USP Perspective: advancing the quality of dietary supplements

Luciana Takara
Gerente Sr., Government & Regulatory Affairs

Rafael Finocchiaro Maranho
Strategic Customer Development Executive

Agenda

- Introdução sobre USP
- Suplementos Alimentares
  - Processo de Desenvolvimento de Monografias
  - Guias de Submissão
  - O que submeter?
  - Importância de Padrões Públicos
- Conclusões
- Convite: Call for Candidates / Stakeholder Fórum
- Perguntas & Respostas





Introdução sobre USP

Missão da USP

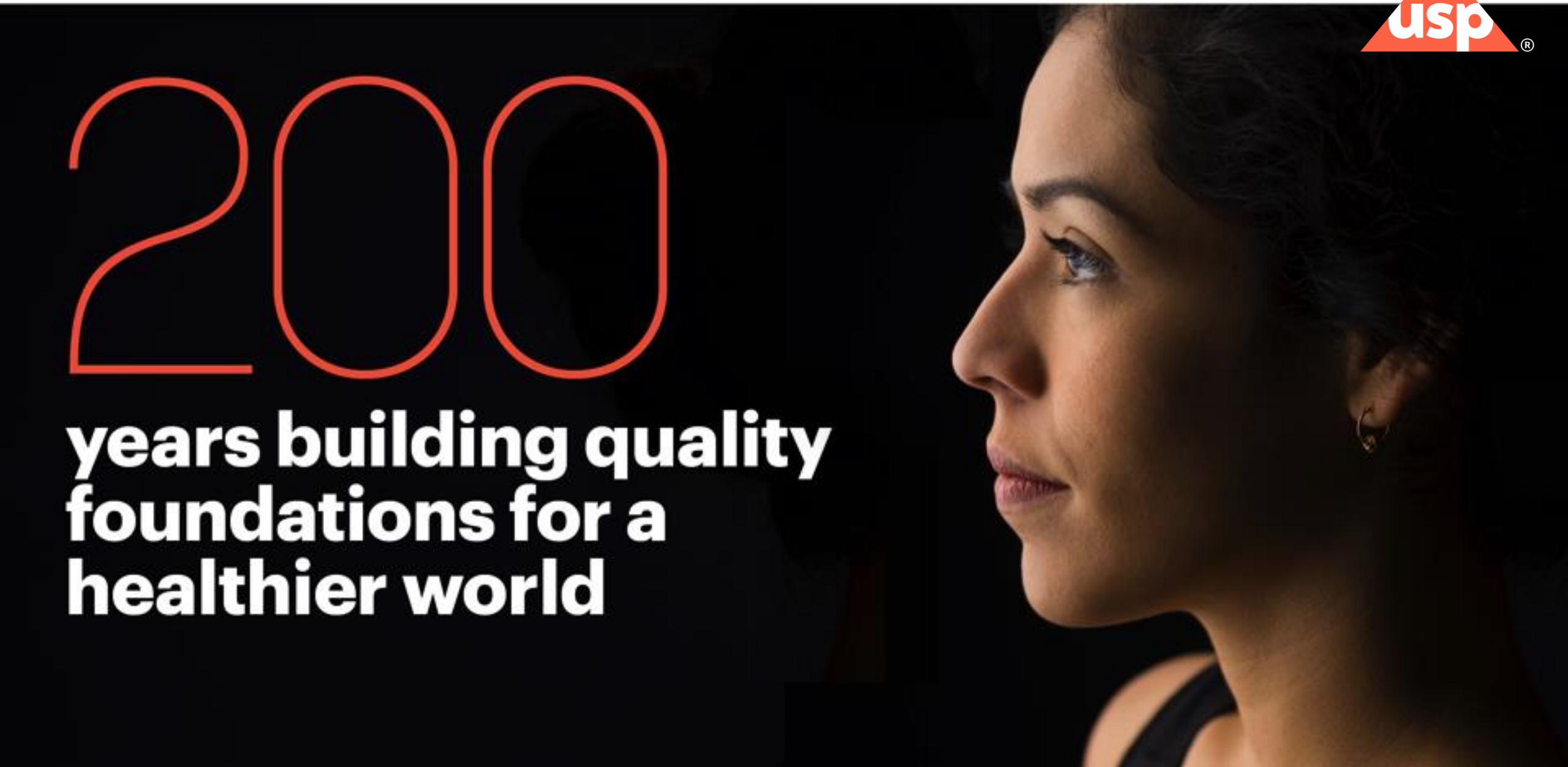
Melhorar a saúde global através de padrões públicos e programas relacionados que ajudam a assegurar a qualidade, segurança e benefícios de medicamentos e alimentos.



© 2018 USP

200

years building quality foundations for a healthier world

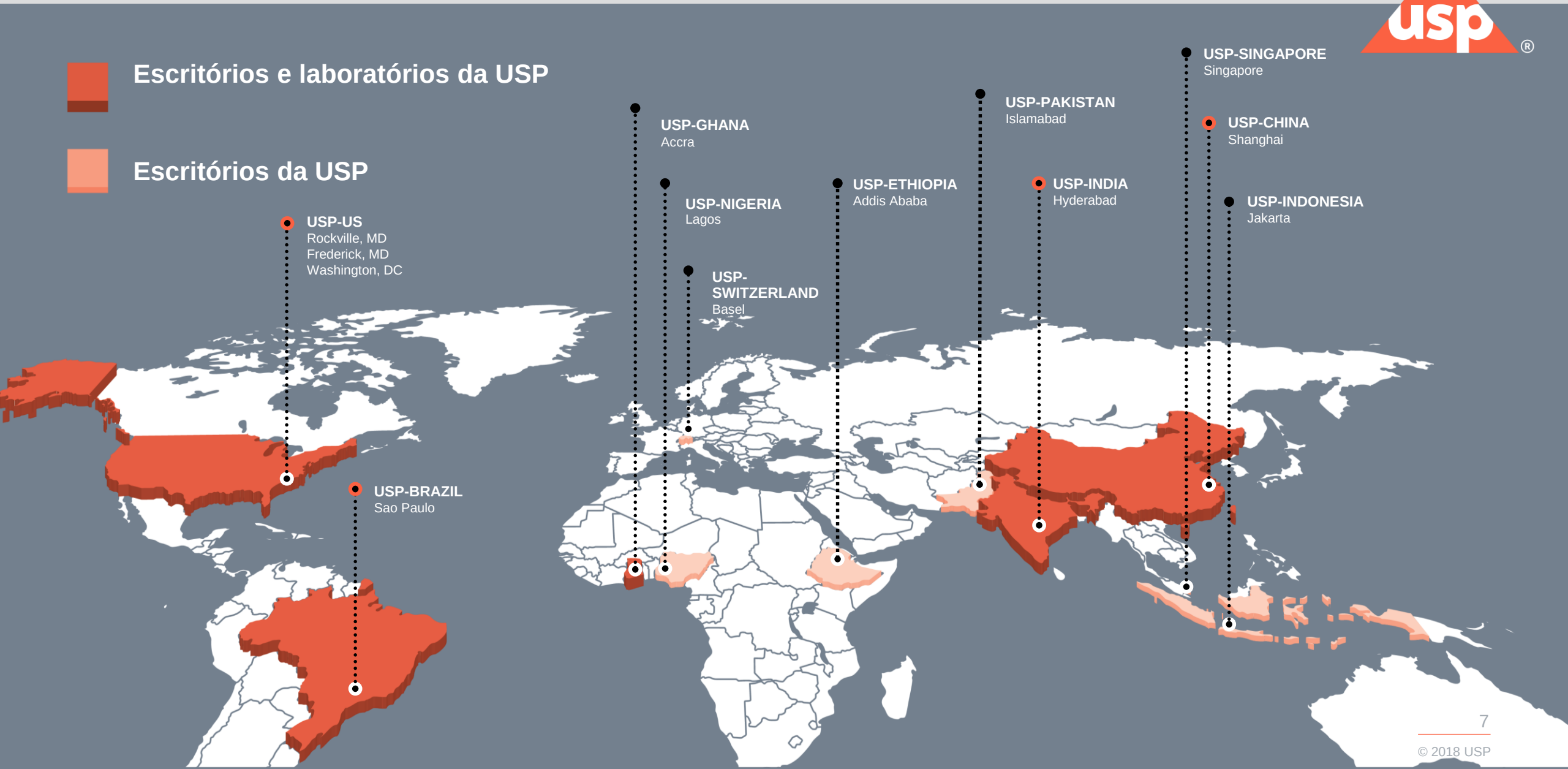


USP hoje: Avançando na visão de nosso fundador

- Fundada em 1820, sem fins lucrativos, privada, independente e auto-financiada;
- Focada em normas de qualidade para melhorar a saúde pública global;
- 1.200+ colaboradores ao redor do mundo;
- Escritório central em Rockville, EUA;
- Laboratórios colaborativos nos EUA, Índia, China, Brasil e Gana;
- Escritórios na Suíça, Etiópia, Indonésia, Filipinas e Nigéria;
- Trabalha em conjunto com mais de 900 voluntários da indústria, academia, governo que auxiliam na proteção da saúde pública;
- Internacionalmente reconhecida e com trabalhos globais.

© 2017 USP

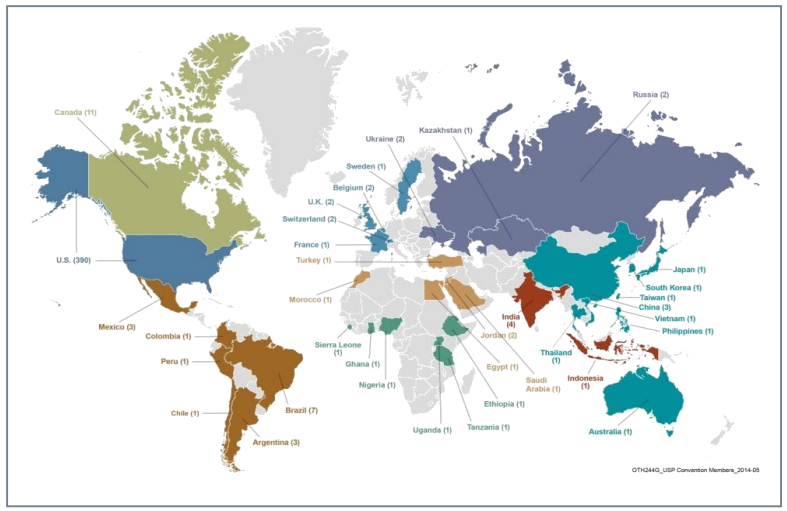
USP trabalha globalmente

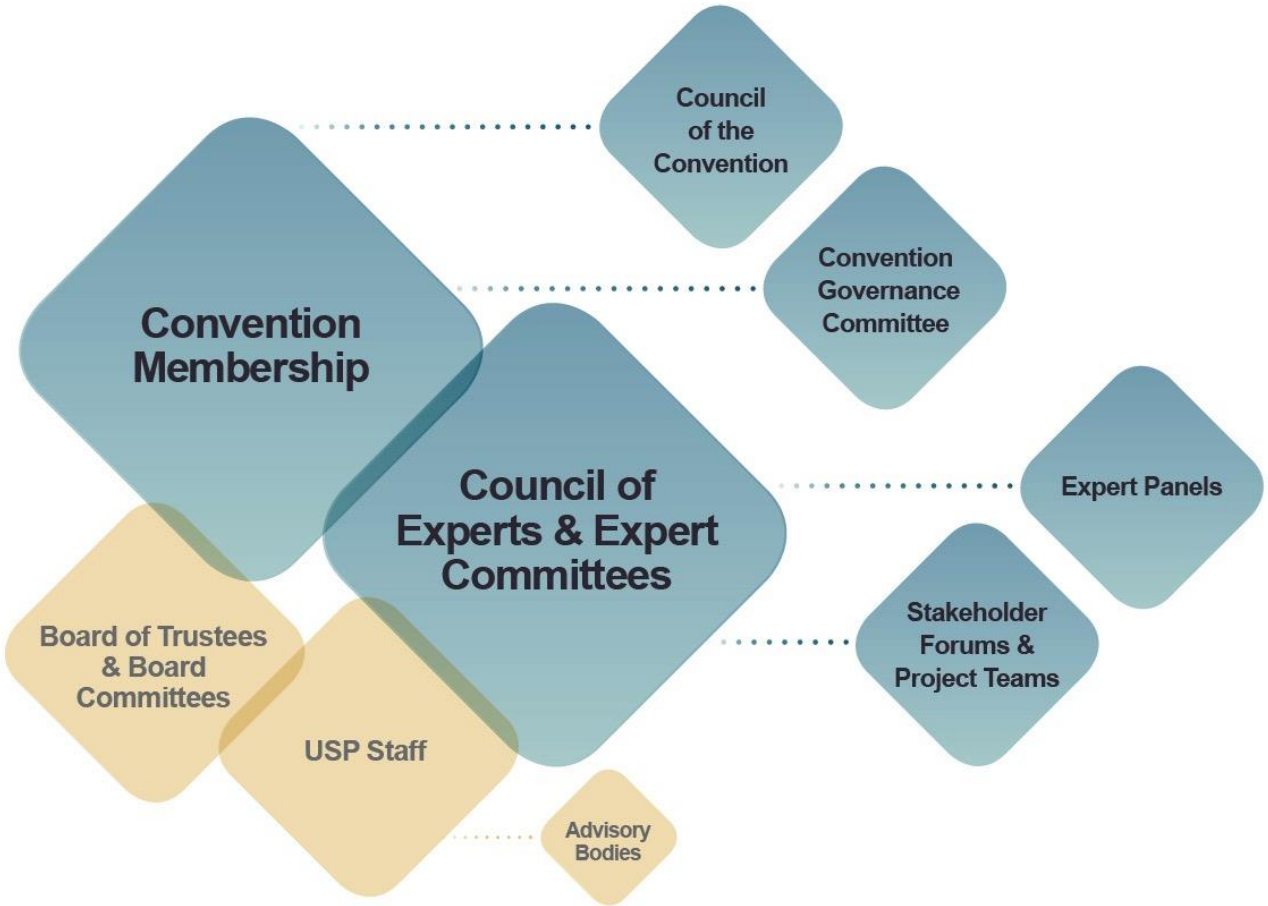


© 2018 USP

Governança e Conselho Consultivo

USP Convention Members





© 2017 USP

Presença global do staff da USP

1200+ Staff

70%
US-Based

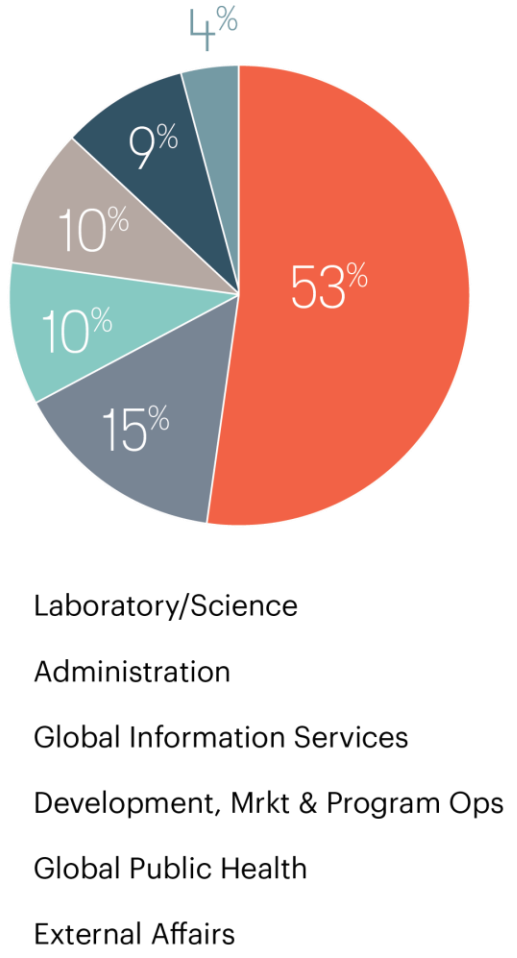
6%
China-Based

4%
Brazil-Based

15%
India-Based

5%

Other global sites: Ethiopia, Europe, Ghana, Indonesia, Nigeria, Singapore

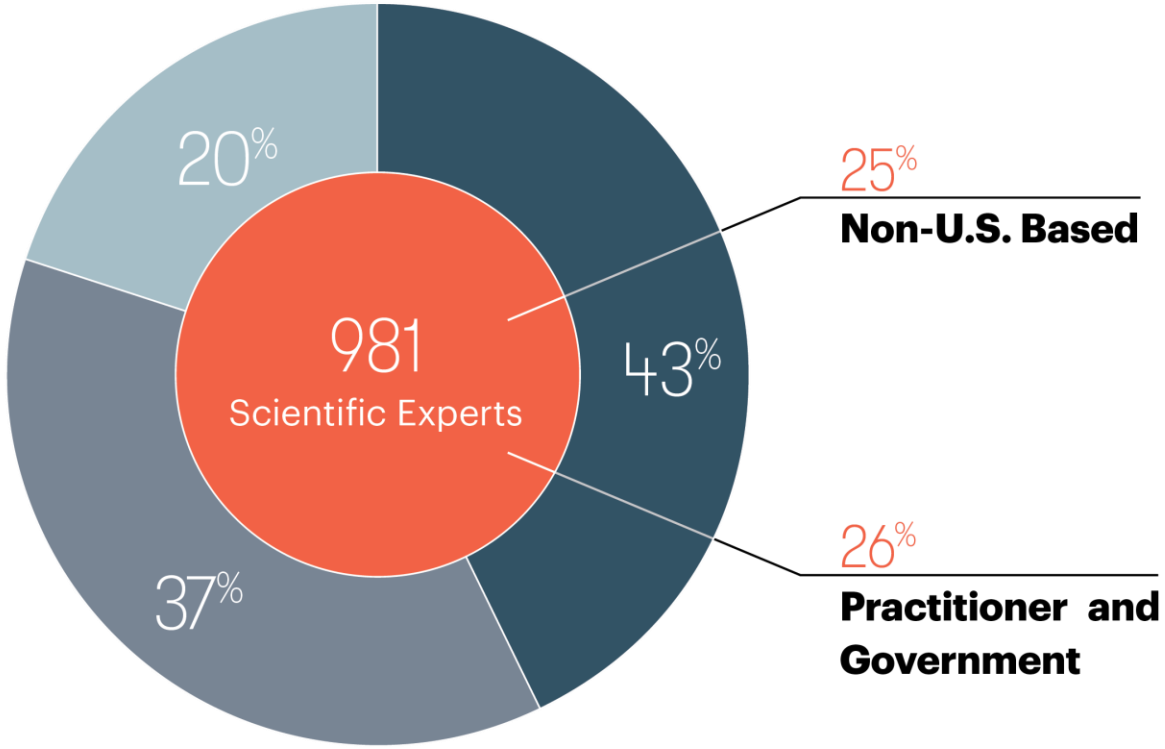


© 2017 USP

Voluntários da USP

981 Scientific Experts–Volunteers and Government Liaisons

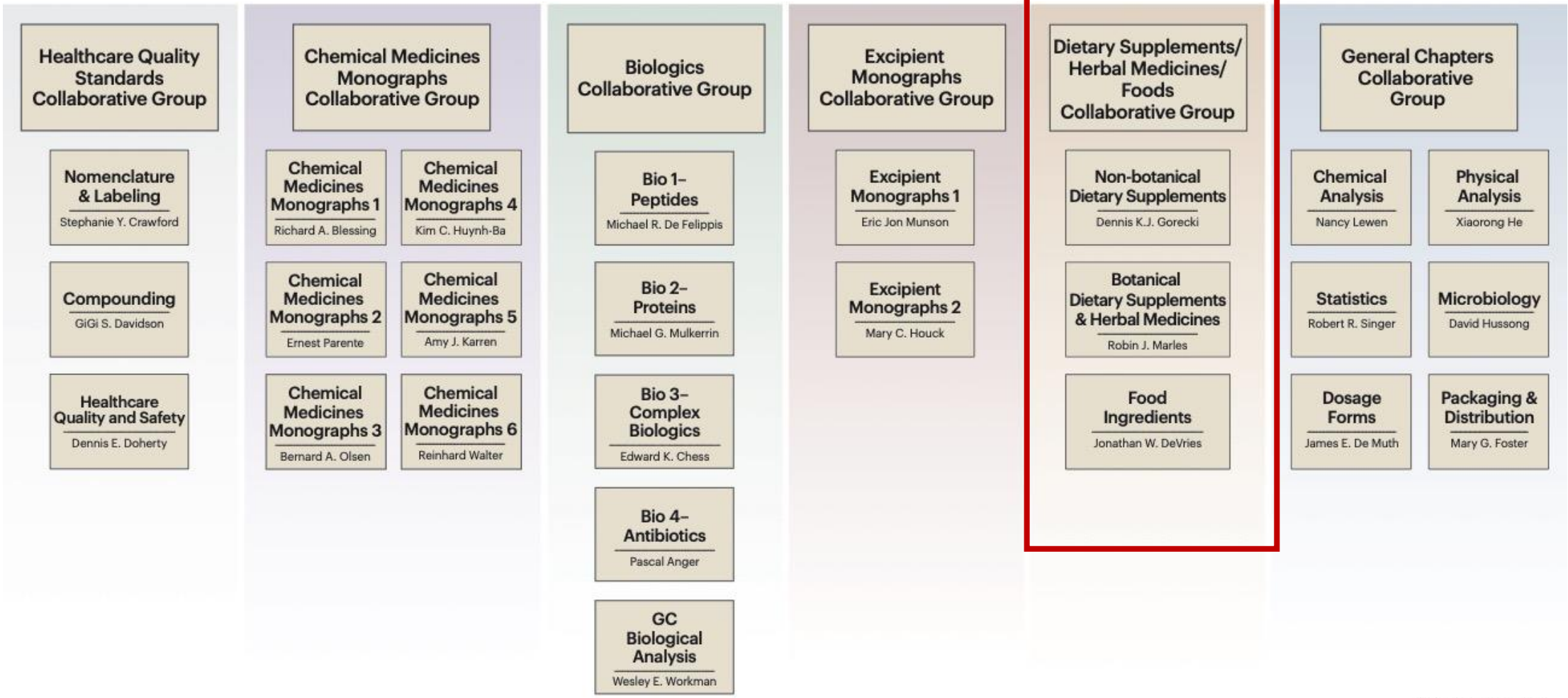
- 428 Expert Committee Members
- 362 Expert Panels-Only Members
- 191 Government Liaisons



© 2018 USP

Voluntários fazem acontecer na USP

Comitês de Especialistas e Grupos Colaborativos

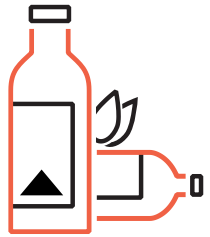


Definindo qualidade para…

Produtos Farmacêuticos



Ingredients de alimentos



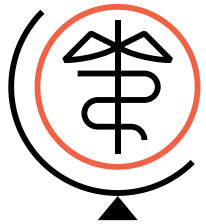
Qualidade em serviços de saúde



Suplementos Alimentares e Medicamentos Fitoterápicos



Saúde pública global



© 2017 USP

…através de padrões…

- Padrões documentais (Mais de 500 monografias para suplementos alimentares)
  - **USP-NF** - para medicamentos, excipientes e suplementos alimentares
  - **DSC** - Suplementos alimentares
  - **Herbal Medicines Compendium** – Produtos naturais
  - **FCC** – Ingredientes alimentícios
- Padrões de referência - material
  - **>3.800** Padrões de Referência USP
  - **>330** itens especificamente para Suplementos Alimentares disponíveis em catálogo

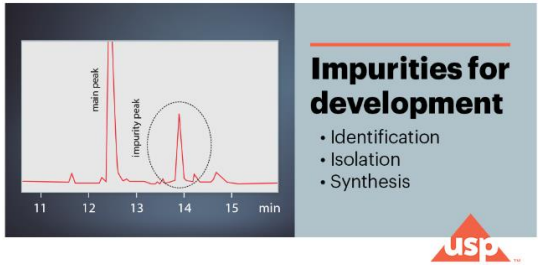




© 2017 USP

…e nossos programas e serviços relacionados

- Impurities for development (IfD)
  - Identificação, isolamento, síntese de impurezas para medicamentos em desenvolvimento



- USP Education (https://www.uspbrasil.com.br/cursos/)
  - ~6,000 participantes/ano; >100 cursos
- Programa de Verificação
  - USP Verified Mark em >400 milhões frascos





- Global Public Health (GPH)
  - Programa Promoting Quality of Medicines (PQM): USAID financiou atividades em países de baixa e média renda para garantir a qualidade e aumentar o acesso de medicamentos considerados prioritários.



© 2017 USP

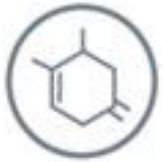
2

Suplementos Alimentares na USP

Processo de Desenvolvimento de Monografias

Stakeholders

Academia
Industria
Autoridades Reguladoras



Início do desenvolvimento de monografia*

Revisão técnica



Draft da monografia e revisão pelo Comitê de Especialistas



Proposta da Monografia

- Food Chemical Codex Forum (FCCF) ou Pharmacopeial Forum (PF) para comentários públicos



Monografia aprovada

- Pelo Comitê de Especialistas e publicado no FCC ou no USP-NF

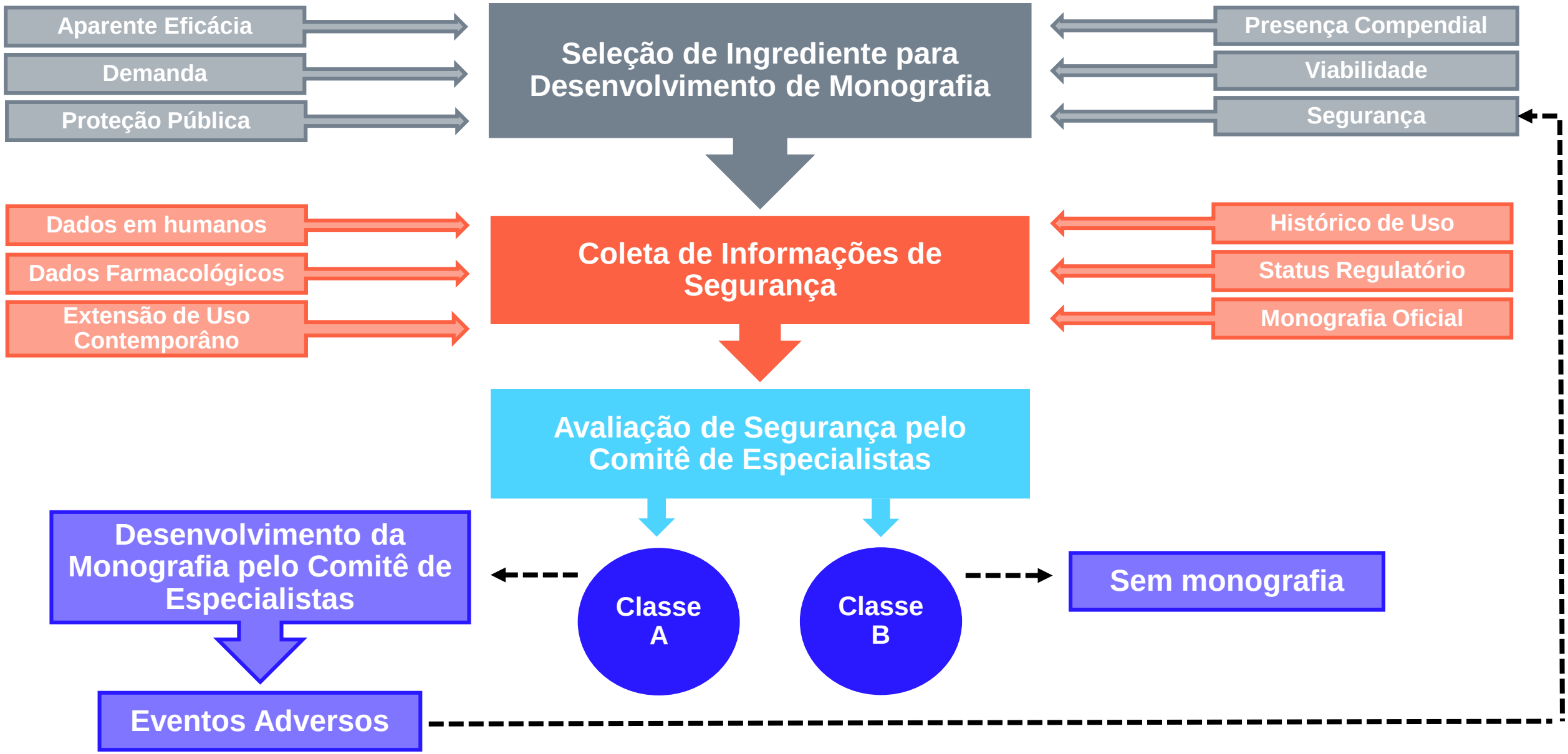


Requisição de Revisão

- requisição de revisão pode ser iniciada pela USP ou stakeholders para qualquer das monografias publicadas no FCC ou USP-NFA

© 2017 USP

Processo de Desenvolvimento de Monografias

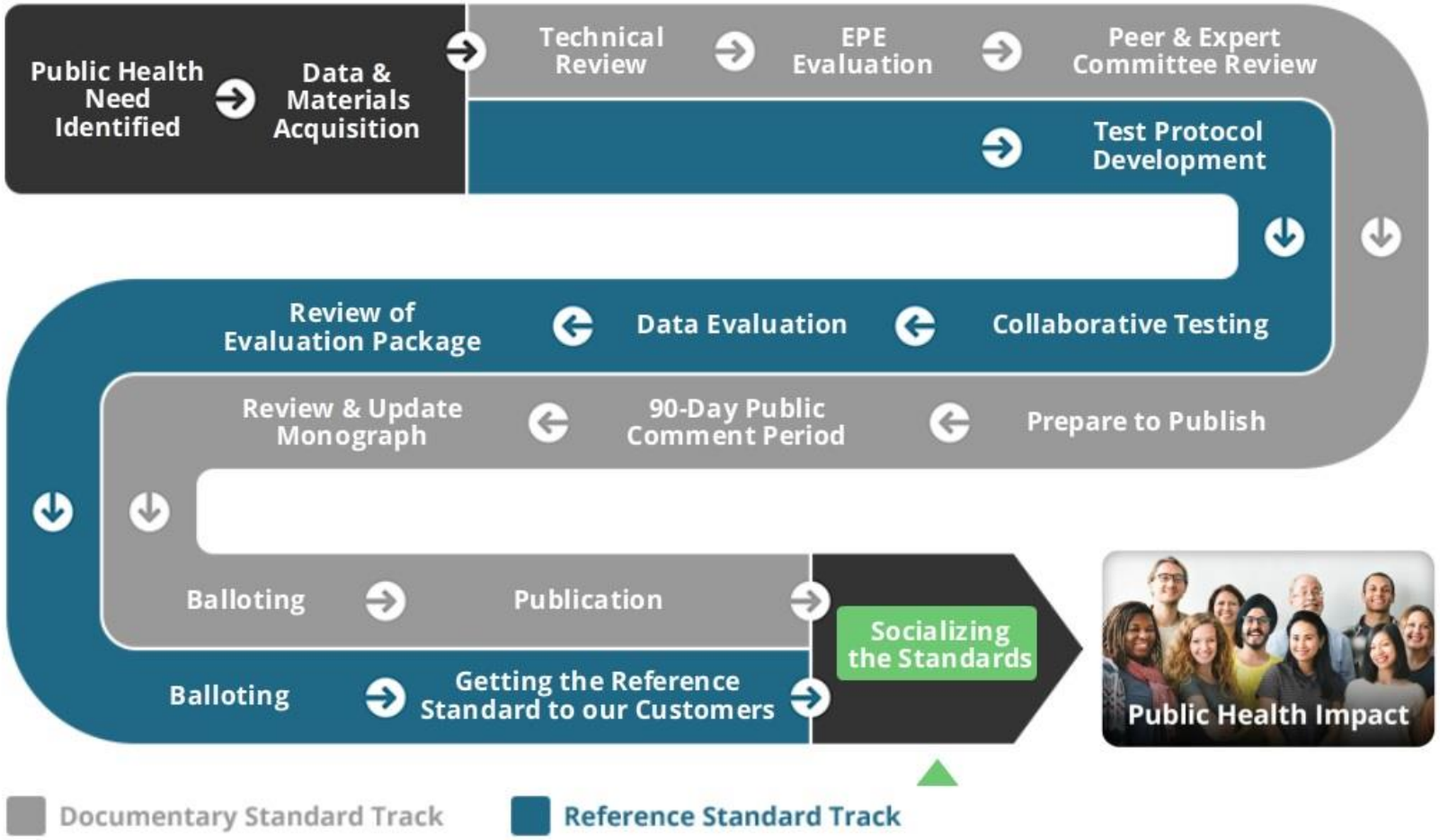


Esforço Coordenado: Monografias e Padrões de Referência



Developing Reference Standards

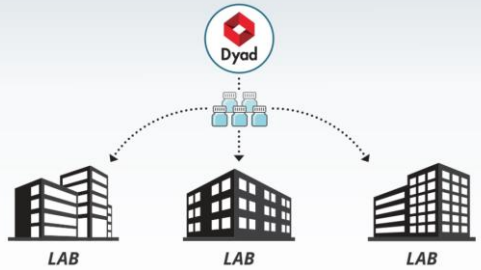




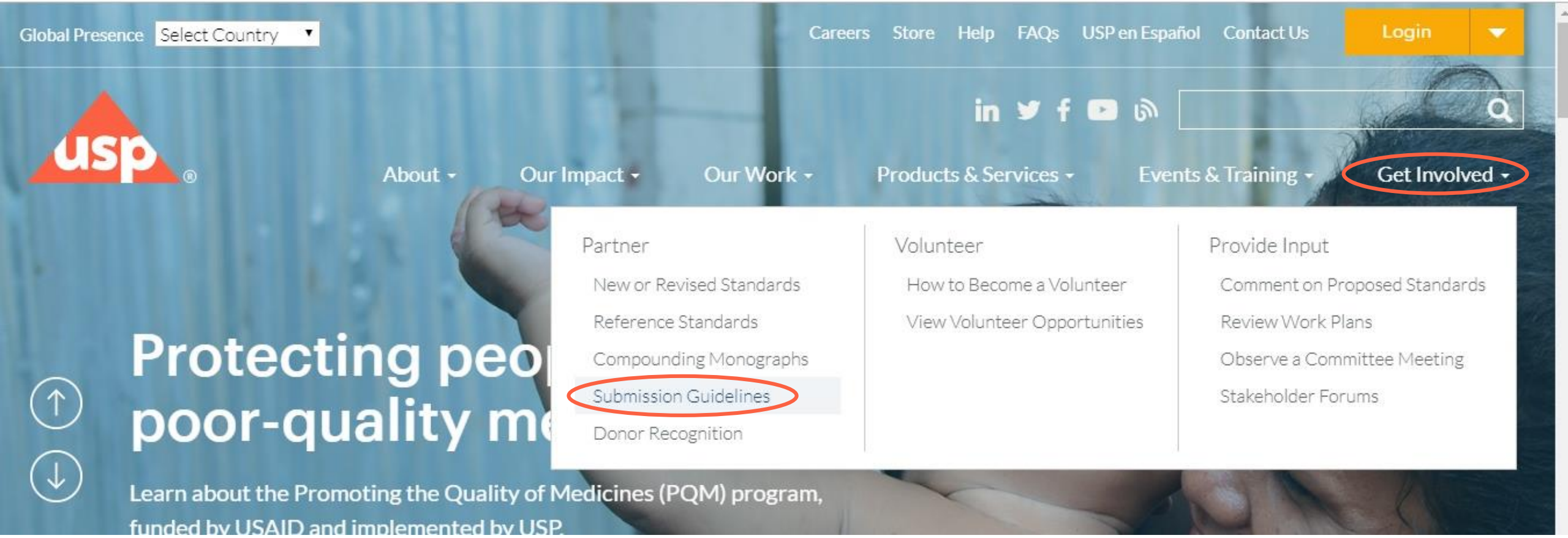
Collaborative Testing

Collaborative testing is generally conducted in at least three labs, which includes Reference Standards Laboratories (RSL). This team is part of Global Laboratory Operations (GLO).

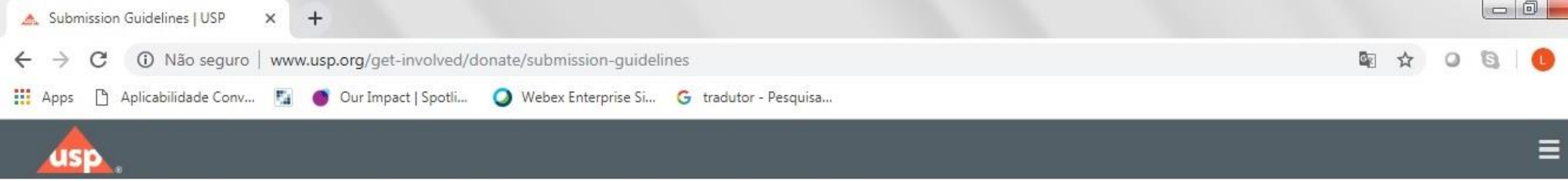
USP also has collaborative testing labs in India, Brazil, China, and Ghana



© 2017 USP



Acesse: www.usp.org
Get Involved
Submission guidelines



- **Dietary Supplements, Herbal Medicines, and Food Ingredient Guidelines**
  - Botanical Dietary Supplements: Botanical drugs, botanical dietary supplements, and herbal medicine ingredients
  - Non-Botanical Dietary Supplements: Vitamins, minerals, amino acids, and specialty ingredients (e.g., chondroitin, creatine, probiotics)
  - Admission of Dietary Supplement Ingredients to the USP–NF Monograph Development Process: Criteria used to determine whether a dietary ingredient qualifies for admission to the USP–NF process for quality monograph development
  - Food Ingredients monographs and other revisions to FCC: Foods, food additives, food colors, processing aids (e.g., enzymes), and functional ingredients that affect the human body. Also, view FCC submission checklist.
  - Guideline for Assigning Titles to USP Dietary Supplement Monographs:This Guideline streamlines the naming of DS monograph articles in the USP–NF and in the DSC. It provides a written systematic approach to developing monograph titles for dietary ingredients and dietary supplement dosage forms newly admitted to USP. In order to minimize the potential for confusion and controversy, the nomenclature approach is informed by the practices of the dietary supplement industry and the labeling requirements of applicable federal regulations.

Acesse: www.usp.org
Get Involved
Submission guidelines

Guia para a Admissão de Ingredientes Suplementares Alimentares ao Processo de Desenvolvimento de Monografia USP – NF

- O objetivo do Guia é estabelecer os critérios que a USP usa para determinar se um ingrediente se qualifica ou não para admissão no processo para o desenvolvimento de uma monografia de qualidade
- Admissão no processo de desenvolvimento de monografias não garante inclusão na United States Pharmacopeia and National Formulary (USP–NF). A aprovação subsequente da monografia para inclusão no USP – NF é determinado pelo processo de votação da USP.
- O Guia estabelece um sistema Classe A e B que categoriza os ingredientes de suplementos alimentares de acordo com seu nível de segurança e descreve o processo pelo qual os ingredientes são classificados.

https://www.usp.org/sites/default/files/usp/document/get-involved/submission-guidelines/guideline-for-the-admission-of-dietary-supplement-ingredients.pdf

© 2017 USP

Seleção e Priorização de Ingredientes de Suplementos Alimentares

- A seleção inicial e a priorização de ingredientes de suplementos alimentares para admissão no processo de desenvolvimento de monografias do USP-NF são baseadas em várias considerações, incluindo, entre outras, as seguintes:

1. Extensão de uso, com base nas vendas no mercado ou outros fatores
2. Uso histórico
3. Conhecimento de composição química
4. Existência de outros padrões farmacopeicos
5. Evidência de benefício
6. Interesse de um órgão governamental
7. Potenciais riscos para a saúde associados ao seu uso

© 2017 USP

Processo de Desenvolvimento de Monografia USP – NF

Classe A

Classe A: Admitido no processo de desenvolvimento de monografias do USP-NF

- Ingredientes para os quais a evidência disponível não indica um risco grave para a saúde * ou outro problema de saúde pública que impeça o desenvolvimento de uma monografia USP-NF e que possa ser aprovado para inclusão nos compêndios.

Classe B

Classe B: Não admitido no processo de desenvolvimento de monografias

- Ingredientes para os quais a evidência disponível indica um risco grave para a saúde* ou outras preocupações em saúde pública que impedem o desenvolvimento de monografia.

- * Risco grave para a saúde:

(A) resultar em: (i) morte; (ii) risco de vida; (iii) internação hospitalar; (iv) uma persistente deficiência ou incapacidade significativa; ou (v) uma anomalia congênita ou defeito congênito; ou

(B) exigir, com base em julgamento médico razoável, uma intervenção médica ou cirúrgica para impedir um desfecho descrito no subparágrafo (A).

© 2017 USP

O que submeter?

1) Documentação de status regulatório
2) Conteúdo da Monografia
3) Validação do Método
4) Dados de suporte
5) Resumo dos dados técnicos



O que submeter?

1) Documentação de status regulatório
2) Conteúdo da Monografia
3) Validação do Método
4) Dados de suporte
5) Resumo dos dados técnicos



Documentação de status regulatório

Status Regulatório

- Como exemplo foi utilizado o sistema regulatório dos EUA?
  - ✓Aditivo alimentar
  - ✓Aditivo corante
  - ✓Substância geralmente reconhecida como segura (GRAS)
  - ✓Sanção Priorizada
- Outros países / internacionais

Documentação Regulatória

- Não é obrigatório, mas auxilia na análise
- EUA:
  - ✓Pacote de notificação GRAS enviado e resposta da FDA
  - ✓Documentação do Self GRAS
- Outros países:
  - ✓Pacote enviado para avaliação e resposta regulatória

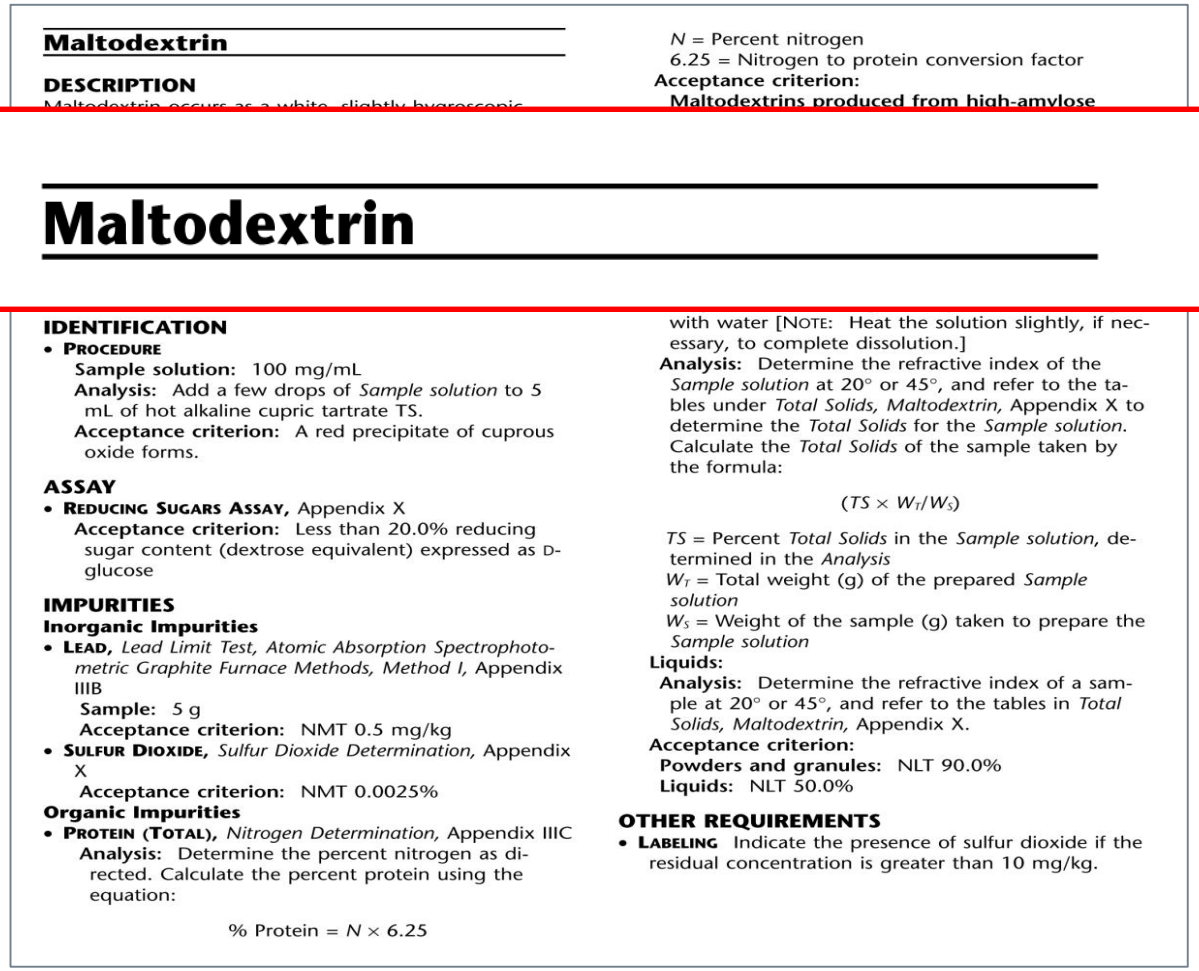
© 2017 USP

O que submeter?

1) Documentação de status regulatório
2) Conteúdo da Monografia
3) Validação do Método
4) Dados de suporte
5) Resumo dos dados técnicos



Conteúdo da Monografia - Título



Maltodextrin

DESCRIPTION

N = Percent nitrogen
6.25 = Nitrogen to protein conversion factor
Acceptance criterion:
Maltodextrins produced from high-amylose

Maltodextrin

IDENTIFICATION
- **PROCEDURE**
  Sample solution: 100 mg/mL
  Analysis: Add a few drops of *Sample solution* to 5 mL of hot alkaline cupric tartrate TS.
  Acceptance criterion: A red precipitate of cuprous oxide forms.

ASSAY
- **REDUCING SUGARS ASSAY,** Appendix X
  Acceptance criterion: Less than 20.0% reducing sugar content (dextrose equivalent) expressed as D-glucose

IMPURITIES
Inorganic Impurities
- **LEAD,** *Lead Limit Test, Atomic Absorption Spectrophotometric Graphite Furnace Methods, Method I,* Appendix IIIB
  Sample: 5 g
  Acceptance criterion: NMT 0.5 mg/kg
- **SULFUR DIOXIDE,** *Sulfur Dioxide Determination,* Appendix X
  Acceptance criterion: NMT 0.0025%

Organic Impurities
- **PROTEIN (TOTAL),** *Nitrogen Determination,* Appendix IIIC
  Analysis: Determine the percent nitrogen as directed. Calculate the percent protein using the equation:

$$\% \text{ Protein} = N \times 6.25$$

with water [NOTE: Heat the solution slightly, if necessary, to complete dissolution.]
Analysis: Determine the refractive index of the *Sample solution* at 20° or 45°, and refer to the tables under *Total Solids, Maltodextrin,* Appendix X to determine the *Total Solids* for the *Sample solution.* Calculate the *Total Solids* of the sample taken by the formula:

$$(TS \times W_T/W_S)$$

TS = Percent *Total Solids* in the *Sample solution,* determined in the *Analysis*
W_T = Total weight (g) of the prepared *Sample solution*
W_S = Weight of the sample (g) taken to prepare the *Sample solution*

Liquids:
Analysis: Determine the refractive index of a sample at 20° or 45°, and refer to the tables in *Total Solids, Maltodextrin,* Appendix X.
Acceptance criterion:
Powders and granules: NLT 90.0%
Liquids: NLT 50.0%

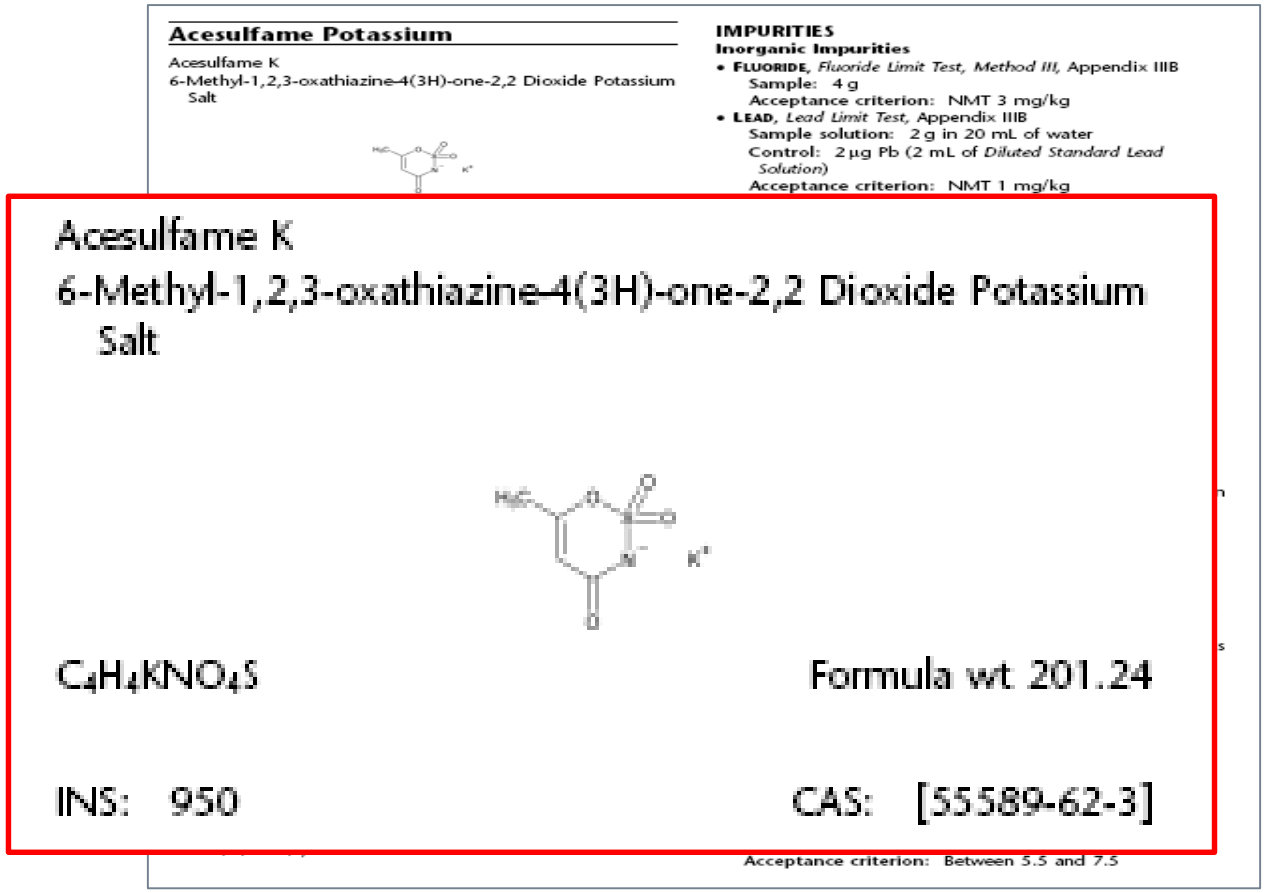
OTHER REQUIREMENTS
- **LABELING** Indicate the presence of sulfur dioxide if the residual concentration is greater than 10 mg/kg.

- Nome / título
- Harmonização com o JECFA
- Não-proprietário
- Deve ser uma descrição científica precisa do material
- Nome atribuído por uma autoridade reguladora
- Nome comum - nome usado para item de comércio

© 2017 USP

Conteúdo da Monografia – Dados químicos

- Caráter informativo
- Dados químicos
  - ✓ Nome químico
  - ✓ Sinônimos
  - ✓ Estrutura molecular, fórmulas químicas e massas moleculares
  - ✓ CAS
  - ✓ INS
  - ✓ FEMA
  - ✓ UNII



Acesulfame Potassium

Acesulfame K
6-Methyl-1,2,3-oxathiazine-4(3H)-one-2,2 Dioxide Potassium Salt

IMPURITIES
Inorganic Impurities
- **FLUORIDE,** *Fluoride Limit Test, Method III,* Appendix IIIB
  Sample: 4 g
  Acceptance criterion: NMT 3 mg/kg
- **LEAD,** *Lead Limit Test,* Appendix IIIB
  Sample solution: 2 g in 20 mL of water
  Control: 2 µg Pb (2 mL of *Diluted Standard Lead Solution*)
  Acceptance criterion: NMT 1 mg/kg

Acesulfame K
6-Methyl-1,2,3-oxathiazine-4(3H)-one-2,2 Dioxide Potassium Salt

$C_4H_4KNO_4S$ Formula wt 201.24

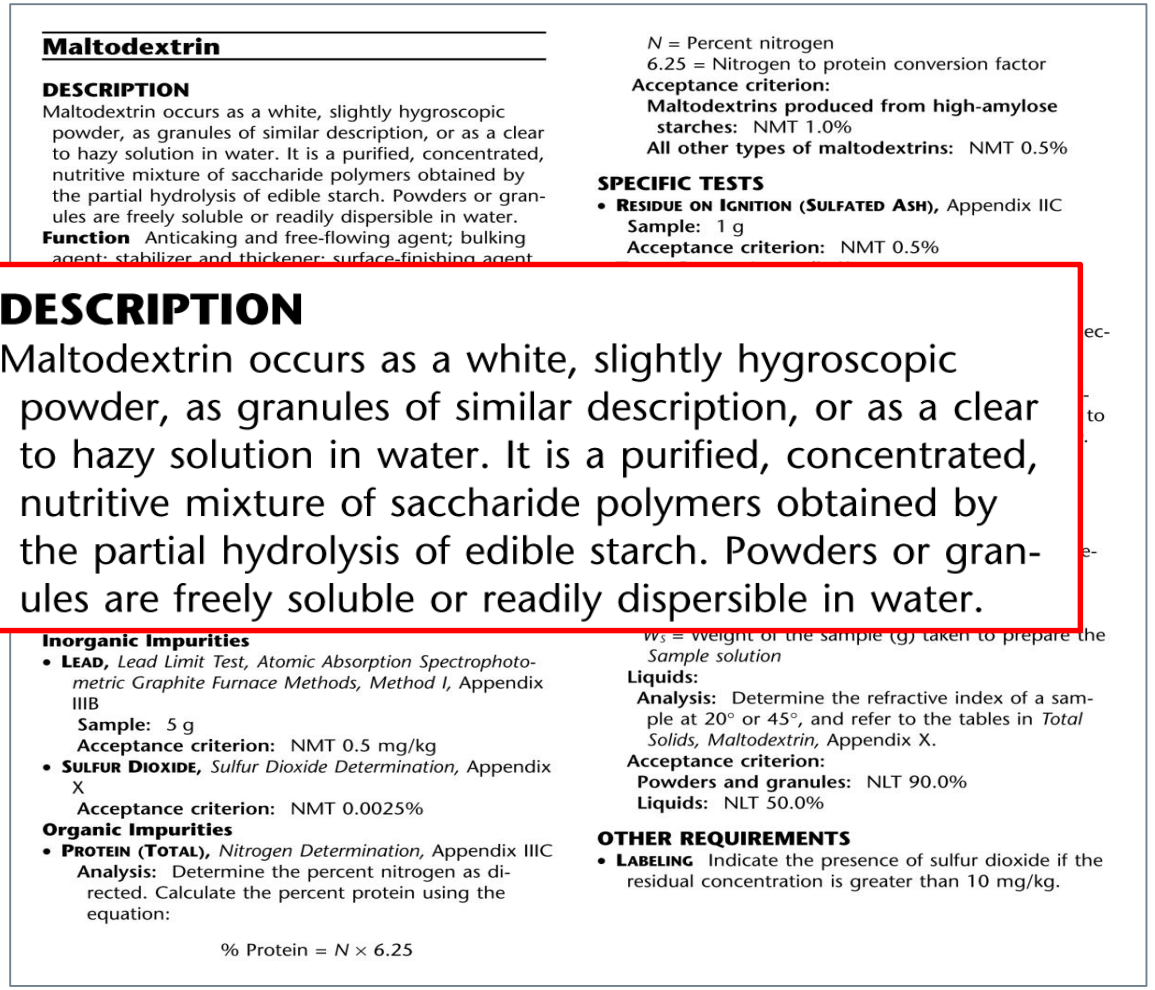
INS: 950 CAS: [55589-62-3]

Acceptance criterion: Between 5.5 and 7.5

© 2017 USP

Conteúdo da Monografia - Descrição

- Caráter informativo
- Características físicas
  - ✓Cor
  - ✓Estado físico / forma
- Origem
- Indicações aproximadas de solubilidade, pH, ponto de fusão, entre outros
- Presença de substâncias adicionadas: antioxidantes, agentes anti-aglomerantes
  - ✓ FCC prevê a presença de tais substâncias
  - ✓ Restrições: misturas proprietárias
- Informação não proprietária do método de fabricação



Maltodextrin

DESCRIPTION

Maltodextrin occurs as a white, slightly hygroscopic powder, as granules of similar description, or as a clear to hazy solution in water. It is a purified, concentrated, nutritive mixture of saccharide polymers obtained by the partial hydrolysis of edible starch. Powders or granules are freely soluble or readily dispersible in water.

Function Anticaking and free-flowing agent; bulking agent; stabilizer and thickener; surface-finishing agent

N = Percent nitrogen
6.25 = Nitrogen to protein conversion factor

Acceptance criterion:
Maltodextrins produced from high-amylose starches: NMT 1.0%
All other types of maltodextrins: NMT 0.5%

SPECIFIC TESTS

- **Residue on Ignition (Sulfated Ash),** Appendix IIC
  Sample: 1 g
  Acceptance criterion: NMT 0.5%

DESCRIPTION

Maltodextrin occurs as a white, slightly hygroscopic powder, as granules of similar description, or as a clear to hazy solution in water. It is a purified, concentrated, nutritive mixture of saccharide polymers obtained by the partial hydrolysis of edible starch. Powders or granules are freely soluble or readily dispersible in water.

Inorganic Impurities

- **Lead,** *Lead Limit Test, Atomic Absorption Spectrophotometric Graphite Furnace Methods, Method I,* Appendix IIIB
  Sample: 5 g
  Acceptance criterion: NMT 0.5 mg/kg
- **Sulfur Dioxide,** *Sulfur Dioxide Determination,* Appendix X
  Acceptance criterion: NMT 0.0025%

Organic Impurities

- **Protein (Total),** *Nitrogen Determination,* Appendix IIIC
  Analysis: Determine the percent nitrogen as directed. Calculate the percent protein using the equation:

$$\% \text{ Protein} = N \times 6.25$$

W_S = weight of the sample (g) taken to prepare the *Sample solution*

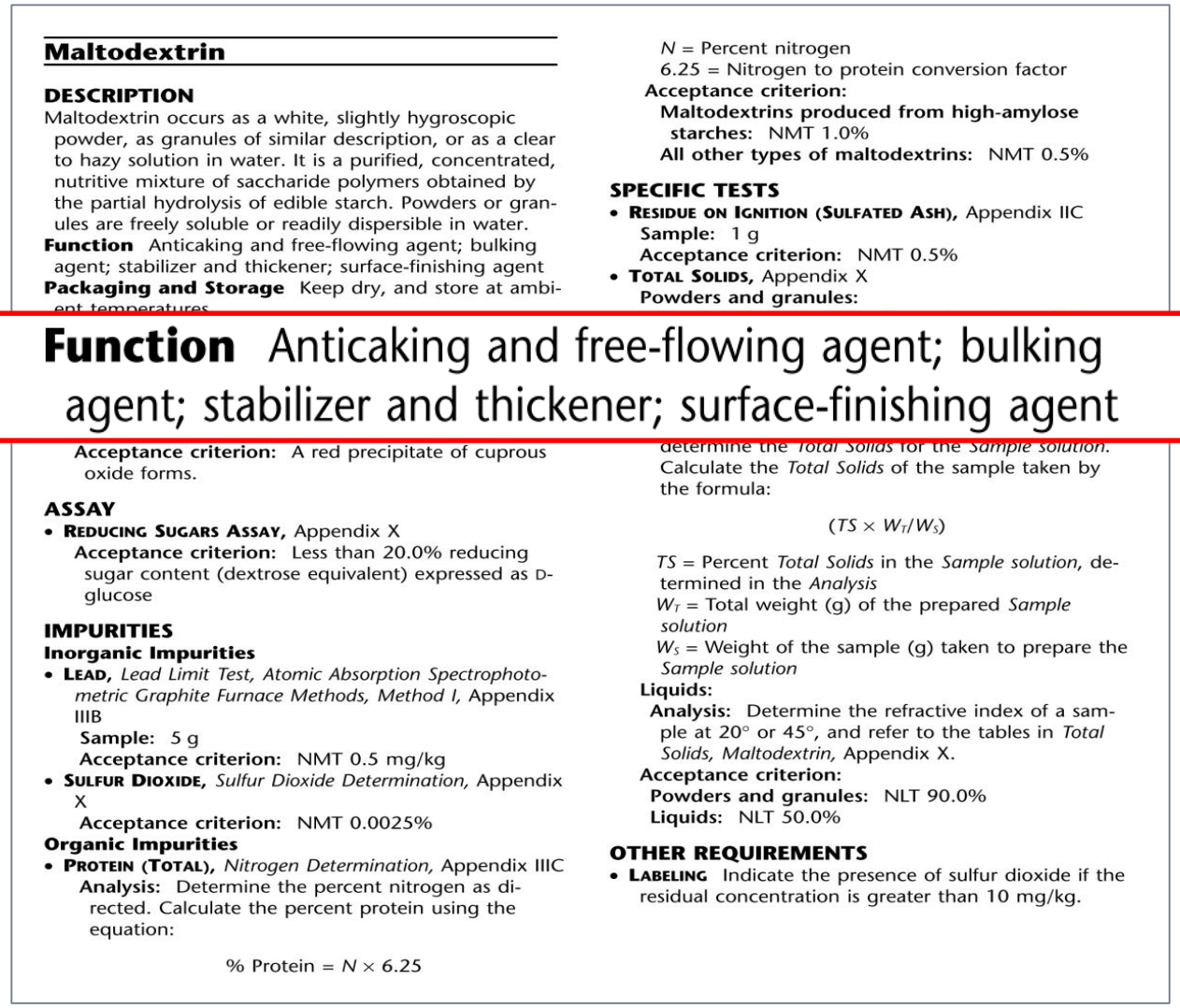
Liquids:
Analysis: Determine the refractive index of a sample at 20° or 45°, and refer to the tables in *Total Solids, Maltodextrin,* Appendix X.
Acceptance criterion:
Powders and granules: NLT 90.0%
Liquids: NLT 50.0%

OTHER REQUIREMENTS

- **Labeling** Indicate the presence of sulfur dioxide if the residual concentration is greater than 10 mg/kg.

© 2017 USP

Conteúdo da Monografia - Função



Maltodextrin

DESCRIPTION

Maltodextrin occurs as a white, slightly hygroscopic powder, as granules of similar description, or as a clear to hazy solution in water. It is a purified, concentrated, nutritive mixture of saccharide polymers obtained by the partial hydrolysis of edible starch. Powders or granules are freely soluble or readily dispersible in water.

Function Anticaking and free-flowing agent; bulking agent; stabilizer and thickener; surface-finishing agent

Packaging and Storage Keep dry, and store at ambient temperatures.

Function Anticaking and free-flowing agent; bulking agent; stabilizer and thickener; surface-finishing agent

Acceptance criterion: A red precipitate of cuprous oxide forms.

ASSAY

- **Reducing Sugars Assay,** Appendix X
  Acceptance criterion: Less than 20.0% reducing sugar content (dextrose equivalent) expressed as D-glucose

IMPURITIES

Inorganic Impurities

- **Lead,** *Lead Limit Test, Atomic Absorption Spectrophotometric Graphite Furnace Methods, Method I,* Appendix IIIB
  Sample: 5 g
  Acceptance criterion: NMT 0.5 mg/kg
- **Sulfur Dioxide,** *Sulfur Dioxide Determination,* Appendix X
  Acceptance criterion: NMT 0.0025%

Organic Impurities

- **Protein (Total),** *Nitrogen Determination,* Appendix IIIC
  Analysis: Determine the percent nitrogen as directed. Calculate the percent protein using the equation:

$$\% \text{ Protein} = N \times 6.25$$

N = Percent nitrogen
6.25 = Nitrogen to protein conversion factor

Acceptance criterion:
Maltodextrins produced from high-amylose starches: NMT 1.0%
All other types of maltodextrins: NMT 0.5%

SPECIFIC TESTS

- **Residue on Ignition (Sulfated Ash),** Appendix IIC
  Sample: 1 g
  Acceptance criterion: NMT 0.5%
- **Total Solids,** Appendix X
  Powders and granules:

determine the *Total Solids* for the *Sample solution*. Calculate the *Total Solids* of the sample taken by the formula:

$$(TS \times W_T/W_S)$$

TS = Percent *Total Solids* in the *Sample solution*, determined in the *Analysis*
W_T = Total weight (g) of the prepared *Sample solution*
W_S = Weight of the sample (g) taken to prepare the *Sample solution*

Liquids:
Analysis: Determine the refractive index of a sample at 20° or 45°, and refer to the tables in *Total Solids, Maltodextrin,* Appendix X.

Acceptance criterion:
Powders and granules: NLT 90.0%
Liquids: NLT 50.0%

OTHER REQUIREMENTS

- **Labeling** Indicate the presence of sulfur dioxide if the residual concentration is greater than 10 mg/kg.

- Apenas informativo
- Propriedades técnicas principais no produto ou processo de fabricação
- Aplicação principal
  - ✓ Exemplo: Fonte de…

© 2017 USP

Conteúdo da Monografia – Embalagem e Armazenamento

Maltodextrin

DESCRIPTION

Maltodextrin occurs as a white, slightly hygroscopic powder, as granules of similar description, or as a clear to hazy solution in water. It is a purified, concentrated, nutritive mixture of saccharide polymers obtained by the partial hydrolysis of edible starch. Powders or granules are freely soluble or readily dispersible in water.

Function Anticaking and free-flowing agent; bulking agent; stabilizer and thickener; surface-finishing agent

Packaging and Storage Keep dry, and store at ambient temperatures.

IDENTIFICATION

Packaging and Storage: Store in well-closed containers in a cool, dry place.

mL of hot alkaline cupric tartrate TS.

Acceptance criterion: A red precipitate of cuprous oxide forms.

ASSAY

- **Reducing Sugars Assay,** Appendix X

  Acceptance criterion: Less than 20.0% reducing sugar content (dextrose equivalent) expressed as D-glucose

IMPURITIES

Inorganic Impurities

- **Lead,** *Lead Limit Test, Atomic Absorption Spectrophotometric Graphite Furnace Methods, Method I,* Appendix IIIB

  Sample: 5 g

  Acceptance criterion: NMT 0.5 mg/kg
- **Sulfur Dioxide,** *Sulfur Dioxide Determination,* Appendix X

  Acceptance criterion: NMT 0.0025%

Organic Impurities

- **Protein (Total),** *Nitrogen Determination,* Appendix IIIC

  Analysis: Determine the percent nitrogen as directed. Calculate the percent protein using the equation:

$$\% \text{ Protein} = N \times 6.25$$

N = Percent nitrogen

6.25 = Nitrogen to protein conversion factor

Acceptance criterion:

Maltodextrins produced from high-amylose starches: NMT 1.0%

All other types of maltodextrins: NMT 0.5%

SPECIFIC TESTS

- **Residue on Ignition (Sulfated Ash),** Appendix IIC

  Sample: 1 g

  Acceptance criterion: NMT 0.5%
- **Total Solids,** Appendix X

  Powders and granules:

  Sample solution: 60 g of sample made to 100 g with water [NOTE: Heat the solution slightly, if nec-

bles under *Total Solids, Maltodextrin,* Appendix X to determine the *Total Solids* for the *Sample solution.* Calculate the *Total Solids* of the sample taken by the formula:

$$(TS \times W_T/W_S)$$

TS = Percent *Total Solids* in the *Sample solution,* determined in the *Analysis*

W_T = Total weight (g) of the prepared *Sample solution*

W_S = Weight of the sample (g) taken to prepare the *Sample solution*

Liquids:

Analysis: Determine the refractive index of a sample at 20° or 45°, and refer to the tables in *Total Solids, Maltodextrin,* Appendix X.

Acceptance criterion:

Powders and granules: NLT 90.0%

Liquids: NLT 50.0%

OTHER REQUIREMENTS

- **Labeling** Indicate the presence of sulfur dioxide if the residual concentration is greater than 10 mg/kg.

- Apenas informativo
- Identificar condições que possam acelerar a degradação do material
  - Exposição ao ar, temperatura crítica
  - Reduzir o risco de contaminação
  - Mais Informações na seção "*General Provisions and Requirements Applying to Specifications, Tests, and Assays of the Food Chemicals Codex*"

© 2017 USP

Conteúdo da Monografia - Identificação

Maltodextrin

DESCRIPTION

Maltodextrin occurs as a white, slightly hygroscopic powder, as granules of similar description, or as a clear to hazy solution in water. It is a purified, concentrated, nutritive mixture of saccharide polymers obtained by the partial hydrolysis of edible starch. Powders or granules are freely soluble or readily dispersible in water.

Function Anticaking and free-flowing agent; bulking agent; stabilizer and thickener; surface-finishing agent

Packaging and Storage Keep dry, and store at ambient temperatures.

IDENTIFICATION

- **PROCEDURE**

  Sample solution: 100 mg/mL

  Analysis: Add a few drops of *Sample solution* to 5 mL of hot alkaline cupric tartrate TS.

  Acceptance criterion: A red precipitate of cuprous oxide forms.

N = Percent nitrogen
6.25 = Nitrogen to protein conversion factor

Acceptance criterion:
Maltodextrins produced from high-amylose starches: NMT 1.0%
All other types of maltodextrins: NMT 0.5%

SPECIFIC TESTS

- **RESIDUE ON IGNITION (SULFATED ASH),** Appendix IIC
  Sample: 1 g
  Acceptance criterion: NMT 0.5%
- **TOTAL SOLIDS,** Appendix X
  Powders and granules:
  Sample solution: 60 g of sample made to 100 g with water [NOTE: Heat the solution slightly, if necessary, to complete dissolution.]
  Analysis: Determine the refractive index of the *Sample solution* at 20° or 45°, and refer to the tables under *Total Solids, Maltodextrin,* Appendix X to determine the *Total Solids* for the *Sample solution.* Calculate the *Total Solids* of the sample taken by the formula:

IDENTIFICATION

- **PROCEDURE**

  Sample solution: 100 mg/mL

  Analysis: Add a few drops of *Sample solution* to 5 mL of hot alkaline cupric tartrate TS.

  Acceptance criterion: A red precipitate of cuprous oxide forms.

rected. Calculate the percent protein using the equation:

$$\% \text{ Protein} = N \times 6.25$$

- Objetivo: demonstrar a identidade do material
- Testes típicos:
  - Espectroscopia na região do infravermelho ou UV
  - Titulação
  - Cromatografia
  - Testes do *Appendix IIIA*

© 2017 USP

Conteúdo da Monografia - Teor

Maltodextrin

DESCRIPTION

Maltodextrin occurs as a white, slightly hygroscopic powder, as granules of similar description, or as a clear to hazy solution in water. It is a purified, concentrated, nutritive mixture of saccharide polymers obtained by the partial hydrolysis of edible starch. Powders or granules are freely soluble or readily dispersible in water.

Function Anticaking and free-flowing agent; bulking agent; stabilizer and thickener; surface-finishing agent

Packaging and Storage Keep dry, and store at ambient temperatures.

IDENTIFICATION

- **PROCEDURE**
  Sample solution: 100 mg/mL
  Analysis: Add a few drops of *Sample solution* to 5 mL of hot alkaline cupric tartrate TS.
  Acceptance criterion: A red precipitate of cuprous oxide forms.

ASSAY

- **REDUCING SUGARS ASSAY,** Appendix X
  Acceptance criterion: Less than 20.0% reducing sugar content (dextrose equivalent) expressed as D-glucose

IMPURITIES

N = Percent nitrogen
6.25 = Nitrogen to protein conversion factor
Acceptance criterion:
Maltodextrins produced from high-amylose starches: NMT 1.0%
All other types of maltodextrins: NMT 0.5%

SPECIFIC TESTS

- **RESIDUE ON IGNITION (SULFATED ASH),** Appendix IIC
  Sample: 1 g
  Acceptance criterion: NMT 0.5%
- **TOTAL SOLIDS,** Appendix X
  Powders and granules:
  Sample solution: 60 g of sample made to 100 g with water [NOTE: Heat the solution slightly, if necessary, to complete dissolution.]
  Analysis: Determine the refractive index of the *Sample solution* at 20° or 45°, and refer to the tables under *Total Solids, Maltodextrin,* Appendix X to determine the *Total Solids* for the *Sample solution.* Calculate the *Total Solids* of the sample taken by the formula:

$$(TS \times W_T/W_S)$$

TS = Percent *Total Solids* in the *Sample solution,* determined in the *Analysis*
W_T = Total weight (g) of the prepared *Sample solution*
W_S = Weight of the sample (g) taken to prepare the

ASSAY

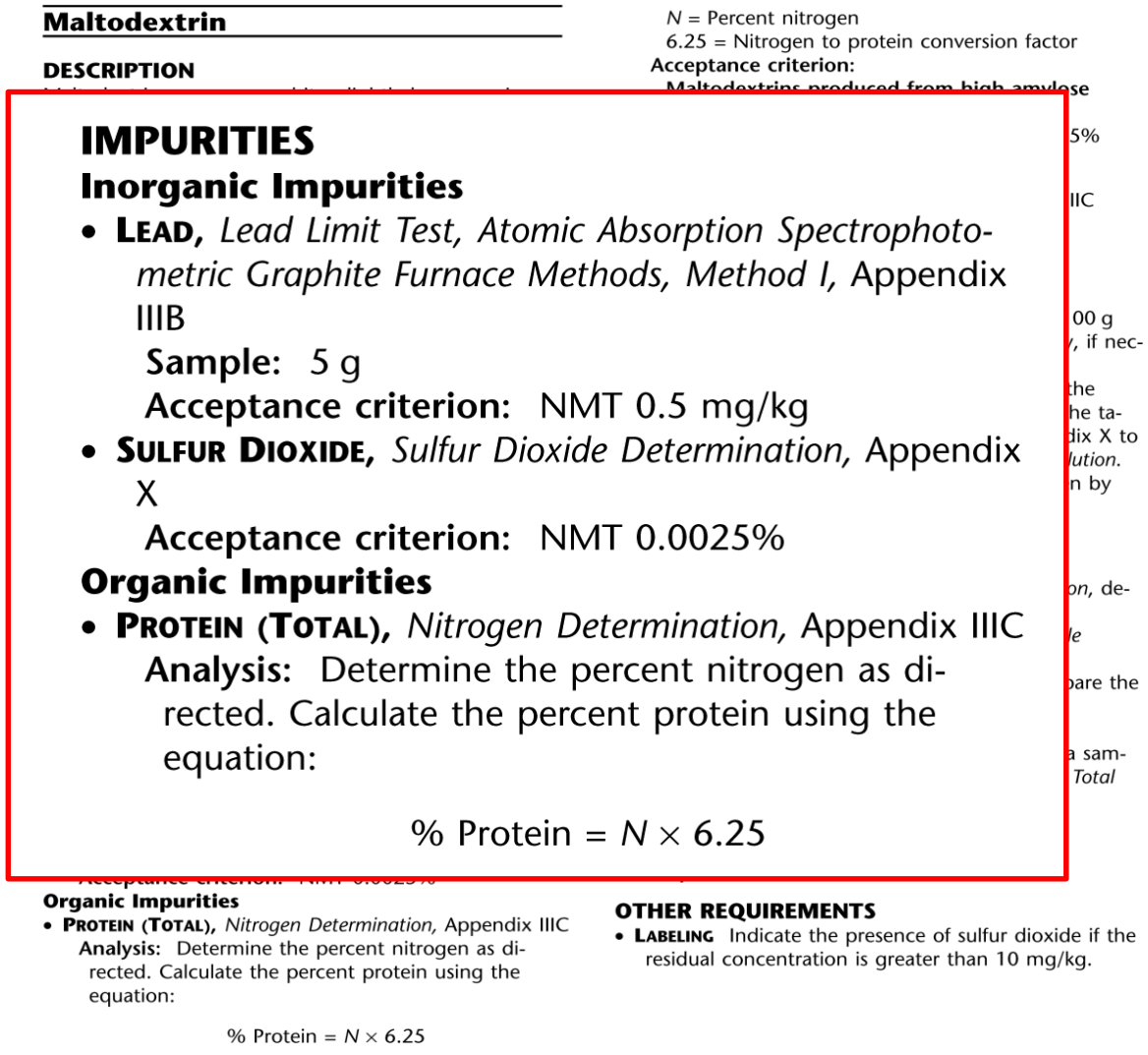
- **REDUCING SUGARS ASSAY,** Appendix X
  Acceptance criterion: Less than 20.0% reducing sugar content (dextrose equivalent) expressed as D-glucose

% Protein = $N \times 6.25$

- **Objetivo**: quantificar os componentes funcionais principais do material
- Testes típicos:
  - HPLC
  - CG

© 2017 USP

Conteúdo da Monografia – Impurezas orgânicas e inorgânicas



Maltodextrin

DESCRIPTION

N = Percent nitrogen
6.25 = Nitrogen to protein conversion factor
Acceptance criterion:

IMPURITIES

Inorganic Impurities

- **LEAD,** *Lead Limit Test, Atomic Absorption Spectrophotometric Graphite Furnace Methods, Method I,* Appendix IIIB
  Sample: 5 g
  Acceptance criterion: NMT 0.5 mg/kg
- **SULFUR DIOXIDE,** *Sulfur Dioxide Determination,* Appendix X
  Acceptance criterion: NMT 0.0025%

Organic Impurities

- **PROTEIN (TOTAL),** *Nitrogen Determination,* Appendix IIIC
  Analysis: Determine the percent nitrogen as directed. Calculate the percent protein using the equation:

$$\% \text{ Protein} = N \times 6.25$$

Organic Impurities

- **PROTEIN (TOTAL),** *Nitrogen Determination,* Appendix IIIC
  Analysis: Determine the percent nitrogen as directed. Calculate the percent protein using the equation:

$$\% \text{ Protein} = N \times 6.25$$

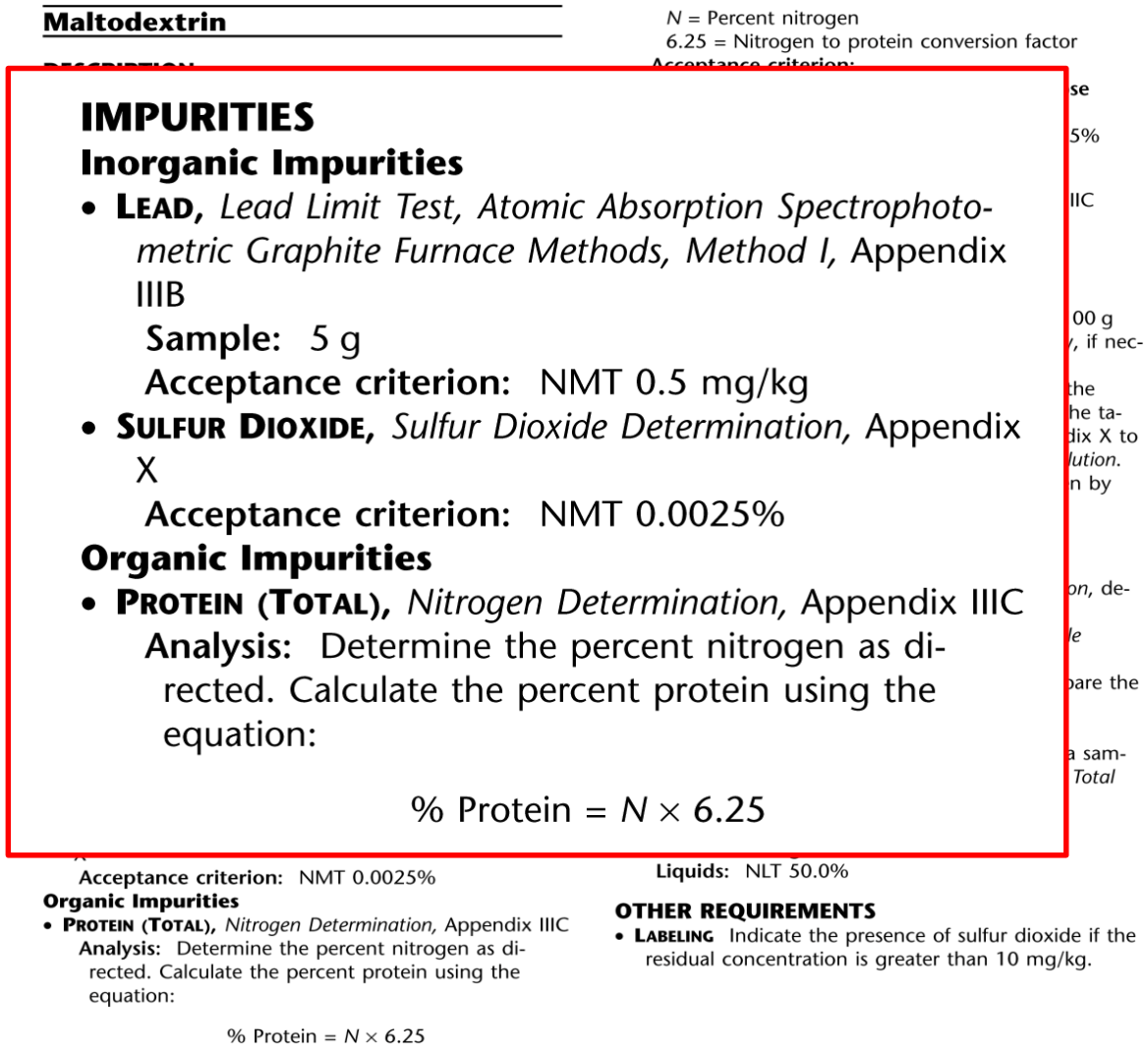
OTHER REQUIREMENTS

- **LABELING** Indicate the presence of sulfur dioxide if the residual concentration is greater than 10 mg/kg.

- **Objetivo**: limitar os potenciais contaminantes em níveis aceitáveis pelas cGMP
- Assumindo-se que o fabricante segue as cGMP, as impurezas são inerentes:
  - Às Matérias-primas
  - Ao Método de fabricação

© 2017 USP

Conteúdo da Monografia – Impurezas orgânicas e inorgânicas



Maltodextrin

N = Percent nitrogen
6.25 = Nitrogen to protein conversion factor

IMPURITIES

Inorganic Impurities

- **LEAD,** *Lead Limit Test, Atomic Absorption Spectrophotometric Graphite Furnace Methods, Method I,* Appendix IIIB
  Sample: 5 g
  Acceptance criterion: NMT 0.5 mg/kg
- **SULFUR DIOXIDE,** *Sulfur Dioxide Determination,* Appendix X
  Acceptance criterion: NMT 0.0025%

Organic Impurities

- **PROTEIN (TOTAL),** *Nitrogen Determination,* Appendix IIIC
  Analysis: Determine the percent nitrogen as directed. Calculate the percent protein using the equation:

$$\% \text{ Protein} = N \times 6.25$$

Acceptance criterion: NMT 0.0025%

Organic Impurities

- **PROTEIN (TOTAL),** *Nitrogen Determination,* Appendix IIIC
  Analysis: Determine the percent nitrogen as directed. Calculate the percent protein using the equation:

% Protein = $N \times 6.25$

Liquids: NLT 50.0%

OTHER REQUIREMENTS

- **LABELING** Indicate the presence of sulfur dioxide if the residual concentration is greater than 10 mg/kg.

- Inorgânicas:
  - Metais pesados
  - Pb, As, Cd, Hg
  - Água
  - Dióxido de enxofre, Selenio, Amônia
- Orgânicas:
  - Solventes residuais
  - Impurezas
  - Produtos de degradação

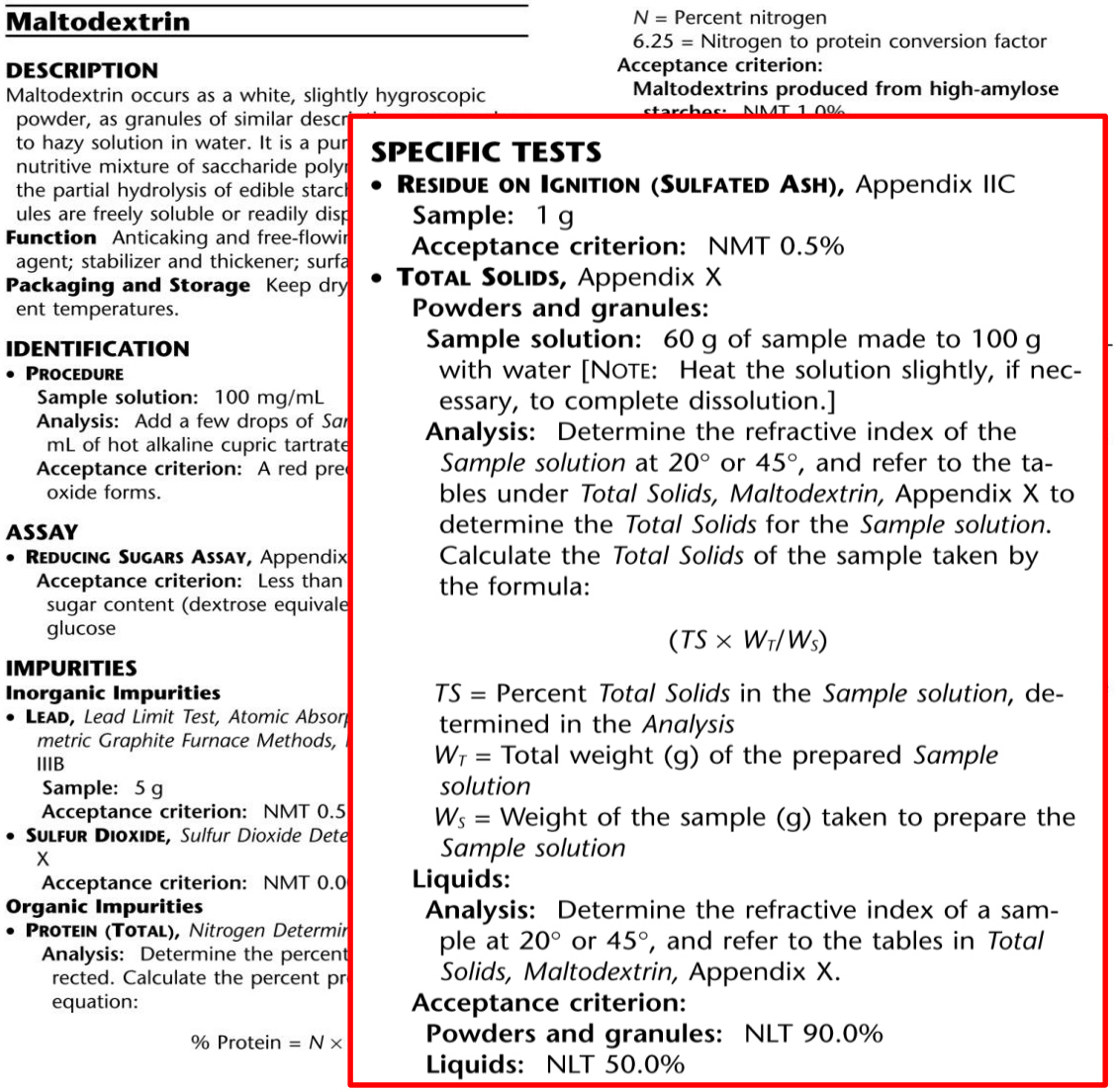
© 2017 USP

Testes comuns por tipo de monografia

Testes	Vitaminas	Minerais	Não-botânicos	Botânicos
Identidade	IR, HPLC TR, UV, químicos	Químicos	IR, HPLC TR, UV, químicos	Microscopia, TLC, HPLC, GC
Teor	Espectroscopia, HPLC, Microbiologia	Absorção Atômica, ICP, Titulação	Espectroscopia, HPLC, Titulação	HPLC, GC
Pureza	Pureza cromatográfica, Testes limite, Microbiogia, Metais pesados	Testes químicos de limite, Absorção Atômica, ICP	Pureza cromatográfica, Testes limite, Microbiogia, Metais pesados,dioxinas	Toxinas, Aflatoxinas, Metais pesados, Pesticidas, Material estranho, Resíduo por ignição, Microbiologia, Marcadores negativos
Performance	Embalagem, rótulo, Uniformidade de conteúdo, Dissolução, Desintegração	Embalagem, rótulo, Uniformidade de conteúdo, Dissolução, Desintegração	Embalagem, rótulo, Uniformidade de conteúdo, Dissolução, Desintegração	Embalagem, rótulo, Uniformidade de conteúdo, Material extraível, Dissolução, Desintegração

© 2017 USP

Conteúdo da Monografia – Testes específicos



Maltodextrin

DESCRIPTION

Maltodextrin occurs as a white, slightly hygroscopic powder, as granules of similar descri... to hazy solution in water. It is a pur... nutritive mixture of saccharide polyr... the partial hydrolysis of edible starch... ules are freely soluble or readily disp...

Function Anticaking and free-flowin... agent; stabilizer and thickener; surfa...

Packaging and Storage Keep dry... ent temperatures.

IDENTIFICATION

- **PROCEDURE**

  Sample solution: 100 mg/mL

  Analysis: Add a few drops of *Sar...* mL of hot alkaline cupric tartrate...

  Acceptance criterion: A red prec... oxide forms.

ASSAY

- **REDUCING SUGARS ASSAY,** Appendix...

  Acceptance criterion: Less than... sugar content (dextrose equivale... glucose

IMPURITIES

Inorganic Impurities

- **LEAD,** *Lead Limit Test, Atomic Absorp... metric Graphite Furnace Methods,* ... IIIB

  Sample: 5 g

  Acceptance criterion: NMT 0.5...

- **SULFUR DIOXIDE,** *Sulfur Dioxide Dete...* X

  Acceptance criterion: NMT 0.0...

Organic Impurities

- **PROTEIN (TOTAL),** *Nitrogen Determin...*

  Analysis: Determine the percent... rected. Calculate the percent pr... equation:

$$\% \text{ Protein} = N \times$$

N = Percent nitrogen

6.25 = Nitrogen to protein conversion factor

Acceptance criterion:

Maltodextrins produced from high-amylose starches: NMT 1.0%

SPECIFIC TESTS

- **RESIDUE ON IGNITION (SULFATED ASH),** Appendix IIC

  Sample: 1 g

  Acceptance criterion: NMT 0.5%

- **TOTAL SOLIDS,** Appendix X

  Powders and granules:

  Sample solution: 60 g of sample made to 100 g with water [NOTE: Heat the solution slightly, if necessary, to complete dissolution.]

  Analysis: Determine the refractive index of the *Sample solution* at 20° or 45°, and refer to the tables under *Total Solids, Maltodextrin,* Appendix X to determine the *Total Solids* for the *Sample solution.* Calculate the *Total Solids* of the sample taken by the formula:

$$(TS \times W_T/W_S)$$

TS = Percent *Total Solids* in the *Sample solution,* determined in the *Analysis*

W_T = Total weight (g) of the prepared *Sample solution*

W_S = Weight of the sample (g) taken to prepare the *Sample solution*

  Liquids:

  Analysis: Determine the refractive index of a sample at 20° or 45°, and refer to the tables in *Total Solids, Maltodextrin,* Appendix X.

  Acceptance criterion:

  Powders and granules: NLT 90.0%

  Liquids: NLT 50.0%

- Objetivo: fornecer uma descrição mais completa do material
- Diferencia materiais semelhantes
- Detecta adulterações

- Exemplos:
  - Viscosidade
  - Perda por secagem
  - Resíduo por ignição
  - Índice de peróxido
  - Rotação ótica

© 2017 USP

Conteúdo da Monografia – Outros requisitos

Maltodextrin

DESCRIPTION

Maltodextrin occurs as a white, slightly hygroscopic powder, as granules of similar description, or as a clear to hazy solution in water. It is a purified, concentrated, nutritive mixture of saccharide polymers obtained by the partial hydrolysis of edible starch. Powders or granules are freely soluble or readily dispersible in water.

Function Anticaking and free-flowing agent; bulking agent; stabilizer and thickener; surface-finishing agent

Packaging and Storage Keep dry, and store at ambient temperatures.

IDENTIFICATION

- **PROCEDURE**

  Sample solution: 100 mg/mL

  Analysis: Add a few drops of *Sample solution* to 5 mL of hot alkaline cupric tartrate TS.

  Acceptance criterion: A red precipitate of cuprous oxide forms.

ASSAY

- **REDUCING SUGARS ASSAY,** Appendix X

  Acceptance criterion: Less than 20.0% reducing sugar content (dextrose equivalent) expressed as D-glucose

OTHER REQUIREMENTS

- **LABELING** Indicate the presence of sulfur dioxide if the residual concentration is greater than 10 mg/kg.

Organic Impurities

- **PROTEIN (TOTAL),** *Nitrogen Determination,* Appendix IIIC

  Analysis: Determine the percent nitrogen as directed. Calculate the percent protein using the equation:

$$\% \text{ Protein} = N \times 6.25$$

N = Percent nitrogen

6.25 = Nitrogen to protein conversion factor

Acceptance criterion:

Maltodextrins produced from high-amylose starches: NMT 1.0%

All other types of maltodextrins: NMT 0.5%

SPECIFIC TESTS

- **RESIDUE ON IGNITION (SULFATED ASH),** Appendix IIC

  Sample: 1 g

  Acceptance criterion: NMT 0.5%

- **TOTAL SOLIDS,** Appendix X

  Powders and granules:

  Sample solution: 60 g of sample made to 100 g with water [NOTE: Heat the solution slightly, if necessary, to complete dissolution.]

  Analysis: Determine the refractive index of the *Sample solution* at 20° or 45°, and refer to the tables under *Total Solids, Maltodextrin,* Appendix X to determine the *Total Solids* for the *Sample solution.* Calculate the *Total Solids* of the sample taken by the formula:

$$(TS \times W_T/W_S)$$

TS = Percent *Total Solids* in the *Sample solution,* determined in the *Analysis*

W_T = Total weight (g) of the prepared *Sample*

OTHER REQUIREMENTS

- **LABELING** Indicate the presence of sulfur dioxide if the residual concentration is greater than 10 mg/kg.

- Evidenciar características específicas
- Texto na etiqueta do produto

© 2017 USP

O que submeter?

1) Documentação de status regulatório
2) Conteúdo da Monografia
3) Validação do Método
4) Dados de suporte
5) Resumo dos dados técnicos



Validação do Método

- Racional para a Validação
- Procedimento analítico sugerido
  - ✓ Pode ser executado por um analista competente
  - ✓ Deve incluir todos os detalhes relevantes
- Dados e evidências
  - ✓ Cumprimento das características de desempenho da Validação

Data Elements Required for Assay Validation

Analytical Performance Parameter	Assay Category I	Assay Category II		Assay Category III
		Quantitative	Limit Tests	
Accuracy	Yes	Yes	*	*
Precision	Yes	Yes	No	Yes
Specificity	No	Yes	No	*
Limit of Detection	Yes	Yes	Yes	*
Limit of Quantitation	No	No	Yes	*
Linearity	Yes	Yes	No	*
Range	Yes	Yes	*	*
Ruggedness	Yes	Yes	Yes	Yes

*May be required, depending on the nature of the specific test.

Categoria I: Métodos para os principais componentes
Categoria II: Métodos para impurezas
Categoria III: Métodos para avaliação de desempenho

© 2017 USP

O que significa um método cientificamente validado?

<1225> Validation of Compendial Procedures

Table 2. Data Elements Required for Validation

Analytical Performance Characteristics	Category I	Category II		Category III	Category IV
		Quantitative	Limit Tests		
Accuracy	Yes	Yes	[a]	[a]	No
Precision	Yes	Yes	No	Yes	No
Specificity	Yes	Yes	Yes	[a]	Yes
Detection limit	No	No	Yes	[a]	No
Quantitation limit	No	Yes	No	[a]	No
Linearity	Yes	Yes	No	[a]	No
Range	Yes	Yes	[a]	[a]	No

[a] May be required, depending on the nature of the specific test.

- *Accuracy*
- *Precision*
- *Specificity*
- *Detection Limit*
- *Quantitation Limit*
- *Linearity and Range*
- *Robustness*



© 2017 USP

O que submeter?

- Documentação de status regulatório
- Conteúdo da Monografia
- Validação do Método
- Dados de suporte
- Resumo dos dados técnicos



O que submeter?

Dados de Suporte

- **Objetivo**: Demonstrar que o material comercializado pode atender aos critérios de aceitação propostos
- Dados de pelo menos três lotes de produção independentes de material grau alimentício
- Certificado de Análise (CoA)

Resumo de Dados Técnicos

- **Objetivo**: Auxiliar na avaliação de novas monografias propostas
- Encorajado, mas não obrigatório
- Não para uma avaliação de segurança

© 2017 USP

Padrões públicos USP para Suplementos Alimentares

- Monografias + Capítulos Gerais + Padrões de Referência = conjunto abrangente de métodos cientificamente validados, Padrões de Referência e especificações para avaliação da Qualidade
  - Identidade
  - Pureza, Teor, Composição
  - Limites de contaminante
  - Desempenho
  - Características específicas

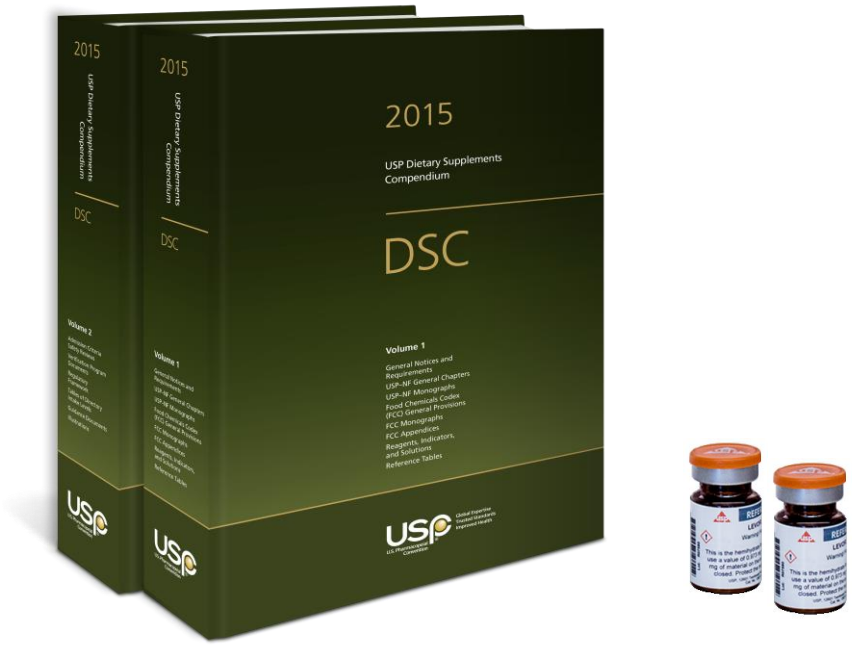




© 2017 USP

Dietary Supplements Compendium

- Lançamento da versão **Online** em 2019
- **75 novas monografias** para suplementos alimentares (**500** no total)
- **27** Capítulos Gerais
- Mais de **175 monografias** para excipientes
- Mais de **200 monografias** do Food Chemicals Codex (FCC)
- Inclui mais de **150 páginas** de placas cromatográficas e ilustrações



© 2017 USP

Conclusões



Dados de Segurança



Tempo Médio: 18 meses



Não envolve Custos para o sponsor



Confidencialidade das informações durante o processo de revisão



Valor dos padrões públicos – Vantagens para indústria e para regulador

© 2017 USP

call for candidates

2020–2025

Join us on the Journey

Collaborate with highly dedicated leaders from science, medicine, healthcare practitioners, industry and academia to help us establish standards that make it possible for 2 billion people around the world to have access to quality medicines, dietary supplements and foods.

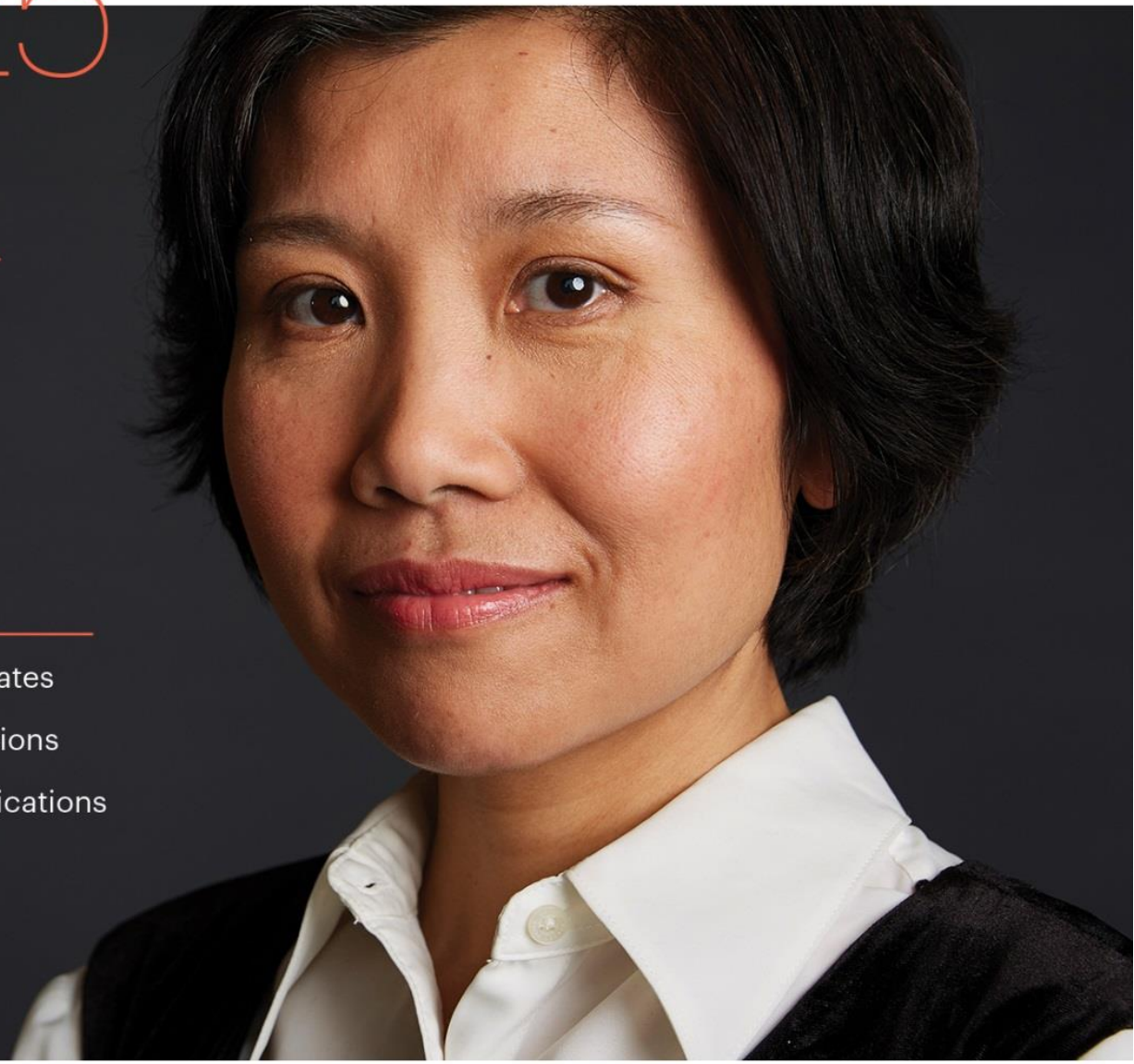
Important dates:

Jul 2018: USP launched the 2020-2025 Call for Candidates

Jan 2020: Deadline for Expert Committee chair applications

May 2020: Deadline for Expert Committee member applications

Jul 2020: 2020–2025 Council of Experts and Expert Committees begin their work



usp®

For additional information visit **callforcandidates.usp.org** or contact **USPVolunteers@usp.org.**

Participe: Stakeholder Fórum de Suplementos Alimentares

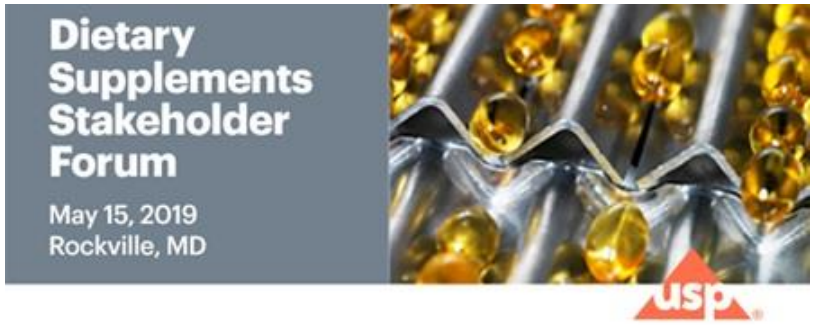
Objetivos:

- Proporcionar fórum para stakeholders discutirem abertamente questões e compartilharem perspectivas relacionadas aos padrões de suplementos alimentares da USP.
- Reunir feedback das partes interessadas para os esforços atuais e futuros de definição de padrões da USP.

Quem deve participar?

- Fabricantes, organizações, provedores de serviços e outras stakeholders que trabalham com suplementos alimentares

http://www.usp.org/get-involved/stakeholder-forums/dietary-supplements/face-to-face-meeting-2019?vsmaid=1814&vcid=76490



Share your perspectives on Dietary Supplement Standards

Contribute to the future of USP standards that help ensure the quality of dietary supplements. Your personal, professional and scientific insight will help find solutions to develop priority standards issues.

USP Dietary Supplement Stakeholder Forum Meeting - Onsite or online!

Event Details
Date: May 15, 2019
Time: 9:00 AM- 4:30 PM
Location: USP Headquarters Meeting Center
Address: 12601 Twinbrook Pkwy
Rockville, MD 20852

USP encourages manufacturers, service providers and other interested parties who work with dietary supplements to attend because stakeholder input is essential to the development of USP dietary supplement standards.

Register Here

© 2017 USP

Thank You



Empowering a healthy tomorrow