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SUMMARY

The battle for more affordable drugs for consumers has been raging since the first generic drugs were produced. Generic drugs are follow-on products manufactured to have the same clinical effect as brand name reference product drugs.¹ Traditional brand name and generic drugs are small molecule products that are easy to replicate and can be identically manufactured every time. Biologic drugs are of a different class than small molecule drugs. Biologics are large molecules that are derived from or produced in a living environment. Because of the complexity of biologics, they are much more difficult to replicate, even between batches produced by the same manufacturer.²

The Federal Food and Drug Administration (FDA) regulates biologic drugs for safety and efficacy. In so doing, the FDA has promulgated regulations concerning the potential approval of biologic drugs that will follow current biologic drugs onto the market. These biologic drugs that are meant to be more affordable versions of current biologic drugs are called “biosimilars.” The FDA is in the process of determining the approval process for a certain subset of biosimilars referred to as “interchangeable biosimilars” which can be substituted for original biologics without the prescribing physician’s request. Federal law does not preempt state law on the issue of biosimilars. Battles are ensuing at the state level between large biologic drug companies on one side and potential biosimilar competitors as well as payors on the other side. State regulation could be extremely effective in barring competition in the production and marketing of biosimilars that would have a damaging effect on consumers. California is one of 18

¹ Amgen. How are Biologic Medicines Different from Other Medications? <<http://www.buildingbiologics.com/how-biologics-differ.html>>.

² Id.

states to have considered biosimilar legislation that proposes state regulation of interchangeable biosimilars.³

The most controversial piece of the proposed biosimilar legislation in these states is a provision requiring the dispensing pharmacist to notify the prescribing physician that an interchangeable biosimilar was dispensed within a few days of the substitution. Lobbyists have been very involved in proposed biosimilar legislation throughout the country. An examination of the purpose behind lobbyist support of biosimilar legislation indicates that biotech lobbyists are likely supporting SB 598 and other biosimilar legislation in order to maintain market share in the biotech industry. Industries that back this preemptive legislation are fueling the perception that interchangeable biosimilars are not as safe or effective as the original biologic product. Biosimilar legislation at the state level is setting a dangerous precedent of preemptive lawmaking backed by pharmaceutical industries with an interest in dominating the biologic drug market and the future market for biosimilars. This legislation could restrict consumer access to safe and less expensive biosimilars and harm competition in the biosimilar market.

III. What is Senate Bill 598?

Senate Bill 598 (SB 598) concerns the regulation of biosimilar substitution for biologic drugs in California. Senate Bill 598 allows FDA approved interchangeable biologics to be substituted for pioneer biologic drugs if the prescriber allows for substitution on the prescription, and notification of the substitution is given to the prescriber within five days of the dispensing of the interchangeable biosimilar.⁴ This bill

³ [Table I: State Biosimilar Legislation](#)

⁴ U.S. Senate. California Legislature, 2013–2014 regular session. Senate Bill 598.

was strongly supported in the Senate and the Assembly with 29 out of 39 senators voting yes in the full roll call vote, and 60 yes votes out of 78 total votes in the full Assembly roll call.⁵ Although SB 598 had strong support in the Assembly and the Senate, California Governor Edmund Brown vetoed the bill on October 12, 2013.⁶ California's proposed bill is one of many attempts at biosimilar legislation in the U.S.^{Error! Bookmark not defined.} California's bill has received more attention than other state bills because of a strong biotechnology presence in the state, including biotech giants Amgen and Genentech. Additionally, "California accounts for more than 28 percent of the country's biotechnology pipeline."⁷

A. LOBBYING EFFORTS IN SUPPORT OF SENATE BILL 598

It is easy to understand why SB 598 would garner such strong legislative backing in light of the lobbying efforts that were extended in support of the bill. One lobbyist group called for constituents to send letters in support of the bill to Governor Brown by posting an infographic on its website suggesting that the bill will "allow greater patient access to biosimilar medicines in the pharmacy setting" and will "allow pharmacists to substitute FDA-approved interchangeable biosimilars like they already do with generics".⁸ The group that released this infographic is the Biotechnology Industry Association (BIO), a 501(c)(6) trade association representing the lobbying interests of

⁵ Open Government. California Senate Bill 598 Votes and Actions. <<http://ca.opengovernment.org/sessions/20132014/bills/sb-598/votes>>.

⁶ Veto Letter SB 598: Governor Edmund Brown. California. October 12, 2013. <http://gov.ca.gov/docs/SB_598_2013_Veto_Message.pdf>.

⁷ BayBio, California Health Institute and Pricewaterhouse Coopers. California Biomedical Industry 2012 Report. Page 24. <<http://www.chi.org/uploadedFiles/report2012/MW-12-0125%20CHI%20report%20interactive%20v2.pdf>>.

⁸ Biotechnology Industry Organization. Why California Needs SB 598. September 24th 2013. <<http://www.bio.org/articles/why-california-needs-sb-598>>.

over a thousand biotechnology companies in areas from health to agriculture.⁹ The website for BIO advertises Amgen and Genentech as some of the Association's sponsors.¹⁰ Another lobbying group that is associated with the interests of Amgen and Genentech is the Alliance for Safe Biologic Medicines (ASBM). This group lists Amgen, Genentech and the Biotechnology Industry Association as three of its thirteen general member partners.¹¹

The claim that greater access to biosimilars will be promoted through SB 598 is contrary to the likely effect that SB 598 will have on the market for interchangeable biosimilars. It is not plausible that the pharmaceutical companies would support greater access to biosimilars when the provisions of the bill actually propose more stringent regulation of interchangeable biosimilars. Industries that support SB 598 have an interest in preserving their share of the market in the reference products that have patents near expiration.

Amgen is one of SB 598 greatest supporters and has been a leader in biologic drugs for years. Amgen has three biologic drug patents expiring between 2013 and 2016 that had total sales of more than six million dollars in the U.S. in 2012 and over 700,000 sales in California in 2012.¹² The bill's opposition suggests that Amgen supports SB 598 because the bill's provisions make it more difficult for biosimilar producers to get public

⁹Biotechnology Industry Organization. About BIO. <<http://www.bio.org/articles/about-bio>>.

¹⁰ Biotechnology Industry Organization. Biosimilars.<<http://www.bio.org/category/biosimilars>>.

¹¹ Alliance for Safe Biologic Medicines. Member Partners. <<http://safebiologics.org/member-partners.php>>.

¹² Express Scripts Research Report. Ten-Year Potential Savings from Biosimilars in California. Page 6. September 26, 2013. < <http://patentdocs.typepad.com/files/ten-year-potential-savings-from-biosimilars-in-california.pdf>>.

support for their drugs.¹³ The provision implicated is the requirement that physicians receive notification when their patient has received an interchangeable biologic as a substitute for a reference biologic drug. Biosimilar manufacturers, and others in opposition to the bill fear that the notification requirement will indicate that the drug is unsafe in comparison to the reference drug.¹⁴ Support for the bill from companies such as Amgen and Genentech could be seen as a way to hold onto the patent life by keeping biosimilar competitors out of the market.

Amgen is in the process of developing six biosimilar drugs with a planned release date of 2017.¹⁵ This complicates the stance of SB 598 opponents because it suggests that the regulations proposed by SB 598 would be applicable to six new biosimilars manufactured by Amgen. If SB 598 truly is an entry barrier for biosimilars, it would seem that Amgen is supporting a bill that would later confine the sale of its own products. Some commentators have suggested that there is good reason for Amgen's support of SB 598, even with the company's recent involvement in biosimilar production. "Tony Cooper, Amgen's head of global commercial operations, argued that Amgen's decades of expertise in manufacturing biologics gives it a structural advantage relative to its biosimilar competitors."¹⁶ This statement from one of Amgen's employees suggests that Amgen might feel confident about its production of biosimilars and the possibility of

¹³Bio-PharmaReporter.com. Cali Gov vetoes biosimilar bill, thwarting Amgen and Genentech. October 16th, 2013. <<http://www.biopharma-reporter.com/Markets-Regulations/Cali-Gov-vetoes-biosimilar-bill-thwarting-Amgen-and-Genentech>>.

¹⁴ California Public Employees' Retirement System: Office of Governmental Affairs. Letter of Opposition. August 21, 2013. <http://www.gphaonline.org/media/cms/SB0598_Ltr_Author_8-6-13.pdf>.

¹⁵ Amgen. Amgen Biosimilars. <http://www.amgen.com/science/amgen_biosimilars_pioneer.html>.

¹⁶ Propthink. Amgen and the Biosimilar Threat: Lessons from Affymax. March 8, 2013. <<http://propthink.com/amgen-and-the-biosimilar-threat-lessons-from-affymax/5391/>>.

meeting FDA requirements for interchangeability before the release of its products in 2017.

It is also pertinent to recognize that the biologic patent terms for many reference products expire prior to 2017, when Amgen plans to release its biosimilars.¹⁷ SB 598 was amended to have a sunset provision under which SB 598 would expire in 2017 unless the California Legislature renewed the legislation. This means that Amgen biosimilars would enter the market just as the requirements of notification for interchangeable biologics are set to expire under the proposed rules in SB 598. Biosimilar manufacturers that enter the market before 2017, including those manufacturers that are creating biosimilars that will compete with Amgen's current patented biologics, would need to comply with SB 598's regulations.

There are many more supporters of Senate Bill 598 that include biotechnology companies, physician specialty groups and patient advocate groups.¹⁸ In addition to Amgen, biotechnology companies Genentech and Merck have been proponents of the California biosimilar legislation. Merck's motivations for supporting SB 598 could be similar to Amgen's. Merck signed a deal with South Korea's Samsung Bioepis which was announced February of 2013 that is meant to expand biosimilar development and marketing for Merck and Samsung.¹⁹ Merck is taking on the commercialization aspect of

¹⁷ Generics and Biosimilars Initiative. U.S. \$67 Billion Worth of Biosimilar Patents Expiring Before 2020. October 18, 2013. <<http://www.gabionline.net/Biosimilars/General/US-67-billion-worth-of-biosimilar-patents-expiring-before-2020>>.

¹⁸ Bill Analysis, Senate Bill 598 California. <http://www.leginfo.ca.gov/pub/13-14/bill/sen/sb_0551-0600/sb_598_cfa_20130624_104220_asm_comm.html>.

¹⁹ Merck. Merck and Samsung Bioepis Enter Biosimilars Development and Commercialization Agreement. February 20, 2013. <<http://www.merck.com/licensing/our-partnership/samsung-partnership.html>>.

the project, while Samsung Bioepis will be involved in the development and testing of biosimilar drugs.²⁰ As with Amgen, it is difficult to find a business justification for Merck's support of SB 598 when it is in the process of expanding its business to the biosimilar industry. Merck has not released information regarding a date when its biosimilars will be available. However, because the joint venture between Merck and Samsung Bioepis is so recent, it is likely that the biosimilars produced through this collaboration will not be available until after the 2017 sunset provision of SB 598.

Genentech, a biotechnology company that has been a pioneer in the field of biologic drugs for years is another supporter of SB 598. Genentech's support of SB 598 is not complicated by the potential release of Genentech biosimilars. Genentech has not released any indication that they are entering the biosimilar market soon like Merck and Amgen. Genentech currently holds three biologic patents that are set to expire in 2015 and 2019.²¹ These three patents had sales that totaled more than seven million dollars in 2012.²²

Lobbyists in support of SB 598 claim to support patient rights to access of safe and effective interchangeable biosimilars.²³ However, this language seems to counter the interests of the industry that is supporting SB 598. Manufacturers of biologic drugs do not have an interest in providing greater access to the interchangeable biologics that will be produced by their competitors. The stakes are high for these companies and

²⁰ Id.

²¹ Express Scripts Research Report. Ten-Year Potential Savings from Biosimilars in California. Page 6. September 26, 2013. <<http://patentdocs.typepad.com/files/ten-year-potential-savings-from-biosimilars-in-california.pdf>>.

²² Id.

²³ Biotechnology Industry Organization. Why California Needs SB 598. September 24th 2013. <<http://www.bio.org/articles/why-california-needs-sb-598>>.

organizations in preserving their biologic drug patents and entering the biosimilar market. Criticism of Amgen and Genentech's position on SB 598 and other biosimilar legislation is well founded in light of the underlying interests of each of these manufacturers.

B. LOBBYING EFFORTS AGAINST SENATE BILL 598

Even though there is strong support for Senate Bill 598, there are also some resilient groups in opposition to SB 598. The Generic Pharmaceutical Association (GPhA) and California Public Employees Retirement System (CalPERS) are two of the largest groups in opposition to SB 598 in California. Some other groups that do not support SB 598 include the California Pharmacists Association, Teva Pharmaceuticals, Blue Cross, Kaiser Permanente, Walgreens and CVS.²⁴ The interests represented by these groups explain their position as opponents of SB 598. Groups like CalPERS, Blue Cross and Kaiser Permanente are payors that end up financing the high cost biologics and eventually passing on the cost to consumers through higher premiums. Pharmacist groups and employers like Walgreens, CVS and the California Pharmacists Association represent pharmacists who are not interested in taking on additional administrative requirements that they will not be compensated for. Biosimilar companies like Teva oppose SB 598 because they want to enter a market where they have a reasonable expectation that their product will succeed and bring in revenue for the manufacturer. All of these industries would be better served with more competition in the area of biosimilar manufacturing and sales.

²⁴ Bill Analysis, SB 598. California. June 25, 2013. <http://www.leginfo.ca.gov/pub/13-14/bill/sen/sb_0551-0600/sb_598_cfa_20130624_104220_asm_comm.html/>.

The Academy of Managed Care Pharmacy (AMCP), a national professional organization for pharmacists, is another group in opposition to SB 598 that represents the interests of one of the groups most directly impacted by the proposed legislation. In a letter to Governor Brown, the AMCP stated: “a requirement that the pharmacist must notify the prescriber within five business days of the substitution is unnecessary and overly burdensome.”²⁵ Pharmacist groups are wary of reporting requirements for filling prescriptions that may place an additional administrative burden on pharmacy practice.

The Generic Pharmaceutical Association is at the forefront of opposition to SB 598, and in other states considering biosimilar legislation. GPhA is a trade association for generic drug manufacturers and distributors that lobbies for greater access to generic pharmaceuticals.²⁶ In a letter to Governor Brown of California, GPhA requested a veto of SB 598 expressing concerns that SB 598 is “premature, would erect substitution barriers, implements an unnecessary pharmacy practice, and would create doubt about the safety and effectiveness of more affordable interchangeable biosimilars.”²⁷ The first concern of the GPhA is the prematurity of the bill. GPhA contends that SB 598 is premature because the FDA has not yet reviewed applications for biosimilars; consequently, it has not yet approved any interchangeable biosimilars.²⁸

²⁵ Academy of Managed Care Pharmacy Letter to Governor Brown of California. September 6, 2013. <<http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=17142>>.

²⁶ Generic Pharmaceutical Association. The Association. <<http://www.gphaonline.org/about/the-gpha-association>>.

²⁷ Generic Pharmaceutical Association. RE: Veto Request: Senate Bill 598. September 19, 2013. <http://www.gphaonline.org/media/cms/GPhA_Honorable_Brown_Veto_Letter_9_20_13.pdf>.

²⁸ Id.

One of the greater concerns about the prematurity of state law is the effect it will have on market entry when manufacturers are ready to bring interchangeable biosimilars to the public. A regulatory environment with requirements that vary from state to state is not conducive to market entry. Manufacturers of interchangeable biosimilars will be hesitant to enter the market without settled law in place that is uniform across the country for fear that the regulatory environment may squeeze their products out of the market. Biosimilar market entry would be best promoted if the federal regulations of the FDA preempted state law. However, there are arguments in opposition to GPhA's view suggesting that state level biosimilar regulation is necessary to protect the public. Public safety is not less of a concern prior to the release of biosimilar products; in fact, there is an argument that the safety of consumers is best protected by implementing regulations prior to the release of biosimilars. However, the FDA is in the best position to regulate the safety and efficacy of such products, not the states. Patient safety is something that does not differ based on the state the patient resides in. Regulation of drug products by the FDA promotes patient safety the most thoroughly at a national level.

The California Public Employees Retirement System is one of the payors for biologic drugs on the list of those in opposition to SB 598. CalPERS administers the health plans of more than 1.3 million public employees in California.²⁹ Because payment for health care is generally provided by insurers rather than paid for directly by consumers, organizations like CalPERS, Blue Cross and Kaiser Permanente handle the cost of biological drugs that will be used by consumers, passing on some of the cost

²⁹ California Public Employees Retirement System. About Us. October 21, 2013. <<http://www.calpers.ca.gov/index.jsp?bc=/about/home.xml>>.

through premiums and deductibles on insurance and benefits plans. In a letter opposing SB 598, CalPERS stated that over ninety percent of the organization's spending on specialty drugs went to biologic prescriptions yearly.³⁰ This spending on biologics totaled over 230 million dollars in the year 2011.³¹ CalPERS is concerned that the notification requirements for pharmacists may reduce the number of biosimilars that are distributed to consumers.³² These notification requirements would provide a disincentive for biosimilar manufacturers looking to enter the market and provide lower cost alternatives to the public. Even if one or two manufacturers decide to enter the market, in biosimilars, price will not be driven down until there is more competition. This means encouraging as many market entrants as possible. If only one or two firms provide biologic drugs, it would have the effect of promoting brand loyalty and maintaining high biologic drug costs for CalPERS and other payors, a cost that would eventually be passed onto its members.

Without an alternative for biologic medicines, the costs to insurers and consumers will remain high making it difficult for consumers to access the drugs that they need to maintain their health. Although regulations can provide consumers and prescribers confidence that they are providing and receiving the best care, some cost barriers may take away the benefit of additional protections on patient welfare.

C. PRESCRIBER NOTIFICATION REQUIREMENT:

One of the most prominent provisions in Senate Bill 598 and of biosimilar legislation other states is the requirement that the prescribing physician be notified when

³⁰ California Public Employees Retirement Service Letter in Opposition to SB 598. August 21, 2013. < http://www.gphaonline.org/media/cms/SB0598_Ltr_Author_8-6-13.pdf>.

³¹ Id.

³² Id.

a pharmacist substitutes an interchangeable biosimilar for the reference product on the prescription. This requirement is troubling for three reasons: First, the requirement suggests that there is something categorically different about interchangeable biologics and reference products that makes the former less safe or effective than the latter. Second, the requirement prematurely indicates that the FDA will not follow its own standards and will allow biosimilars into the market that do not meet the Public Health Service Act's high standard of interchangeability. Third, the notification requirement adds an unnecessary and burdensome administrative requirement for pharmacists. All three of these features of the notification requirement contribute to the anticompetitive nature of SB 598.

I. THE PHYSICIAN REPORTING REQUIREMENT OF SB 598 SUGGESTS THAT INTERCHANGEABLE BIOSIMILARS ARE LESS SAFE THAN REFERENCE PRODUCTS AND THEREFORE NEED A MORE BURDENSOME REGULATORY STRUCTURE.

Requiring prescriber notification for interchangeable biosimilar substitution when there is not a prescriber notification for generic substitution suggests that interchangeable biosimilars are not substitutable in the same way as generic drugs. Although small molecule drugs and biologic drugs are very different, the standards of interchangeability promulgated by the FDA require a rigorous showing of safety and efficacy. The same showing is required for generic substitution.

In a statement issued after Governor Brown's veto of SB 598, Amgen expressed its disappointment in the veto and claimed that "the bill would have given Californians with serious illnesses increased access to biologic and biosimilar medicines in a way that

maintained patient medical records and facilitated manufacturer accountability.”³³

Amgen seems to be suggesting that physicians need to more closely monitor their patient’s reactions to interchangeable biologics than their reactions to reference products. Conjointly, Amgen’s statement suggests manufacturers of interchangeable biologics need to be held to a higher standard of accountability for patient safety than the manufacturers of reference products.

It could be suggested that manufacturer tracking and physician notification would increase responsiveness to adverse health effects that may result from interchangeable biologics. Although monitoring of drug use could promote safety, the regulation suggests that interchangeable biosimilars need more safety precautions than the original biologic drug. According to the Public Health Service Act, as amended by the Biologics Price Competition and Innovation Act of 2009, an interchangeable biologic is defined by its ability to be substituted for a reference drug without any concern of adverse health effects.³⁴ An interchangeable biosimilar is found to be interchangeable because of its ability to be substituted without physician notification.³⁵ Because biosimilars that meet the standards of interchangeability are for all medical purposes transposable, it is unclear why an interchangeable biosimilar would be less safe than the reference product.

³³ Amgen. Amgen Statement on Veto for California Biosimilars Bill. <
http://www.amgen.com/media/statement_on_veto_california_biosimilars.html>.

³⁴ “For a biological product that is administered more than once to an individual, 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.” 42 U.S.C.A. § 262 (West)

³⁵ “The term “interchangeable” or “interchangeability”, in reference to a biological product that is shown to meet the standards described in subsection (k)(4), means that the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.” 42 U.S.C.A. § 262 (West)

Therefore, the reporting requirement does not serve the purpose of protecting the public, as is alleged by Amgen and other proponents of SB 598.

It is possible that manufacturer accountability could be beneficial to the public and could promote patient safety. However, this system could increase the safety monitoring for any drug or biologic drug and it is not logical to apply the requirements to only a small subset like interchangeable biologics. In fact, there is already a system in place to track the manufacturer and dosage of each drug on the market. This system, the National Drug Code (NDC) Directory, was established in 1972 through the National Drug Listing Act. The National Drug Listing Act requires drug products to have a unique identification number that correlates to a specific drug manufacturer and includes dosage information and information about the active ingredients in the drug.³⁶ Because the NDC

³⁶ (A) in the case of a drug contained in the applicable list and subject to section 355 or 360b of this title... a reference to the authority for the marketing of such drug or device and a *copy of all labeling for such drug or device*;

(B) in the case of any other drug or device contained in an applicable list--

(i) which drug is subject to section 353(b)(1) of this title... a copy of all labeling for such drug or device, a *representative sampling of advertisements for such drug or device*, and, upon request made by the Secretary for good cause, a copy of all advertisements for a particular drug product or device, or

(ii) which drug is not subject to section 353(b)(1) of this title... the *label and package insert for such drug or device and a representative sampling of any other labeling for such drug or device*;

(C) in the case of any drug contained in an applicable list which is described in subparagraph (B), a *quantitative listing of its active ingredient or ingredients*, except that with respect to a particular drug product the Secretary may require the submission of a quantitative listing of all ingredients if he finds that such submission is necessary to carry out the purposes of this chapter;

(D) if the registrant filing a list has determined that a particular drug product or device contained in such list is not subject to section 355 or 360b of this title, ... a brief statement of the basis upon which the registrant made such determination if the Secretary requests such a statement with respect to that particular drug product or device; and

(E) in the case of a drug contained in the applicable list, *the name and place of business of each manufacturer of an excipient of the listed drug with which the person listing the drug conducts business, including all establishments used in the production of such excipient, the unique facility identifier of each such establishment, and a point of contact e-mail address for each such excipient manufacturer*.

21 U.S.C.A. § 360 (West) (emphasis added)

system is already federally established it would be simple to use it to promote patient safety and manufacturer accountability for interchangeable biosimilars as well as for the biologics, brand drugs and generics to which it already applies. Because the requirements for NDC codes include a statement of the manufacturer, the dosage and active ingredients in the drug, it is clear that interchangeable biosimilars would be distinguishable from reference biologics through different NDC codes. Although it is not required, most pharmacies already keep information regarding NDC codes for each prescription drug dispensed. In order to track the manufacturer of biologic drugs for the purposes of addressing safety issues, pharmacies could easily be required to maintain this information for all prescription drugs including reference products and biosimilars.

Although it is possible that this information could be used for all products, it is possible that the real distinction in safety and efficacy lies between small molecule drugs (brand and generic) and large molecule biologic drugs. The manufacturing process for biologic drugs is much more complex than that of small molecule drugs.³⁷ The process of manufacturing biologics requires so many more steps than small molecule drug manufacturing.³⁸ Additionally, environment plays the same or greater role in manufacture than the components of the molecule.³⁹ For these reasons, the same manufacturer cannot exactly duplicate the results of biologic manufacturing, even for the same drug.⁴⁰

³⁷ Amgen. How are Biologic Medicines Different from Other Medications? <<http://www.buildingbiologics.com/how-biologics-differ.html>>.

³⁸ Id.

³⁹ Amgen. How are Biologic Medicines Different from Other Medications? <<http://www.buildingbiologics.com/how-biologics-differ.html>>.

⁴⁰ Id.

Therefore, it would be prudent to retain NDC codes for all biologic drugs, not only those for interchangeable biosimilars.

Another step that could be taken to monitor the safety of all biologic drugs would be for pharmacists to maintain records of lot numbers in addition to the NDC code. Manufacturers indicate that a drug was produced in a certain batch by assigning the drug a lot number. This information is generally used so an entire supply of a manufacturer's drug will not be recalled every time something goes wrong with just a single batch. Because all biologic drugs vary to some extent by the batch, having pharmacists retain a record of the batch numbers for the biologic drugs they prescribe could improve manufacturer accountability even more than retention of the NDC code. Once again, this is a regulatory measure that would work most efficiently if applied to all biologic drugs, not just interchangeable biosimilars.

The reporting requirements in SB 598 and other state bills are being proposed and backed by biologic manufacturers in order to place additional regulations on competitors, not to increase patient safety and efficacy. There are alternatives for tracking biologic drug use that would be more easily implemented than physician notification and would better attain the goals of providing safe and efficacious use of biologic products. If safety of biologic drugs is a concern, it is only cogent to require *all* biologic products to submit to such requirements. There is no clear reason for suggesting that interchangeable biosimilars will be less safe than the reference products they are modeled after.

II. THE PHYSICIAN NOTIFICATION REQUIREMENT SUGGESTS THAT THE FDA'S HIGH STANDARDS FOR INTERCHANGEABILITY ARE NOT SUFFICIENT FOR BIOSIMILARS AND THEREFORE IT IS NECESSARY FOR STATE LAW TO INTERVENE PREMATURELY.

The prematurity of Senate Bill 598 and other state legislation regarding biosimilars is a real concern. The FDA has not yet approved a biosimilar and it is premature add state level regulation when the federal law is not yet at a stage where it is possible to discover its shortcomings that could properly be filled by state law. It would be prudent to see if additional state level restrictions on biosimilar substitution are necessary *after* the FDA has approved an interchangeable biosimilar. The legislation could be more properly designed to achieve its purpose of patient safety if, after release of biosimilar products, it is deemed that those products are not safe.

What is more troubling about the prematurity of the bill than the timing of approval for biosimilars is that the FDA has not yet developed a clear approval process for interchangeable biosimilars. The FDA guidance has mentioned that it is not clear what information will be necessary to determine whether or not a biosimilar can be considered interchangeable.⁴¹ It is reasonable for California to protect the health and well being of its citizens, but it is rash for the state to implement regulations concerning biosimilars before the FDA has finalized its biosimilar application review process. It would be prudent to wait for further FDA guidance before designing a law that is meant to provide more protection to consumers than the FDA regulations.

Enactment of state laws concerning biosimilars before a process for interchangeable biosimilar approval has been developed questions the purpose of state legislation. If the intent behind SB 598 and similar state legislation is to encourage safe

⁴¹ Guidance for Industry; Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009. February 2012. <<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM273001.pdf>>.

and efficacious use of interchangeable biologic products, it would seem prudent to understand what the FDA considers to be relevant differences between biosimilars, interchangeable biosimilars and reference products. This inquiry should be answered before determining whether or not additional state regulations are necessary to promote safety and effectiveness.

Another concern about Senate Bill 598 and other state biosimilar legislation is the seeming inconsistency it has with existing FDA regulation. If biosimilar drugs were to be approved by the FDA and not meet the standards of interchangeability, there may be a medical justification for requiring notice of prescription. However, SB 598 extends past the requirement that biosimilars meet an interchangeability standard by requiring exactly what the Public Health Service Act does not require in the definition of interchangeability. Interchangeability is meant to allow for the substitution of a biosimilar drug without the intervention of the prescribing physician.⁴²

Amgen noted in its response to the Governor's veto that "SB 598 was intended to be consistent with the federal law definition of interchangeable as reflecting FDA's scientific determination that the product may be substituted without the intervention of the prescriber."⁴³ However, Amgen does not explain how SB 598 is consistent with FDA regulation. This claim is difficult to find support for in the bill's language in light of the FDA's definition of interchangeability.

⁴² "The term "interchangeable" or "interchangeability', in reference to a biological product that is shown to meet the standards described in subsection (k)(4), means that the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product." 42 U.S.C.A. § 262 (West)

⁴³ Amgen. Amgen Statement on Veto for California Biosimilars Bill.

<http://www.amgen.com/media/statement_on_veto_california_biosimilars.html>.

The enactment of state legislation prior to the clarification of federal guidance is premature and will likely result in anticompetitive effects for new market entrants. It is unlikely that manufacturers of interchangeable biosimilars will be comfortable risking billions of dollars of a product that will be released into an uncertain regulatory environment that could vary for all fifty states. The patent clock on reference products will soon be expiring, and it is important for less expensive alternatives to be made available to customers as soon as possible. State legislation could serve as the citadel that protects the market power of single firms past the time when their patents have expired. When federal legislation has already promulgated sufficient safety standards, states should serve the role of fostering competition, not excluding it through unnecessary regulation.

The standards for interchangeability that have already been developed, including the definition of interchangeability suggest that the FDA will regulate biosimilars that can be substituted at a very high standard. At this time there is no reason to think that the FDA will not follow these standards and only approve safe and efficacious interchangeable biologic products. Premature state legislation of biosimilars stands as nothing more than an entry barrier for competition in the biosimilar market.

III. PHARMACISTS ARE UNDULY BURDENED BY THE NOTIFICATION REQUIREMENTS OF SB 598 AND IT IS POSSIBLE TO IMPOSE LESS ENCUMBERING PRODUCT TRACKING REQUIREMENTS THAT BETTER SERVE THE GOALS OF PATIENT SAFETY.

Those who oppose SB 598 and other similar legislation are concerned about barriers to entry for more affordable biologics.⁴⁴ Requiring reports to be made every time a pharmacist substitutes a biosimilar places an unnecessary and burdensome administrative requirement on pharmacists. Notification would require pharmacists to report their substitution within a short period of time (three to five days for most proposed state legislation). This requirement is in addition to the requirement that pharmacies keep their own record of the substitution. This is harmful to the biosimilar industry because substitution will be more difficult than just dispensing the brand name biologic. Pharmacists may be more reluctant to substitute interchangeable biosimilars for a reference product because of the administrative burden of reporting the substitution within the required time frame.

Alternative methods of drug tracking and record maintenance for patient safety are less burdensome than the requirements of SB 598. If pharmacies were required to maintain NDC codes for prescriptions of biologics and perhaps a lot number record as well, it would place only a slight burden on pharmacies. Many pharmacies already retain this information for their own use, and it would not be difficult to implement this system nationally.

The extensive lobbying efforts that have supported biosimilar legislation throughout the U.S. could be seen as an effort to maintain market power in biologic product sales and development. Companies like Amgen and Genentech are behind this effort through their own lobbying efforts, but also as the backbone of other organizations

⁴⁴ Generic Pharmaceutical Association. RE: Veto Request: Senate Bill 598. September 19, 2013.<http://www.gphaonline.org/media/cms/GPhA_Honorable_Brown_Veto_Letter_9_20_13.pdf>.

such as Biotechnology Industry Association and the Alliance for Safe Biologic Medicines. Pharmaceutical companies have a lot at stake because of patent exclusivity. Patent law encourages innovation by rewarding successful creators of new and effective products. However, the efforts to restrain competition through regulation and legislation will harm innovation by not allowing a low cost substitute product to more easily make its way into the hands of consumers.