State-level legislation on follow-on biologic substitution

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INTRODUCTION

In 2009, the Biologics Price Competition and Innovation Act (BPCIA) paved the way for market entry of generic biologics by establishing a pathway for their regulatory approval. Proliferating with the advent of recombinant DNA technology, biologic drugs are derived from living organisms to create vaccines, blood products, allergenic products, monoclonal antibodies, cytokines, growth factors, enzymes, immunomodulators, thrombolytics, proteins, arsphenamine (and derivatives), toxins, and antitoxins.1 Larger and more complex than traditional pharmaceutical molecules, biologics are more difficult to create (and replicate) than small-molecule drugs.2 Their clinical effects are determined not only by their primary chemical structure but also by glycosylation patterns found in their structural folds.3 Thus, follow-on biologics, also referred to as biosimilars, can never be exact replicas of a reference product.4 Unlike generic drugs, biologics with pharmacokinetic equivalence may nevertheless exhibit varying pharmacodynamics, clinical efficacy, and immunogenicity (the product’s power to cause an immune reaction), not only between follow-on and reference products, but also within a particular reference product manufactured at different times or locations.5

The BPCIA defines biosimilars as biological products that are highly similar to reference products with no clinically meaningful differences in terms of safety, purity, or

1 Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111–148, 124 Stat. 119 (amending Public Health Service Act § 351, 42 U.S.C. §262(i)(1) (2012) [hereinafter BPCIA]).
2 Leigh Revers & Eva Furczon, An Introduction to Biologics and Biosimilars. Part II: Subsequent Entry Biologics: Biosame or Biodifferent?, 143 Can. Pharm. J. 184 (2010).
3 George Dranitsaris, Eitan Amir, & Kristin Dorward, Biosimilars of Biological Drug Therapies, 71 Drugs 1527, 1528–29 (2011).
4 Id. at 1530.
5 Id.
potency. The Food and Drug Administration (FDA) is authorized to designate a biosimilar as ‘interchangeable’ with a reference product if ‘the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch’. Importantly, if deemed interchangeable, a follow-on ‘biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product’.

While the FDA’s European counterpart has already approved 16 follow-on biologics, no follow-on biologics have yet been approved in the United States. In anticipation of their arrival, though, several states have sought over the past year to legally limit the extent to which pharmacies may actually treat follow-on biologics as interchangeable.

OVERVIEW OF STATE-LEVEL LEGISLATION ON FOLLOW-ON BIOLOGIC SUBSTITUTION

All states have generic substitution laws applicable to small-molecule drugs that either permit or prohibit pharmacists from substituting a reference product with a generic listed as bioequivalent in the Orange Book. Forty states require mandatory generic substitution for drugs covered by Medicaid. These generic substitution laws generally do not apply to follow-on biologics, however, as they usually require a higher level of chemical equivalence than is provided by the biologics standard of ‘interchangeability’.

In 2013, follow-on biologic substitution bills were introduced in 18 states; they were enacted in Florida, North Dakota, Oregon, Utah, and Virginia. By and large, these bills sought to establish strict procedures for pharmacy substitution not otherwise required by the BPCIA, such as requirements for patient consent or physician notification despite the BPCIA’s designation of interchangeable biologics as substitutable without

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6 BPCIA at 42, U.S.C. § 262(k)(4) (2012).
7 Id.
8 Id. at 42, U.S.C. § 262(i)(3).
9 European Medicines Agency, European Public Assessment Reports, http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/epar_search.jsp&mid=WC0b01ac058001d125 (accessed 6 April 2014).
10 Public Workshop: Follow-On Biologics: Impact of Recent Legislative and Regulatory Naming Proposalson Competition, 78 Fed. Reg. 68840, 68842 (15 November 2013).
11 Jesse C. Vivian, Generic-Substitution Laws, 33 US Pharm. 30 (2008). The FDA maintains current information about generic equivalents in a compendium commonly known as the Orange Book. Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, FDA (February 2014), http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm (accessed 13 February 2014).
12 Jessica Mazer, Pharmaceutical Care Mgmt. Ass’n, Generic Substitution: The Science and Savings, D.C. Governors’ Staff Briefing (9 March 2011), http://amcp.org/WorkArea/DownloadAsset.aspx?id = 10530 (accessed 13 February 2014).
13 Jason Kanter & Robin Feldman, Understanding and Incentivizing Biosimilars, 64 Hastings L. J. 57, 75 (2012).
14 For up-to-date information on state-level biosimilar legislation, see Kurt R. Karst, The Biosimilars State Legislation Scorecard, FDA L. Blog (4 September 2013) http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2013/09/biosimilars-state-legislation-scorecard.html (accessed 13 February 2014).
a physician’s intervention. While the details of various provisions differ from state to state, all of the follow-on biologic substitution bills have in common two features: (1) they permit substitution only if the FDA has designated the biosimilar as interchangeable, and (2) they prohibit substitution if the prescribing physician has specifically indicated a preference for the reference product. In addition, some of the bills include provisions regarding physician notification; patient notification or consent; additional labeling requirements, such as the name of the reference product being substituted; and retention of records regarding the substitution. Table 1 summarizes the key differences between the bills as of 20 February 2014.

Notably, follow-on biologic substitution legislation has not been limited to the United States. Like the United States, the European Union allows for substitution but allows member states to determine how they would like to regulate such substitution.40 Similarly, biologic substitution regulations in Canada are set by provinces.41

**POLICY CONSIDERATIONS**

The promise of follow-on biologics in increasing access to life-saving therapy is enormous. In 2013, there were approximately 125 different FDA-approved prescription biologic products available in the U.S. market (not counting separate approvals for new

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15 The base-line requirement not included in this list is that the dispensed product be labeled as such.
16 S.B. 1438, 51st Leg., 1st Sess. (Ariz. 2013).
17 S.B. 149, 89th Gen. Ass., Reg. Sess. (Ark. 2013).
18 S.B. 386, 89th Gen Ass., Reg. Sess. (Ark. 2013).
19 A.B. 1139, Leg., Reg. Sess. (Cal. 2013).
20 S.B. 598, Leg., Reg. Sess. (Cal. 2013); A.B. 1139, Leg., Reg. Sess. (Cal. 2013).
21 H.B. 1121, 69th Gen. Ass. (Colo. 2013).
22 S.B. 118, 147th Gen. Ass. (Del. 2013).
23 H.B. 365, Leg. ( Fla. 2013); S.B. 732, Leg. ( Fla. 2013).
24 S.B. 1934, 98th Gen. Ass., Reg. Sess. (Ill. 2013–2014).
25 S.B. 272, 118th Gen Ass., 1st Reg. Sess. (Ind. 2013).
26 H.B. 1315, 118th Gen Ass., 1st Reg. Sess. (Ind. 2013).
27 S.B. 781, Gen. Ass., Reg. Sess. (Md. 2013).
28 H.B. 1927, 188th Gen. Ct. (Mass. 2013).
29 H.B. 3667, 188th Gen. Ct. (Mass. 2013).
30 H.B. 3734, 188th Gen. Ct. (Mass. 2013).
31 Miss. Code Ann. § 73-21-118 (West 2013).
32 N.D. Cent. Code Ann. § 19-02.1-14.3 (West 2013).
33 Or. Rev. Stat. Ann. § 342.2 (West 2013).
34 H.B. 746, Gen. Ass., Reg. Sess. (Pa. 2013); S.B. 405, Gen. Ass., Reg. Sess. (Pa. 2013).
35 S.B. 190, 83rd Leg., Sess. (Tex. 2013).
36 H.B. 542, 83rd Leg., Sess. (Tex. 2013).
37 Utah Code Ann. § 58-17b-605.5 (West 2013).
38 VA Code Ann. § 54.1-3408.04 (West 2013).
39 S.B. 5469, 63rd Leg., Reg. Sess. (Wash. 2013); H.B. 1528, 63rd Leg., Reg. Sess. (Wash. 2013).
40 Lynne Taylor, *Germany: ‘EU’s Most Favourable Market for Biosimilars’,* Pharma Times (30 May 2013), http://www.pharmatimes.com/article/13-05-30/GermanyEU_s_most_favourable_market_for_biosimilars.aspx (accessed 13 February 2014).
41 Can. Life & Health Ins. Ass’n, CLHIA Report, *Ensuring the Affordability, Accessibility and Sustainability of Prescription Drugs in Canada*, at 25, http://www.clhia.ca/dominio/html/clhia/CLHIA_LP4W_LND_Webstation.nsf/resources/CLHIA_Prescription_Drug_Paper/$file/CLHIA_Prescription_Drug_Policy_PaperEN.pdf (accessed 13 February 2014).
## Table 1. State-level legislation on follow-on biologic substitution

|                        | Physician Notification/Authorization | Patient Notification/Consent | Enhanced Labeling Requirements | Record Retention | Liability | Other Provisions | Bill Status |
|------------------------|-------------------------------------|-----------------------------|--------------------------------|------------------|-----------|------------------|-------------|
| Arizona                | written or electronic notice within 3 days | written and oral notice of substitution | 'substituted for [reference product]' | 7 years | n/a | pharmacy board required to maintain online list of substitutable biosimilars | failed |
| Arkansas               | *written or electronic notice within 3 days, physician must pre-authorize; any form of notice within 1 day | *notice of & consent to substitution | *indicate substitution | *2 years | n/a | *pharmacy board has discretion to deviate from list of FDA-authorized substitutes | *failed |
| California             | *n/a, any form of notice within 5 days | *notice of substitution | */n/a | */n/a | */same as for dispensing biologic as indicated | */applicable to Medicaid | *pending (vetoed by governor) |

Notes:
- * indicates the bill is pending.
- */ indicates the bill is failed.
| State          | Physician Notification/Authorization | Patient Notification/Consent | Enhanced Labeling Requirements | Record Retention | Liability | Other Provisions | Bill Status |
|---------------|-----------------------------------|------------------------------|--------------------------------|-----------------|-----------|------------------|-------------|
| Colorado      | any form of notice within 3 days   | notice of substitution       | n/a                            | 5 years         | same as for dispensing a drug prescribed in generic form | n/a         | pending        |
| Delaware      | electronic, fax, written or phone notice within 2 days | written notice of substitution | ‘substituted for [brand prescribed]’ | 3 years         | same as for dispensing prescription as written | n/a         | failed         |
| Florida       | n/a                               | notice of substitution, price difference & right of refusal | n/a                            | 2 years         | n/a       | n/a              | enacted     |
| Illinois      | any form of notice within 5 days   | notice of substitution       | n/a                            | 5 years         | n/a       | n/a              | pending     |
| Indiana       | *any form of notice within 3 days; prescription must indicate ‘may substitute’  
               | ‘written or electronic notice’ | ‘notice of substitution’       | n/a              | */5 years   | n/a              | */failed    |

* S.B. 272  
ˆ H.B. 1315
Table 1. continued

| State       | Physician Notification/Authorization | Patient Notification/Consent | Enhanced Labeling Requirements | Record Retention | Liability | Other Provisions | Bill Status          |
|-------------|--------------------------------------|-----------------------------|--------------------------------|------------------|-----------|------------------|---------------------|
| Maryland    | any form of notice within 5 days      | written notice of substitution | ‘substituted for [brand prescribed]’ | 5 years          | same as for dispensing as written | n/a                | failed              |
| Massachusetts | *H.B. 192728                           | **electronic notice within a reasonable time once electronic health records are fully interoperable | n/a                             | n/a              | n/a                   | n/a                | **/***pending       |
|             | *H.B. 366729                           | **written notice of substitution |                                 |                  | n/a                   | n/a                |                     |
|             | **H.B. 373430                          |                             |                                 |                  | n/a                   | n/a                |                     |
| Mississippi | any form of notice within 5 days      | notice of & consent to substitution |                              | 10 years         | n/a                   | n/a                | enacted             |
| North Dakota | electronic notice within 1 day        | notice of substitution & right of refusal |                              | 5 years          | n/a                   | n/a                | enacted             |
| Oregon      | any form of notice within 3 days      | notice of substitution       |                                | 3 years          | n/a                   | n/a                | enacted             |
| State       | Physician Notification/Authorization | Patient Notification/Consent | Enhanced Labeling Requirements | Record Retention | Liability | Other Provisions | Bill Status |
|------------|--------------------------------------|------------------------------|--------------------------------|------------------|-----------|------------------|-------------|
| Pennsylvania | */^written notice within 3 days       | */^notice of substitution, price difference & right of refusal *written consent to substitution | */^n/a                          | */^2 years        | */^only increased if an incorrect interchangeable biosimilar is substituted | */^pharmacies must post statement regarding substitution law and list of brand name and equivalent, and they must have available a list of price comparison; pharmacy board retains discretion to revise list of authorized substitutions | */^pending |
| Texas       | */^written or electronic notice within 3 days (sunsets December 2015) | */^notice of option to substitute & requirement of patient choice; order form notice for mail-order | */^"substituted for [brand prescribed]" | */^'for the period specified by law for pharmacy records' | */^'same as if dispensed as prescribed | */^pharmacies must display notice regarding substitution law | */^failed |

* S.B. 190[^35]  
* H.B. 542[^36]
| State          | Physician Notification/Authorization | Patient Notification/Consent | Enhanced Labeling Requirements | Record Retention | Liability | Other Provisions | Bill Status |
|---------------|-------------------------------------|-------------------------------|--------------------------------|------------------|-----------|------------------|-------------|
| Utah          | any form of notice within 3 days     | consent to substitution;     | name of prescribed product    | n/a              | same as if | n/a              | enacted     |
|               |                                     | for mail-order, notice by    |                                |                  | dispensed as|                 |             |
|               |                                     | phone/email if by            |                                |                  | prescribed |                 |             |
| Virginia      | any form of notice within 5 days     | consent to substitution &    | ‘substituted for [brand      | 2 years          | n/a       | n/a              | enacted     |
|               |                                     | notice of price difference   | prescribed]’                   |                  |           |                 |             |
| Washington    | written or electronic notice        | notice of substitution       | n/a                            | 2 years          | n/a       | ‘a state purchased | failed      |
|               | within 3 days                       |                               |                                |                  |           | health care program|             |
|               |                                     |                               |                                |                  |           | may impose limited |             |
|               |                                     |                               |                                |                  |           | 32 restrictions on|             |
|               |                                     |                               |                                |                  |           | an endorsing      |             |
|               |                                     |                               |                                |                  |           | practitioner’s    |             |
|               |                                     |                               |                                |                  |           | authority to write |             |
|               |                                     |                               |                                |                  |           | a 33 prescription  |             |
|               |                                     |                               |                                |                  |           | to dispense as    |             |
|               |                                     |                               |                                |                  |           | written only under|             |
|               |                                     |                               |                                |                  |           | [certain] circumstances’ |         |

doses), with over half of these approved within the past decade.\textsuperscript{42} Biologics have become especially important in the fields of oncology,\textsuperscript{43} rheumatology,\textsuperscript{44} and endocrinology.\textsuperscript{45} On average, therapeutic biologics are more than 20 times as expensive as pharmaceutical drugs, with treatments ranging from tens to hundreds of thousands of dollars per year, with an average annual cost of $16,425.\textsuperscript{46} In 2010, eight of the top ten highest expenditure Medicare Part B drugs were biologics, with the highest expenditure drug claiming $2 billion in Medicare funds.\textsuperscript{47} The highest average annual expenditure per Medicare beneficiary in 2010 was for a biologic costing $216,833.\textsuperscript{48}

The high cost of biologics can be partially explained by higher manufacturing and quality control costs, as well as a lack of competition from generics; industry estimates of R&D for new biologics are comparable to those for new pharmaceutical drugs.\textsuperscript{49} While stressing the importance of cost-effectiveness analysis keyed to differences in bioequivalence,\textsuperscript{50} many commentators have begun calling for substitution of less expensive follow-on biologics as an important strategy for reducing healthcare costs,\textsuperscript{51} particularly in the field of oncology, which has seen exponentially increasing medicine prices.\textsuperscript{52} A 2008 study estimated that substitution of follow-on biologics in the top 12 biologic categories could result in U.S. savings of over $100 billion in the first decade.\textsuperscript{53} Generic erythropoietin is projected to save eight billion Euros in Germany alone by 2020.\textsuperscript{54} Recognizing the large potential for cost savings from increased competition, the Federal Trade Commission has called for public comments on new legislation impacting follow-on biologics.\textsuperscript{55}

\textsuperscript{42} See FDA, User Fee Billable Biologic Products and Potencies Approved Under Section 351 of the PHS Act (December 2013), http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm122936.htm; FDA, CDER Therapeutic Biologic Products (2013), http://www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm164641.pdf (accessed 13 February 2014).
\textsuperscript{43} Dietger Niederwieser, Biosimilar Agents in Oncology/Haematology: From Approval to Practice, 86 Eur. J. Haematol. 277 (2010).
\textsuperscript{44} Thomas Dorner et al., The Role of Biosimilars in the Treatment of Rheumatic Diseases, 72 Ann. Rheum. Dis. 322 (2013).
\textsuperscript{45} David R. Owens et al., The Emergence of Biosimilar Insulin Preparations—A Cause for Concern?, 14 Diabetes Technol. Ther. 989 (2012).
\textsuperscript{46} Robert J. Shapiro et al., The Potential American Market for Generic Biological Treatments and the Associated Cost Savings, at 4 (2008), http://www.sonecon.com/docs/studies/0208_GenericBiologicsStudy.pdf (accessed 13 February 2014).
\textsuperscript{47} U.S. Gov’t Accountability Office, Medicare: High-Expenditure Part B Drugs, GAO-13-46R, at 7 (2012), http://www.gao.gov/assets/650/649459.pdf (accessed 13 February 2014).
\textsuperscript{48} Id. at 10.
\textsuperscript{49} Wendy H. Schacht & John R. Thomas, Cong. Research Serv., Follow-On Biologics: The Law and Intellectual Property Issues, CRS Rep. for Cong. 7-5700 at 2 (2012).
\textsuperscript{50} For a discussion of the differences between generics and biosimilars, see Anoop Misra, Are Biosimilars Really Generics?, 10 Expert Opin. Biol. Ther. 489 (2010).
\textsuperscript{51} Erwin A. Blackstone & Joseph P. Fuhr, Jr., Biosimilars and Innovation: An Analysis of the Possibility of Increased Competition in Biopharmaceuticals, 2 Future Med. Chem. 1641 (2010).
\textsuperscript{52} Eg, Paul Cornes, The Economic Pressures for Biosimilar Drug Use in Cancer Medicine, 7 Target. Oncol. 57 (2012).
\textsuperscript{53} Shapiro et al. (2008), supra note 46.
\textsuperscript{54} Giovanni Lapadula & Gian Franco Ferraccioli, Biosimilars in Rheumatology: Pharmacological and Pharmacoeconomic Issues, 30 Clin. Exp. Rheumatol. S102 (2012).
\textsuperscript{55} Public Workshop, supra note 10.
How substitution laws are designed will determine the extent to which they promote or limit follow-on biologic substitution. For instance, shorter time frames for physician notification and longer requirements for record retention may make it more costly for pharmacies to substitute follow-on biologics. In the context of generic substitution, requirements that substitutions be labeled as such may increase patient anxiety, perhaps even causing a nocebo-like effect in which drug effectiveness is decreased by the patient’s belief that it is ineffective. Patient consent requirements in generic substitution laws, like those found in Virginia’s biologic substitution legislation, have been found to result in 25% less substitution. Similarly, any requirements that physicians authorize substitution, such as the one found in one of Arkansas’s failed bills, may play into some physicians’ generalized mistrust of generic alternatives.

Broadly speaking, laws with fewer requirements and therefore less compliance costs are more likely to incentivize substitution. Massachusetts’ proposed bill, which prohibits any additional requirements not also applicable to all generics, may be the most likely to incentivize substitution if passed. At the same time, too little detail can leave unintentional regulatory gaps. For instance, Michelle Derbyshire observes that because ‘around 26% of top biologicals are distributed through mail order, the impact of these state bills may depend on how they regulate mail-order pharmacies’. Only Utah’s new law and Texas’s failed House bill specifically address mail-order prescription substitution.

Regardless of any incentive-distorting effects of the specific requirements of substitution laws, they raise a number of bioethical questions regarding informed consent and patient autonomy. When the FDA designates a biosimilar as interchangeable, it may not be able to account for long-term risks that have yet to be observed, or potential increased efficacy of the current reference product over the original reference product, perhaps due to more experience producing the biologic. Medical professional societies have called for increased pharmacovigilance to reduce these unknown risks. Pharmacovigilance programs, in turn, may be able to advise state pharmacy board decisions to prohibit certain substitutions—as explicitly provided for by Pennsylvania’s bill—faster than the FDA is able to review a biosimilar’s designation of interchangeability. Moreover, patient autonomy—which is best safeguarded by consent

56 Hans C. Ebbers et al., Interchangeability, Immunogenicity and Biosimilars, 30 Nat. Biotech. 1186 (2012).
57 See J. Wessenfield et al., The Nocebo Effect: A Reason for Patients’ Non-Adherence to Generic Substitution? 65 Pharmazie 451 (2010).
58 William H. Shrank et al., State Generic Substitution Laws Can Lower Drug Outlays Under Medicaid, 29 Health Aff. 1383 (2010); Christine M.L. Kelton, State Medicaid Programs Missed $220 Million in Uncaptured Savings as Generic Fluoxetine Came to Market, 2001–05, 32 Health Aff. 1204 (2013).
59 See, eg, Michel J. Berg et al., Generic Substitution in the Treatment of Epilepsy: Patient and Physician Perceptions, 13 Epilepsy Behav. 693 (2008).
60 Michelle Derbyshire, U.S. State Legislation on Biosimilars Substitution, 2 Generics Biosimilars Initiative J. (2013).
61 For an overview of common risks associated with biosimilars, see Rustom Mody, Brajesh Varshney & Dhananjay Patankar, Understanding Variations in Biosimilars: Correlation with Risk and Regulatory Implications, 22 Risk Safety Med. 27 (2010).
62 David R. Holmes, ACCF/ACA 2011 Health Policy Statement on Therapeutic Interchange and Substitution: A Report of the American College of Cardiology Foundation Clinical Quality Committee, 58 J. Am. Coll. Cardiol. 1287 (2011).
requirements—would be compromised by default, notice-free Medicaid substitution if states were to extend such requirements to follow-on biologics in the absence of an explicit provision also extending any notice or consent requirements to public assistance programs.

Finally, questions of liability—both on the part of the pharmacies and the follow-on biologic manufacturers—are implicated by substitution laws. Only a handful of the state-level laws specify that a pharmacist’s liability for substituting a biologic is the same as for substituting a traditional small-molecule drug. Moreover, manufacturers of follow-on biologics face uncertainty regarding their liability for failure-to-warn claims. In the context of small-molecule drugs, state tort claims would be preempted by federal law, which, under Mutual Pharmaceutical Co. v. Bartlett, shields generic drug manufacturers from liability if they adhere to the FDA’s mandatory labeling requirements. It is unclear whether warning labels used on follow-on biologics would be governed by a different standard, particularly in states that do not have specific labeling requirements. Even if failure-to-warn claims concerning follow-on biologics were governed by the Bartlett standard, the manufacturers of interchangeable biosimilars remain in a legal limbo until the FDA sets their labeling requirements.

CONCLUSION

As more states consider follow-on biologic substitution legislation, biotech companies are lobbying for greater restrictions on pharmacists’ discretion to substitute follow-on biologics for their brand name products, claiming that such restrictions are necessary to protect patient safety. Amgen, a leading biotech firm, has found itself on both sides of the debate as it begins to develop its own branded follow-on biologics. While mixed messages from powerful stakeholders may cause delays in new legislation, states have time to choose their approach: Europe’s early experience with follow-on biologics suggests that the U.S. market will first be composed primarily of biosimilars that fail to meet the BPCIA’s requirements for interchangeability (and therefore would not be subject to substitution at all). Indeed, a number of provisions—especially those relating to physician notification—will sunset before any follow-on biologics are even approved by the FDA as interchangeable. Nevertheless, it is important for biologics manufacturers to have a sense of how states plan on regulating follow-on biologics so that they can adequately assess their prospects for research and development.

Moving forward, states will have to decide how to strike an adequate balance between access and affordability of biologic products on the one hand, and adequate safety and efficacy on the other. For the most part, this will require more information on the cost-effectiveness of substitution in the context of biologics. Importantly, this will also require official guidance from the FDA regarding how brand and follow-on

63 See Mutual Pharm. Co. v. Bartlett, 133 S. Ct. 2466 (2013).
64 Andrew Pollack, Biotech Firms, Billions at Risk, Lobby States to Limit Generics, New York Times (29 January 2013), http://www.nytimes.com/2013/01/29/business/battle-in-states-on-generic-copies-of-biotech-drugs.html?hpw (accessed 13 February 2014).
65 Melanie Senior, Biosimilars Battle Rages On, Amgen Fights Both Sides, 31 Nat. Biotech. 269 (2013).
66 See Francis Megerlin et al., Biosimilars and the European Experience: Implications for the United States, 42 Health Aff. 1803 (2013).
biologics will be named. As commentators note, biosimilar substitution laws as currently written will not actually allow for substitution if the FDA decides that follow-on biologics cannot use the same name as reference products.\(^{67}\) The biotech industry and countless patients who rely on life-saving biologics should stay tuned as states maneuver within an increasingly disjointed regulatory limbo.

**ACKNOWLEDGEMENTS**

The JLB Editors-in-Chief wish to acknowledge Holly Lynch, JD, M. Bioethics, who coordinated the new development pieces in this issue. She considered proposals from Harvard Law School students, selected authors, provided feedback on outlines and drafts, and liaised with JLB.

\(^{67}\) Pollack, *supra* note 64.