February 2, 2019

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CITIZENS PETITION TO ENSURE UNADULTERATED SOURCES OF METHSCOPOLAMINE BROMIDE

Action Requested

In compliance with 21.CFR 10.30 the petitioner respectfully requests that FDA's Office of Generic Drugs (OGD) consistently ensure that the requirements to manufacture Methscopolamine Bromide USP are adhered to by all Active Pharmaceutical Ingredient ("API") and finished product manufacturers of Methscopolamine Bromide tablets.

Statement of Grounds

FDA's jurisdiction

Section 501(b) of the Food, Drug, and Cosmetic Act (the Act) deems an official drug (i.e., a drug purported to be or represented as a drug the name of which is recognized in an official compendium) to be adulterated if it fails to conform to compendial standards of quality, strength or purity. Compendial tests or assay methods are used when determining such conformance under 501(b); the standards are stated in individual monographs as well as portions of the General Notices section of the USP/NF. Standards and test methods have been established for such characteristics as potency, sterility, *dissolution*, weight variation and content uniformity.[1]

2016 Guidance

To ensure the consistency in the manufacturing and production of botanical drugs, the Center for Drug Evaluation and Research released a guidance in December 2016 titled "Botanical Drug Development" (hereinafter the "Guidance"). The Guidance reiterates scientific principles to ensure that manufactured botanical drugs are both safe, and efficacious and are neither adulterated nor misbranded. To achieve this goal and to ensure "therapeutic consistency", the Guidance considers the "totality of the evidence" and makes recommendations including, in relevant part, relating to: (1) Botanical Raw Material Control, (2) Quality Control by Chemical Tests, and (3) Biological Assays and Chemical Data.

[1] CPG Sec. 420.100 Adulteration of Drugs Under Section 501(b) and 501(c) of the Act. *Direct Reference Seizure Authority for Adulterated Drugs Under Section 501(b) https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-afda-ice/documents/webcontent/ucm074367.pdf (Last Review January 12, 2019)

Specific considerations include:

(1) Characterization, identification tests, and specification criteria for biological raw materials with appropriate updates being provided to the FDA;
(2) Testing "for residual pesticides, including parent pesticides and their major toxic metabolites" and as may be outlined in USP <561> and for any pesticides routinely used in the countries of origin of botanical raw materials"

Methscopolamine Bromide Expectations

Petitioner is aware that at least one of the FDA approved API manufacturer and finished product manufacturer of Methscopolamine Bromide tablets is compliant with the expectations outlined in the Guidance. However, there is concern that not all API manufacturer and finished product manufacturers of Methscopolamine Bromide (collectively, "Manufacturers") are compliant with the Guidance. For example, the Duboisia flower (hereinafter "the Flower") is a known starting material for this API and may be harvested in regions located in Australia susceptible to significant amounts of pesticides. As such, Manufacturers should test for residual pesticides and have established validated identification tests, and acceptance limits. On faith and belief, it is understood that these requirements are not consistently met by all Manufacturers.

Conclusion

Recent twitter commentary by FDA Commissioner Scott Gottlieb, MD states that the FDA conducts "high risk inspections."[2] Per Dr. Gottlieb, in relevant part, "The primary factors contributing to a facility's risk profile include: … the manufacturing process, and the compliance history of the facility."[3] Manufacturers using natural sources such as Flowers hence posit a risky manufacturing process. Manufacturers may hence be subject to high risk inspections. Accordingly, Petitioner requests that FDA consistently ensure that all Manufacturers are in full compliance with the outlined requirements in the Guidance.

Environmental Impact

The petitioner does not believe that there will be any significant environmental impact.

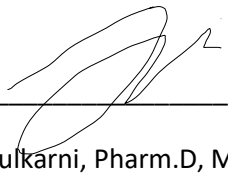
Economic Impact

The petitioner does not believe that there will be any significant economic impact.

[2] https://twitter.com/SGottliebFDA/status/1083388859931656192
[3] https://twitter.com/SGottliebFDA/status/1083056007696257024

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.



_____ (Signature)

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