Portfolio Media. Inc. | 111 West 19th Street, 5th floor | New York, NY 10011 | www.law360.com
Phone: +1 646 783 7100 | Fax: +1 646 783 7161 | customerservice@law360.com

How Orange Book Listings Affect Patent Density, Exclusivity

By **Omar Robles, Emily Rothkin and Daniel Yu** (August 12, 2020, 4:30 PM EDT)

Omar Robles

Emily Rothkin

Daniel Yu

The In re: Humira decision in the U.S. District Court for the Northern District of Illinois turned the spotlight on the issue of patent thickets and the potential effect of those thickets on competition. While many in our industry are contemplating how this will shape the future, we analyze historical data to uncover recent trends in patent density and the foreseeable impact on exclusivity in small-molecule drugs.

The U.S. Food and Drug Administration publication, commonly referred to as the Orange Book, lists all FDA-approved small-molecule drugs.[1]

It also identifies, among other things, the periods of statutory exclusivity for which the listed drugs qualify, as well as each patent that the sponsor of a drug's new drug application, or NDA, claims as covering the drug substance, drug product or method of use of the product.[2]

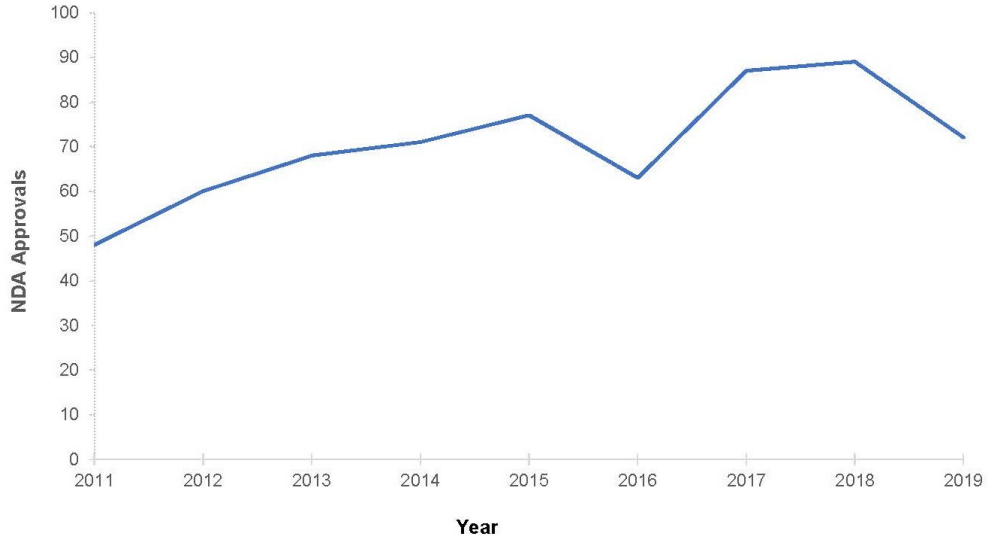
As a general matter, which is well documented elsewhere, these exclusivities can prevent the approval and sale of generic versions of a drug product that has been approved under an NDA.[3]

Using electronic snapshots of the Orange Book for each year between 2011 and 2019, we have identified the FDA-approved NDAs that were in the Orange Book during this period, including those approved prior to 2011. In addition, we have identified the patent(s) claimed by the sponsor of each NDA, hereafter referred to as listing the patent(s) in the Orange Book.

Our findings focus on assessing the density of patents listed for recently NDA-approved drug products and the average period of exclusivity that listed patents statutorily provide for these drug products. In analyzing the combined Orange Book data, we have found several salient trends.

First, the number of NDA approvals per year rose moderately: NDA approvals increased 50% from 48 in 2011 to 72 in 2019.[4] Many studies have noted the increase in approved drugs over time.[5] Indeed, while 2017 was noted as a record-breaking year with the most drugs approved in over 20 years, this record was subsequently broken in 2018.[6] These studies are consistent with the trend shown below, that NDA submissions are increasing with time.

Figure 1. **NDA Approvals**
2011-2019

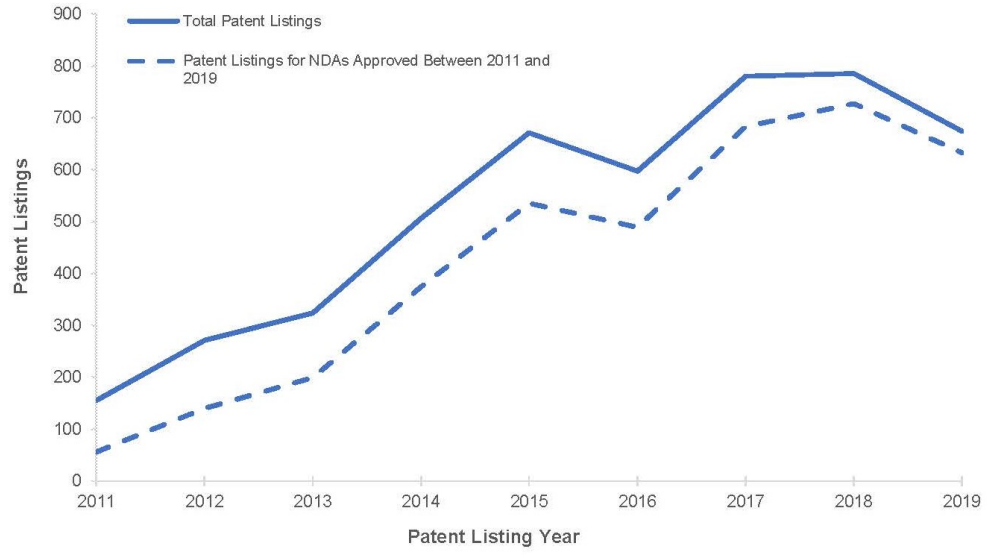


Second, the number of new patent listings per year for NDAs approved between 2011 and 2019 increased from 56 in 2011 to 632 in 2019, an increase of 1,029%. While this certainly shows that the growth of new patent listings outpaced the growth of NDA approvals, it does not necessarily indicate that there are, on average, more patents listed for NDAs approved more recently compared to those approved less recently.

New patent listings do not have to occur only at the time an NDA is approved and, as counted in the quantities above, the number of new patent listings also includes patents listed for NDAs that were approved prior to 2011.[7] Consequently, the observed trend could be driven by patents listed for relatively older NDAs.

To unpack this trend, we take a closer look at the number of patents associated with NDAs approved before and after 2011. Our analysis shows that only a relatively small number of patents were listed for NDAs approved prior to 2011 and that number remained relatively constant year to year.

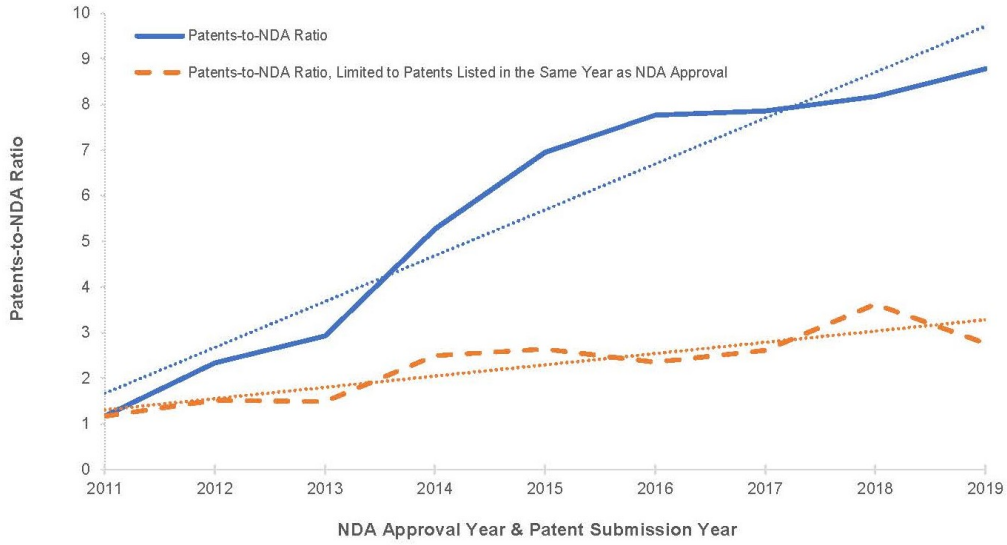
Figure 2: **New Patent Listings**
2011-2019



These results suggest that the number of listed patents per NDA has trended upward since 2011, a result that is confirmed by the results in Figure 3. The average number of patents listed per NDA approved between 2011 and 2019 increased 633% from 1.2 to 8.8.

Additionally, we assess only patents listed within a year of an NDA's approval and find that the average patent density increased from 1.2 in 2011 to 2.8 in 2019,[8] an increase of 133%. Therefore, most of the growth in average patent density between 2011 and 2019 is from patents being listed more than a year after NDA approval.

Figure 3: **Patent Density for NDAs Approved 2011-2019**

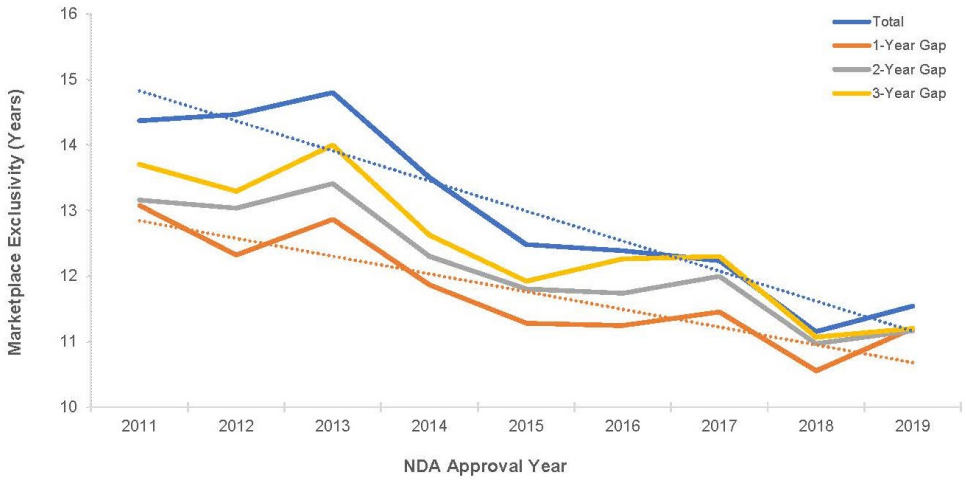


Listing additional patents after an NDA is approved can be a means of extending the period of exclusivity, a practice that is sometimes referred to as patent evergreening. Some have alleged that this practice is anti-competitive since it may extend the time period foreclosing competition from generic versions of the NDA-approved drug product.[9]

To explore the issue of patent evergreening, we examine the trend in average patent exclusivity. Figure 4 plots the average patent exclusivity for NDAs approved between 2011 and 2019. For this analysis, patent exclusivity is defined as the time period between the date of an NDA's approval and the latest expiration date of the patent(s) listed for the NDA. Average patent exclusivity of NDA-approved drug products grew modestly between 2011 and 2013, but then decreased from 14.8 years to 11.5 years between 2013 and 2019.

This suggests that patent evergreening, to the extent it exists, has not caused a sustained increase in average patent exclusivity for NDA-approved drug products. Of course, this result does not show the effects of patent evergreening on individual products, nor does this general trend reveal the effect of the growth of patent listings on exclusivity against the counterfactual in which patent listings did not increase.

Figure 4: **Average Patent Exclusivity for NDAs Approved 2011-2019**



The data available from the Orange Book snapshots do allow for further analysis of this trend. In particular, it is possible to examine average patent exclusivity from patents listed at specific intervals after NDA approval, e.g., within one year, two years and three years. These trends are added to Figure 4. These results still show a decrease in average patent exclusivity for NDA-approved drug products starting with NDAs approved in 2014.

However, they also reveal that, conditional on the year in which an NDA was approved, patents listed after the approval of an NDA, on average, tend to increase patent exclusivity for the NDA. Although this may be an unsurprising result, it indicates that, all else equal, increasing patent density may be lengthening patent exclusivity periods.

In summary, our analysis indicates that growth in patent listings has significantly outpaced growth in NDAs and that patent density for recent NDA-approved drug products has increased. Nevertheless, we do not see evidence that patent evergreening, to the extent that it exists, has caused a sustained increase in average patent exclusivity for NDA-approved drug products. However, we do find that, conditional on the year in which an NDA was approved, the listing of patents after NDA approval tends to increase patent exclusivity on average.

Our analysis has identified several interesting trends, though our findings also raise additional questions that are beyond the reach of analysis of the Orange Book data. Some of these questions relate to the scope and direction of innovation that supports the development of new pharmaceutical products and the treatments for which those products are used.

For instance, it would be interesting to gain further insight into the distribution of innovation underlying the increase in patent density in order to better understand the extent to which patent listing has been driven by the development of new formulations, new therapeutic applications and methods of use for existing drug products, and new chemical entities. It is also relevant to consider the extent to which the exclusivity afforded by patents is fostering innovation.

For example, to what extent does the incentive of patent protection promote incremental innovation related to existing drug products? These and other questions are fertile ground for additional research.

Omar Robles, Ph.d., is a senior consultant at NERA Economic Consulting Inc.

Emily Rothkin is a J.D. candidate at Boston University School of Law. She previously worked as a

senior analyst at NERA.

Daniel Yu is an MBA candidate at the Wharton School of the University of Pennsylvania. He previously worked as a senior analyst at NERA.

The opinions expressed are those of the author(s) and do not necessarily reflect the views of the firm, its clients or Portfolio Media Inc., or any of its or their respective affiliates. This article is for general information purposes and is not intended to be and should not be taken as legal advice.

[1] The "Orange Book" is officially titled the "Approved Drug Products with Therapeutic Equivalence Evaluations." Although it was first published before the passage of the Hatch-Waxman Act in 1984, the scope of the publication was expanded by its passage. Herein, I refer to the most recent (40th) edition of the Orange Book (available at https://www.fda.gov/media/71474/download) as the "Orange Book 40th Edition."

[2] Orange Book 40th Edition, pp. vi, AD 1; Marianne S. Terrot, "SCP 31 Sharing Session: Publicly Accessible Databases of Patent Status Information concerning Medicines and Vaccines: Overview of the Orange Book and the Off-Patent/Off-Exclusivity List," FDA, available at https://www.wipo.int/edocs/mdocs/scp/en/scp_31/scp_31_h_orange.pdf; "Frequently Asked Questions on Patents and Exclusivity," FDA, available at https://www.fda.gov/drugs/development-approval-process-drugs/frequently-asked-questions-patents-and-exclusivity.

In general, for the included patents, the Orange Book reports the patent number, submission date (i.e., the date the FDA received the request to list the patent), and expiration date. It also reports the expiration date of any statutory exclusivity. Orange Book 40th Edition, pp. AD 2, ADA 1.

[3] See, e.g., "Patents and Exclusivity," FDA/CDER SBIA Chronicles, 19 May 2015, available at https://www.fda.gov/media/92548/download; Rebecca S. Eisenberg, "Patents and Regulatory Exclusivity," The Oxford Handbook of the Economics of the Biopharmaceutical Industry, Edited by Patricia Danzon and Sean Nicholson, Oxford: Oxford University Press, 2012, pp. 167–98, available at https://repository.law.umich.edu/book_chapters/126/.

[4] The count of NDAs is inclusive of all NDA classifications. NDAs have multiple classifications, which include, but are not limited to, drug products that contain a new molecular entity (Type 1); contain a new active ingredient (Type 2); or are available in a new dosage form (Type 3). For more information on NDA classification codes, see "MAPP 5018.2," FDA, available at https://www.fda.gov/media/94381/download.

A drug product that is available in different strengths will have a single NDA for all the FDA-approved strengths of the product. However, the NDA approval date will differ across the strengths of the drug product if the strengths were approved on different dates. Our analysis is based on the earliest approval date associated with each NDA.

[5] One study found the number of National Drug Codes more than doubled between 2008 to 2016. (See, Hernandez, Immaculada, et.al., "The Contribution Of New Product Entry Versus Existing Product Inflation In The Rising Costs of Drugs," Health Affairs, Vol. 38, No. 1 (2019.)

[6] "2017 Saw the Most Drugs Approved in Over 20 Years," Fortune, available at http://fortune.com/2018/01/02/new-drug-approvals/. "FDA Approved Record Number of Drugs in 2018," Medscape, available at https://www.medscape.com/viewarticle/907364; "2018 FDA drug approvals," Nature, available at https://www.nature.com/articles/d41573-019-00014-x.

[7] For patents issued after the approval of an NDA, the NDA holder is required to list the patent within 30 days of the issuance of the patent for its listing to be considered timely. See, "Frequently Asked Questions on Patents and Exclusivity," U.S. Food & Drug Administration, available at https://www.fda.gov/drugs/development-approval-process-drugs/frequently-asked-questions-patents-and-exclusivity#Why_doesn_t_the_Orange_Book_include_patent_submission_dates_for_most_records, Question 8.

[8] To the extent that NDAs were approved late in 2019, it is not possible to count the total number

of patents listed within one full year of NDA approval since information for all of 2020 is not yet available at the time of this publication.

[9] See, e.g., Roger Collier, "Drug patents: the evergreening problem," Canadian Medical Association Journal, Vol. 185, No. 9, 11 June 2013, available at https://www.cmaj.ca/content/185/9/E385; Alfred B. Engelberg, "A Shortfall in Innovation Is the Cause of High Drug Prices," Health Affairs, 28 February 2019, available at https://www.healthaffairs.org/do/10.1377/hblog20190228.636555/full/.
