Letters

RESEARCH LETTER

Biologic Patent Thickets and Terminal Disclaimers

Spending on biologics in 2021 represented $260 billion or 46% of all spending on prescription drugs in the US.[1] Biosimilar competition can lower prices, but biosimilar entry is often delayed by expansive patent thickets (dozens or hundreds of patents directed toward the same product). Many of these patents claim innovations that are closely related to one another.[2,3] Although the US Patent and Trademark Office is required to reject patents that are obvious follow-ons from earlier versions, they may grant such patents when applicants file terminal disclaimers.

Supplemental content

A *terminal disclaimer* is a stipulation that the follow-on patent will expire at the same time as the original patent. This tool, which is not permitted in other countries, allows drug manufacturers to quickly obtain new patents that offer trivial changes over existing innovations.[4] These patents can trigger lengthy and costly litigation and add uncertainty for biosimilar manufacturers who must invalidate or design around all patents in a biologic's portfolio.

In recognition of this problem, a bipartisan group of US senators recently urged the US Patent and Trademark Office to limit or eliminate the use of terminal disclaimers in pharmaceutical patents.[5] Even though biologic patent thickets have received increased scrutiny, the role of terminal disclaimers in these patent thickets has not been systematically examined. We analyzed the use and timing of terminal disclaimers in all biologic patents involved in litigation from 2010 to 2023.

Methods | We used the Legal Analytics Platform (Lex Machina) to identify patents involved in biosimilar litigation beginning in 2010 (when the modern biosimilar pathway was established) until April 2023. We focus on litigated patents because, unlike the manufacturers of small-molecule drugs, the manufacturers of biologics are only required to list their patents with the US Food and Drug Administration (FDA) when they face litigation.

Claims define the legal scope of patents, and we determined whether each claim was related to the drug's manufacturing technique, method of treatment, formulation, composition of matter, or delivery device (**Table**). Because patents often contain many claims, each patent could be associated with multiple subject matter claims. We used data from the US Patent and Trademark Office prosecution history to determine if patents had terminal disclaimers and when patents were issued relative to FDA approval of the relevant biologic.[6] The analyses were completed using Excel version 16 (Microsoft).

Results | Manufacturers of 12 biologics brought litigation against manufacturers of 48 biosimilars from 2010 to 2023. Of the 271 patents involved in litigation, 129 (48%) contained terminal disclaimers. Patents with terminal disclaimers had fewer claims on composition of matter compared with patents without terminal disclaimers (4% vs 8%) and more claims on method of treatment (33% v 26%) and formulation (30% vs 10%) (Table). The number of patents with terminal disclaimers spiked 12 years after product approval, coinciding with the end of FDA-granted statutory biologic exclusivity (**Figure**). During year 13, there were 44 patents issued with terminal disclaimers compared with 15 patents without terminal disclaimers.

Discussion | Almost half of all biologic patents involved in litigation from 2010 to 2023 had terminal disclaimers. These patents spiked just as 12-year statutory exclusivity periods were ending. The scale and timing of these patenting practices suggest that biologic firms may be using patents with terminal disclaimers to strengthen barriers to biosimilar entry.

Table. Type of Claims in Patents With vs Without Terminal Disclaimers

	No. of patents litigated	Patents by terminal disclaimer status, No. (%)	
		With a terminal disclaimer	Without a terminal disclaimer
Unique patents	271	129 (48)	142 (52)
Subject matter of patent claim[a]			
Manufacturing technique[b]	130	46 (36)	84 (52)
Method of treatment[c]	84	42 (33)	42 (26)
Formulation[d]	55	39 (30)	16 (10)
Composition of matter[e]	18	5 (4)	13 (8)
Delivery device[f]	7	1 (1)	6 (4)

[a] Some of the patents include claims that cover more than 1 subject matter.

[b] Covers the methods for producing the biologic (eg, purification method).

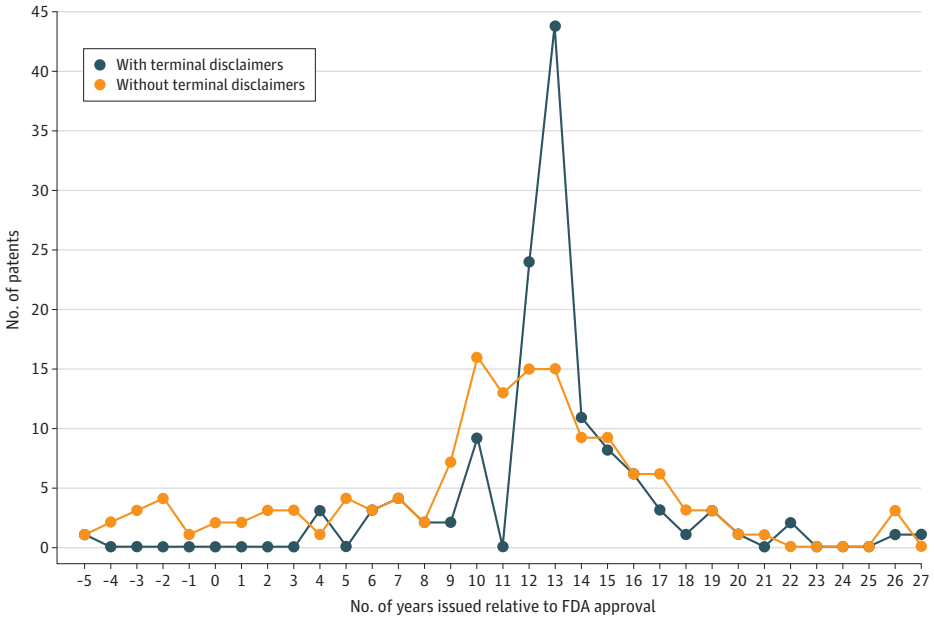
[c] Covers the use of the biologic to treat a specific disease or population.

[d] Covers the biologic's active ingredient along with the excipients (eg, buffers or carriers) that make up the dosage form that is administered to the patient.

[e] Covers the biologic's active ingredient (eg, the amino acid backbone of an antibody).

[f] Covers the delivery devices used for the administration of a biologic (eg, the injector pen).

Figure. Number of Patents With vs Without Terminal Disclaimers Involved in Litigation Relative to Drug Approval From the US Food and Drug Administration (FDA)



This figure shows when litigated patents with vs without terminal disclaimers were granted relative to the approval of biologics by the FDA. Both types of patents experienced sharp increases during the study period followed by declines through year 20. The pronounced peak for patents with terminal disclaimers occurred in years 12 and 13, coinciding with the end of FDA-granted statutory exclusivity.

By adding patents with terminal disclaimers beginning in year 12, biologic manufacturers introduce uncertainty precisely when biosimilar challenges begin. Biosimilar firms must then contest or design around a wave of new patents containing claims that become enforceable just as statutory exclusivity periods are ending.

A limitation of this study is that it only examined litigated patents; however, these are the key patents that impede biosimilar entry. Congress could reduce the barriers to biosimilar entry by capping the number of patents that brand-name manufacturers can assert against biosimilar firms (eg, just 1 patent among those linked by terminal disclaimers). Minimizing the use and effect of terminal disclaimers could help improve patient access to lower-cost biosimilar drugs and reduce health care spending.

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