COMPOUNDING PHARMACY OWNER SUMMIT 2024

Compounding Cases: A Survey of Legal Action By and Against Compounding Pharmacies

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Agenda:

1. Athenex v. Azar – The FDA has a lot of discretion!
2. Allergan v. Sincerus – Pharma wants similar discretion.
3. The Implied Preemption Cases – Pharma can't wear FDA's shoes!
   a. Nexus v. Everybody
   b. Hope v. Fagron
4. SCA Pharmaceuticals v. FDA – Let's keep FDA discretion in check!
5. Absolute Pharmacy v. California BOP – And states too!
6. Evexias Health Solutions v. FDA – Hot off the press!

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Athenex Inc. v. Azar, No. 19-cv-00603, (D.D.C. Aug. 1, 2019)

- FDA determined vasopressin did not meet criteria set forth in Guidance For Industry and found no clinical need to allow compounding from bulk
- Athenex argued that there is a clinical need for compounded vasopressin, as the commercially available product (Vasostrict) contained chlorobutanol, which is expressly contraindicated in some patients
  - adverse reactions – anaphylactic shock, cardiovascular effects, neurological effects, pregnancy
  - Risk from use clearly outweighs any possible theoretical benefit of using Vasostrict in these patients
  - Under FDA's own standards, there is a "clinical need" to compound vasopressin from bulk
- FDA disagreed, so Athenex filed suit

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Athenex Inc. v. Azar, No. 19-cv-00603, (D.D.C. Aug. 1, 2019)

- Athenex Argument 1:
  - Because vasopressin is the active ingredient of an FDA-approved drug, its therapeutic value had already been confirmed by the Agency
- Court disagreed:
  - … "reading 'clinical need' this way does not create a category of active pharmaceutical ingredients for which there is not a 'clinical need.'"
  - "Congress plainly thought that there are some bulk drug substances for which there is a 'clinical need' and others for which there is not."

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Athenex Inc. v. Azar, No. 19-cv-00603, (D.D.C. Aug. 1, 2019)

- Athenex Argument 2:
  - Congress intended for clinical need to be determined by medical practitioners
  - FDA erroneously usurping that role as a mischaracterization of FDA's role in evaluating clinical need
- Court disagreed:
  - FDA decision does not interfere with a physician's decision to administer Vasostrict, or even a compounded version of the drug
  - Agency is deciding on "the type of drug that reaches the marketplace."
  - Athenex's interpretation of clinical need would open the floodgates to outsourcing facilities compounding with every bulk substance contained within FDA-approved drugs

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Athenex Inc. v. Azar, No. 19-cv-00603, (D.D.C. Aug. 1, 2019)

- Athenex Argument 3:
  - 503B contains independent provisions to safeguard the drug approval system, particularly the Essential Copy prohibition
- Court disagreed:
  - Essential Copy prohibition complemented, rather than duplicated, the clinical need evaluation
- Other notable findings by Court:
  - FDA interpretation should receive deference from the Court
  - Court recognized the need to protect the premarket approval process for new drug products from unfair competition by drugs compounded from bulks
  - Court found persuasive FDA's argument that Congress deliberately cabined the use of bulk drug substances in part to protect against the economic incentives for outsourcing facilities routinely to compound from bulks

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Allergan v. Sincerus

- Allergan alleged that Sincerus was unlawfully manufacturing and selling unapproved new drugs.
- Particularly, Sincerus was not fully compliant with Section 503B by compounding bulk drugs before the final clinical need list had been issued by FDA, and was therefore not eligible for the exemptions therein.
- Allergan also alleged that Sincerus was violating the Lanham Act by engaging in false and misleading advertising and promotion of the unapproved new drugs
  - ANY violation of the FDCA resulted in ALL Sincerus activities to be illegal
- Judge ruled no violation of the Lanham Act for a 503B facility to market the use of a substance on FDA's interim Bulk List 1 for compounding
- Judge also ruled that even if a facility does violate some portion of the FDCA, it does not mean that all marketing materials used, or compounding services provided, for other substances compounded by the 503B facility violate the Lanham Act

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The Implied Preemption Cases

- Nexus v. Everybody
  - Nexus obtained FDA approval on Ephedrine 5mg/ml RTU injection. Nexus then sued various 503Bs compounding API-to-sterile and sterile-to-sterile preparations alleging violation of multiple state unfair competition laws.
- Hope v. Fagron
  - Hope holds FDA approval on sodium thiosulfate injection. The *only* approved indication is acute cyanide poisoning.
  - The product is used off-label to treat calciphylaxis, a serious condition in which calcium accumulates in small blood vessels of the fat and skin tissues. Calciphylaxis causes blood clots, painful skin ulcers and may cause serious infections that can lead to death. Calciphylaxis is prevalent in patients suffering from end-stage renal disease.
  - Hope's sodium thiosulfate contains potassium, which is contraindicated in patients receiving dialysis.
  - Based on provider demand, Fagron developed a potassium-free sodium thiosulfate.

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The Implied Preemption Cases

- Hope sought injunctive relief and damages based on claims that Fagron's noncompliance with the Federal Food, Drug & Cosmetic Act ("FDCA") and corresponding FDA policy resulted in violations of unfair competition laws in 5 states.
  - Hope Argument 1: Sodium Thiosulfate API was, at times, not on the 503B Bulks List
  - Hope Argument 2: Fagron's compounded sodium thiosulfate product was essentially a copy of Hope's commercially-available product (503B and 503A)
  - Hope Argument 3: Anticipatory compounding and compounding inordinate amounts (503A)
- Conclusion from above arguments is that Fagron cannot enjoy the exemptions under Section 503B and 503A, resulting in the distribution of unapproved drug products.
  - Such activity resulted in violation of various state laws, giving rise to unfair competition claims.
- Fagron argued that neither Hope nor the court has the right to enforce the FDCA. Instead, only the FDA has the right to enforce the FDCA. This is the principle of "Implied Preemption."

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The Implied Preemption Cases

- California lower courts – differing opinions re: Implied Preemption arguments.
  - The Nexus defendants prevailed on Motion to Dismiss.
  - A judge in the same Court disagreed with the Nexus judge's conclusion and denied Fagron's similar Motions to Dismiss and for Summary Judgment.
  - Fagron ultimately tried the case.
- Both cases were appealed to the Ninth Circuit Court of Appeals. Both the Nexus defendants and Fagron prevailed.
  - Nexus decision: https://cdn.ca9.uscourts.gov/datastore/opinions/2022/09/13/20-56227.pdf; Fagron decision is unpublished "Slip Opinion."
  - "Because the FDCA forbids private rights of action under that statute, a private action brought under [other laws] may not be pursued when, as here, the claim would require litigation of the alleged underlying FDCA violation in a circumstance where the FDA has not itself concluded that there was such a violation."

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The Implied Preemption Cases

  - "The issuance of this and other FDA documents shows that it has been attentive to the difficult issues of interpreting and enforcing the "essentially a copy" provision. All of Nexus's claims depend on a determination of whether Central Admixture's ephedrine sulphate is "essentially a copy" of Nexus's Emerphed. The plain text of the FDCA leaves that determination in the first instance to the FDA's balancing of risks and concerns in its enforcement process."
  - "Because Hope seeks to 'enforce its interpretation' of the FDCA's rules for manufacturing compounded drugs against a competitor, the FDCA's prohibition on private enforcement and the doctrine of implied preemption bar the suit."
- Nexus relented. Hope did not and is now seeking a Petition for Writ of Certiorari to the U.S. Supreme Court. Fagron's brief is due on April 15.
- Interesting tidbit – Hope is represented by Novo Nordisk's former counsel (King & Spalding). Were the semaglutide cases a driver for keeping the Hope case alive?

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SCA Pharmaceuticals, LLC v. FDA

- FDA inspected SCA's Windsor, CT facility for 4 weeks during September and October 2023.
- A Form 483 with 10 observations was issued October 20, 2023. SCA alleges that most observations were for minor, isolated, and easily redressable observations.
- 8 days before SCA's 483 response was due, FDA demanded that SCA "voluntarily" cease production at the Windsor facility and recall all products in the market. This would result in the recall of 2.5 million units.
- Failure to "voluntarily" comply would immediately result in a Section 705(b) Notice warning the public not to use any of the firm's products due to what FDA terms the possibility of "serious and potentially life-threatening infections or death."
- SCA complied with the facility shutdown and immediately began remediation.

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SCA Pharmaceuticals, LLC v. FDA

- SCA requested that the FDA share the Health Hazard Evaluation ("HHE") that is meant to be FDA's predicate for any forced market action. FDA refused to produce the HHE.
- Negotiations were not successful and FDA's release of the 705(b) Notice was imminent, so SCA sued FDA for violation of the APA and Due Process.
- The Court noted that FDA did not follow its normal regulatory procedures – there was no interactive discussion of the 483; there was no HHE prepared; and that FDA was demanding a recall and a shutdown before the time expired for SCA to respond to the 483.
- The Court referred to the threatened 705(b) Notice as "blackmailing a company into complying with a recall that the agency cannot statutorily order."
- In response to FDA's ripeness argument, the Court asked: "Do we have to wait until the company is put out of business for them to bring this lawsuit?"

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Absolute Pharmacy v. California State Board of Pharmacy (Absolute Pharm. v. Sodergren, 2023 Cal. Super. LEXIS 54865)

- Presented novel issue—can a state board enforce the Section 503A of the FDCA via its disciplinary statute allowing it to discipline a licensee for an alleged violation of federal law?
- The Superior Court of Los Angeles County found that the California State Board of Pharmacy could not use its disciplinary authority to enforce Section 503A because it lacked an independent state law basis for finding that any violation occurred.
- First ruling of its kind.

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Evexias Health Solutions, LLC, et al v. FDA

- On March 29, 2024, Evexias sued FDA in the U.S. District Court for the Northern District of Texas for violation of the APA in its management of the 503A Bulks List, particularly the recent inclusion of AOD-9604, CJC-1295, ipamorelin acetate, and Thymosin Alpha-1 on Interim 503A Bulks List 2 (drug substances that "have been identified by FDA as presenting a significant safety risk.").
- Unlike other drug substances moved to 503A Bulks List 2, the 4 peptides at issue in this matter were not brought before PCAC and, of course, not put through Notice and Comment Rulemaking required by the APA.

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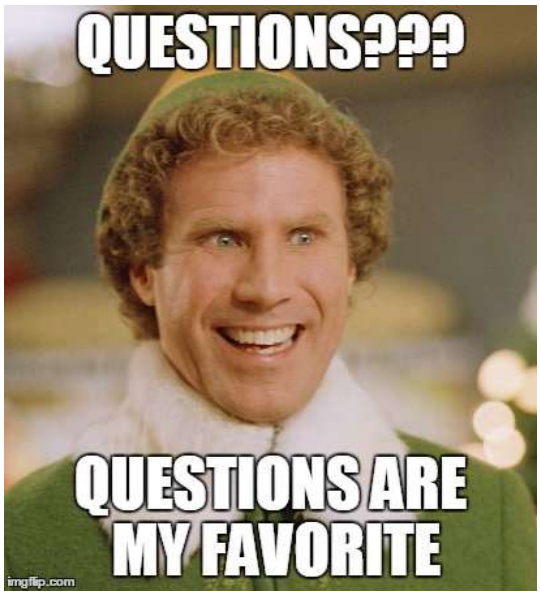

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