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November 17, 2000

BY HAND

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room 1061
5630 Fishers Lane
Rockville, MD 20857

**RE: INITIAL RESPONSE OF C. B. FLEET COMPANY, INCORPORATED,
TO CITIZEN PETITION FILED ON BEHALF OF BRAINTREE
LABORATORIES, INC.**

DOCKET NO. 00P-1472(CP1)

Dear Sir/Madam:

We represent C. B. Fleet Company, Incorporated, of Lynchburg, Virginia. ("Fleet"). Fleet has become aware of a Citizen Petition filed August 23, 2000, on behalf of Braintree Laboratories, Inc. ("Braintree"), which has been assigned the above-referenced docket number. The purpose of this Initial Submission by Fleet is to indicate that Fleet disagrees not only with the assertions of fact upon which the action is requested, but the actions requested in that Citizen Petition as well. The other purpose of this Initial Submission is to indicate that Fleet will file a more complete response to that petition by January 19, 2000, and to outline what would be contained in that more complete submission. Until receipt of Fleet's more complete submission, Fleet requests that the Agency defer any consideration

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or action on the Braintree Citizen Petition, unless it decides to deny that petition—as Fleet believes it should.

In that Petition, Braintree has requested the Commissioner to issue a determination that drug products containing sodium phosphates and labeled for use as bowel preparations be: 1) subject to prescription limitations within the meaning of Section 503(b) of the Federal Food and Drug and Cosmetic Act (“the Act”) on the basis of sodium phosphates’ alleged documented toxicity and potentiality for harmful effects when used in bowel preparations and 2) regulated as “new drugs” within the meaning of Section 201(p) of the Act on the basis that when used for bowel preparation, sodium phosphates allegedly cannot be considered generally recognized as safe, whether marketed OTC or subject to prescription limitations. In addition, the Braintree Citizen Petition requests the Commissioner to require a boxed warning on the labeling for all sodium phosphates bowel preparation products calling special attention to the allegedly serious safety concerns associated with the dose and contraindications of these products.

For almost ten years, Braintree has attempted to get FDA to take actions of the sort requested by them in this Citizen Petition. This is despite the fact that the sodium phosphates oral solution product—marketed as Fleet® Phospho-Soda®—has been marketed since 1869 with an impressive safety and effectiveness record as both a laxative

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and a bowel purgative. Because numerous clinical studies have shown that Fleet® Phospho-Soda® is not only equal or superior to the polyethylene glycol (“PEG”) bowel preparations marketed by Braintree as GOLYTELY® and NULYTELY®, but much more well tolerated by patients and with a much higher rate of completion, Fleet® Phospho-Soda® is becoming a standard bowel preparation for use prior to colonoscopy and other diagnostic and surgical procedures.

Sodium phosphates for use as a bowel preparation were included under the Proposed Monograph on Laxative Drug Products for Over-the-Counter Human Use as far back as 1975. See proposed 21 C.F.R. §334.16(a), 40 Fed. Reg. 12940 (March 21, 1975) and proposed 21 C.F.R. §334.80(a), 40 Fed. Reg. 12942. See, also, 40 Fed. Reg. 12911. Such professional labeling for use of sodium phosphates was also included in the Tentative Final Monograph on Laxative Drug Products for Over-the-Counter Human Use. See proposed 21 C.F.R. §§334.80(a)(2) and (b)(2), and (c), 50 Fed. Reg. 2157 (January 15, 1985).

Since that time, due to improper overdosing or other misuse of Fleet® Phospho-Soda® in patients in whom it should not have been used, the Agency has required package size limitations in sodium phosphates solution for oral use and has issued labeling requirements relevant to directions for use. See 21 C.F.R. §201.37, as

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promulgated at 61 Fed. Reg. 27483 (May 21, 1998). Fleet has cooperated with the Agency on these initiatives, and has at all times provided the Agency with information on the safety of the sodium phosphates oral solution upon request and has complied with all of the labeling rules requested by the Agency, and subsequently required by rule.

It is Fleet's position that the Agency's action to date have been adequate to protect the public health and that the actions requested by Braintree in its Citizen Petition are not only baseless but not required.

As to the request by Braintree that Commissioner order the product be limited to prescription use and be regulated as a "new drug," Fleet believes that as used in accordance with the Agency's current rules its Fleet® Phospho-Soda® product is not a new drug, as it has been tentatively found generally recognized as safe and effective as a laxative and a bowel preparation (purgative). It is widely used for this purpose, and preferred by many physicians who perform colonoscopies, endoscopies and other diagnostic procedures, as well as colorectal and other surgeons, over PEG bowel preparations and other preparations. In addition, there are plethora of adequate and well controlled studies, constituting "substantial evidence", upon which experts recognize it as safe and effective for this use, and, as such, to state it is a "new drug" is contrary to law and fact. Braintree's request should be seen for what it is: an attempt by a competitor to

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force its primary competition to spend money defending the safety and efficacy of a product that has been marketed safely and effectively for over 130 years.

As to the need for revising labeling as to “Warnings”, the Agency has already addressed that issue—and done so recently. 21 C.F.R. §201.307 requires for this type of product the following statement under “Warnings” in **boldface** type as the **first statement**:

Taking more than the recommended dose in 24 hours can be harmful.

The rule contains similar admonition requirements in the “Directions” section. See 21 C.F.R. §201.307(b)(3)(i) and (ii). Fleet has complied with all of the requirements as a review of the packaging of Fleet® Phospho-Soda® makes clear. See Exhibit A. Braintree is thus requesting the Agency to revisit an issue the Agency has just recently—1998—considered, almost exclusively on data that was available to the Agency when the Agency issued 21C.F.R. §201.307, as a final rule, in May 1998. There is nothing new in the medical literature, or in the adverse reports to Fleet, or to the Agency, that should require the Agency to use its limited resources to revisit an issue the Agency has just thoroughly considered. Indeed, the labeling requested in the Braintree Citizen Petition:

Do not exceed recommended dose. Before use, appropriate tests should be performed to rule out electrolyte, renal or cardiovascular abnormality. Serious and life-threatening adverse events have occurred with sodium phosphate in the presence of these conditions.

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does not differ in much detail from the labeling currently required by 21 C.F.R. §201.307 and/or used by Fleet in its labeling and professional labeling. See Physicians Desk Reference, 2000 Edition, P. 1068, attached as Exhibit B. Thus, there is no need for any consideration of revised labeling for these products. Last, Braintree has not made any argument to justify on a legal basis the need for a black box warning.

In short, Fleet believes the Braintree Citizen Petition is nothing more than a frivolous attempt by a competitor, whose products have encountered professional and consumer acceptance problems, to cause its primary competitor regulatory problems. It is but one more step in its decade long campaign aimed at attempting to force Fleet's valuable and important bowel cleansing product from the market for no reason other than to prevent competition. As if that were not enough, the Braintree Citizen Petition requests the Agency to revisit a matter it has just considered without submitting any substantial new data in support of its latest unfounded attempt to coerce the Agency in unwarranted and unnecessary action.

In short, Fleet believes the Commissioner should respond summarily to the Petition and deny the requested actions in their entirety.

As indicated, Fleet will submit a more complete response by January 19, 2000, although it does not believe one should be necessary to deny the relief requested in the

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Braintree Citizen Petition. In that response, Fleet will discuss history of submissions it has made to FDA, including submissions made to highlight FDA to the safety issues, Fleet's labeling of the products, Fleet's compliance with package size limitations, various submissions Braintree has made repeatedly before on the exact same issue, and a discussion of what Fleet has done in response to various FDA requests.

It will also discuss the safety of sodium phosphates bowel preparations and explain deaths/serious injuries reported on the product. These reports and medical literature have involved cases of overdose, where the product was contraindicated, and problems with misuse of the product.

It will also detail how Fleet labeling warns physicians to monitor for electrolyte problems and that clinical practice failures are just that and nothing encouraged or condoned by Fleet. It will refute Braintree's argument about induced lesions. It will explain in detail that the product is safe when and as directed. It will describe how Braintree is emphasizing safety concerns that are not warranted for more anticompetitive reasons. It will emphasize that much of the "literature" upon which Braintree relies is based on data of a paid consultant/employee of Braintree, Jack Di Palma, M.D., whose bias is obvious on its face.¹ Last, it will discuss current labeling for Fleet®

¹ Please note that Dr. DiPalma is listed as the Contact for Medical Emergencies for Braintree in the 2000 *Physicians' Desk Reference* (Exhibit C).

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Phospho-Soda® and why it accomplishes adequate safety precautions, why tests for electrolyte, renal or cardiovascular abnormality are not needed prior to use if the product is used as directed, and therefore a black box warning is not required or legally justifiable.

In short, it will in greater detail substantiate the arguments included herein, on both scientific and medical, and legal grounds, as to why the Braintree Citizen Petition should be denied in its entirety.

As noted above, Fleet believes that this Initial Submission alone should be sufficient to summarily deny the Braintree Citizen Petition, but it will, in order to assist the Agency, supply a more detailed response by January 19, 2000, and, unless the Agency decides to deny the Citizen Petition in the interim, as Fleet believes it should, requests that the Agency defers any consideration of the Braintree Citizen Petition until Fleet's more complete submission is filed.

Respectfully submitted,



Peter S. Reichertz
Michael D. Bernstein

Counsel to C.B. Fleet Company, Incorporated