Via Electronic Submission to: www.regulations.gov

August 31, 2020

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Approved Drug Products With Therapeutic Equivalence Evaluations (the "Orange Book"); Establishment of a Public Docket; Request for Comments (Docket No. FDA-2020-N-1069)

Dear Sir or Madam:

The American Pharmacists Association (APhA) appreciates the opportunity to provide the Food and Drug Administration (FDA) with our comments and recommendations for making improvements to *Approved Drug Products With Therapeutic Equivalence Evaluations* (the "Orange Book"). Founded in 1852, APhA represents pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians, and others interested in improving medication use and advancing patient care. APhA members provide care in all practice settings, including community pharmacies, hospitals, long-term care facilities, specialty pharmacies, community health centers, physician offices, ambulatory clinics, managed care organizations, hospice settings, and the uniformed services.

Below are our comments on the questions posed by FDA in the *Federal Register* notice:

What types of people or entities use the Orange Book?

On July 18-20, 2020, APhA conducted a pulse survey of our members regarding their use of the Orange Book. Of the 122 respondents, only 22% reported that they currently use the Orange Book. Some respondents reported being unfamiliar with the Orange Book or not needing to use it in their current position.

What sections of the Orange Book do these different types of people or entities use?

Of respondents who reported using the Orange Book, the following percentages use these different sections of the book:

92% Prescription Drug Product List
42% OTC Drug Product List
15% Drug Products with Approval under Section 505 of the FD&C Act List
23% Discontinued Drug Product List
8% Orphan Products Designations and Approvals List
12% Drug Products Which Must Demonstrate *in vivo* Bioavailability Only if Product Fails to Achieve Adequate Dissolution
4% Appendices

For what reasons do these people or entities use the Orange Book?

Of respondents who reported using the Orange Book, the following percentages use it to:

96% Look up therapeutic equivalence evaluations for prescription drugs
17% Look up patent and/or exclusivity information
30% Check if a drug has been discontinued

What additional information or features (e.g., additional search functions) could be incorporated into the Orange Book to make it more useful?

Although APhA's survey did not ask whether our members were using the online version of the Orange Book or the mobile app, there was consensus that making the Orange Book more accessible and easier to use and navigate would be very helpful. One pharmacist stated: "I wish you could just click on a product you know/have, and then it will take you to the next page where there is a list of every available product and narrow to each category (A, AB, etc.)."

Additional recommendations to improve the Orange Book include the following:

- Add the option to search by National Drug Code (NDC).
- Improve the display format so it is easier to read and interpret.
- Provide better explanations of the different therapeutic equivalence codes.
- Educate pharmacists and other users about the Orange Book's uses and functionalities, including through short YouTube videos.

Is the information in the Orange Book regarding therapeutic equivalence generally useful?

90% of respondents to this question reported that the therapeutic equivalence information was very or somewhat useful, while 10% reported that the therapeutic equivalence information was not too useful or not at all useful.

How useful is the second letter of a therapeutic equivalence evaluation code?

85% of respondents to this question reported that the second letter of a therapeutic equivalence evaluation code was very or somewhat useful, while 15% reported that it was not too useful or not at all useful.

How could the therapeutic equivalence information be made more user-friendly or otherwise be tailored to meet the needs of people or entities that use the Orange Book (e.g., the therapeutic equivalence evaluation code)?

APhA recommends that FDA improve the Orange Book by improving search functionality and allowing users to customize their searches through the use of filters.

- One survey respondent stated: "If I bring up a generic drug, I don't want to see every permutation of it initially. Instead show me the parent options first (for example the different forms of Depakote) and then list in different tables the generics that are AB rated and the ones that are not with a clear legend. Within the separate tables, make it so I can search manufacturer name or NDC. I would like another type of search and that is to search by NDC. It would be nice to have the two tables -- one where it lists all AB and another that lists all else with the parent (brand name) listed first in bold."

The recommendation to include therapeutic equivalence tables/charts was echoed by other APhA members.

Some respondents recommended that the Orange Book provide better explanations of the different therapeutic equivalence codes, while others recommended that an easier, clearer coding system be developed.

Additional recommendations to make the therapeutic equivalence information more user-friendly and/or tailored to meet pharmacists' needs include the following:

- As stated above, add the option to search by National Drug Code (NDC).
- Add a drop-down menu that displays therapeutically equivalent products with the manufacturer indicated.
- Make sure brand and generic drug names are up to date.
- Finally, one pharmacist stated: "I think having an additional resource for error prone equivalent products, such as oral contraceptives or grouping by class for therapeutic interchange would be helpful."

If you use the information regarding therapeutic equivalence, how do you use it?

Pharmacists use therapeutic equivalence (TE) information to determine whether a generic drug may be substituted for a brand name or other drug product to meet a patient's needs and save money. APhA survey respondents reported using TE information to select AB-rated generics for dispensing, purchasing, and formulary development purposes. Therapeutic equivalence information is helpful when a pharmacist is reviewing formulary options and determining which drug(s) may be substituted without a change in the prescription order. The information is also helpful for purposes of generic interchange in the case of backordered or out-of-stock drugs.

For example, one APhA survey respondent stated that he/she uses TE information to confirm which generics are equivalent to which brands when different dosage forms exist for a specific drug. Another respondent explained that he/she uses TE information to determine generic equivalency for medications such as diltiazem and nifedipine which have many generic forms.

Is there any other information regarding the Orange Book that would be useful for FDA to consider?

The Discontinued Drug Product List in the Orange Book contains both discontinued and withdrawn applications (if a determination has been made that they were not withdrawn for safety or efficacy reasons). APhA recommends that FDA indicate which applications have been discontinued and which have been withdrawn.

Additional recommendations include the following:

- Link the Orange Book data to the drug shortage list to assist in the identification/selection of alternate products for use.
- Include the history of an individual product's profile by outlining changes in the product over time.
- Include "Authorized Generics" of a brand name drug in the Orange Book[1].
- Make the Orange Book available in other languages.
- Educate pharmacists and other users about the Orange Book's uses and functionalities, including through short YouTube videos.
- Some APhA survey respondents noted that the Orange Book is not always integrated into pharmacy software systems. APhA recommends that FDA consider conducting education and outreach to software vendors to encourage Orange Book integration.

[1] See *FDA List of Authorized Generic Drugs*, accessed on Aug. 25, 2020 at https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/fda-list-authorized-generic-drugs.

Does the information regarding therapeutic equivalence promote drug competition? And if so, how?

The therapeutic equivalence information in the Orange Book can help to promote drug competition and substitution and lead to lower prices. However, APhA is concerned that brand name drug manufacturers sometimes try to inappropriately tilt in their favor the delicate balance established by the Hatch-Waxman Amendments[2] between promoting innovation and ensuring generic drug competition. Brand name drug manufacturers' practice of listing numerous patents in the Orange Book contributes to delays in bringing generic drug products to market. To help address inappropriate blocking of competition, APhA recommends that FDA, in a timely manner, remove patents from the Orange Book that have been invalidated by the Patent Trial and Appeal Board.

Conclusion

APhA appreciates the opportunity to provide our comments and recommendations for improving the Orange Book. If you have any questions or need additional information, please contact me at kbolte@aphanet.org or (301) 648-0673.

Sincerely,

Karin L. Bolte

Karin L. Bolte, JD
Director, Health Policy

[2] Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, P.L. 98-417.