HollisterStier Allergy

MITE EXTRACTS

ITEM NO. 6691, 6692, 6720

Two distinct strengths and a variety of vial sizes let you choose what best fits the needs of your practice...and your patients.

ITEM NO.	DESCRIPTION	CONCENTRATION
6691	Standardized 50/50 Mite Mix, D. pteronyssinus and D. farinae	5,000 AU/mL (each species) or 15,000 AU/mL (each species)
6692	Standardized Mite, D. pteronyssinus	10,000 AU/mL or 30,000 AU/mL
6720	Standardized Mite, D. farinae	10,000 AU/mL or 30,000 AU/mL

HollisterStier grows mites in our own facilities according to our exacting standards, allowing us to control the product at every step of the process. Our manufacturing plant is regulated by both CBER and CDER.

Two Strengths. Maximum Flexibility.

- Effective diagnosis and treatment mean you reach and benefit more patients. Studies have shown that puncture skin testing with D. farinae at 30,000 AU/mL identified more than twice as many mite sensitive patients when compared to 10,000 AU/mL.[1] We offer both to give you more options.
- Available in 10,000 AU/mL and 30,000 AU/mL to help you meet immunotherapy guidelines.
- Also available in a variety of vial sizes, meaning you can match both strength and size to best meet your needs.
- Like all of our glycerinated antigens, our mite doesn't contain phenol… which can denature the proteins in allergenic extracts.[2]

WARNING Important Safety Information
(See full prescribing information for complete boxed warning.)

This product is intended for use only by licensed medical personnel experienced in administering allergenic extracts and trained to provide immediate emergency treatment in the event of a life-threatening reaction. Allergenic extracts may potentially elicit a severe life-threatening systemic reaction, rarely resulting in death. Therefore, emergency measures and personnel trained in their use should be available immediately in the event of such a reaction. Patients should be instructed to recognize adverse reaction symptoms and cautioned to contact the physician's office if symptoms occur. Standardized glycerinated extracts may be more potent than regular extracts and therefore, are not directly interchangeable with non-standardized extracts, or other manufacturers' products. This product should never be injected intravenously. Refer to the package insert for full prescribing information.

See footnotes on reverse

QUALITY. PURITY. RELIABILITY.

SEE INSERT INSIDE.

HollisterStier Allergy

3525 North Regal Street | Spokane, WA 99207-5788
hsallergy.com | 800.495.7437

Footnotes

1 Jones, J. and Wallen, N. (1991). Comparison of puncture skin test (PST) reactivity to standardized D. farina (DF) extracts at 30,000 AU/ml (30k) and 10,000 AU/mL (10k). *AAAAI.*

2 Nelson, H. (2004). Preparing and Mixing Allergen Vaccines for Subcutaneous Immunotheraphy. In R. Lockey, *Allergens and Allergen Immunotherapy* (3rd ed., p. 472). NY.

Adverse reactions on our products can be reported by calling 800-495-7437, or by emailing adversereactions@jhs.jubl.com. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 800-FDA-1088.

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INSTRUCTIONS AND DOSAGE SCHEDULE

ALLERGENIC EXTRACTS STANDARDIZED MITES

HollisterStier

WARNINGS

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Standardized glycerinated extracts may be more potent than regular extracts and therefore, are not directly interchangeable with non-standardized extracts, or other manufacturers' products.

This product should never be injected intravenously.

Refer also to the WARNINGS, PRECAUTIONS, ADVERSE REACTIONS and OVERDOSE Sections for further discussion.

DESCRIPTION: Mite extract is a sterile solution containing the extractables of *Dermatophagoides farinae* or *Dermatophagoides pteronyssinus*, 0.5% sodium chloride, 0.275% sodium bicarbonate, and 50% glycerin by volume as a preservative. Source material for the extract is the whole bodies of the mites. The mites are grown on a medium of brine shrimp eggs and wheat germ, and are handled and cleaned in a manner that the maximum carryover of the medium components is less than 1%. The medium contains no material of human origin.

Sterile, diluted mite extracts available for intradermal testing contain 0.9% sodium chloride, not more than 0.5% glycerin by volume, 0.03% albumin (human), not more than 0.003% sodium bicarbonate, and 0.4% phenol as a preservative.

Skin test trials were conducted to evaluate the skin reactivity of medium components mixed in the approximate proportion used for mite growth. Twenty-three individuals who were puncture test reactive ($\Sigma E \geq 40$mm) to either *D. farinae or D. pteronyssinus* were tested with an extract of medium components at an estimated 1% carryover level. None of these patients had a ΣE response more than 3mm larger than the negative control by puncture test with the concentrate of the medium components extract. One of the 23 patients had a reaction with $\Sigma E \geq 20$mm when tested intradermally with a 1:100 (v/v) dilution of the concentrate of the medium components extracts.

Standardized *D. farinae and D. pteronyssinus* extract concentrates (stock concentrates) containing 30,000 Allergy Units/mL (AU/mL) are supplied in dropper vials for scratch, prick or puncture tests. Stock concentrates are also available in multiple-dose vials containing 10,000 AU/mL and 30,000 AU/mL to be diluted for intradermal testing and immunotherapy.

Standardized *D. farinae and D. pteronyssinus* extract dilutions (at 30 AU/mL and 300 AU/mL) are supplied for intradermal diagnostic tests described in Section DOSAGE AND ADMINISTRATION, Diagnosis, Part 2.a.

Product Concentration:

1. **Allergy Units (AU/mL).** The potency of extracts labeled in Allergy Units (AU/mL) is determined by in vitro comparison to a reference standard established by the Center for Biologics Evaluation and Research (CBER) of the Food and Drug Administration.
2. **Bioequivalent Allergy Units (BAU/mL).** Other standardized allergenic extracts are labeled in Bioequivalent Allergy Units/mL (BAU/mL) based on their comparison (by *in vitro* assay or major allergen content) to CBER, FDA Reference Preparations. The FDA reference extracts have been assigned Bioequivalent Allergy Units based on the CBER $ID_{50}EAL$ method.[5] Briefly, highly sensitive patients are skin tested to the reference preparation using an intradermal technique employing 3-fold extract dilutions. Depending on the dilution which elicits a summation of erythema diameter of 50, Bioequivalent Allergy Units are assigned as follows:

BAU/mL	D_{50}
100,000	13-15
10,000	10.9-12.9
1,000	8.8-10.8
100	6.7-8.7

3. **Concentrate.** Concentrate label terminology applies to allergenic extract mixtures where the individual allergens being combined vary in strength or the designation of strength.

e.g.	Concentrate
50%	Short Ragweed 1:20 w/v
25%	Std. Cat Hair 10,000 BAU/mL
25%	Std. Mite D. farinae 10,000 AU/mL

Should the physician choose to calculate the actual strength of each component in the "Concentrate" mixture, the following formulation may be used:

Actual Allergen Strength in Concentrate Mixture = Allergen Manufacturing Strength x % Allergen in Formulation (by volume or parts)

CLINICAL PHARMACOLOGY:[26] The mechanisms by which hyposensitization is achieved are not completely understood. It has been shown that repeated injections of appropriate allergenic extracts will ameliorate the intensity of allergic symptoms upon contact with the allergen[6, 7, 8, 9]. Clinical studies which address the efficacy of immunotherapy are available. The allergens which have been studied are cat, mite, and some pollen extracts[10, 11, 12, 13, 14, 15].

IgE antibodies bound to receptors on mast cell membranes are required for the allergic reaction, and their level is probably related to serum IgE concentrations. Immunotherapy has been associated with decreased levels of IgE, and also with increases in allergen specific IgG "blocking" antibody.

The histamine release response of circulating basophils to a specific allergen is reduced in some patients by immunotherapy, but the mechanism of this change is not yet clear.

The relationships among changes in blocking antibody, reaginic antibody, and mediator-releasing cells, and successful immunotherapy need study and clarification.

Mites belonging to the genus *Dermatophagoides* are found in approximately 80% of house dust samples throughout the world[22, 23]. *D. farinae* is common in much of the United States[24], although D. pteronyssinus is predominant in certain coastal regions, and both species are commonly found in homes[25]. Persons suspected of having allergy to house dust should be tested for sensitivity to each mite.

INDICATIONS AND USAGE:[16, 17, 18, 26] Standardized glycerinated allergenic extracts are indicated for use in diagnosis and immunotherapy of patients presenting symptoms of allergy (hay fever, rhinitis, etc.) to specific environmental allergens. The selection of allergenic extracts to be used should be based on a thorough and carefully taken history of hypersensitivity, and confirmed by skin testing[20, 21].

The use of mixed or unrelated antigens for skin testing is not recommended since, in the case of a positive reaction, it does not indicate which component of the mix is responsible for the reaction, while, in the case of a negative reaction, it fails to indicate whether the individual antigens at full concentration would give a positive reaction. Utilization of such mixes for compounding a treatment may result, in the former case, in administering unnecessary antigens and, in the latter case, in the omission of a needed allergen.

Allergens to which a patient is extremely sensitive should not be included in treatment mixes with allergens to which there is much less sensitivity, but should be administered separately. This allows individualized and better control of dosage increases, including adjustments in dosage becoming necessary after severe reactions which may occur to the highly reactive allergen.

CONTRAINDICATIONS: There are no known absolute contraindications to immunotherapy. See PRECAUTIONS for pregnancy risks.

Patients with cardiovascular diseases or pulmonary diseases such as symptomatic asthma, and/or those who are receiving cardiovascular drugs such as beta blockers, may be at higher risk for severe adverse reactions. These patients may also be more refractory to the normal allergy treatment regimen. Patients should be treated only if the benefit of treatment outweighs the risks[1].

Any injections, including immunotherapy, should be avoided in patients with a bleeding tendency.

Since there are differences of opinion concerning the possibility of routine immunizations exacerbating autoimmune diseases, immunotherapy should be given cautiously to patients with autoimmune diseases, and only if the risk from exposure to the allergen is greater than the risk of exacerbating the autoimmune process.

WARNINGS: See WARNINGS at the beginning of this instruction sheet.

Allergenic extract should be temporarily withheld from patients or the dose adjusted downward if any of the following conditions exist: (1) severe symptoms of rhinitis and/or asthma; (2) infection or flu accompanied by fever, or (3) exposure to excessive amounts of clinically relevant allergen prior to a scheduled injection. Do not

start immunotherapy during a period of symptoms due to exposure. Since the individual components of the extract are those to which the patient is allergic, and to which he or she will be exposed, typical allergic symptoms may follow shortly after the injection, particularly when the antigen load from exposure plus the injected antigen exceeds the patient's antigen tolerance.

THE CONCENTRATE SHOULD NOT BE INJECTED AT ANY TIME UNLESS TOLERANCE HAS BEEN ESTABLISHED. DILUTE CONCENTRATED EXTRACTS WITH STERILE ALBUMIN SALINE WITH PHENOL (0.4%) FOR INTRADERMAL TESTING.

INJECTIONS SHOULD NEVER BE GIVEN INTRAVENOUSLY. Subcutaneous injection is recommended. Intracutaneous or intramuscular injections may produce large local reactions or be excessively painful.

AFTER INSERTING NEEDLE SUBCUTANEOUSLY, BUT BEFORE INJECTING, ALWAYS WITHDRAW THE PLUNGER SLIGHTLY. IF BLOOD APPEARS IN THE SYRINGE, CHANGE NEEDLE AND GIVE THE INJECTION IN ANOTHER SITE.

IF CHANGING TO A DIFFERENT LOT OF STANDARDIZED EXTRACT: Even though it is the same formula and concentration, the first dose of the new extract should not exceed 50% of the last administered dose from the previous extract.

IF THE STANDARDIZED EXTRACT PREVIOUSLY USED WAS FROM ANOTHER MANUFACTURER: Since manufacturing processes and sources of raw materials differ among manufacturers, the interchangeability of extracts from different manufacturers cannot be insured. The starting dose of the standardized glycerinated extract therefore should be greatly decreased even though the extract is the same formula and dilution. Initiate therapy as though patient had not been receiving immunotherapy, or determine initial dose by skin test using serial dilutions of the extract. In highly sensitive individuals, the skin test method may be preferable. See DOSAGE AND ADMINISTRATION and ADVERSE REACTIONS Sections.

IF A PROLONGED PERIOD OF TIME HAS ELAPSED SINCE THE LAST INJECTION: Patients may lose tolerance for allergen injections during prolonged periods between doses. The duration of tolerance is an individual characteristic and varies from patient to patient. In general, the longer the lapse in the injection schedule, the greater dose reduction required. If the interval since last dose is over four weeks, perform skin tests to determine starting dose.

IF THE PREVIOUS EXTRACT WAS OUTDATED: The dating period for allergenic extracts indicates the time that they can be expected to remain potent under refrigerated storage conditions (2° - 8° C). During the storage of extracts, even under ideal conditions, some loss of potency occurs. For this reason, extracts should not be used beyond their expiration date. If a patient has been receiving injections of an outdated extract, he may experience excessive local or systemic reactions when changed to a new, and possibly more potent extract. In general, the longer the material has been outdated, the greater the dose reduction necessary for the fresh extract.

IF THE PREVIOUS EXTRACT WAS NON-STANDARDIZED: Standardized extracts may be more potent than non-standardized extracts. Initiate therapy as though the patient had not been receiving immunotherapy, or determine initial dose by skin test using serial dilutions of the extract. See PRECAUTIONS and DOSAGE AND ADMINISTRATION Sections.

IF ANY OTHER CHANGES HAVE BEEN MADE IN THE EXTRACT CONCENTRATE FORMULA: Changes other than those listed above may include situations such as a redistribution of component parts or percentages, a difference in extracting fluid (i.e., change from non-glycerin extracts to 50% glycerin extracts), combining two or more stock concentrates, or any other change.

It should be recognized that any change in formula can affect a patient's tolerance of the treatment. The usual 1/2 of the previous dose for a new extract may produce an adverse reaction; extra dilutions are recommended whenever starting a revised formula. The greater the change, the greater the number of dilutions required.

Proper selection of the dose and careful injection should prevent most systemic reactions. It must be remembered, however, that allergenic extracts are highly potent in sensitive individuals, and that systemic reactions of varying degrees of severity may occur, including urticaria, rhinitis, conjunctivitis, wheezing, coughing, angioedema, hypotension, bradycardia, pallor, laryngeal edema, fainting, or even anaphylactic shock and death. Patients should be informed of this, and the precautions should be discussed prior to immunotherapy. (See PRECAUTIONS below.) Severe systemic reactions should be treated as indicated in the ADVERSE REACTIONS Section.

PRECAUTIONS:

1. **General**

The presence of asthmatic signs and symptoms appear to be an indicator for severe reactions following allergy injections[1, 32, 33, 34, 35]. An assessment of airway obstruction either by measurement of peak flow or an alternate procedure may provide a useful indicator as to the advisability of administering an allergy injection.

Concentrated extracts must be diluted prior to use; See DOSAGE AND ADMINISTRATION Section for detailed instructions on the dilution of standardized glycerinated allergenic extracts.

Any evidence of local or generalized reaction requires a reduction in dosage during the initial stages of immunotherapy, as well as during maintenance therapy.

Allergenic extracts diluted with Albumin Saline with Phenol (0.4%) may be more potent than extracts diluted with diluents which do not contain stabilizers. When switching from non-stabilized to stabilized diluent, consider weaker initial dilutions for both intradermal testing and immunotherapy.

Sterile solutions, vials, syringes, etc., should be used and aseptic precautions observed in making dilutions.

To avoid cross-contamination, do not use the same needle to withdraw materials from vials of more than one extract, or extract followed by diluent.

A sterile tuberculin syringe graduated in 0.01 mL units should be used to measure each dose from the appropriate dilution. Aseptic techniques should always be employed when injections of allergenic extracts are being administered.

A separate sterile syringe should be used for each patient to prevent transmission of homologous serum hepatitis and other infectious agents from one person to another.

Patient reactions to previous injections should be reviewed before each new injection. A conservative dosage schedule should be followed by the physician until a pattern of local responses is established which can be used to monitor increases in dosage.

Rarely, a patient is encountered who develops systemic reactions to minute doses of allergen and does not demonstrate increasing tolerance to injections after several months of treatment. If systemic reactions or excessive local responses occur persistently at very small doses, efforts at immunotherapy should be stopped.

PATIENTS SHOULD BE OBSERVED IN THE OFFICE FOR 30 MINUTES AFTER EACH TREATMENT INJECTION. Most severe reactions will occur within this time period, and rapid treatment measures should be instituted. See ADVERSE REACTIONS Section for such treatment measures.

2. **Information for Patients**

Patients should be instructed in the recognition of adverse reactions to immunotherapy, and in particular, to the symptoms of shock. Patients should be made to understand the importance of a 30 minute observation period, and be warned to return to the office promptly if symptoms occur after leaving.

3. **Carcinogenesis, Mutagenesis, Impairment of Fertility.**

Long-term studies in animals have not been conducted with allergenic extracts to determine their potential for carcinogenicity, mutagenicity or impairment of fertility.

4. **Pregnancy[30]**

Allergenic Extracts. Animal reproduction studies have not been conducted with allergenic extracts. It is also not known whether allergenic extracts can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Allergenic extracts should be given to a pregnant woman only if clearly needed.

For women who have been getting maintenance doses of allergen without side effect, the occurrence of pregnancy is not an indication to stop immunotherapy.

5. **Nursing Mothers**

There are no current studies on secretion of the allergenic extract components in human milk, or of their effect on the nursing infant. Because many drugs are excreted in human milk, caution should be exercised when allergenic extracts are administered to a nursing woman.

6. **Pediatric Use**

Since dosage for the pediatric population is the same as for adults[26, 27], the larger volumes of solution may produce excessive discomfort. Therefore, in order to achieve the total dose required, the volume of the dose may need to be divided into more than one injection per visit.

7. **Geriatric Use**

The reactions from immunotherapy can be expected to be the same in elderly patients as in younger ones. Elderly patients may be more likely to be on medication that could block the effect of epinephrine which could be used to treat serious reactions, or they could be more sensitive to the cardiovascular side effect of epinephrine because of pre-existing cardiovascular disease[29].

8. **Drug Interactions**

Patients on non-selective beta blockers may be more reactive to allergens given for diagnosis or treatment, and may be unresponsive to the usual doses of epinephrine used to treat allergic reactions[19].

Certain medications may lessen the skin test wheal and erythema responses elicited by allergens and histamine for varying time periods. Conventional antihistamines should be discontinued at least 5 days before skin testing. Long acting antihistamines should be discontinued for at least 3 weeks prior to skin testing[2]. Topical steroids should be discontinued at the skin test site for at least 2-3 weeks before skin testing[2, 3].

Tricyclic antidepressants such as Doxepin should be withheld for at least 7 days before skin testing[31]. Topical local anesthetics may suppress the flare responses and should be avoided in skin test sites[4].

ADVERSE REACTIONS:

1. **Local Reactions**

Some erythema, swelling or pruritus at the site of injection are common, the extent varying with the patient. Such reactions should not be considered significant unless they persist for at least 24 hours. Local reactions (erythema or swelling) which exceed 4-5 cm in diameter are not only uncomfortable, but

also indicate the possibility of a systemic reaction if dosage is increased. In such cases the dosage should be reduced to the last level not causing the reaction and maintained at this level for two or three treatments before cautiously increasing again.

Large persistent local reactions may be treated by local cold, wet dressings and/or the use of oral antihistamines. They should be considered a warning of possible severe systemic reactions and an indication of the need for temporarily reduced dosages.

A mild burning immediately after the injection is to be expected. This usually leaves in 10 to 20 seconds.

2. **Systemic Reactions**

With careful attention to dosage and administration, systemic reactions occur infrequently, but it cannot be overemphasized that in sensitive individuals, any injection could result in anaphylactic shock. Therefore, it is imperative that physicians administering allergenic extracts understand and be prepared for the treatment of severe reactions.

Other possible systemic reactions which may occur in varying degrees of severity are laryngeal edema, fainting, pallor, bradycardia, hypotension, angioedema, cough, wheezing, conjunctivitis, rhinitis, and urticaria. Adverse reaction frequency data for allergenic extract administration for testing and treatment show that risk is low.[1, 28]

If a systemic or anaphylactic reaction does occur, apply a tourniquet above the site of injection and inject 1:1000 epinephrine-hydrochloride intramuscularly or subcutaneously into the opposite arm. Loosen the tourniquet at least every 10 minutes. Do not obstruct arterial blood flow with the tourniquet.

EPINEPHRINE DOSAGE:

ADULT DOSAGE: 0.3 to 0.5 mL should be injected. Repeat in 5 to 10 minutes if necessary.

PEDIATRIC DOSAGE: The usual initial dose is 0.01 mg (mL) per kg body weight or 0.3 mg (mL) per square meter of body surface area. Suggested dosage for infants to 2 years of age is 0.05 to 0.1 mL; for children 2 to 6 years, 0.15 mL; and children 6 to 12 years, 0.2 mL. Single pediatric doses should not exceed 0.3 mg (mL). Doses may be repeated as frequently as every 20 minutes, depending on the severity of the condition and the response of the patient.

After administration of epinephrine, profound shock or vasomotor collapse should be treated with intravenous fluids, and possibly vasoactive drugs. Airway patency should be insured. Oxygen should be given by mask. Intravenous antihistamine, theophylline and/or corticosteroids may be used if necessary after adequate epinephrine and circulatory support has been given.

Emergency resuscitation measures and personnel trained in their use should be available immediately in the event of a serious systemic or anaphylactic reaction not responsive to the above measures [Ref. *J. Allergy and Clinical Immunology*, 77(2): p. 271-273, 1986].

Rarely are all of the above measures necessary; the tourniquet and epinephrine usually produce prompt responses. However, the physician should be prepared in advance for all contingencies. Promptness in beginning emergency treatment measures is of utmost importance.

Severe systemic reactions mandate a decrease of at least 50% in the next dose, followed by cautious increases. Repeated systemic reactions, even of a mild nature, are sufficient reason for the cessation of further attempts to increase the reaction-causing dose.

3. **Adverse Event Reporting**

Report all adverse events to Jubilant HollisterStier LLC, Customer Technical Services Department at 1 (800) 992-1120. A voluntary adverse event reporting system for health professionals is available through the FDA MEDWATCH program. Preprinted forms (FDA Form 3500) are available from the FDA by calling 1 (800) FDA-1088. Completed forms should be mailed to MEDWATCH, 5600 Fisher Lane, Rockville, MD 20852-9787 or Fax to: 1 (800) FDA-0178.

OVERDOSAGE: See ADVERSE REACTIONS Section.

DOSAGE AND ADMINISTRATION:

1. **General**

Sterile aqueous diluent containing human serum albumin [Albumin Saline with Phenol (0.4%)], or diluent of 50% glycerin may be used when preparing dilutions of the concentrate for immunotherapy. For intradermal testing dilutions, Albumin Saline with Phenol is recommended.

Dilutions should be made accurately and aseptically, using sterile diluent, vials, syringes, etc. Mix thoroughly and gently by rocking or swirling.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

2. **Diagnosis**

To identify highly sensitive individuals and as a safety precaution, it is recommended that a scratch, prick or puncture test using a drop of the extract concentrate be performed prior to initiating intradermal testing. Prick tests are performed by placing a drop of extract on the skin and piercing through the drop into the skin with a slight lifting motion. Puncture testing is performed by placing a drop of extract concentrate on the skin and puncturing the skin through the drop with a small needle such as a Prick Lancetter. Fifteen minutes after puncture is made the diameter of wheal and erythema reactions are measured, and the sensitivity class of the patient determined by the table presented at end of Diagnosis Section. Less sensitive individuals (Class 0 to 1+) can be tested intradermally with the recommended dilutions of the extract concentrate (See intradermal testing instructions).

The skin test concentration of 30,000 AU/mL in dropper vials is used for scratch, prick or puncture testing. Puncture tests performed on 12 selected highly sensitive subjects showed the following:

Species	Mean Σ Wheal ± 1 Std. Dev. (mm)	Mean Σ Erythema ± 1 Std. Dev. (mm)
D. farinae	22.4 ± 10.7	82.3 ± 21.7
D. pteronyssinus	24.0 ± 9.9	89.3 ± 24.5

Σ equals the sum of the longest diameter and the mid-point orthogonal diameter.

Extract for intradermal testing should be prepared by diluting the 30,000 AU/mL stock concentrate, provided in multiple-dose vials, with sterile aqueous diluent (refer to the dilution table displayed in the immunotherapy section below).

To administer the intradermal strength dilutions, a 1 mL tuberculin syringe with a short 27-gauge needle should be used. The needle is inserted intradermally at a 30° angle, bevel down, and 0.02 to 0.05 mL of the extract is injected. Fifteen minutes following injection, the diameter of wheal and erythema reactions are measured, and the patient's sensitivity class is determined by the table on the following page.

Intradermal skin test results in selected highly sensitive subjects are presented for reference purposes:

		AU/mL that Elicited ΣE=50 mm	
Allergen	Number of Persons	Mean	2 Std. Dev. Range
D. farinae	12	0.0609	0.0015 - 2.6016
D. pteronyssinus	12	0.0333	0.0003 - 4.0077

Intradermal extract should be used as follows:

a. **Patients with a negative scratch, prick or puncture test:**

Patients who do not react to a valid scratch, prick or puncture test should be tested intradermally with 0.02 to 0.05 mL of a 30 AU/mL extract solution. If this test is negative, a second intradermal test may be performed using a 300 AU/mL extract solution. The negative control used with this latter dilution should contain 0.5% glycerin.

b. **Patients tested only by the intradermal method:**

Patients suspected of being highly allergic should be tested with 0.02 to 0.05 mL of a solution containing 0.03 AU/mL. A negative test should be followed by repeat tests using progressively stronger concentrations until the maximum recommended strength of 300 AU/mL is reached. The negative control used with this latter dilution should contain 0.5% glycerin.

Skin tests are graded in terms of the wheal and erythema response noted at 10 to 20 minutes. Wheal and erythema size may be recorded by actual measurement of the extent of both responses.

Refer to the following table to determine the skin test sensitivity class. The corresponding ΣE (sum of the longest diameter and the mid-point orthogonal diameters of erythema) is also presented.

Class	Wheal Diameter	Erythema Diameter	Corresponding ΣE
0	<5 mm	<5 mm	<10 mm
±	5-10 mm	5-10 mm	10-20 mm
1+	5-10 mm	11-20 mm	20-40 mm
2+	5-10 mm	21-30 mm	40-60 mm
3+	10-15 mm[a]	31-40 mm	60-80 mm
4+	> 15 mm[b]	>40 mm	> 80mm

a. or with pseudopods
b. or with many pseudopods

3. **Immunotherapy**

Allergen extracts should be administered using a sterile syringe with 0.01 mL gradations and a 25-27 gauge x 1/2" to 5/8" needle. The injections are given subcutaneously. The most common sites of injection are the lateral aspect of the upper arm or thigh. Intracutaneous or intramuscular injections may produce large local reactions which may be very painful.

Dosage of allergenic extracts is a highly individualized matter and varies according to the degree of sensitivity of the patient, his clinical response, and tolerance to the extract administered during the early phases of an injection regimen. The starting dose should be based on skin tests of the extract to be used for immunotherapy. To prepare dilutions for intradermal and therapeutic use, make a 1:10 dilution by adding 1.0 mL of the concentrate to 9.0 mL of Sterile Albumin Saline with Phenol (0.4%). Subsequent serial dilutions

are made in a similar manner. (See Table I.) To determine the starting dose, begin intradermal testing with the most dilute extract preparation. Inject 0.02 mL and read the reaction after 15 minutes. Intradermal testing is continued with increasing concentrations of the extract until a reaction of 11-20 mm erythema (ΣE 20-40 mm) and/or a 5 mm wheal occurs. This concentration at a dose of 0.03 mL then can serve as a starting dose for immunotherapy and be increased by 0.03 mL to as high as 0.12 mL increments each time, until 0.3 mL is reached. At this time a dilution 10 times as strong can be used, starting with 0.03 mL. Proceed in this way until a tolerance dose is reached or symptoms are controlled. Suggested maintenance dose is 0.2 mL of the concentrate. Occasionally, higher doses are necessary to relieve symptoms. Special caution is required in administering doses greater than 0.2 mL. The interval between doses normally is 3 to 7 days.

This is offered as a suggested schedule for average patients and will be satisfactory in most cases. However, the degree of sensitivity varies in many patients. The size of the dose should be adjusted and should be regulated by the patient's tolerance and reaction. The size of the dose should be decreased if the previous injection resulted in marked local or the slightest general reaction. Another dose should never be given until all local reactions resulting from the previous dose have disappeared.

In some patients, the dosage may be increased more rapidly than called for in the schedule. In seasonal allergies, treatment should be started and the interval between doses regulated, so that at least the first twenty doses will have been administered by the time symptoms are expected. Thus, the shorter the interval between the start of immunotherapy and the expected onset of symptoms, the shorter the interval between each dose. Some patients may even tolerate daily doses. A maintenance dose, the largest dose tolerated by the patient that relieves symptoms without producing undesirable local or general reactions, is recommended for most patients. The upper limits of dosage have not been established; however, doses larger than 0.2 mL of the glycerin concentrate may be painful due to the glycerin content. The dosage of the allergenic extract does not vary significantly with the respiratory allergic disease under treatment. The size of this dose and the interval between doses will vary and can be adjusted as necessary. Should symptoms develop before the next injection is scheduled, the interval between doses should be decreased. Should allergic symptoms or local reactions develop shortly after the dose is administered, the size of the dose should be decreased. In seasonal allergies, it is often advisable to decrease the dose to one-half or one-quarter of the maximum dose previously attained if the patient has any seasonal symptoms.

The interval between maintenance doses can be increased gradually from one week to 10 days, to two weeks, to three weeks, or even to four weeks if tolerated. Repeat the doses at a given interval three or four times to check for untoward reactions before further increasing the interval. Protection is lost rapidly if the interval between doses is more than four weeks. (See WARNINGS Section.)

The usual duration of treatment has not been established. A period of two or three years of injection therapy constitutes an average minimum course of treatment.

TABLE I
TEN-FOLD DILUTION SERIES
Standardized Extracts Labeled 30,000 AU/mL

Dilution	Extract	+ Diluent	=	AU/mL Concentration
0	Concentrate	+ 0 mL	=	30,000
1	1 mL concentrate	+ 9 mL	=	3,000
2	1 mL dilution #1	+ 9 mL	=	300
3	1 mL dilution #2	+ 9 mL	=	30
4	1 mL dilution #3	+ 9 mL	=	3
5	1 mL dilution #4	+ 9 mL	=	0.3
6	1 mL dilution #5	+ 9 mL	=	0.03
7	1 mL dilution #6	+ 9 mL	=	0.003

4. **Pediatric Use**
   The dose for the pediatric population is the same as for adults. (See PRECAUTIONS.)
5. **Geriatric Use**
   The dose for elderly patients is the same as for adult patients under 65[29].

HOW SUPPLIED: Standardized allergenic extracts are supplied for diagnostic and therapeutic use:

Diagnostics:
Extracts: *D. pteronyssinus and D. farinae*
Scratch, prick or puncture tests, 30,000 AU/mL [50% glycerin (v/v)] in 5 mL dropper vial.
Intradermal Tests [Aqueous] of 30 AU/mL in 5 mL vial, and 300 AU/mL in 5 mL vial.

Bulk Therapeutics [50% glycerin (v/v)] in multiple dose vials:
Extracts: *D. pteronyssinus and D. farinae*
10 mL vial, 30,000 AU/mL or 10,000 AU/mL
30 mL vial, 30,000 AU/mL or 10,000 AU/mL
50 mL vial, 10,000 AU/mL

A mixture of the two mite species, in equal parts, resulting in *D. pteronyssinus* at 15,000 AU/mL and *D. farinae* at 15,000 AU/mL is available for therapeutic use in 10 mL and 30 mL vials. A mixture of the two species is also available at 5,000 AU/mL each species in 10 mL, 30 mL and 50 mL.

Storage:
The expiration date of the mite extract in 50% glycerin is listed on the container label. The extract should be stored at 2° - 8°C and kept in this temperature range during office use. Dilutions containing less than 50% glycerin are less stable, and if loss of potency is suspected, should be checked by skin testing with equal units of a freshly prepared dilution on known mite allergic individuals.
The expiration date of the intradermal tests is listed on container labels. Store at 2° - 8°C.

LIMITED WARRANTY: A number of factors beyond our control could reduce the efficacy of this product or even result in an ill effect following its use. These include storage and handling of the product after it leaves our hands, diagnosis, dosage, method of administration and biological differences in individual patients. Because of these factors, it is important that this product be stored properly and that the directions be followed carefully during use.

No warranty, express or implied, including any warranty of merchantability or fitness, is made. Representatives of the Company are not authorized to vary the terms or the contents of any printed labeling, including the package insert, for this product except by printed notice from the Company's headquarters. The prescriber and user of this product must accept the terms hereof.

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