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CONSUMER HEALTHCARE PRODUCTS ASSOCIATION

October 23, 2000

Charles Ganley, M.D.
Director, Division of Over-the-Counter Drug Products
Center for Drug Evaluation and Research (HFD-560)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857-1706

Re: Docket No. 78N-036L

Dear Dr. Ganley:

Some time ago FDA asked the Laxative Task Group of the Consumer Healthcare Products Association (CHPA, formerly the Nonprescription Drug Manufacturers Association) to comment on the agency's determination and comments pertaining to psyllium (see attached letter from William E. Gilbertson, Pharm.D., July 28, 1995, regarding Docket No. 78N-036L). The agency specifically sought comments on the following topics:

1. Methodology to more accurately assay the amount of hydrophilic mucilloid, for a possible revision of USP monograph standards for psyllium preparations;

2. Change in dosage ranges;

3. Assessment of need for name changes so names are appropriate and consistent; and

4. Review of compendial purity standards for *plantago*-seed, psyllium husk, and psyllium hydrophilic mucilloid for oral suspension to ensure consistent and reasonable standards.

This letter provides the CHPA Psyllium Subgroup's responses on each of these topics.

Assay of hydrophilic mucilloid

FDA is requesting that manufacturers of psyllium products work with the USP Convention to possibly revise the monograph standards for psyllium preparations to more accurately measure hydrophilic mucilloid content, i.e., to consider including measurements of mucilloid content in gram-weight (the compendial standards measure the mucilloid content using swell volume methodology) and/or converting the swell volume to gram-weight.

CHPA members who manufacture over-the-counter (OTC) psyllium products consider the current swell volume methodology sufficient for measuring the content of psyllium husk and fragmented psyllium husk for oral suspension. The swell volume test is well established with much historical data; it is a test that manufacturing plants can use very effectively. Company studies demonstrate that swell volume is precise (precision is 1.6% Relative Standard Deviation).

In addition, a CHPA member company is working to establish a USP monograph for a finished product, "Psyllium Hydrophilic Mucilloid Granules," a granular mixture of psyllium husk and seed. This proposed product monograph also relies on swell volume methodology as a measure of psyllium content. The swell volume assay contained in the proposed Psyllium Hydrophilic Mucilloid Granules monograph is similar to the swell volume test used in the current USP monograph for Psyllium Hydrophilic Mucilloid for Oral Suspension, but differs to accommodate differences in the product formulations. The swell volume assay for Psyllium Hydrophilic Mucilloid Granules was reviewed during a 1999 FDA inspection of the manufacture and was found to be acceptable.

We believe there is confusion around the term "psyllium hydrophilic mucilloid." FDA's July 28, 1995 letter to CHPA stated that "because the final (laxative) monograph will only contain active ingredients that have USP monographs, only *plantago* seed, psyllium husk and psyllium hydrophilic mucilloid for oral suspension would be included at this time." We would like to point out that the USP monograph defines Psyllium Hydrophilic Mucilloid for Oral Suspension as "a dry mixture of Psyllium Husk with suitable additives" (see attached USP monograph). This describes a finished product and thus would not be included in the OTC laxative monograph, which is specific to active ingredients. "*Plantago* Seed" and "Psyllium Husk" USP monographs refer to active ingredients.

CHPA members consider the active ingredient in "Psyllium Hydrophilic Mucilloid for Oral Suspension" to be "psyllium hydrophilic mucilloid" and would like the option of keeping this and "psyllium (hemicellulose)" as active ingredients in the final laxative monograph. Clarity is required around the names and active ingredient definitions (see Appendix).

Change in dosage ranges

FDA proposes dosages for psyllium-containing products be based on the levels of mucilloid that can be extracted from psyllium seeds. The FDA is proposing 2.5-14 g of psyllium hydrophilic mucilloid for a daily dosage for adults and children 12 years of age and over and 1.25-7 g for children 6 to under 12 years of age and a maximum daily dosage of 30 g of *plantago* seed (as opposed to 2.5-30 g and 1.25-15 g, for products containing any psyllium ingredient identified in 334.10 (f) in the Tentative Final Monograph [TFM]). The agency states that a daily dose of 2.5-14 g provides for a range that generally reflects dosages for mucilloid content that are suggested for use for occasional constipation.

We recommend the dose ranges stated in the TFM (2.5-30 g of psyllium for a daily dosage for adults and children 12 years of age and over and 1.25-15 g for children 6 to under 12 years of age) remain in effect. Support for this is the health claim for soluble fiber from psyllium, wherein the agency disagreed with comments that argued that limits should be placed on permissible levels of psyllium husk in foods (*Federal Register*, Vol. 63, No. 32, February 18, 1998, pp. 8103-8121). The agency stated in this reference that a preliminary review of the Kellogg Company's GRAS affirmation petition revealed that it contains significant evidence supporting the safety of the consumption of up to 25g/day of psyllium husk in a variety of food categories (p. 8112) . Also, the 1993 Life Sciences Research Office (LSRO) psyllium husk report concluded a daily intake of up to 25 g/d of psyllium husk is safe (LSRO. The Evaluation of the Safety of Using Psyllium Seed Husk as a Food Ingredient. Bethesda, MD., December 1993).

Need for name changes

FDA suggested the USP Convention assess the need for official name changes so the names are appropriate and consistent.

CHPA agrees name changes are needed to assure consistency. Psyllium is defined in both *The American Heritage College Dictionary* and *Webster's Ninth New Collegiate Dictionary*, while the word "plantago" is found in neither. Thus, we think consumers are unlikely to be familiar with the term "plantago" and recommend that all products containing psyllium be labeled with the word "psyllium."

We recommend that the USP Monograph currently entitled "*Plantago* Seed" be renamed "Psyllium Seed." We also recommend the psyllium active ingredients in the OTC laxative monograph that are now called "Plantago ovata husks" and "Plantago seed" be called "Psyllium husk" and "Psyllium seed."

Compendial purity standards

According to FDA, one laxative manufacturer noted that different grades of psyllium lead to inconsistencies in dosing. The information in the letter from Rowell Laboratories was misinterpreted. FDA stated in their letter to CHPA, "As an example, the manufacturer stated that a psyllium-containing product containing a 50% grade of psyllium would require a dosage of approximately 7 g in order to be comparable to a dosage of 3.5 g of psyllium at an 85% to 95% purity level." Actually, the Rowell letter said drug products are available that contain 50% psyllium (not psyllium that is 50% pure). The only reason one would need to take more grams of the product is because excipients are present.

CHPA agrees that a review of compendial purity standards is needed to ensure consistent and reasonable standards. *Plantago* seed (psyllium seed) currently does not have the same purity standards as husk, and wherever feasible the standards applicable to husk should be applied to seed, e.g., microbial limits.

Please let me know if you or others at FDA have questions about any of these comments regarding psyllium as an active ingredient in OTC laxative products.

Sincerely yours,

Lorna C. Totman

Lorna C. Totman, Ph.D., DABT
Director of Scientific Affairs

Appendix: Definitions

Attachments: A—Letter from Gilbertson, FDA, to Soller, NDMA, July 28, 1995
B—USP monographs for Psyllium Hydrophilic Mucilloid for Oral Suspension, Plantago Seed, and Psyllium Husk

cc: FDA Dockets Management Branch (3 copies)

LT/lct

DEPARTMENT OF HEALTH & HUMAN SERVICES

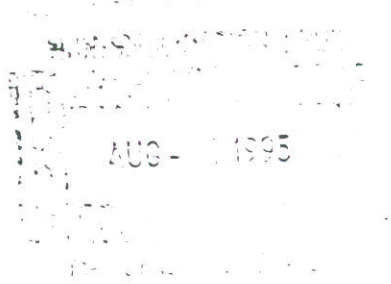
Public Health Service

Food and Drug Administration
Rockville MD 20857

A

July 28, 1995

R. William Soller, Ph. D.
Senior Vice President and
Director of Science & Technology
Nonprescription Drug Manufacturers Association
1150 Connecticut Avenue, NW
Washington, D.C. 20036



Re: Docket No. 78N-036L

Dear Dr. Soller:

As you are aware, we are in the process of developing the final rule for over-the-counter (OTC) laxative drug products. In response to the tentative final monograph (TFM) (50 FR 2124) and amended TFM for OTC laxative drug products (51 FR 35136), two manufacturers questioned the appropriateness of the proposed daily dosage of 2.5 to 30 g for psyllium-containing preparations. One manufacturer stated that these dosages were inconsistent with the dosing ranges of marketed psyllium-containing laxative drug products and with dosages provided in the scientific literature. The manufacturer also noted that the various available commercial grades of psyllium (i.e., 50, 85, and 95 percent) lead to inconsistencies in dosing. As an example, the manufacturer stated that a psyllium-containing product containing a 50 percent grade of psyllium would require a dosage of approximately 7 g in order to be comparable to a dosage of 3.5 g of psyllium at an 85 to 95 percent purity level. Another manufacturer requested that the proposed divided dosing range in the amended TFM should be sufficiently flexible to accommodate its marketed psyllium-containing laxative drug product.

Based on a review of the scientific literature and our survey of the OTC marketplace, we also have concerns about the appropriateness of the Panel's recommended daily dosage of 2.5 to 30 g for all psyllium-containing preparations.

In the tentative final monograph (TFM) for OTC laxative drug products, the agency agreed with the Panel's recommended daily dosages of 2.5 to 30 g for psyllium preparations, which included plantago seed, plantago ovata husks, psyllium (hemicellulose), psyllium hydrophilic mucilloid (psyllium hydrocolloid), psyllium seed, psyllium seed (blond), and psyllium seed husks (50 FR 2154). However, because the final monograph will only contain active ingredients that have U.S.P. monographs, only plantago seed, psyllium husk, and psyllium hydrophilic mucilloid for oral suspension would be included at this time.

Based upon our review of the scientific literature and our survey of the OTC marketplace for psyllium-containing laxative drug products, we determined that the primary constituent responsible for the bulk-forming laxative action is psyllium hydrophilic mucilloid. We also found that most OTC marketed psyllium preparations list the psyllium hydrophilic mucilloid or husks (which is the primary source of the mucilloid) as the active ingredient and that dosages are based primarily on the content of psyllium hydrophilic mucilloid.

We have determined from articles in the literature (copies enclosed) that the maximum percentage (approximate 32 percent) of the mucilloid that can be extracted from equivalent daily dosages of psyllium (plantago) seeds (7 to 45 g) found in the literature references is approximately 2.24 to 14.4 g of the hydrophilic mucilloid. From these approximate dosage ranges, we have concluded that the Panel's minimum daily dosage of 2.5 g (40 FR 12908) is appropriate for psyllium hydrophilic mucilloid and that allowing a maximum daily dose of 14 g provides for a daily dosing range (i.e., 2.5 to 14 g) that generally reflects dosages for mucilloid content found in the OTC drug marketplace for use for the relief of occasional constipation. We note that although the literature information pertaining to the 32 percent extraction of mucilloid from seeds was published in 1932, based on a recent telephone conversation with Dr. Scrinivasan of the United States Pharmacopeial Convention (U.S.P.C.), that information still appears to be applicable. However, we are interested in knowing whether there is any improved methodology (since 1932) to more accurately assay the amount of the hydrophilic mucilloid extracted.

In the final monograph, we plan to base the dosages for psyllium-containing products on the content of psyllium hydrophilic mucilloid for a daily dosage of 2.5 to 14 g for adults and children 12 years of age and over and 1.25 to 7 g for children 6 to under 12 years of age. We believe that this dosing range based on psyllium hydrophilic mucilloid content provides sufficient flexibility to generally accommodate the existing OTC psyllium-containing laxative drug products. We also consider the Panel's recommended maximum daily dosage of 30 g as still applicable to plantago seed. Therefore, the dosages for plantago seed would be based on the hydrophilic mucilloid content with a maximum daily dosage limitation of 30 g of the seed. We are requesting your comments regarding these dosage ranges.

We have also sent a letter to the U.S.P.C. requesting its review and comment on the U.S.P. monographs for plantago seed, psyllium husks, and psyllium hydrophilic mucilloid for oral suspension (copy enclosed). Because the compendial standards only measure the hydrophilic mucilloid content using the swell volume methodology, we are also requesting the U.S.P.C. to consider using or including equivalent content measurements in gram-weights. We are asking for your association's assistance in requesting that manufacturers work with the U.S.P.C. to revise the monograph standards for psyllium preparations to more accurately measure hydrophilic mucilloid content and consider including equivalent measurements in gram-weight and to assess the need for official name changes so that the names are appropriate and consistent. We are also recommending that the compendial purity standards for plantago seed and psyllium hydrophilic mucilloid be reviewed and evaluated to ensure consistent and reasonable standards. We request that manufacturers forward to the U.S.P.C. appropriate information on any improved analytical methods to assay and measure psyllium hydrophilic mucilloid content. This appears to be an area that your Laxative Task Force may want to review.

We also would appreciate any comments regarding the agency's determinations and comments pertaining to psyllium. Because we want to consider this information in preparing the final monograph, we would appreciate an expeditious response.

All comments and information should be submitted in three copies, identified with the docket number shown at the beginning of this letter, to the Dockets Management Branch, (HFA-305), Food and Drug Administration, Room 1-23, 12420 Parklawn Drive, Rockville, MD 20857.

Should you have any questions, please contact Gloria Chang of my staff at 301-594-0897.

Your assistance will be greatly appreciated.

Sincerely yours,

William E. Gilbertson, Pharm.D.
Director
Monograph Review Staff
Office of OTC Drug Evaluation
Center for Drug Evaluation and Research

Enclosures

Charles Ganley, M.D.
October 23, 2000

Appendix

Definitions

Plantago seed - cleaned, dried, ripe seed, with psyllium husk constituting approximately 15-35% of the seed by weight; known in commerce as (Spanish or French or Blonde) Psyllium Seed or as Indian *Plantago* Seed.

Psyllium seed - synonymous with *plantago* seed. Psyllium is the preferred term in the United States.

Psyllium husk - cleaned, dried seed coats; the active ingredient in most psyllium bulk-forming laxatives.

Psyllium seed husk - synonymous with psyllium husk.

Psyllium hydrophilic mucilloid for oral suspension – a dry mixture of psyllium husk with suitable excipients or additives (bulk-forming laxative product).

Mucilage - the water-soluble intracellular polysaccharide in psyllium husk.

2P33730

PSYLLIUM HYDROPHILIC MUCILLOID FOR ORAL SUSPENSION

>> **Psyllium** Hydrophilic Mucilloid for Oral Suspension is a dry mixture of **Psyllium** Husk with suitable additives.

PACKAGING AND STORAGE -- Preserve in tight containers.

IDENTIFICATION -- Microscopically, it shows the presence of fragmented **Psyllium** Husk, as described for Histology -- Husk in the section, Botanic characteristics, under **Psyllium** Husk.

MICROBIAL LIMITS <61> -- It meets the requirements of the tests for absence of Salmonella species and of Escherichia coli.

SWELL VOLUME -- Transfer 250 mL of simulated intestinal fluid TS without enzymes to a glass-stoppered, 500-mL graduated cylinder. Gradually, with shaking, add an amount of **Psyllium** Hydrophilic Mucilloid for Oral Suspension, equivalent to 3.5 g of **psyllium** husk, and shake until a uniform, smooth suspension is obtained. Dilute with the same fluid to 500 mL. Shake the cylinder for about 1 minute every 30 minutes for 8 hours. Allow the gel to settle for 16 hours (total time 24 hours). Determine the volume of the gel: it is not less than 110 mL.

2P33700

PSYLLIUM HUSK

>> **Psyllium** Husk is the cleaned, dried seed coat (epidermis) separated by winnowing and thrashing from the seeds of Plantago ovata Forskal, known in commerce as Blond **Psyllium** or Indian **Psyllium** or Ispaghula, or from Plantago **psyllium** Linne or from Plantago indica Linne (Plantago arenaria Waldstein et Kitaibel) known in commerce as Spanish or French **Psyllium** (Fam. Plantaginaceae), in whole or in powdered form.

PACKAGING AND STORAGE -- Preserve in well-closed containers, secured against insect attack (see Preservation under Vegetable and Animal Drugs in the General Notices).

BOTANIC CHARACTERISTICS --

Histology -- Husk -- The epidermis is composed of large cells having transparent walls filled with mucilage, and the cells swell rapidly in aqueous mounts and appear polygonal to slightly rounded in a surface view, when viewed from above (from below they appear elongated to rectangular). The swelling takes place mainly in the radial direction. The mucilage of the epidermal cells stains red with ruthenium red and lead acetate TS. The very occasional starch granules that are present in some of the epidermal cells, and that may be found embedded in the mucilage, are small and simple or compounded with four or more components.

Powdered **Psyllium** Seed Husk -- It is a pale to medium buff-colored powder, having a slight pinkish tinge and a weak characteristic odor. Occasional single and 2- to 4-compound starch granules, the individual grains being spheroidal plano to angular convex from 2 to 10 um in diameter, are found embedded in the mucilage. Entire or broken epidermal cells are filled with mucilage. In surface view, the epidermal cells appear polygonal to slightly rounded. Mucilage stains red with ruthenium red and lead acetate TS. Some of the elongated and rectangular cells representing the lower part of epidermis and also radially swollen epidermal cells can be found.

IDENTIFICATION --

A: Mounted in cresol -- Cells, viewed microscopically, are composed of polygonal prismatic cells having 4 to 6 straight or slightly wavy walls.

B: Mounted in alcohol and irrigated with water -- Viewed microscopically, the mucilage in the outer part of the epidermal cells swells rapidly and goes into solution.

MICROBIAL LIMITS <61> -- The total combined molds and yeasts count does not exceed 1000 per g, and it meets the requirements of the test for absence of Salmonella species and Escherichia coli.

TOTAL ASH <561>: not more than 4.0%.

ACID-INSOLUBLE ASH <561>: not more than 1.0%.

WATER, Method II <921>: not more than 12.0%.

LIGHT EXTRANEOUS MATTER -- [NOTE -- Perform this test in a well-ventilated hood.] Transfer 15.0 g to a 250-mL separator. Add about 90 mL of a liquid mixture of carbon tetrachloride and ethylene

dichloride (about 2:1), having a specific gravity of 1.45. Shake for 30 seconds, and allow to settle for 30 seconds. Repeat the shaking and settling twice more. Drain all the material and liquid except the floating layer. Add 25 mL of the liquid mixture, stir carefully, allow to settle, and drain as before. Repeat the washing of the floating layer
twice more, but use only 10 mL of the liquid mixture each time. Transfer
the washed floating layer to a tared beaker, heat on a steam bath until the odor of the liquid no longer persists, dry at 40 degrees for 3 hours, allow to cool in a desiccator, and weigh: the limit is 15%.

HEAVY EXTRANEOUS MATTER -- [NOTE -- Perform this test in a well-ventilated hood.] Transfer 10.0 g to a 250-mL separator. Add about 80 mL of carbon tetrachloride, and shake for 1 minute. Allow to stand for 5 minutes. Drain into a tared 1000-mL beaker the nonmucilaginous material that sinks to the bottom, taking care not to drain any of the floating material. Heat in a hot air oven, at a temperature not exceeding 90 degrees, until the odor of the liquid no longer persists, allow to cool in a desiccator, and weigh: the limit is 1.1%.

INSECT INFESTATION -- Transfer 25 g to a 250-mL beaker, add sufficient solvent hexane to saturate, add an additional 75 to 100 mL of solvent hexane, and allow to stand for 10 minutes, stirring occasionally with a stirring rod. Wet a sheet of filter paper with alcohol, and filter the mixture with the aid of vacuum. Discard the filtrate. Transfer the residue to the original beaker with the aid of alcohol. Add alcohol to bring the volume to 150 mL above the level of the transferred residue. Boil for 10 minutes. Filter through alcohol-wetted paper as above. Prepare a trap flask, consisting of a 2000-mL graduated, narrow-mouth conical flask into which is inserted a rubber disk supported on a stiff metal rod about 4 mm in diameter and longer than the height of the flask, the rod being threaded at the lower end and furnished with nuts and washers to hold the disk in place, and the disk being of the proper shape and size to prevent liquid in the body of the flask from spilling when it is pressed up against the neck from the inside. Transfer the residue to the trap flask, completing the transfer with the aid of hot water. Add sufficient hot water to bring the volume to 1000 mL. Add 20 mL of hydrochloric acid. Raise the rod, and support it so that the rubber disk is held above the liquid level. Rinse the rubber disk with hot water. Spray the inside of the neck of the flask with an antifoam spray. Boil for 30 minutes, and cool to room temperature. Add 40 mL of solvent hexane, and agitate for 1 minute by tilting the flask and moving
the rod vertically with wrist action. Allow to stand for 5 minutes. Add water to bring the level of liquid to the neck of the flask, and allow to stand for 20 minutes. Simultaneously rotate the disk to free it from settled material, and raise it as far as possible into the neck of the flask. Prepare a sheet of ruled filter paper, with lines approximately 5
mm apart for filtration by moistening it with water and placing it on a vacuum funnel. Transfer the material trapped in the neck of the flask to
the filter with the aid of water. If necessary, wash the paper with alcohol to remove traces of hexane. Place the paper on a 100-mm petri dish that has been wetted with a solution containing equal volumes of glycerin and alcohol. Add 35 mL of solvent hexane to the flask, and gently stir with the trapping rod. Add water to bring the liquid level into the neck of the flask. Allow to stand for 15 minutes. Using the same technique as before, transfer the trapped material onto a separate paper. Examine the papers at 30X magnification: in the case of powdered

Psyllium Husk, not more than 400 insect fragments, including mites and psocids, can be seen; in the case of whole **Psyllium** Husk, not more than 100 insect fragments, including mites and psocids, can be seen.

SWELL VOLUME -- Transfer 250 mL of simulated intestinal fluid TS without enzymes to a glass-stoppered, 500-mL graduated cylinder. Gradually, with shaking, add 3.5 g of the **Psyllium** Husk until a uniform, smooth suspension is obtained. Dilute with the same fluid to 500 mL. Shake the cylinder for about 1 minute every 30 minutes for 8 hours. Allow the gel to settle for 16 hours (total time 24 hours). Determine the volume of the gel: it is not less than 40 mL per g for powdered **Psyllium** Husk, and not less than 35 mL per g for whole **Psyllium** Husk.

2P17500
PLANTAGO SEED

>> Plantago Seed is the cleaned, dried, ripe seed of Plantago **psyllium** Linne, or of Plantago indica Linne (Plantago arenaria Waldstein et Kitaibel), known in commerce as Spanish or French **Psyllium** Seed; or of Plantago ovata Forskal, known in commerce as Blond **Psyllium** or Indian Plantago Seed (Fam. Plantaginaceae).

PACKAGING AND STORAGE -- Preserve in well-closed containers, secure against insect attack (see Vegetable and Animal Drugs -- Preservation in the General Notices).

BOTANIC CHARACTERISTICS --

Unground Plantago **psyllium** Seed -- Ovate to ovate-elongate, concavo-convex; mostly from 1.3 to 2.7 mm in length, rarely up to 3 mm, and from 600 um to 1.1 mm in width. It is light brown to moderate brown, darker along the margin, and very glossy; the convex dorsal surface exhibiting a lighter colored longitudinal area extending nearly the length of the seed and representing the embryo lying beneath the seed coat, and showing a sometimes indistinct transverse groove nearer the broader end. The concave ventral surface has a deep cavity, in the center of the base of which is an oval, yellowish white hilum.

Unground Plantago indica Seed -- Ovate-oblong to elliptical, concavo-convex; from 1.6 to 3 mm in length and from 1 to 1.5 mm in width. Externally it is dark reddish brown to moderate yellowish brown, occasionally somewhat glossy, often dull, rough, and reticulate; the convex dorsal surface having a longitudinal lighter colored area extending lengthwise along the center and beneath the seed coat, and a median transverse groove, dent, or fissure. The ventral surface has a deep concavity, the edges somewhat flattened and frequently forming a sharp indented angle with the base of the cavity, the latter showing a light colored oval hilum.

Unground Plantago ovata Seed -- Broadly elliptical to ovate, boat-shaped, from 2 to 3.5 mm in length and from 1 to 1.5 mm in width. It is pale brown to moderate brown with a dull surface, the convex surface having a small, elongated, glossy brown spot. The concave surface has a deep cavity, in the center of the base of which occurs a hilum covered with a thin membrane.

Odor and taste -- All varieties of Plantago Seed are nearly odorless.

Histology -- Plantago Seed is reniform in median transverse sections. Its seed coat has a colorless epidermis of mucilaginous cells whose radial and outer walls break down to form layers of mucilage when

brought into contact with water, and a reddish brown to yellow pigment layer in the seeds of Plantago indica and Plantago **psyllium**, a broad endosperm with thick-walled outer palisade cells, and irregular inner endosperm cells; and a straight embryo extending lengthwise through the center. The endosperm and embryo cells contain fixed oil and aleurone grains, the latter being rounded, oval, pyriform, or irregularly shaped, from 2 to 8 um in diameter.

WATER ABSORPTION -- Place 1 g of Plantago Seed in a 25-mL graduated cylinder, add water to the 20-mL mark, and shake the cylinder at intervals during 24 hours. Allow the seeds to settle for 12 hours, and note the total volume occupied by the swollen seeds: the seeds of Plantago **psyllium** occupy a volume of not less than 14 mL, those of Plantago ovata not less than 10 mL, and those of Plantago indica not less than 8 mL.

TOTAL ASH <561>: not more than 4.0% of total ash.

ACID-INSOLUBLE ASH <561>: not more than 1.0% of acid-insoluble ash.

FOREIGN ORGANIC MATTER <561>: not more than 0.50%.