

February 9, 2005

Division of Dockets Management
Food and Drug Administration (HFA-305)
5630 Fishers Lane
Room 1061
Rockville, MD 20852



7361 Calhoun Place,
Suite 500
Rockville, Maryland 20855-2765
301.838.3120
fax: 301.838.3182

CITIZEN PETITION

Dear Sir or Madam:

The undersigned submits this petition on behalf of our client in quadruplicate, pursuant to 21 CFR 10.30 and in accordance with the regulations at 21 CFR 314.161, requesting the Commissioner of the Food and Drug Administration to provide a determination whether the listed drug product has been withdrawn for safety or effectiveness reasons as outlined in the enclosed.

Please contact us if you have any questions or need any additional information.

Sincerely,


Anthony C. Celeste
Senior Vice President

Enclosures

2005P.0061

CP1

17/B, Mahal Industrial Estate,
Mahakali Caves Road,
Andheri (East), Mumbai 400 093 India
Tel (91-22) 5645 5645
Fax (91-22) 5645 5685



February 4, 2005

CITIZEN PETITION

The undersigned submits this petition under section 505(j)(2)(C) of the Federal Food Drug, and Cosmetic Act ("The FDC Act") and 21 CFR § 314.93, and 21 CFR §§ 10.20 and 10.30 to request that the Commissioner of Food and Drugs make a determination that the discontinued formulations of Sandostatin (Octreotide Acetate Injection), 50, 100, 500 mcg/ml, 1ml ampoule & 200, 1000 mcg/ml, 5 ml vial, is suitable for submission as an Abbreviated New Drug Application (ANDA).

A. Action Requested

This petition seeks a determination that the discontinued formulations of Sandostatin (Octreotide Acetate Injection), 50, 100, 500 mcg/ml, 1ml ampoule & 200, 1000 mcg/ml, 5 ml vial, containing sodium chloride and glacial acetic acid/sodium acetate buffer system, is suitable for evaluation under an ANDA. The reference listed drug product upon which this petition is based is available as Sandostatin[®] (Octreotide Acetate Injection), 50, 100, 500 mcg/ml, 1ml ampoule & 200, 1000 mcg/ml, 5 ml vial, containing sodium chloride and glacial acetic acid/sodium acetate buffer system, (NDA 019667). The undersigned believes that the discontinued formulation of Sandostatin[®] (Octreotide Acetate Injection) was not withdrawn for reasons of safety or effectiveness.

B. Statement of Grounds

It is known from the Code of Federal Regulations that when an ANDA makes a reference to a discontinued label of a drug, FDA may still approve the ANDA upon determination that the formulation was not withdrawn for reasons of safety or effectiveness (21 U.S.C. Section 355 (j)(6) and 21 CFR §§ 314.122 and 314.161)¹.

The discontinued formulation, Sandostatin (Octreotide Acetate Injection), 50, 100, 500 mcg/ml, 1ml ampoule & 200, 1000 mcg/ml, 5 ml vial by Novartis was first approved on October 21, 1988 under NDA 019667 containing sodium chloride and a glacial acetic acid/sodium acetate buffer system. Novartis later reformulated Sandostatin Injection and this new formulation included a change in buffer system and tonicity agents. The original buffer system contained acetic acid, which was replaced by lactic acid and the tonicity agent sodium chloride was replaced by mannitol. The exact formula is provided in Tables 1 and 2 of the attached sheet. The regulation 21 CFR § 314.94(a)(9)(iii) permits ANDA applicants to seek approval for parenteral products that differ in buffer system.²

The proposed product is identical to the discontinued formulation of Sandostatin in its formula, which contains sodium chloride and a glacial acetic acid/sodium acetate buffer

¹ Although the regulations are consistent with relief sought, this citizen petition is submitted pursuant to section 505(j)(2)(C) of the Federal Food Drug, and Cosmetic Act ("The FDC Act") and 21 CFR § 314.93

² 21 CFR § 314.94(a)(9)(iii): "Inactive ingredient changes permitted in drug products intended for parenteral use". an applicant may seek approval of a drug product that differs from the reference listed drug in preservative, buffer, or antioxidant provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product.

17/B, Mahal Industrial Estate,
Mahakali Caves Road,
Andheri (East), Mumbai 400 093 India
Tel (91-22) 5645 5645
Fax (91-22) 5645 5685



system and is identical in indication, active ingredient and route of administration to the listed drug Sandostatin[®], and the concentration of the proposed product is in accordance with the prior FDA approved labeling for Sandostatin[®]. (See attachment Table III).

In this regard, the petitioner respectfully draws the agency's attention to the following facts:

1. The innovator asserted that it initiated the formulation change precisely because of safety issue i.e. reports of pain at the site of the injection. In a report of the clinical study³ of the two parenteral preparations of octreotide acetate namely the formulation containing the acetic acid buffer (herein after referred to as "discontinued formula") and the formulation containing the lactic acid buffer (herein after referred to as "currently listed formula"), the innovator reported (page 17 of the report) that 9 out of 16 patients suffered **mild pain** at the injection site in the "discontinued formula" group and one out of 16 cases suffered pain in the "currently listed formula" group.
2. Also in the said report it has been stated that the bioavailabilities of both the formulations (discontinued and currently listed) are equivalent (page 17 of the report).

In consideration of the above factual findings, the petitioner respectfully submits that the suffering of pain at the injection site is only a matter of patient compliance and should not be connoted to safety of the product. This is further supported from the observations of practicing physicians (attached certificates) in India treating patients using both the octreotide acetate formulations (the discontinued formula) (see attachments Table IV) and Sandostatin[®] (currently listed formula) that there is no difference in pain at the site of the injection in respect of both the formulations when administered subcutaneously.

In support of the above contention, the petitioner herein quotes the unit wise sales figure of its octreotide acetate (50 mcg) product, "discontinued formula" in India over the period ranging from the year 2000 to 2004, with sales figure in 569,273 Ampoules.

In conformance with the above referenced provisions, this petition seeks FDA to make a determination that the discontinued formulation of Sandostatin (Octreotide Acetate Injection) containing sodium chloride and a glacial acetic acid/sodium acetate buffer system was not voluntarily withdrawn by Novartis for reasons of safety or effectiveness and that the use of that labeling by the proposed product would not render the proposed product less safe or effective and would be therapeutically equivalent to the currently marketed immediate-release octreotide acetate product, Sandostatin (octreotide acetate) injection.

In view of the above, this petition seeks a determination that the discontinued formulation of Sandostatin (Octreotide Acetate Injection), 50, 100, 500 mcg/ml, 1ml ampoule & 200, 1000 mcg/ml, 5 ml vial, is suitable for submission as an Abbreviated New Drug Application (ANDA).

³ Report on "Bioequivalence study of the two parenteral preparations of SMS 201-995", Sandoz Pharmaceutical Ltd., Tokyo, Japan, March 1988

17/B, Mahal Industrial Estate,
Mahakali Caves Road,
Andheri (East), Mumbai 400 093 India
Tel (91-22) 5645 5645
Fax (91-22) 5645 5685



C. Environmental Impact

This petition is entitled to a categorical exclusion under 21 CFR 25.30 and 25.31

D. Economic Report

The petitioner agrees to provide an economic analysis if requested by the agency.

E. Certification

The undersigned certifies that, 'to the best knowledge and belief of the undersigned, this petition includes all information and review upon which the petitioner relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Abhay Muthal", written over a horizontal dashed line.

Dr. Abhay. Muthal
Dy. General Manager , Regulatory Affairs.

A handwritten signature in black ink, appearing to read "Swati Veera", written over a horizontal dashed line.

Swati. Veera
Patent Attorney



Table I

Formulation of Discontinued Sandostatin (Octreotide Acetate Injection)

For single dose:

Each ml of aqueous solution contains :	
Octreotide Acetate equivalent to Octreotide	50 mcg / 100 mcg / 500 mcg
Inactive Ingredients:	
Glacial Acetic acid	2.0 mg
Sodium Acetate	2.0 mg
Sodium Chloride	7.0 mg
Water for Injection	q.s. to 1ml

For multi dose:

Each ml of aqueous solution contains :	
Octreotide Acetate equivalent to Octreotide	200 mcg / 1000 mcg
Inactive Ingredients:	
Glacial Acetic acid	2 mg
Sodium Acetate	2 mg
Sodium Chloride	7 mg
Phenol	5 mg
Water for Injection	q.s. to 1ml

Table II

Formulation of Currently Listed Sandostatin (Octreotide Acetate Injection)

For single dose:

Each ml of aqueous solution contains :	
Octreotide Acetate equivalent to Octreotide	50 mcg / 100 mcg / 500 mcg
Inactive Ingredients:	
Lactic acid USP	3.4 mg
Mannitol USP	45 mg
Sodium bicarbonate USP	q.s. to pH 4.2 ± 0.3
Water for Injection	q.s. to 1ml

For multi dose:

Each ml of aqueous solution contains :	
Octreotide Acetate equivalent to Octreotide	200 mcg / 1000 mcg
Inactive Ingredients:	
Lactic acid USP	3.4 mg
Mannitol USP	45 mg
Phenol USP	5 mg
Sodium bicarbonate USP	q.s. to pH 4.2 ± 0.3
Water for Injection	q.s. to 1ml