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February 20, 2002

VIA MESSENGER

Dockets Management Branch  
Food and Drug Administration  
Department of Health and Human Services  
HFA-305, Room 1061  
5630 Fishers Lane  
Rockville, MD 20852

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**CITIZEN PETITION**

Dear Sir or Madam:

The undersigned submits this petition in quadruplicate, pursuant to Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act and 21 CFR § 314.93, on behalf of a client, to request that the Commissioner of Food and Drugs permit the filing of an Abbreviated New Drug Application (ANDA) for a drug that has the same strengths as a drug listed in FDA's publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations," but differs in dosage form.

**A. Action Requested**

By this petition, the Commissioner of the Food and Drug Administration (FDA) is hereby requested to declare that Baclofen Orally Disintegrating Tablets, 10 mg and 20 mg, are suitable for submission as an ANDA. The Reference Listed Drug (RLD) products on which this petition is based are Lioresal® (baclofen USP) 10 mg and 20 mg Tablets. Therefore, the petitioner requests a change from the RLD, Novartis' Lioresal Tablets, only in its dosage form (from tablet to orally disintegrating tablet).

**B. Statement of Grounds**

The Federal Food, Drug and Cosmetic Act provides for the submission of an ANDA for a drug product that differs in dosage form from that of the listed drug provided the FDA

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has approved a petition that proposed filing such an application. A copy of the most recent internet listing of the "Approved Drug Products with Therapeutic Equivalence Evaluations" (Orange Book), included in Attachment 1, lists the RLD, Novartis' Lioresal Tablets. The proposed drug product is an orally disintegrating form of the tablets, in the same dosage strengths as the RLD. The proposed product contains the same active ingredient as the RLD and is intended for the same route of administration. Thus, the proposed product will be labeled with the same conditions of use as the listed drug and is expected to have the same therapeutic effect when used as indicated in the labeling.

A copy of the RLD labeling is included in Attachment 2. The labeling of the proposed product is expected to be the same as that for the RLD with the exception of the section denoting the manufacturer, and the change in dosage form, which will instruct the user to place the orally disintegrating tablet on the tongue, allowing it to rapidly disintegrate and be swallowed. A copy of the draft proposed package insert is provided in Attachment 3.

In support of the change in dosage form requested in this petition, the petitioner would like to point out that the Agency has previously approved ANDA suitability petitions allowing for a change in dosage form in many instances. A suitability petition was recently approved for the drug product famotidine (docket 00P-1422) to allow a change from a tablet to an orally disintegrating tablet. The petitioner is seeking the change in dosage form in an effort to make an alternate dosage form (rapidly disintegrating tablet) available to those individuals that may have difficulty in swallowing an intact tablet or prefer the proposed dosage form.

The petitioner is also requesting a waiver of the requirement to conduct pediatric studies in accordance with the Regulations Requiring Manufacturers to Assess the Safety and Effectiveness of New Drug and Biological Products in Pediatric Patients; Final Rule (Pediatric Final Rule) 63 FR 66632 published December 2, 1998, and the waiver requirements set forth in 21 CFR § 314.55(c)(2)(i), as "the drug product does not represent a meaningful therapeutic benefit over existing treatments for pediatric patients and is not likely to be used in a substantial number of pediatric patients".

In support of the request to waive the requirement of pediatric studies, the petitioner notes that the RLD is indicated in the treatment of "...the alleviation of signs and symptoms of spasticity resulting from multiple sclerosis, particularly for the relief of flexor spasms and concomitant pain, clonus, and muscular rigidity." According to the National Institute of Neurological Disorders and Stroke, symptoms of multiple sclerosis (MS) rarely begin before age 15<sup>1</sup>. It is estimated that there are between 250,000 and 350,000 people suffering from this disease in the US. An article published by the American Academy of Neurology states that the onset of MS prior to the age of 15 occurs in 3 to 5% of cases<sup>2</sup>. The Pediatric Final Rule states that a "substantial number of pediatric patients will be defined as 50,000 pediatric patients with the disease for which the drug or biological product is indicated" (63 FR 66647). Using the figures noted

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above in a worst-case scenario, the pediatric population suffering from the indicated disease would be 17,500, which falls far below the definition of "substantial number" in the Pediatric Final Rule.

The labeling for the Lioresal tablet also states that it "may be of some value in patients with spinal cord injuries and other spinal cord diseases." According to the Spinal Cord Injury Information Network, there are approximately 183,000 to 230,000 cases of persons with spinal cord injuries in the US<sup>3</sup>. The Washington School of Medicine has published statistics stating that only 4.9% of these injuries occur in the 0-15 age group<sup>4</sup>. Using these figures, the worst-case scenario of the pediatric population suffering from spinal cord injuries would be approximately 11,270, also well below the substantial number as defined in the Pediatric Final Rule. Combining the estimated "worst-case" figures from both possible indicated conditions results in a figure less than 29,000.

The Scott-Levin Physician Drug and Diagnosis Audit<sup>5</sup> (PDDA) provides market research figures by counting the number of drug occurrences. Drug occurrences are defined as the number of mentions for a specific drug, regardless of location (hospital, doctor office, etc.) and issuance (prescription, sample, doctor recommendation, etc.). For the calendar year 2000, the PDDA estimated number of mentions of baclofen in the 0-16 age group numbered 19,000. Figures through November are available for 2001 and show that the estimated number of mentions in the 0-16 age group numbered 11,000.

It should also be noted that the RLD labeling for baclofen includes the statement that safety and effectiveness have not been established for patients under the age of 12. When considering the total pediatric populations affected by the indicated or possible conditions, the numbers would be smaller still if evaluating only the pediatric subpopulation in the neonate to 11-year age group. Taking into consideration the size of pediatric population suffering from the indicated or possible conditions, coupled with the market data, and the lack of established efficacy in the pediatric population provided in the RLD labeling, the petitioner feels a request for a waiver is reasonable and warranted.

### **C. Environmental Impact**

The petitioner claims a categorical exclusion under 21 CFR § 25.31.

### **D. Economic Impact**

The information will be provided upon request by the Agency.

### **E. Certification**

The undersigned certifies, that to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it

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includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,



Richard S. Morey

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### References

1. Multiple Sclerosis: Hope Through Research. National Institute of Neurological Disorders and Stroke, National Institutes of Health web site. Available at: [http://accessible.ninds.nih.gov/health\\_and\\_medical/pubs/multiple\\_sclerosis.htm](http://accessible.ninds.nih.gov/health_and_medical/pubs/multiple_sclerosis.htm). Accessed January 14, 2002. (Attachment 4)
2. Ruggieri M ; Polizzi A ; Pavone L ; Grimaldi L ME. Multiple sclerosis in children under 6 years of age. Neurology 1999 Aug. 53: 478-484. (Attachment 5)
3. Spinal Cord Injury Information Network. Available at: <http://www.spinalcord.uab.edu>. Accessed February 5, 2002. (Attachment 6)
4. The Rehabilitation Learning Center. Washington School of Medicine. Available at: <http://www.neuro.wustl.edu/ric/DempGr.html>. Accessed February 5, 2002. (Attachment 7)
5. Scott-Levin Physician Drug and Diagnosis Audit, PDDA, Scott-Levin Inc., 2001. (Attachment 8)