DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Center for Tobacco Products
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

August 28, 2014

NOT SUBSTANTIALLY EQUIVALENT

Star Scientific, Inc.
Attention: Robert E. Pokusa, General Counsel
1255 23rd Street, N.W.
Suite 875
Washington, DC 20037
via UPS

FDA Submission Tracking Number (STN): SE0000283

Dear Mr. Pokusa:

We have completed our review of your Report Preceding Introduction of Certain Substantially Equivalent Products into Interstate Commerce (SE Report), submitted under section 905(j) of the Food, Drug, and Cosmetic Act (FD&C Act), for the following tobacco product:

Applicant:	Star Scientific, Inc.
Tobacco Product Name[1]:	Ariva Wintergreen
Tobacco Product Category:	Smokeless
Tobacco Product Sub-Category:	Dissolvable (Tablets)
Package Size:	10 Tablets
Package Type:	Carton with one 10-Count Blister Pack

We have completed the review of your SE Report and have determined that it does not establish that the product specified above is substantially equivalent to the predicate tobacco product, Original Ariva. We have described below our basis for this determination.

[1] Brand/sub-brand or other commercial name used in commercial distribution

1. Your SE Report lacks full characterization of all ingredients in all components and subcomponents. For example, the grade/purity and supplier of each ingredient would help fully characterize the new and predicate tobacco products.

2. Your SE Report provides the measured pH values for the new tobacco product but not for the predicate tobacco product. The percentage of free nicotine depends on the product pH, especially between pH 7 and 9. The measured pH values or the free nicotine levels based on measured pH values for the predicate tobacco product would help to demonstrate whether the new and predicate tobacco products are substantially equivalent.

3. Your SE Report indicates that there are many changes in ingredients in terms of quantity or type or both. The new tobacco product includes different (b) (4) (b) (4) and (b) (4) and significantly different amounts of (b) (4) and (b) (4) (b) (4) (b) (4) than the predicate tobacco product. Additionally, the new tobacco product includes a (b) (4) which contains (b) (4) These differences may affect the release rates and amounts of the tobacco constituents. However, evidence and scientific rationale is not provided to demonstrate that these differences do not cause the new tobacco product to raise different questions of public health.

4. Your SE Report provides average HPHC quantities, standard deviations, and 95% confidence limits for the new tobacco product. However, your SE Report only provides average HPHC quantities for the predicate tobacco product. We cannot determine whether the differences in HPHC quantities between the new and predicate tobacco products are significant with only the average values. Full test data (including test protocols, quantitative acceptance (pass/fail) criteria, national/international standards used and any deviation(s) from those standards, data sets, and a summary of the results, standard deviations or confidence limits) would help in evaluating HPHC quantities in the new and predicate tobacco products.

5. Your SE Report provides two separate sets of nicotine data in (b) and (b) (4) reports. (b) (4))) However, your SE Report did not provide an explanation for the discrepancies between the two sets of data. Additionally, the values reported in (b) (4) are reported in mg per gram unit with no indication of whether the values are as received or dry weight adjusted. It is not clear which nicotine data set to use for the determination of substantial equivalence.

6. Your SE Report provides TSNA quantities for the new tobacco product. However, the SE Report states that the (b) (4) (b) (4) , and the TSNAs levels were reported

as “NQ” for the predicate tobacco product. Several other HPHCs are presented as “NQ” and “BDL” (below the detection limit) as well. The data cannot be fully evaluated without complete information about the methodologies used to generate the HPHC data, including the limit of detection and limit of quantitation, accuracy and precision of the methods.

7. Your SE Report lacks information about stability for the predicate and new tobacco products. Additional information about stability testing is needed to fully characterize the predicate and new tobacco products. Such information would include detailed stability testing, including test protocols, quantitative acceptance criteria, data sets and a summary of the results for all stability testing performed.

8. Your SE Report lists complex ingredients but does not distinguish between complex ingredients made to your specifications and those that are not. Furthermore, your SE Report lacks the information about complex ingredients made to your specifications as explained in FDA’s *Guidance for Industry Listing of Ingredients in Tobacco Products*.

9. Your SE Report provides some information on the design parameters for the predicate and new tobacco products. However, your SE Report does not include all of the design parameters required to fully characterize the predicate and new tobacco products. In order to adequately characterize the products, it is necessary to compare key design parameters, including the following information about the predicate and new tobacco products that is omitted in your SE Reports:

    a. Target specification and upper and lower range limits for tobacco particle size (mm)
    b. Target specification for portion weight (mg)
    c. Upper and lower range limits for final tobacco moisture (%)
    d. Upper and lower range limits for portion length (mm)
    e. Upper and lower range limits for portion width (mm)
    f. Upper and lower range limits for portion thickness (mm)

    It is not clear if there are differences in these design parameters for the predicate and new tobacco product.

10. Your SE Report includes design parameter specifications but do not include raw data confirming that specifications are met. More specifically, the test data (i.e., measured values of design parameters), including test protocols, quantitative acceptance criteria (pass/fail), data sets, and a summary of the test results is not provided for the following design parameters for the predicate tobacco product:

    a. Tobacco particle size (mm)
    b. Final tobacco moisture (%)
    c. Portion weight (mg)

Certificates of analysis from the material supplier may provide such information.

11. Your SE Report indicates that there were substantial increases in several HPHCs, specifically (b) (4) However, your SE Report did not include evidence and scientific rationale for why the increases in these HPHCs do not cause the new tobacco product to raise different questions of public health with regard to product toxicity.

12. Your SE Report indicates that the levels of carcinogenic compounds such as acetaldehyde, NNN, and NNK were reported for the new tobacco product but not for the predicate tobacco product. These chemicals are known to be carcinogenic. Without levels of these HPHCs in the predicate tobacco product, it cannot be determine whether or not the predicate and new tobacco products have different characteristics with regard to product toxicity.

13. Your SE Report indicates that (b) (4) is used in the new tobacco product but not the predicate tobacco product. However, your SE Report does not provide the source and type of the (b) (4) used for the manufacturing of the new tobacco product. Furthermore, your SE Report does not include evidence and scientific rationale for why the presence of (b) (4) does not cause the new tobacco product to raise different questions of public health.

14. Your SE Report includes a health information summary that contains statements which convey a modified exposure claim, referring to the new tobacco product repeatedly as "(b) (4) Use of a claim such as this requires a marketing order based on a Modified Risk Tobacco Product Application (MRTPA) under section 911(g)(2) of the Federal Food, Drug, and Cosmetic Act. Without such an order, this language cannot be used.

15. Your SE Report indicates that the (b) (4) of the new tobacco product differ from those of the predicate tobacco product. However, your SE Report does not include evidence and scientific rationale for why the differences in (b) (4) do not cause the new tobacco product to raise different questions of public health (e.g., an impact on tobacco use behavior, such as initiation among non-users, or increased use or decreased cessation among users).

16. Your SE Report indicates the (b) (4) is increased in the new tobacco product compared to the predicate tobacco product. (b) (4) , which is an HPHC based, in part, on its potential to increase the addictiveness of nicotine, is increased in the new tobacco product. However, your SE Report does not include evidence and scientific rationale demonstrating that these differences in HPHC levels do not cause the new tobacco product to raise different questions of public health with regard to consumer addiction.

17. Your SE Report indicates that the new tobacco product has differences in (b) (4) compared to the predicate tobacco product. Also, the new tobacco product includes (b) (4) designed to make the new tobacco product less harsh and improve taste acceptability compared to the predicate tobacco product. Palatability can influence initiation behaviors and abuse liability. In addition, these changes may alter release rate of tobacco constituents with addiction indications, thereby impacting product addictiveness. However, your SE Report does not include evidence and scientific rationale demonstrating that these differences do not cause the new tobacco product to raise different questions of public health.

You have failed to provide sufficient information to support a finding of substantial equivalence; therefore, we are issuing an order finding that this new tobacco product is not substantially equivalent to an appropriate predicate tobacco product. Upon issuance of this order, your tobacco product is misbranded under section 903(a)(6) and adulterated under section 902(6)(A) of the FD&C Act. Therefore, you must immediately stop all distribution, importation, sale, marketing, and promotion of your tobacco product in the United States. Failure to comply with the FD&C Act may result in FDA taking regulatory action without further notice. These actions may include, but are not limited to, civil money penalties, seizure, and/or injunction.

Additionally, FDA requests that within 15 days of this letter you submit a plan detailing the steps you plan to take to ensure that this misbranded and adulterated product is not further distributed, imported, sold, marketed, or promoted in the United States by others. Your plan should include information sufficient to distinguish this misbranded and adulterated product from legally marketed tobacco products, including, but not limited to lot numbers, manufacturing codes, and manufacturing dates. The plan should also include a list of your direct accounts, and contain their contact information. Submit your plan to the address below with a cover letter that includes the following text in the subject line:

COMPLIANCE PLAN for SE0000283.

FDA will post product identifying information on a list of tobacco products that are adulterated and misbranded due to an NSE order. The list can be found by visiting FDA's website at www.fda.gov/tobacco and searching for "Misbranded and Adulterated NSE Tobacco Products" using the search box.

We remind you that you are required to update your listing information in June and December of each year under section 905(i)(3) of the FD&C Act. As part of this listing update, under section 905(i)(3)(B) of the FD&C Act, you must provide information on the date of discontinuance and product identity for any product you discontinue.

If you wish to seek further FDA review of this decision, we suggest that you first request a meeting with the FDA staff who reviewed your submission. If you wish to request supervisory review of this decision under 21 CFR 10.75, please submit the request via the FDA Electronic Submission Gateway (www.fda.gov/esg) using eSubmitter, or mail to:

Food and Drug Administration
Center for Tobacco Products
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

We request that your package be sent as a single submission with a cover letter that includes the following text in your subject line: **REQUEST FOR SUPERVISORY REVIEW for SE0000283**. In addition, we request that your package identify each basis for the request and contain all information on which you wish your request to be based; it may not contain any new data or analysis that was not part of your SE Report.

You may not legally market the new tobacco product described in this SE Report unless (1) FDA issues an order finding the product to be exempt from the requirements of substantial equivalence and you make the required submission under section 905(j)(1)(A)(ii), (2) FDA issues an order finding the product substantially equivalent to a predicate tobacco product (section 910(a)(2)(A) of the FD&C Act), OR (3) FDA issues an order authorizing introduction or delivery for introduction into interstate commerce under a premarket tobacco application (section 910(c)(1)(A) of the FD&C Act).

See the following website for additional information on these three pathways: http://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/NewTobacco ProductReviewandEvaluation/default.htm.

If you have any questions, please contact Idara Udoh, Senior Regulatory Health Project Manager, at (301) 796-3074.

Sincerely,

Digitally signed by David Ashley -S
Date: 2014.08.28 06:56:51 -04'00'

David Ashley, Ph.D.
RADM, U.S. Public Health Service
Director
Office of Science
Center for Tobacco Products