? Are formula cells secure, with access limited to authorized personnel?				
If data are transferred from written data records into a computer database, is the accuracy of data entry verified?				
Are routine accuracy checks performed for the various computer-controlled operations to verify that input to and output from the computer or related system are reliable and accurate? Are the degree and frequency of these verifications appropriate in relation to the complexity and reliability of the computerized system?				
BACKUPS				
Are suitable backup systems in place, such as copies of programs and files, duplicate tapes, or microfilm?				
Has retrievability of information from master tapes and backup tapes been verified?				
CHANGE CONTROL COMPUTER SYSTEMS				
Is there a system to control changes to systems and programs?				
Does the system assure that changes receive the proper review and approval with regard to potential effects before being instituted and that only authorized personnel can make such changes?				

FORM A DSV-5201 ITEM	SATISFACTORY	INADEQUATE	NOT APPLICABLE	COMMENT
If necessary, are personnel trained subsequent to changes?				
Is a log of system and program changes maintained?				
SECURITY				
Is there appropriate security to limit access to computerized systems, protect records from tampering, and prevent data alteration?				
If passwords are used as a security measure, are there provisions for periodic changing of passwords? Does a responsible person (e.g., system administrator) have a list of all passwords in case of emergency?				
If anyone leaves the department or company or otherwise loses authority to access the systems, are there procedures to immediately remove that person's access codes from the system?				

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G. OPERATIONS				
RECEIVING CONTROLS				
Are released items properly segregated from material awaiting testing and disposition?				
Is material adequately identified as to acceptance or rejection?				
Is rejected material adequately controlled?				
Is there an acceptable area/procedure for sampling?				
Are materials properly handled and stored to prevent damage?				
Are stockrooms, storage areas restricted to authorized personnel?				
Are materials properly identified as to their contents to avoid errors?				
Are storage tanks properly identified as to their contents?				
Is piping properly labeled as to content and direction of flow?				
Are materials adequately segregated/identified to prevent mix-ups?				
Is release status controlled by the warehouse locator system?				
Is the locator system accurate as to status of materials?				
Are stocks re-inspected/tested at appropriate intervals?				
Where required, how adequate is the controlled environment storage? (humidity, temperature etc.)				
Are individual part numbers used for each material?				
If multiple lots of an incoming material are received are all the lots tested?				
MANUFACTURING AND INPROCESSING CONTROLS				
Is the product identifiable throughout the manufacturing process?				
Are reaction vessels, intermediate holding tanks, etc. clearly marked as to content?				
Are critical/key intermediate tanks marked with the appropriate status?				
Are manufacturing operations orderly?				
Are manufacturing procedures formalized and controlled?				
Do the employees in the manufacturing area appear to be knowledgeable and quality conscious?				
Are production employees neat and clean in their appearance?				
Is the manufacturing environment acceptable for the type of item being produced?				
Are pipes labeled to show contents and direction of flow?				
Are different grades of the same materials distinguishable in manufacturing to prevent mix-ups?				
Are those production areas that are very dusty properly controlled with exhaust systems and decontamination processes?				
Are waste materials clearly identified in proper containers?				
Are the ceiling fixtures, pipes, etc. free of accumulated dirt and previous product?				
Are the valves and associated pipes in the production free of leaks?				
Are the ceilings and walls in good condition to prevent contamination with paint chips?				
Label Control				
Are labels stored in a secure area away from general storage?				
Are labels proofread and inspected on incoming?				
Are labels formally issued to the packaging/packing lines?				

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Are labels verified prior to use?				
Are labels verified to have the correct lot number and expiry date when used?				
Are labels reconciled after packaging/packing?				
Are returned labels adequately counted and returned to stock properly?				
ANALYTICAL LABORATORIES				
Control of Supplies				
Is there a vendor qualification policy for laboratory supplies?				
Is there a list of approved vendors for laboratory supplies?				
Are reference standards (primary and secondary) appropriately prepared, identified, tested, approved, and stored in a proper manner to ensure stability?				
Are expiration dates adequately monitored so they are not used beyond the expiration dates?				
If reference standards are not USP Reference Standards, has appropriate characterization (including purity and stability) been performed? Are material grades appropriate?				
Are reagents adequately controlled and monitored to assure that they are periodically replaced and that old reagents are not used?				
Are all containers of materials or solutions adequately labeled to determine identity, preparer, and dates of preparation and expiration (if applicable)?				
Are preparations logs maintained, including manufacturer and lot number, preparer and date?				
Are there certificates of analysis available for inspection for reagents?				
Testing				
What is the average turn-around time for samples?				
Are there complete written instructions for sampling, approval or rejection of materials (per acceptance specifications), recording and storage of lab data?				
Have non-compendial procedures been validated based on an SOP, including accuracy, linearity, specificity, ruggedness, and comparison with compendial procedures, OR have compendial procedures been verified to function properly in the company's laboratory?				
Are test procedures readily available to the analysts?				
Are test procedures followed without modification, and if not, is it documented?				
Are any tests performed other than those specified?				
If additional tests are performed, are the results communicated to the appropriate group?				
Is there an SOP describing how numbers are to be rounded?				
Are data and calculations reviewed, verified and signed by a second person?				
Are investigations of Non Conforming Results completed and matters resolved within a period of time per an SOP? Do conclusions and actions appear to be adequate?				
MICROBIOLOGY LABORATORIES				
Is environmental monitoring of the lab conducted? Has the microbial profile of the laboratory been developed?				
How are environmental monitoring standards set?				
Based on an SOP, is the laboratory cleaned and disinfected, including rotation of disinfectants?				
Is there an adequate procedure for disposal of microbiological waste?				

FORM A DSV-5201 ITEM	SATISFACTORY	INADEQUATE	NOT APPLICABLE	COMMENT
Control of Supplies				
Are reagents and microbiological media adequately controlled and monitored to assure that they are periodically replaced and that old reagents are not used?				
Are all containers of materials or solutions adequately labeled to determine identity, preparer, and dates of preparation and expiration (if applicable)?				
Are preparations logs maintained, including manufacturer and lot number, preparer, and date?				
Based on an SOP, is growth support testing with low levels of organisms performed on all media lots and is it documented?				
Is an expiration date assigned to prepared media and are prepared media stored at the manufacturers' recommended storage temperatures?				
Is each lot of microbial Identification systems checked with positive and negative controls?				
Is each lot of biological indicators checked for identity and viability?				
Are positive controls periodically included in autoclave runs?				
Based on an SOP, are there adequate control and documentation of stock cultures, including storage, propagation, assurance of purity, and traceability?				
Testing				
Are there complete written instructions for testing, including procedures, equipment, operating parameters, and acceptance specifications?				
Are procedures verified based on an SOP?				
Are test procedures readily available to the microbiologists?				
Are test procedures followed without modification?				
Is testing conducted with adequate technique and in such a manner and place to preclude laboratory contamination of samples?				
Has preparatory testing been conducted to determine bacteriostatic or fungistatic properties inherent in the material being tested, and effective means to neutralize them?				
Are test materials prepared in accordance with the findings of the preparatory testing?				
If preservatives are present in the product, are inactivators used?				
Are positive and negative controls used for testing? Are their results recorded?				
If there are any "house" organisms, are they included in routine testing?				
Is identification of isolates from microbiological testing performed if appropriate (e.g., if unusually high microbial levels are found in a solid oral ingredient or raw material)?				
If any unusual or objectionable organisms are identified, is an investigation performed and documented and is management notified?				
Are data and calculations reviewed, verified and signed by a second person?				
Are investigations of Non Conforming Results completed and matters resolved within a reasonable period of time per an SOP? Do conclusions and actions appear to be adequate?				
H. QUALITY SYSTEMS				
RESPONSIBILITIES AND AUTHORITY				

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Are the QA/QC organization's authority and responsibilities clearly defined in writing?				
Is there an adequate system for reviewing and implementing all quality related matters/documents?				
Is there a mechanism to assure that only current specifications are in use?				
Are data reviewed and trends monitored? Are adverse trends addressed, and is appropriate management notified?				
COMPLAINT HANDLING				
Is there an adequate program, described in an SOP, for handling complaints, complaint investigations, and implementing corrective actions where indicated? Is there a target time frame for responding?				
Is the effectiveness of corrective actions verified?				
If no complaint investigation is conducted, is there a written record explaining why not and the name of the person making the decision?				
Are trend analyses performed?				
Are periodic reports of complaints and investigations provided to the appropriate parties, including management per an SOP?				
CHANGE CONTROL				
Is there an adequate system, described in an SOP, for controlling changes to raw materials, specifications, test procedures, documents, facilities and equipment, manufacturing processing steps, packaging and labeling materials, including an evaluation of the need for re-qualification or re-validation?				
Is QA involved in the change control process?				
Is there a system in place to assure that any changes are approved by the client prior to implementation?				
QUALITY AUDIT PROGRAM				
Is there an internal quality audit program that covers all areas of the operation to verify that SOPs and other procedures and policies are being followed, and to determine effectiveness of the quality systems?				
Based on the audit findings and recommendations, are steps taken to correct any areas of noncompliance? Are corrective actions documented? Is their effectiveness verified in subsequent audits?				
If any contractors (e.g., manufacturers, laboratories, off-site storage facilities) are used, are they periodically audited and is their performance monitored?				
SAMPLE CONTROL				
Is there an SOP for receipt, identification, and storage of incoming samples?				
How are samples received?				
What is the sample log-in procedure? Is this computerized? Is it validated?				
How are samples stored?				
Is there adequate security for stored samples?				
Is sample flow and chain of custody tracked?				
Are samples reconciled and any discrepancy investigated and reported to the client?				

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Is there an SOP controlling retention of reserve samples?				

I. DOCUMENT CONTROL				
STANDARD OPERATING PROCEDURES (SOPs)				
Are there controlled written SOPs and documents for all areas of the operation?				
Is there an SOP for writing, handling, and updating SOPs? Are SOPs periodically reviewed and updated?				
Is a history of SOP revisions maintained?				
Are current SOPs readily available to employees?				
Is there an adequate system to assure that unneeded or obsolete documents are removed from use?				
If a client's specifications are changed, does the client review and approve the changed document?				
Is there a documentation retention policy?				
TESTING RECORDS				
Is adequate information recorded in test records concerning the sample, test procedure, reagents and instruments used in tests, raw data, calculations, and test results compared with acceptance criteria?				
If chromatograms, charts, and spectra are stored separate from other test records, are there adequate cross-references to their locations?				
Are records legible? Are they appropriately signed and dated where required?				
Are there overwrites, use of white-out, or pencil entries in official records?				
Are changes to data properly initialed, dated, and explained based on an SOP that describes acceptable procedures for recording data and correcting errors in official documents?				
Are records reviewed for completeness before filing?				
Is there adequate security for data and records?				
Are raw data retained for an adequate length of time per an SOP?				
Are records retained for at least one year past the expiration date of the batch or, if Inadequate expiration date has been assigned, as specified in a records retention policy?				

J. DEVIATION MANAGEMENT				
Is there a written SOP for management (documentation, investigation, and conclusion) of deviations?				
Is there a time frame for disposition?				
Are process deviations and Non-Conforming Laboratory Results related in the SOP?				
Are there appropriate approvals of disposition including QA?				
Is trend analysis performed on process and lab deviations?				
K. SHELF-LIFE EVALUATION				
Is there a program to evaluate product shelf life?				

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Is testing performed within defined time frames?				
Are discrepancies in testing resolved per a formal program?				
Is there data that support the shelf-life of submitted products?				
Are stability chambers maintained and calibrated?				
Is there a chamber recovery plan in the event of a failure?				
L. VALIDATION				
VALIDATION DOCUMENTATION				
Is there company policy for validation?				
Is there written validation protocol?				
Are protocols reviewed and approved by the Quality Unit?				
Do validation protocols contain specific critical steps and acceptance criteria?				
Do validation reports cross-reference the protocol?				
Are deviations to the protocols documented and justified?				
EQUIPMENT QUALIFICATION				
Are critical equipment and ancillary systems fully qualified, including Design Qualification (DQ), Installation Qualification (IQ), Operational Qualification (OQ), Performance Qualification (PQ)?				
PROCESS VALIDATION				
Is there a program/SOP for doing process performance studies (e.g. prospective validation, concurrent validation and/or retrospective validation)?				
Are the number of process runs used for validation a function of the complexity of the process or the magnitude of the process change being considered?				
Have process performance studies been done on the products submitted?				
Are critical parameters identified and validated?				
Are critical operations identified and validated?				
Are impurity profiles within established limits?				
Are systems and processes periodically evaluated to verify that they are still operating in a valid manner?				
CLEANING VALIDATION				
Are cleaning procedures validated for those process steps in which contamination poses the greatest risk to ingredient quality?				
Do cleaning protocols describe the equipment to be cleaned, procedures, materials, acceptable cleaning levels, parameters to be monitored and controlled, and analytical methods?				
Are equipment cleaning/sanitation address microbiological and endotoxin contamination?				
Are cleaning procedures monitored at appropriate intervals after validation?				
ANALYTICAL METHOD VALIDATION				
Are analytical equipment qualified?				

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Are analytical methods validated according to USP and/or ICH guidelines?				
Are validation records maintained properly?				
M. IN PROCESS BLENDING				
Is in-process mixing or blending performed appropriately, excluding batches or lots that individually do not conform to specifications?				
Are blending uniformity analysis studies performed?				
N. REJECTION AND RE-USE OF MATERIALS				
REJECTION				
Are rejected materials quarantined and its final disposition recorded?				
REPROCESSING				
Do written procedures identify steps for reprocessing batches?				
Are quality control review and approval required for any and all reprocessing of material?				
Does testing confirm that reprocessed batches conform to established specification?				
Does a written procedure outline steps required to reprocess returned drug products (if it can be determined that such products have not been subjected to improper storage conditions)?				
REWORKING				
Are non conformance investigations performed prior to rework?				
Are analytical and stability tests performed to guarantee that the quality of the product is the same to that product by the original process?				
Is there validation protocol for rework process?				
Are there procedures to compare impurity profile of reworked batch?				
Are there procedures for recover from the mother liquors or filtrates?				
Are recovery processes controlled and monitored to ensure the solvents meet appropriate standards?				
Is the use of recovered mother liquor and solvents documented?				
O. DISTRIBUTION				
Are materials properly released prior to distribution?				
Are material transported in a manner that do not affect the quality?				
Are special transport and storage conditions documented and labeled?				
Is there a system within distribution that permits product recall immediately?				
P. FOLLOW-UP ITEMS FROM PREVIOUS AUDITS				
Has appropriate corrective action been taken for all previous audit findings?				

FORM A DSV-5201 ITEM	SATISFACTORY	INADEQUATE	NOT APPLICABLE	COMMENT

USP DIETARY INGREDIENT VERIFICATION PROGRAM

bservation(s)/Corrective Action Plan(s)/Supplemental Information

USP DIVP BARCODE LABEL
(page 1 only)

AME:	CONTACT:		DOCUMENT REVIEWED	PRODUCT TYPE
ODRESS:	FAX NUMBER:	DATE SENT:	❑ I. Pre-Audit ❑ II. Quality Control ❑ III. Manufacturing	❑ Powder ❑ Liquid ❑ Other _____ _____
NAME:	MANUFACTURE PRODUCT CODE	USP DIVP BARCODE		

ED BY USP DSVP		*TO BE COMPLETED BY MANUFACTURER*		*TO BE COMPLETED BY USP DSVP*
OBSERVATION(S) (Attach additional sheet if necessary)	DIVP PROPOSED CORRECTIVE ACTION(S) (Attach additional sheet if necessary)	MANUFACTURER'S CORRECTIVE ACTION(S) (Attach additional sheet if necessary)	COMPLETION DATE (Target <3 months from Report Date)	FOLLOW UP COMM

TO BE COMPLETED BY USP DSVP	TO BE COMPLETED BY MANUFACTURER	
Reported By: _____ Date: _____ Reviewed By: _____ Date: _____	Contact: _____ Date: _____ Phone Number: _____	Page _____ of _____