Date: 02/26/2020

Section A: Action Required

To whom it may concern,

We respectfully wish to petition the US Food and Drug Administration (FDA) for permission to proceed with an alternative fluoride study to the requirement found in sec. 355.70(a):

> *A fluoride dentifrice drug product shall meet the biological test requirements for animal caries reduction and one of the following tests: Enamel solubility reduction or fluoride enamel uptake. The testing procedures for these biological tests are labeled Biological Testing Procedures for Fluoride Dentifrices ; these testing procedures are on file under Docket No. 80N-0042 in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and are available on request to that office.*

The requirements for an alternative study to sec. 355.70(a) is found in sec. 355.70(c):

> *Alternative testing procedures may be used. Any proposed modification or alternative testing procedures shall be submitted as a petition in accord with 10.30 of this chapter. The petition should contain data to support the modification or data demonstrating that an alternative testing procedure provides results of equivalent accuracy. All information submitted will be subjected to the disclosure rules in part 20 of this chapter.*

The alternative study we request to proceed with is the Featherstone laboratory pH cycling model.

Section B: Statement of Grounds

Currently we as dentists and oral health practitioners are developing toothpaste using stannous fluoride as an active ingredient. It is in violation of our company policy to proceed with any studies involving the use or abuse of animals, we request permission to pursue the Featherstone laboratory pH cycling model to appease the FDA's regulatory standards. As in accordance with sec. 355.70(c), our hope is to provide a toothpaste wherein our clinically proven toothpaste formulas perform as expected. In accordance with as an alternative we request permission to proceed with the Featherstone laboratory pH cycling model, cited as follows; Stookey, George K. "The Featherstone laboratory pH cycling model: A prospective, multi-site validation exercise." American Journal of Dentistry 24.5 (2011): 322.

> *PURPOSE:*
>
> *To demonstrate the robustness of the Featherstone pH cycling model when tested in three independent laboratories and to evaluate the use of "non-inferiority" testing at those laboratories.*
>
> *METHODS:*

The fundamental principles for the Featherstone laboratory pH cycling model to be an appropriate alternative to animal testing is that it must demonstrate equivalent accuracy to the "Gold Standard" (rat caries model) by: (1) providin

g a meaningful representation of the caries process; (2) demonstrating a proportionate response to fluoride dose (or concentration); (3) being able to show that clinically proven formulations perform similarly relative to the controls; and (4) differentiating products that have attenuated fluoride activity.

RESULTS:

This cross-validation study confirmed the ability of the three independent laboratories to discriminate between various concentrations of fluoride-containing dentifrice formulations, demonstrated that clinically proven formulas perform as expected and identified an attenuated fluoride formulation (NaF/CaCO3 dentifrice - 1100 ppm NaF) as inferior compared to the 1100 ppm F (NaF/silica) positive control.

If this test is deemed non satisfactory, or aside from FDA compliance, suggestions for other alternative studies free from the use of animals would be most greatly appreciated.

Section C: Environmental Impact

The Featherstone pH cycling assay will be carried out by an independent third party testing laboratory, the Oral Health Research Institute (OHRI) at the Indiana University School of Dentistry. The OHRI adheres to the Environmental Protection Agency (EPA) hazardous waste generators, and it is currently identified with the EPA ID IND072078967.

Additionally, the EPA does not account for these facilities in the National Priorities List, which is comprised by the sites targeted for long-term federal cleanup activities.

Section D: Economic Impact

Available upon request.

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

Shane Ririe, CFO
grBiosystems Inc.
138 E 12300 S STE C-435
Draper, UT 84020
801.215.9234
sririe@grbiosystems.com