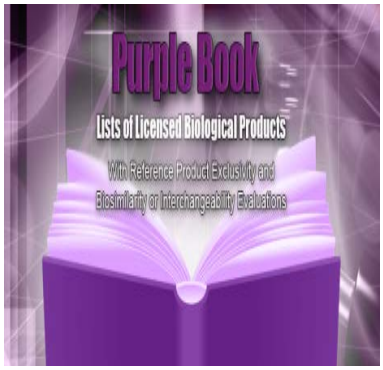
FDA/CDER SBIA CHRONICLES

NOVEMBER 18TH, 2014

Inside This Issue



Did You Know?

Using a color for the nickname of the list draws upon using "The Orange Book" to refer to "Approved Drug Products with Therapeutic Equivalence Evaluations". So during a meeting, a staff member said, "how about **purple**?" The use of bright colors aside, the Agency would like to emphasize that the Purple Book is not the biological equivalent of the Orange Book. The legal regimes governing the licensure of biologics and the approval of drugs are different, and the Purple and Orange Books reflect these differences.

The Purple Book

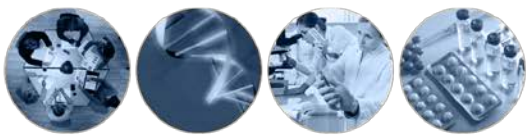
In case you hadn't heard, **purple** is the new color this season for biological products. FDA recently released the "**Purple Book**," a resource that lists innovator biological products, as well as any biosimilar and interchangeable biological products licensed by FDA under the Public Health Service Act (the PHS Act).

The primary purpose of the Purple Book is two-fold: to enable a user to see if a biological product licensed under section 351(k) of the PHS Act has been determined by FDA to be biosimilar to or interchangeable with a reference biological product (an already-licensed innovator biological product approved under section 351(a) of the PHS Act), *and* to provide information on any existing reference product exclusivity protecting a reference biological product.

To understand the Purple Book, let's review the key statutory definitions and concepts related to biological products brought about by the passage of the Biologics Price Competition and Innovation Act of 2009 (BPCI Act). The BPCI Act created both the abbreviated licensure pathway for biologics allowing for the licensure of biosimilar and interchangeable biologics, and for the first time created an exclusivity period for certain qualifying innovator biological products. Until the passage of the BPCI Act, applications for biological products had to contain a full complement of product-specific preclinical and clinical data. These "soup to nuts" applications were approved under section 351(a) of the PHS Act. The BPCI Act, however, amended the PHS Act to create section 351(k) that describes the abbreviated regulatory approval pathway established for biological products. Products evaluated under this pathway can be approved based on less than a full complement of product-specific preclinical and clinical data because of reliance on what is previously known about the reference product (publicly-available information), including FDA's previous finding of safety and effectiveness of the reference product. There are two types of biological products under the 351(k) pathway: biosimilar products and interchangeable biological products. Biosimilarity and interchangeability are assessed with respect to a reference product. A reference product is the single biological product licensed by FDA under section 351(a) of the PHS Act against which a proposed biological product is evaluated in an application submitted under section 351(k).

A ***biosimilar product*** is a biological product that is highly similar to the reference product notwithstanding minor differences in clinically inactive components, and there are no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency of the product. An ***interchangeable biological product*** is a product that has been shown to be biosimilar to the reference product, and can be expected to produce the same clinical result as the reference product in any given patient. In addition, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product should not be greater than the risk of using the reference product without such alternation or switch.

The Purple Book will list biosimilar and interchangeable biological products licensed under section 351(k) of the PHS Act under the reference product to which biosimilarity or interchangeability was demonstrated. The resource lists all reference biological products licensed under section 351(a), side-by-side with all corresponding biosimilars and interchangeable products licensed under section 351(k).



CDER Small Business and Industry Assistance (SBIA)
Division of Drug Information | Office of Communications
10001 New Hampshire Avenue | Hillandale Bldg, 4th Floor | Silver Spring, MD 20993
(866) 405-5367 or (301) 796-6707
CDERSBIA@fda.hhs.gov
www.fda.gov/cdersbia

These lists will also provide information on the reference biological product's date of licensure, and whether there is 12-years exclusivity associated with the reference biological product. The Purple Book consists of two lists organized by FDA center: Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). These lists will be updated periodically when FDA licenses a biological product under section 351(a) or section 351(k) of the PHS Act and/or makes a determination regarding date of first licensure for a biological product licensed under section 351(a) of the PHS Act.

Date of First Licensure and Reference Product Exclusivity: In most instances, the *date of first licensure* will be the initial date the particular product at issue was licensed in the United States. Determining the date of first licensure for a reference product determines whether a particular biological product qualifies for a period of *reference product exclusivity*, and the date on which such exclusivity, if any, will expire.

Reference product exclusivity is described as the period of time from the date of first licensure of a reference product during which a 351(k) sponsor is not permitted to submit, and FDA is not permitted to license a 351(k) application that references the reference product. Specifically, if the reference product has reference product exclusivity, approval of a 351(k) application may not be made effective until the date that is 12 years after the date of first licensure of the reference product. In addition, a sponsor may not submit a 351(k) application to FDA for review until the date that is 4 years after the date of first licensure.

The reference product exclusivity expiry date indicates (1) the date that is 12 years from the date of first licensure as described in 351(k)(7); plus (2) any pediatric exclusivity granted pursuant to section 505(A) of the FD&C Act, if applicable. In other words, the reference product exclusivity expiry date is the date on which a 351(k) application referencing the reference product may be licensed assuming it is not blocked by orphan exclusivity and otherwise meets the requirements for licensure under 351(k).

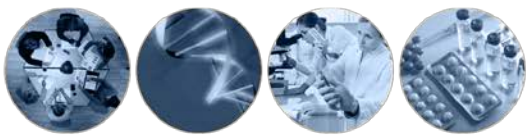
The Purple Book lists will identify the date of first licensure and the date that reference product exclusivity (including any attached pediatric exclusivity) will expire. The list will not identify periods of orphan exclusivity and their expiration dates for biological products. Those dates are available at the searchable database for Orphan Designated and/or Approved Products. Although FDA has not made a determination of the date of first licensure for all 351(a) biological products included on the lists, this does not mean that the biological products on the list are not, or were not, eligible for exclusivity. A determination of the date of first licensure and of when any remaining reference product exclusivity will expire for a biological product submitted under section 351(a) of the PHS Act will generally be made for reasons of regulatory necessity and/or at the request of the 351(a) application license holder.

Determination of the Date of First Licensure: A sponsor may submit the information described in the draft *Guidance for Industry, Reference Product Exclusivity for Biological Products Filed Under Section 351(a) of the PHS Act* to assist FDA in determining the date of first licensure for a biological product. This information will allow FDA to determine whether the product is eligible for its own period of exclusivity or is subject to the exclusion described under section 351(k)(7)(C) of the PHS Act. The sponsor should also provide any other information and data that would assist the FDA in making a determination regarding the date of first licensure for a 351(a) application. The sponsor should provide this information to FDA at the time the 351(a) application submission or, in the case of an already licensed 351(a) application, as correspondence to the application. Alternatively, the sponsor may submit this information an amendment to the 351(a) application. The guidance should be referenced for where this information should be included in the submission.

The Purple Book will serve as a helpful resource to be able to determine the earliest date at which a biosimilar or interchangeable product could be licensed. Because biosimilar and interchangeable biological products will be listed under the corresponding reference product, users can also easily see if there is a biosimilar product or interchangeable biological product licensed. Although FDA has not licensed any biosimilar products or interchangeable biological products to date, FDA is ready to publish this information in this accessible resource once such licensure occurs.

Until next year,
Renu Lal, Pharm.D.
CDER Small Business and Industry Assistance

Issues of this newsletter are archived at http://www.fda.gov/cdersmallbusinesschronicles



CDER Small Business and Industry Assistance (SBIA)
Division of Drug Information | Office of Communications
10001 New Hampshire Avenue | Hillandale Bldg, 4th Floor | Silver Spring, MD 20993
(866) 405-5367 or (301) 796-6707
CDERSBIA@fda.hhs.gov
www.fda.gov/cdersbia