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James T. O'Reilly
University of Cincinnati College of Medicine

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The Formulary Fix Buries Fritz & Harvey: Drug Promotion Escapes its Past Constraints

James T. O'Reilly*

I. Setting the Scene

The young in-house lawyer, a recent W&L Law graduate, enters the meeting on the executive floor of corporate headquarters and observes the vigorous debate among the team of pharmaceutical marketing experts. One group wants to ask senior management to invest \$7 million to conduct an additional clinical trial at three prestigious hospitals, in order to request that the FDA would allow the company to make the newly expanded claim that their ten-year-old acne drug “Alepsima” will cure hangnail.

This is the correct “by the book” route¹ to selling a greater volume of Alepsima, at a greater profit, beginning in an estimated twenty-six months following submission of test results to the Food and Drug Administration (FDA). They expect that a label change will be approved, after the FDA allows the hangnail claim following a detailed medical evaluation of the clinical trial results, and after the FDA’s team of reviewers of the company’s supplemental new drug application feel they have seen enough supporting data, so that their approval of this drug for hangnail will be unassailable.

Another expert group of company marketers wants to push more Alepsima sales today, by overtly promoting its use against hangnails in trade-show booth presentations and sales visits to dermatologists and podiatrists, without awaiting FDA blessings. This group cites an in-house dermatology research team that conducted a less formal review of the technical literature, and found sixteen doctors whose hangnail patients had responded well

* Professor, University of Cincinnati College of Medicine.

1. 21 C.F.R. § 314.70 (2016). The supplemental new drug application must be accompanied by valid clinical data acceptable to FDA scientists.

to their use of Alepsima. The first group replies, “No! Such aggressive claims will get us into trouble.”

At the head of the table, the division Vice-President turns to the young lawyer and says: “How much trouble will we be in, if we use the hangnail claim in sales presentations to sell Alepsima to doctors tomorrow?”

Hundreds of miles away, the maker of Hangtough® ointment has its sales team wondering what defensive moves will be needed, in response to rumors that Alepsima might intrude upon Hangtough’s FDA-approved use as the best-selling brand for hangnails. Is litigating the right strategy? Will the FDA respond to our pleas, and defend us? How much is our lost market share potentially worth?

And, a thousand miles away, the Regional Drug Compliance Director of the FDA is oblivious to both, bemoaning yet another budget cut from the Trump Administration, which reduces the FDA’s ability to monitor claims on drug labels for the latest gene-derived cancer drugs. If she had been asked she would probably respond: “Hangnail? Who cares? When we have death risks surrounding neonatal stem cell infusion, why spend the scarce resources we have on these less impactful decisions?”

So, the conflicts of Lanham Act² remedy, the long shot of FDA and Justice Department cooperation to halt misbranding, and the potential for jeopardizing an income stream of millions to win marginal additional sales in the thousands, makes the young lawyer hesitate. If she or he is as bright as Chris Hurley, there will be a brilliant answer. Charles Dickens would see me as the Ghost of Christmas Past, and Chris as the smiling angel of the pharmaceutical industry’s future. What the Dickens should come from this scenario today?

2. Trademark Act of 1946 (Lanham Act), Pub. L. No. 79-489, 60 Stat. 427 (codified as amended at 15 U.S.C. §§ 1051–1127 (2012)).

II. Yesterday's Blues

Fritz Lanham of Texas³ and Harvey Wiley of Indiana⁴ never met, but their respective legacies in legislation have given the federal courts numerous challenges to decipher. Fritz intended to update the federal trademark laws in the boom years of postwar commerce after World War II; the less busy federal courts had the time and the intellectual power to help Fritz create the legal protection of the statutory rights of trademark owners.

Harvey wanted to stop snake-oil salesmen who hawked their claimed curative potions with loud promises but an absence of supporting data and safety research.⁵ If Harvey and Fritz had met, chances are they would not have regarded the complexities of the 2018-era presentation of drug benefit claims⁶ as a theme for new legislative attention. Their federal judges had the time and the docket capacity to make such intellectually fascinating decisions. Our district court judges today are swamped; just ask them when the vacant seats on their district court bench will be filled. So, a little statutory ambiguity about the additional benefit claims for a drug seems to be fine, since statutes tend to grow ambiguities as they age.

Ambiguities in statutory coverage are as old as Hammurabi or at least the Magna Carta. The king's interpretation of the royal charter controlled the outcome; the royal bench of jurists, like the Royal Assizes of olden times, could offer their interpretation, but the actual creator of that charter was always there to say what had been intended. So, the American Article III judges, begotten by our anti-royalist Constitution, should in theory enjoy the opportunity to bring Harvey and Fritz together, as the Food Drug & Cosmetic

3. Rep. Fritz Lanham represented the 12th Congressional District in Texas and sponsored the Lanham Act. *Id.* §§ 1051–1127.

4. State Chemist of Indiana, later Chief Chemist of the U.S. Department of Agriculture, and first Commissioner of Food & Drugs after adoption of the Pure Foods & Drugs Act. Federal Food and Drugs Act of 1906 (Wiley Act), Pub. L. No. 59-384, 34 Stat. 768 (repealed 1938).

5. A useful biography is found on Wikipedia. *Harvey Washington Wiley*, WIKIPEDIA, https://en.wikipedia.org/wiki/Harvey_Washington_Wiley (last updated Oct. 31, 2017) (last visited Jan. 19, 2018) (on file with the Washington and Lee Law Review).

6. See 21st Century Cures Act, Pub. L. No. 114-255, § 3037, 130 Stat. 1033, 1105 (2016) (codified as amended at 21 U.S.C. § 355 (2012)).

Act⁷ and the Lanham Act⁸ might be used to focus the legal community's attention upon sales of hangnail drugs or other weightier problems.

And so, on this same day as the stage is set for our dermatology drama, Mr. John Jones, suffering from painful hangnail, asks the advanced practice nurse in the local retail store "Minute Clinic" what she can give him for his annoying dermatological problem. "On aisle three we have Hangtough, but take this prescription to the counter and they'll give you Alepsima, and it should be cured more quickly!"

But first, we go back to visit our young lawyer in the drug company conference room. The Vice President's question still hangs in the air: what trouble will we be in by promoting Alepsima?

One of Virginia's brightest young lawyers, after his W&L graduation in a few months, will be answering that question bravely in his excellent analysis of the interweaving of Lanham and Food Drug & Cosmetic Act remedies. Yet this tired and somewhat more experienced counselor with scars and battle stars from many past battles over forty-four years, would hesitate and will say: "It depends!"

III. Warfare in the Pharma Trenches

The commercial wars among pharmaceutical companies of today are different than in ancient times. In the old days, drug marketing lawyers would think "Lanham Act unfair competition" was occurring if our sales representative had found a competitor's sales brochure making the unapproved new claims, typically inside a dermatologist's waiting room. Trade shows, contract reps, detail reps and continuing medical education were the battlefields of old time prescription drug sales.⁹ Nuances of the Lanham Act resonated with courts and earned scholarly attention in esoteric

7. Federal Food, Drug, and Cosmetic Act, Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. § 321 et seq. (2012)).

8. Trademark Act of 1946 (Lanham Act), Pub. L. No. 79-489, 60 Stat. 427 (codified as amended at 15 U.S.C. §§ 1051-1127 (2012)).

9. 2 JAMES T. O'REILLY & KATHARINE A. VAN TASSEL, FOOD & DRUG ADMINISTRATION ch. 15 (4th ed. 2017).

analyses. In the primary article of this issue, W&L's Chris Hurley has spotted those issues very well.

"Back in the day," some tradition-bound drug companies fought the last war, not the new war, and that has made all of the difference. When the Supreme Court in *Weinberger v. Hynson, Westcott & Dunning, Inc.*¹⁰ allowed great deference to an FDA administrative remedy, withdrawal of the New Drug Application (NDA) as punishment for misconduct, the message sent by the FDA and the Court was echoed in company meetings with the FDA for years: beware losing your base product approval. If you dare to push the envelope of permissible claims, then the FDA would win in court, after *Hynson*, when the FDA undertakes the withdrawal of your prior FDA approval of your drug.

Any old-school commentator is in danger of talking "inside baseball" as these nuances evolve, but their relevance will be apparent in retrospective. The Hurley Note's analysis is very well stated. But, the FDA's major years of achieving practical success with threats, came without the FDA having to bring much litigation to police the marketers' efforts for expansion of product benefit claims. In poker terms, the FDA could just call for "*Hynson* deference," and the drug industry player would fold its cards, the benefit would not be claimed, and no court would need to become involved.¹¹

Warriors for the totally compliant drug maker in the olden days might beg the FDA to act against the aggressive hustling of an unapproved claim for a competing drug. But, the agency would choose its targets very strategically, in order to scare many other firms into compliance with one visible victim. The FDA could use misbranding or an "unapproved new drug" violation as the charge,¹² and would have a variety of ways to attack. On rare occasions, there would be a competing drug firm, behind the scenes, begging the FDA to initiate a blockbuster criminal prosecution that, when given publicity, would drive the stock price of the offending drug firm into the ditch. The drug promotion

10. 412 U.S. 609 (1973).

11. See generally James T. O'Reilly, *Losing Deference in the FDA's Second Century: Judicial Review, Politics, and a Diminished Legacy of Expertise*, 93 CORNELL L. REV. 939, 944 (2008).

12. 21 U.S.C. §§ 321, 333, 355 (2012).

conflict's harsh bite was being threatened at a time when promotion of new uses for an approved drug was all about sales and the stock price of the pharmaceutical marketer.

I plead guilty to having been a master practitioner of those black arts of stimulating enforcers to act against bad behavior. For reasons of legal ethics, I cannot reveal whose inbox received a letter bomb and who did a nationwide recall while paying a very large penalty. But, it felt terrific when a month later there came an unsolicited call from a headhunter legal search firm who described a regulatory law job in the home city of my wounded competitor. (I declined to interview after telling the recruiter "I made that opening, I'm not going to fill it!")

That old-style war of off-label promotion is not yet over. On September 22, 2017, we heard the last of a long-running tragedy, the Novelion case.¹³ Novelion bought a tech company and inherited a hugely expensive cancer drug that had been approved only for certain rare cancer cases, one medical use that costs private payers or Medicare between \$250,000 and \$300,000 per rare cancer patient per year. I say "inherited" because the earlier drug firm that launched the drug, Aegerion, imploded. Its sales reps had been hustling the very expensive drug for as-yet-unapproved additional types of cancer. Their hustle to sell more to Medicare and Medicaid patients crossed the line, and three employees hired an attorney and filed a False Claims Act complaint (probably after being terminated).¹⁴

The outcome of the Novelion case was perhaps the last battle using the old ways of war: criminal convictions for two counts of misbranding the drug; a tough federal oversight, the "deferred prosecution agreement" was accepted by Novelion; the firm paid \$36 million in penalties to the Justice Department and \$4.1 million to the Securities & Exchange Commission. Three former employees who quit and blew the whistle received \$4.7 million as their share of the government's recovery.

13. See generally *United States v. Aegerion Pharm., Inc.*, No. 17-10288, 2017 U.S. Dist. LEXIS 191677 (D. Mass. Nov. 20, 2017); see also Press Release, U.S. Dep't Justice, Drug Maker Aegerion Agrees to Plead Guilty; Will Pay More Than \$35 Million to Resolve Criminal Charges and Civil False Claims Allegations (Sept. 22, 2017) (on file with author).

14. See Press Release, U.S. Dep't Justice, *supra* note 13.

I hope we have heard the last; Novelion made no press release, hopes it will slip quietly through the probationary “deferral” period, and hopes that it will not be further prosecuted. The drug remains on the highly specialized cancer market but is not being offered to doctors “off label” while the tight scrutiny period unfolds.

IV. New Ways of War

That was then, this is now. I speak in past tense terms because after December 16, 2016, the “off label” promotion moves from illegal in some doctor’s waiting room to legal in the boardroom of a health insurance conglomerate. Yes, a new law adopted on that day will allow the “Formulary Fix,” the targeted promotional efforts for those as-yet-unapproved medical uses, which now can legally be promoted.

Promotion of the unapproved use is now permitted to be given to the set of most influential and powerful drug “payers” like insurance carriers and state Medicaid agencies, as an expanded set of benefit claims, for expanding the uses of an already-approved drug product. Called the 21st Century Cures Act,¹⁵ the new legislation is an important and subtle change to the 1962–2016 way of operating the process for addition of new benefits for existing licensed drugs. When the new drug approval system was placed in operation under the 1962 statutory amendments, healthcare providers did not take their drug decision-making from large corporate payers like Aetna or Humana or Medicaid; today, the majority of drug prescribing is being done by employed rather than independent doctors.¹⁶ With employment comes the rules of the employer; with those rules comes the Formulary Fix. If the cost to treat this patient is being paid by an entity, it can impose its restraints on what it will purchase and what its employed physicians will prescribe. Hence, the patient gets what the provider sees in the Formulary as the designated drug of choice for the condition reported by the ailing patient.

15. Pub. L. No. 114-255, § 3037, 130 Stat. 1033, 1105 (2016).

16. See generally JAMES O'REILLY & MARY ELLEN KEEGAN, HEALTHCARE EMPLOYMENT GUIDE (BNA 2017).

Just as the World War I invention of the armored tank made horse cavalry obsolete, the Formulary Fix renders the Lanham and misbranding debates less likely to carry much weight in the future.

The 21st Century Cures Act is subtle but strategic. A drug development company's first stage approval of its base line drug wins approval of the new drug application.¹⁷ That company begins selling that drug for that medical indication. The company soon realizes its drug could also cure another ailment. At that point, the company then can choose: it could gather clinical data and ask FDA to expand the permitted label claims of drug benefit¹⁸—the focus of our drug marketing off-label discussion today. Or, the company now is able to take the additional medical uses for that product and present them, not to FDA gatekeepers, but to the intermediary companies called “pharmacy benefit managers,” the intermediate players who actually pay for the Medicaid drugs or who approve the prices that health insurer clients will pay when they purchase drugs.¹⁹

Is the waiting time for FDA's blessing upon one's supplemental new drug application still needed? Times have changed; in ancient times, Ms. Jones once took a prescription for acne medication to the Smith Drug Store and paid real cash for the medication. Today, online promotion to doctors will cut Ms. Jones out of the decision process; electronic messages from the doctor to the insurance company will check if the drug that the doctor wishes to prescribe is “on the (provider's) Formulary”. If it is, then the order is passed along electronically to a mail order pharmacy, and Ms. Jones gets her medicine in one to three days' delivery.

The Formulary acts as the drug benefit payor's economic gate that keeps a \$400 headache drug from being prescribed to customers of XYZ health plan; their Plan makes a privately-determined cost savings decision to not include a certain new headache drug in the Formulary. So, the electronic system of the payer automatically blocks the \$400 option for the headache treatment, while that formulary allows \$4 aspirin or \$7 Tylenol, for example. Sitting at the CVS pharmacy waiting for that prescription to be filled, Ms. Jones has no idea of the hidden role of

17. 21 U.S.C. § 355 (2012).

18. 21 C.F.R. §§ 314.70, 314.80 (2018).

19. See 21st Century Cures Act § 3037 (amending 21 U.S.C. § 352(a)).

Pharmacy Benefit Managers. Recall the scene in the “Wizard of Oz” when the snake oil salesman from Kansas who plays the role of Oz tells Dorothy: “Pay no attention to that man behind the curtain!”²⁰ And so decisions today are fast, and denials are less frequent if the prescriber cooperates.

I realize that this new pharmaceutical sales cycle gets very complex very quickly, which is why so few members of Congress understood what they voted for in Section 3037 of the very complex recent drug legislation. The lobbyists for the drug developers designed this section to serve as a plausible 2016 alternative to the decades-old requirement for drug sponsors to be filing clinical study data with FDA for a “supplemental new drug application.”²¹ They told Congress it was faster and cheaper to allow the “Formulary Fix” for these second and subsequent uses of an already approved drug. Consider a Formulary as an electronic list of privately reviewed drugs, the prescribing of which is commercially acceptable to a large health insurer like Humana, which will accept reimbursement of that drug for certain medical needs.

The Formulary Fix means that the ability to electronically order the certain named drugs on the approved-use list will be available to doctors who work for the entities which take that insurer’s reimbursement, or whose bills are paid by the company under a contract. Doctors who use the drugs on that Formulary list have no problems; but doctors who want to prescribe a different drug that is not in the formulary have to spend non-compensated time to justify their preferred drug. I’ll use another model: doctors treating jaundice can use formulary listed drugs *A* or *B*; but if they want instead to use drug *C*, that is an exception to the Formulary, and they will have to spend their own time negotiating with the corporate staff for an exception which delivers that drug. Yes, hassling a distant phone contact to get another non-Formulary drug for a patient is not being reimbursed, so how often will doctors go “off Formulary” for a call-in support of a different drug for the needs of one patient? Press “00” if you don’t expect it to happen often.

20. L. FRANK BAUM, THE WONDERFUL WIZARD OF OZ (G.M. Co. 1900).

21. 21 C.F.R. §§ 314.70, 314.80.

So, from 2017 forward, if your company holds the new drug approval for an acne product, as our hypothetical case had addressed earlier, your preapproval team no longer need to visit beautiful White Oak, Maryland to argue with FDA review teams. Instead, one MBA will head to New York, Nashville, or Boston to a business office tower where economic choices and medical decisions are being made. Your technical sales person has power in 2017 and hereafter, as a result of Section 3037 of the 21st Century Cures Act, to inform the insurer that your drug cures hangnail and is cheap and easier to administer.

This is now a normalized stream of product benefit information. No one needs to stop to ask FDA's views on clinical efficacy. The net cost for those patients whose insurer will cover their drug is less. The sales reps now must try to convince that company to accept this drug into their "Formulary," a list matching illnesses with drugs, a list that is optional and privately compiled, rather than a federally dictated program. Once you make that sales pitch successfully, the marketplace of all the patients and providers of the XYZ insurance group or a state Medicaid program will be opened to you; and doctors who belong to that health insurer's group must begin or continue to use that selected drug for that "off label" medical indication.

The actual prescriber doctor does not sit in, at the meeting when the drug maker pitches its drug's additional use benefit to the insurer's formulary committee. Hence, the FDA gatekeeper roles of the supplemental NDA are inoperative anachronisms,²² and sales will be spurred. Congress ran right past the previous barrier to adding use information, and "liberated" the drug marketers for private communication to the few specialist medical committee members who are the buyers of their mass quantity of drugs, allowing drug makers to spin the "Formulary Fix".

V. Trump and Trends

Old, tired veterans of those wars have been alarmed at the new Trump Administration leadership's message regarding drug approvals. Past moments of reflection, like the 100th anniversary

22. 21 CFR §§ 314.70, 314.80.

symposium of the FDA in 2006, stimulated reflections on the balance between faster new product approvals, and more certain decisions in the field of drug safety. The earliest presentations to industry audiences by the new Commissioner, a longtime industry advisor and participant, sent a different message and a divergent tone to the FDA's review teams. The words of Commissioner Scott Gottlieb could echo a pharmaceutical industry executive's oft-repeated mantra—speed the data gathering and review, speed the approval, get the drug out today and check the “real world data” next year.²³ It is too early in his leadership term to know where the acceptance of industry will lead, but there are balanced approaches that are at some risk of negative consequences in the Trump Administration's pro-development rhetoric.

VI. *So What?*

Battling over the future use of off-label drug claims will be far less interesting to my hypothetical drug company executive after 2017. She now can gain far more by pressing Humana or Aetna to place the additional drug benefit claim onto their private Formulary. If a doctor is in a hospital or practice group whose Formulary applies controls on what the affiliated physicians can prescribe, as so many practitioners are and will be, then the patient record indicates a certain diagnostic code and the patient gets a prescription for that drug for that non-labeled medical indication, and the sale is made without need for the old ways of chasing the off-label violators. The FDA cares less about hangnail; Jane Insured gets what Doctor Golfclub prescribes; and Golfclub is directed seamlessly by the drug Formulary, which allows her to prescribe this drug *Alepsima* for hangnail.

So, in Shakespeare's terms, I come to not just praise the Note by Hurley, but to bury his model of drug marketing. The

23. Scott Gottlieb, M.D., Comm'r of Food & Drugs, Remarks on Leveraging Quantitative Methods and Modeling to Modernize Generic Drug Development and Review (Oct. 2, 2017); Scott Gottlieb, M.D., Comm'r of Food and Drugs, Speech to the 2017 AdvaMed (MedTech) Conference (Sept. 26, 2017); Scott Gottlieb, M.D., Comm'r of Food and Drugs, Address to National Academy of Sciences, Advancing Public Health Opportunities with Real World Evidence (Sept. 19, 2017).

“Formulary Fix” of Section 3037 of the “21st Century Cures Act”²⁴ is where the marketers of drugs are headed in 2018 and beyond. The claims of additional benefit that had once languished in FDA’s in-box are beating a path to Humana’s or McKesson’s door.

While a supplementary new drug application would be nice to have for the minority of doctors who are not impacted by a Formulary, the months and millions which such a voluminous drug application “supplement” demands²⁵ are considerably less important to net sales goals than they once had been, way back in 2015. The drug promotion effort of this brave new pharma world is not only centralized and simplified, it is also sanctioned by Congress as an alternate route to market success.

How this all will play out remains to be seen, and “all the world’s a stage.”

24. See generally 21st Century Cures Act, Pub. L. No. 114-255, 130 Stat. 1033 (2016).

25. 21 C.F.R. §§ 314.70, 314.80 (2018).