T.H. v. Novartis

(California Supreme Court – 2017)

Exploring new Liability Avenues

May 4, 2018

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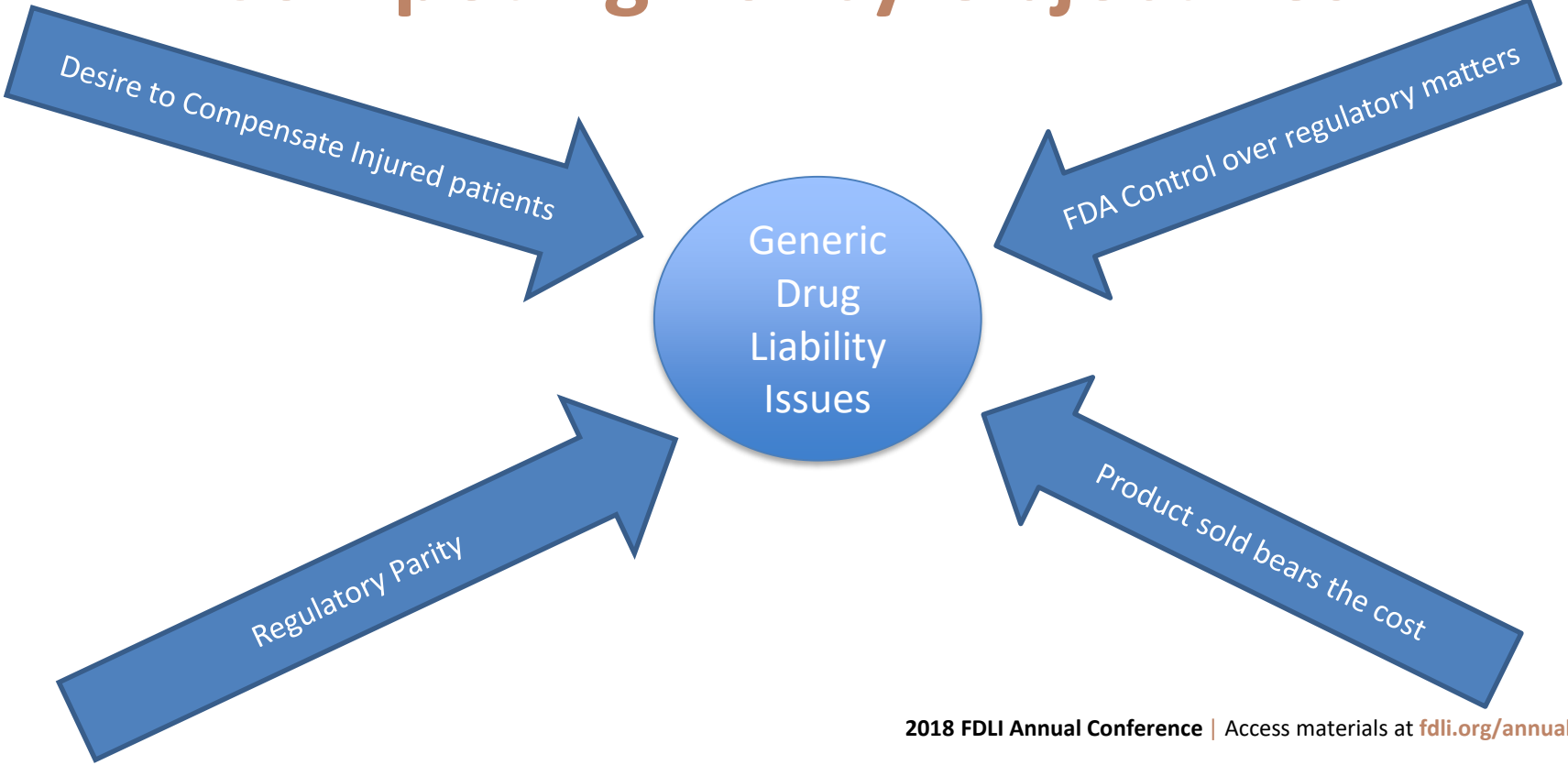
Principal – Leavitt Partners

FDLI

Origins of the Issue
Competing Policy Objectives



Legal background

- Product liability – patient can sue if injured because of inadequate warnings
- Preemption – prevents private lawsuits if FDA controls the label
  - Limited preemption for NDA based drugs (i.e. “name brand drugs)
  - Preemption for ANDA based drugs (i.e. generic drugs)
- Regulatory –
  - Generic dug must match name brand drug (bioavailable and bioequivalence)
- Regulatory – label and warning provisions
  - FDA controls label content – no changes without prior FDA approval
  - Changes being effected (“CBE”) provisions allow NDA holder to implement a label change while FDA is evaluating it
  - ANDA holder must conform its label exactly to the label of the NDA holder
    - No CBE provisions for ANDAs

Core Allegations and Status

- T.H. (and a fraternal twin) sued Novartis alleging a failure to warn of the risks to a fetus of the maternal use of terbutaline (Brethine)
  - 2007 prescribed for premature labor
  - Off-label use of terbutaline
- Mother ingested generic version of terbutaline
- Allegedly the drug caused the plaintiffs to develop autism and other injuries
- Case filed in state court in California
- Defendant challenged adequacy of complaint via demurrer
  - Similar to FRCP 12(b)(6) Motion to Dismiss
  - Facts must be assumed to be true
- Novartis wins at trial court level

Facts of the case

- 1974 – Initial NDA approved for asthma
- 1976 – Initial article about use of terbutaline for premature labor
- 1978 – Contrary article
- 1979 – 2001 –various articles question terbutaline for preterm labor
- 1997 – FDA issues a “Dear Colleague” letter warning of this use
- 2001 – Novartis sells NDA to aaiPharma
- 2005 – aaiPharma declares bankruptcy
- 2007 – Plaintiffs’ mother ingests generic terbutaline
- 2012 – Autism diagnosis

Two Key Questions

1. Does Novartis have a duty to warn patients/doctors of the risks of generic terbutaline
   - The plaintiff didn't take a drug made by Novartis
   - 7-0 decision for plaintiff
2. If so, does that duty continue after Novartis sold the NDA (six years before the key event)?
   - 4-3 decision for plaintiff

Note that majority of case law was in favor of Novartis

Key exception in California in Conte

Overarching Plaintiffs' Dilemma

- Finding a (solvent) defendant to sue
  - Generic manufacturer has preemption defense
  - aaiPharma is bankrupt
  - Novartis didn't make the drug taken by mother
  - Medical malpractice?
  - A search for a deep pocket?
- Also a similar challenge in Wyeth

Summary Positions

- Plaintiff positions (accepted by Court)
  - Victims need compensation
  - NDA holder is the only entity controlling the label
    - Role of CBE provisions
  - Generic company can't change the label
  - Holding the NDA holder responsible will promote adequate warnings
- Defendant position
  - Can't hold the defendant responsible if the defendant didn't make the product
    - Product liability is based on a "product"
    - NDA holder can't spread the risk
  - Once NDA holder sells/transfers the NDA, responsibility ends

Court Decision – Question 1

- Plaintiffs entitled to an adequate warning
- Only the NDA holder (Novartis) can change/amend the label
  - Generic drug company relies on adequacy of warning from NDA
  - Foreseeable that these entities will rely on NDA warning
  - Plaintiff (and physicians) rely on warnings
- Novartis can change the label without FDA approval via the CBE process
- Fact that Novartis drug not ingested doesn't alter the duty owed by Novartis to provide an adequate warning
- Failure to warn must be assumed to be the proximate cause at this stage in the proceedings

Metaphysical Change?

Traditional View

Product Design
Manufacturing
Labeling/
Warnings
Sale or
Distribution

One linked “package” of rights and responsibilities connected to the product

New View

Product Design
Manufacturing
Labeling/
Warnings
Sale or
Distribution

Labeling/
Warning
(Separate
from physical
product and
sale)

Separation of product and label
Two paths now exist

Court Decision – Question 2

- Less unanimity on this question
- Duty continues based on the state of the art in 2001
- Plaintiff must establish that label should have been changed in 2001 or before
  - More complex causation question
  - 2007 ingestion
- Same duty to warn by NDA holder even if NDA transferred but ends with state of the art at the time of transfer
  - Subsequent NDA holder has subsequent duty
  - Perhaps duty to amend label based on pre-transfer information

Next Steps

- Case returned to trial court to permit plaintiff to amend complaint
- Trial court will need to decide
  - Causation
  - Whether state of the art mandated a warning in 2001
  - Whether FDA would have approved a CBE change
  - Did intervening actions/information break the causal connection to Novartis
    - Time delay between 2001 and 2007

Legal Issues and Questions

- The CBE process is a “temporary” “exemption while FDA reviews the label
  - Court may be forced to “guess” what FDA would have done if label change requested
  - Historical deference to FDA – give a chance for FDA to act
  - Judge/jury now asked to decide what FDA would have done with a CBE request
- Drug preemption can get into an assessment of FDA/company interactions
- Looking for the binary point in evolving science
  - When is a label change needed?
  - Gradual development of literature on terbutaline
- Additional pressure to revise generic label obligations
  - Risk of inconsistent labels under a generic CBE process

Other Challenge

- Use of terbutaline for preterm labor is off-label
- Duty to warn of risks of off-label uses?
  - Knowledge of off-label use?
  - 21 CFR 201.128
  - On-going effort to revise regulatory language
- Can the duty to warn be "promotion"?
  - 21 C.F.R. § 201.57(c)(2)(v) ("Indications or uses must not be implied or suggested in other sections of the labeling if not included in [the Indications] section.").
- Issue unaddressed by Court

Implications

- Trial strategy
  - Who does the plaintiff sue?
  - Challenge up front or develop facts?
    - Note that Sindell was also on demurrer/FRCP 12(b)(6)
  - Third party practice
    - Should Novartis sue aaiPharma?
- Metaphysical separation of warning duty and product
  - Implications in other FDA areas (510(k) substantial equivalence?)
  - Implications for other industries?
- On-going challenge of liability for generic drugs and transfers
  - Impact on use of one drug purchased from multiple companies
  - Potential obsolescence of Sindell based market share liability
- Jurisdictional differences
  - MDL and class action implications (mass tort situations)

Implications

- Regulatory strategy
  - File everything approach? Put onus on FDA?
  - When to file CBE
  - FDA discussions become litigation fodder
  - Withdrawing an NDA for non-safety/efficacy reasons
  - Monitoring more than literature – think RWD/RWE
- Business strategy
  - Do you “sell” the old NDA or withdraw it?
  - Sales terms and indemnities
  - Does the seller “guarantee” the solvency of the purchaser?
  - Incentive to withdraw NDAs
  - Impact on insurance (generally claims made policies)

Case to Watch – Gundy v. U.S.

- Sex registration law (SORNA)
  - Granted Attorney General authority to decide whether to apply SORNA to individuals convicted of sex offenses prior to enactment of SORNA
- Delegation clause question
- Is it constitutional to delegate this authority from Congress to the executive.
- Cert granting in 2018
- Cert. question:
  - Whether SORNA's delegation of authority to the Attorney General to issue regulations under 42 U.S.C. §16913(d) violates the nondelegation doctrine
- Very few delegation clause cases
  - U.S. asked Supreme Court not to hear the case
  - Fact that Supreme Court is hearing this case is noteworthy

Gundy v. U.S. - Implications

- Congress delegates many authorities to regulatory agencies in the health care space
  - Create standards
  - Import/export
  - Mandate “guidances”
  - Strategy re drug shortages
- Level of specificity needed from Congress?
- Limitations on delegation impacts past and future regulations
- Relationship to Chevron deference?

Eike *v.* Allergan, Inc.

U.S. Court of Appeals – Seventh Circuit (March 2017)

PROF. WILLIAM M. JANSSEN
CHARLESTON SCHOOL OF LAW

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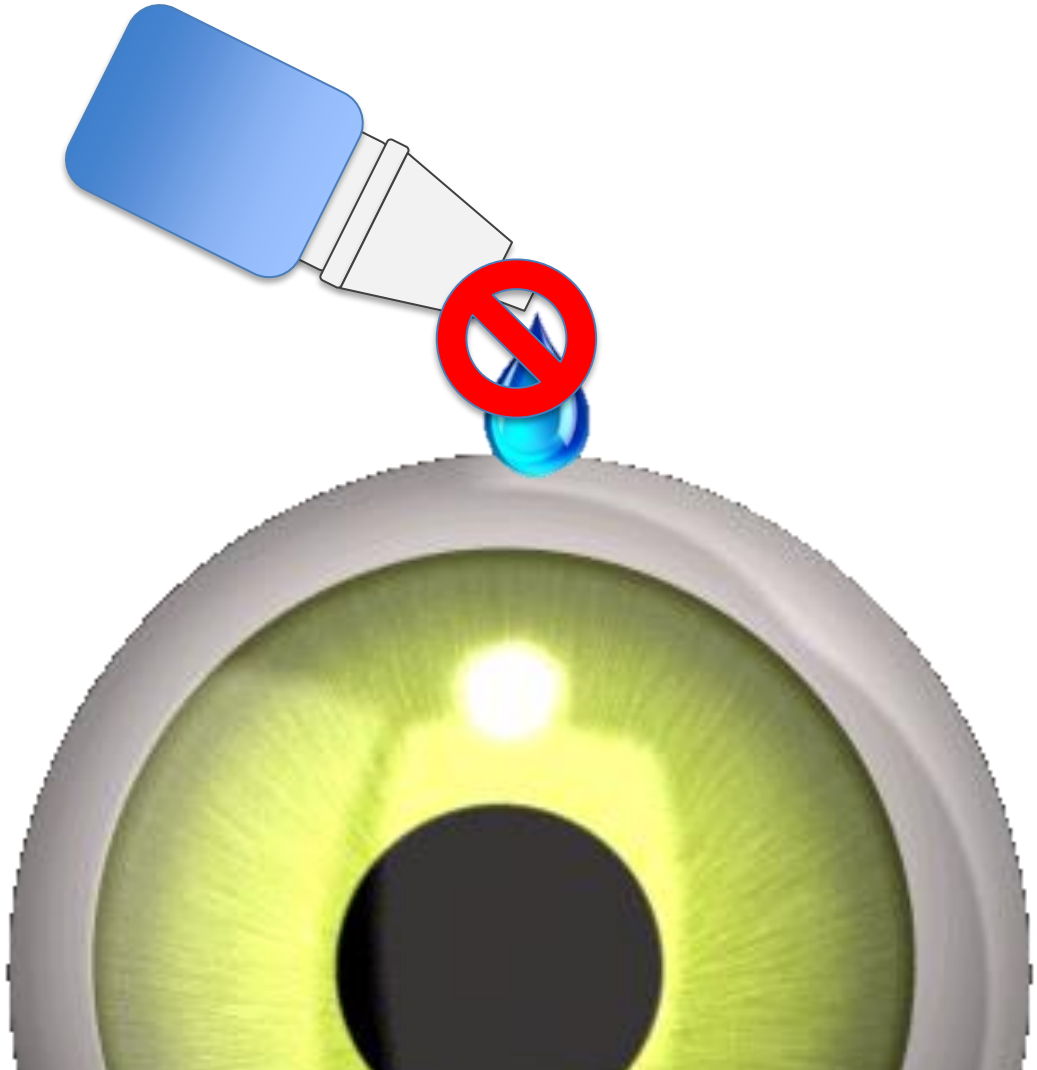


American Journal of Ophthalmology

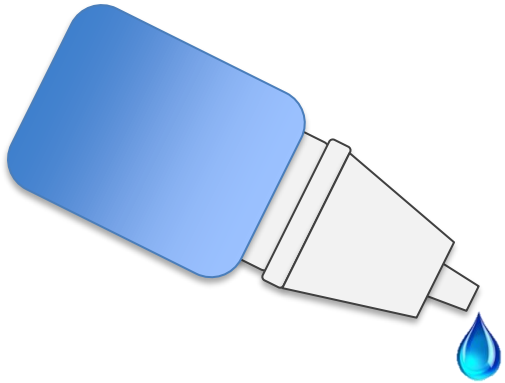
Journal of Glaucoma

Journal of Pharmaceutical Sciences

European Journal of Pharmaceutics and Biopharmaceutics

Archives of Ophthalmology

Survey of Ophthalmology
International Review Journal



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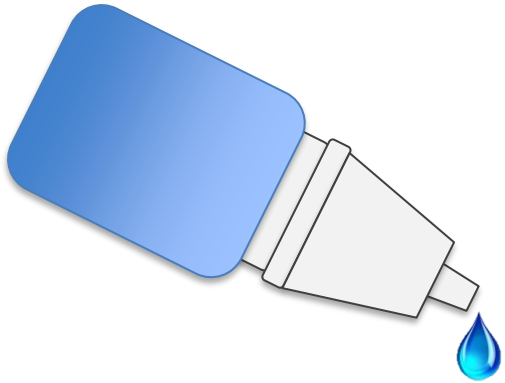


"Unfair trade/business practice"

in violation of State consumer protection laws

No pleaded allegations of –

- ✓ Personal injury to any class member
- ✓ Product failure / ineffectiveness
- ✓ Affirmative misrepresentation
- ✓ Collusion or antitrust violation
- ✓ Anything other than a well-functioning market comprised of multiple competing manufacturers

“Unfair trade/business practice”

in violation of State consumer protection laws

FTC v. Sperry & Hutchinson Co.
405 U.S. 233 (1972) (White, J., for 7-0 Court)

“… measuring a practice against the elusive, but congressionally mandated standard of fairness, [the tribunal may consider] … public values beyond simply those enshrined in the letter or encompassed in the spirit of the antitrust laws.”

“Unfair trade/business practice”

in violation of State consumer protection laws

FTC v. Sperry & Hutchinson Co.
405 U.S. 233 (1972) (White, J., for 7-0 Court)

- Offends public policy
- Is immoral, unethical, oppressive, or unscrupulous
- Causes substantial injury to consumers (or competitors or other businesspersons)

“Unfair trade/business practice”

in violation of State consumer protection laws

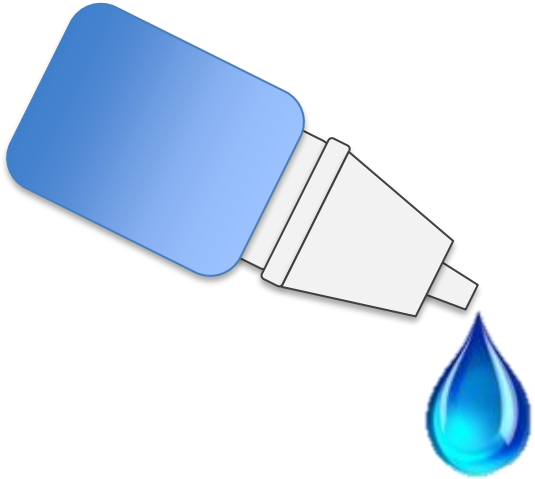
FTC v. Sperry & Hutchinson Co.
405 U.S. 233 (1972) (White, J., for 7-0 Court)

UNFAIR TRADE PRACTICE:

Unnecessarily large dropper-tip size forces consumers to pay for wasted medicine.

COMPANY RESPONSES:

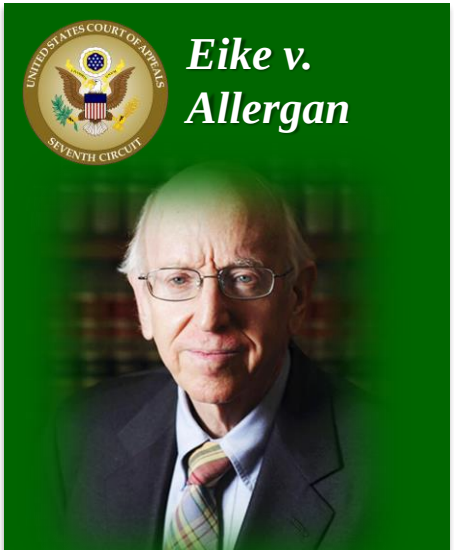
- Patient eye sizes differ.
- Larger drop size enhances likelihood that active ingredient will enter eye.
- Shaky hands by the Elderly + Vision-Impaired.
- FDA approved dropper-tip.



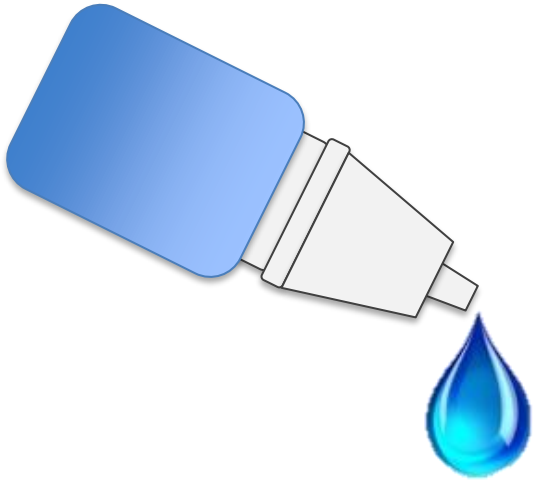
“Unfair trade/business practice”

in violation of State consumer protection laws

“The fact that a seller does not sell the product you want, or at the price you’d like to pay, is not an actionable injury; it is just regret or disappointment—which is all we have here, the class having failed to allege ‘an invasion of a legally protected interest.’”



“You cannot sue a company and argue only—‘it could do better by us’ …”

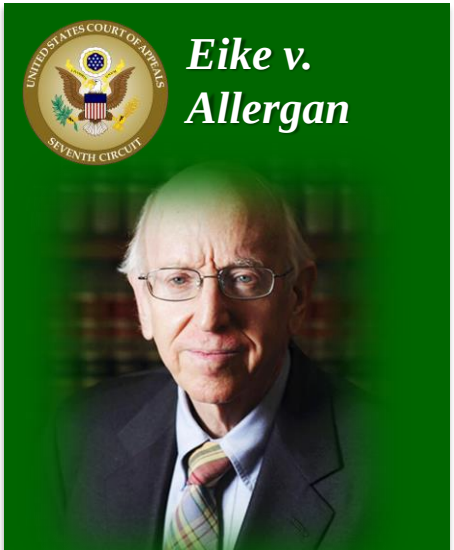


“Unfair trade/business practice”

in violation of State consumer protection laws

U.S. CONSTITUTION

Article III Standing



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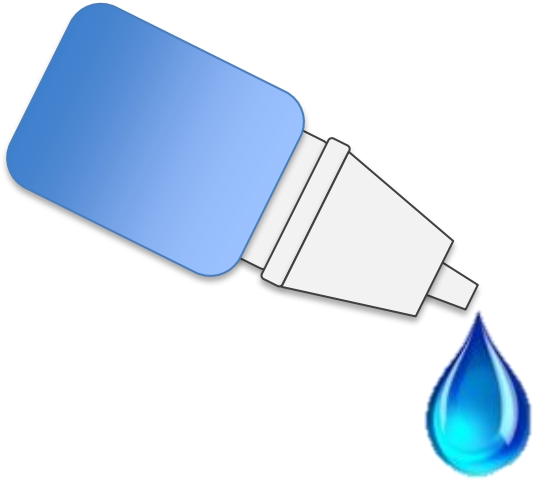


"Unfair trade/business practice"

in violation of State consumer protection laws

Eike v. Allergan

3-0

Article III Standing

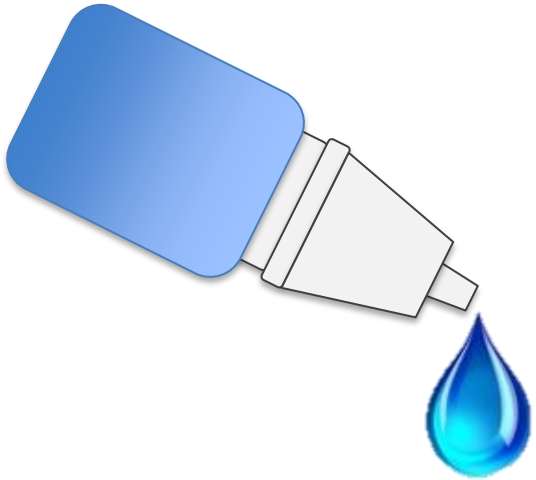
Cottrell v. Alcon Labs

2-1

Satisfies FRCP 8

P's claim: spent money on medicine that could not be used, which violated unfair trade practice statutes.

That's enough for standing.



"Unfair trade/business practice"

in violation of State consumer protection laws

Courts cannot do what Ps request: isolate and change one economic variable while assuming no downstream changes.

Eike v. Allergan

3-0

Article III Standing

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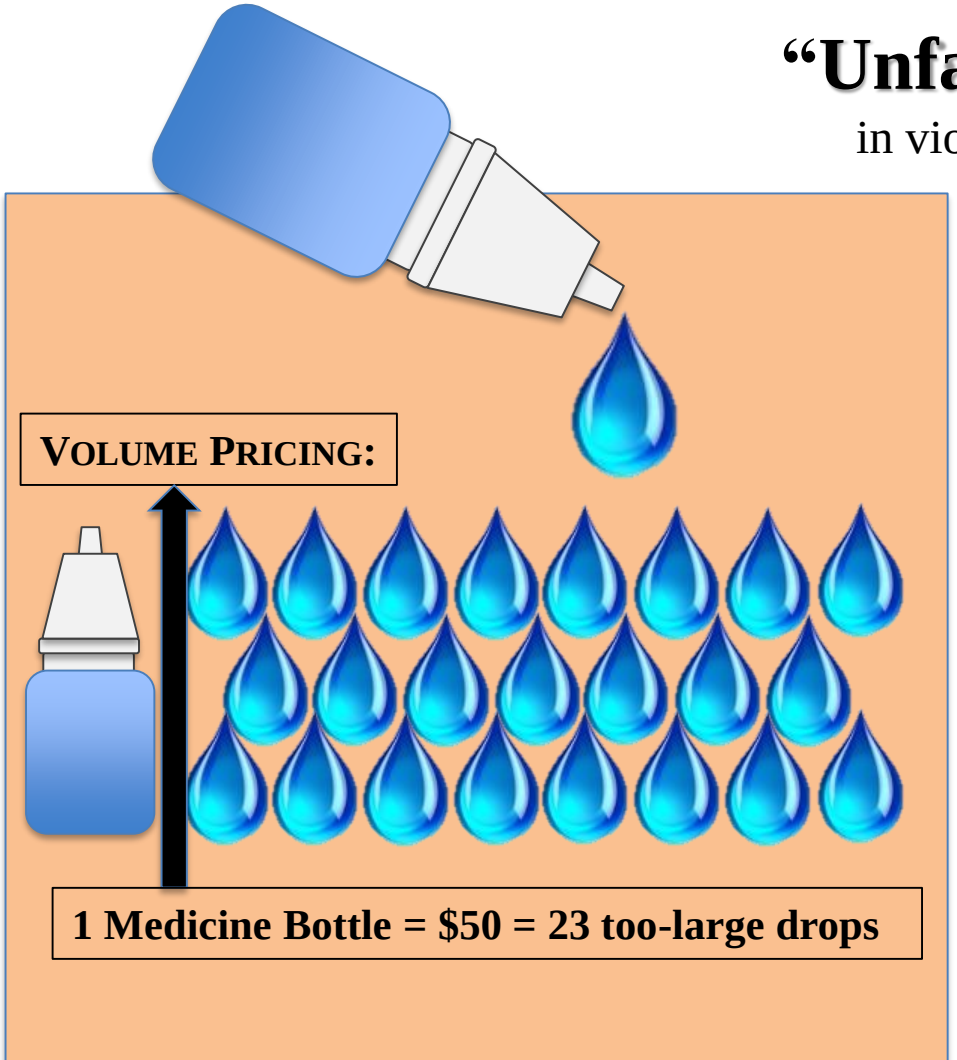
"Unfair trade/business practice"

in violation of State consumer protection laws



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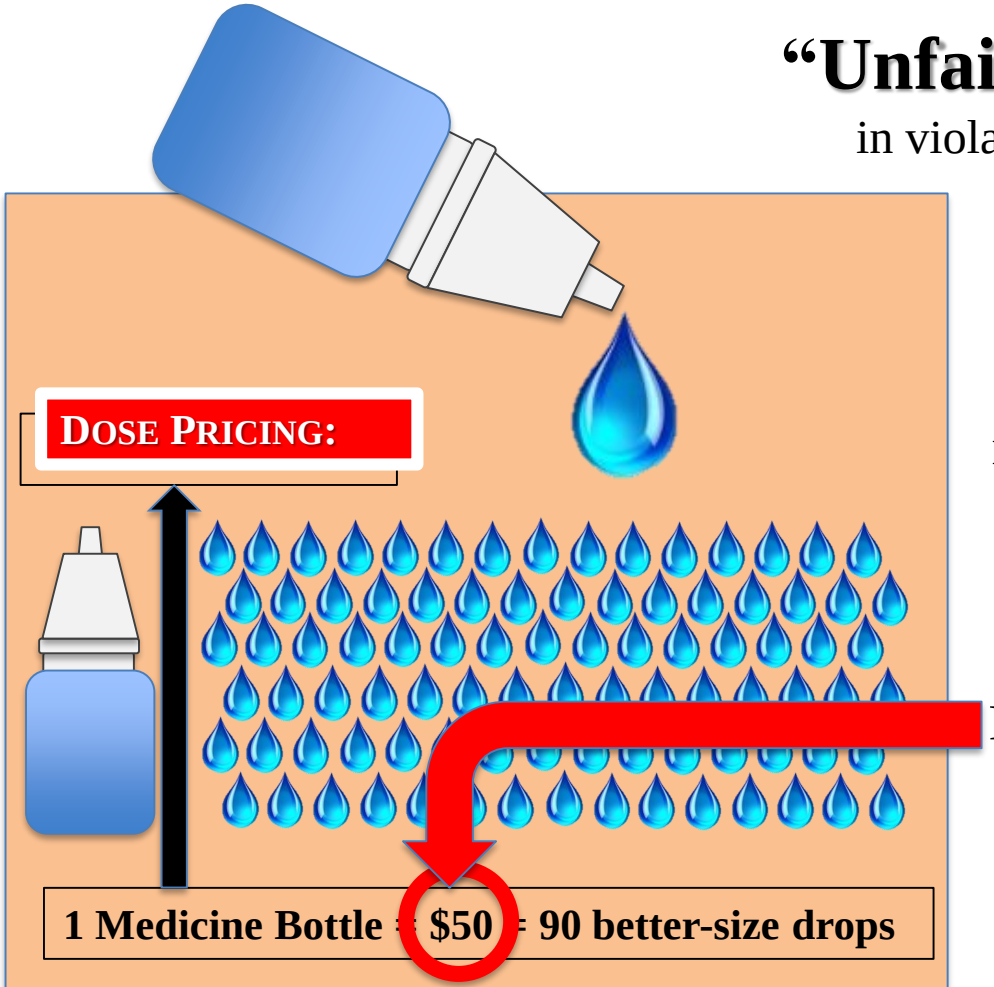
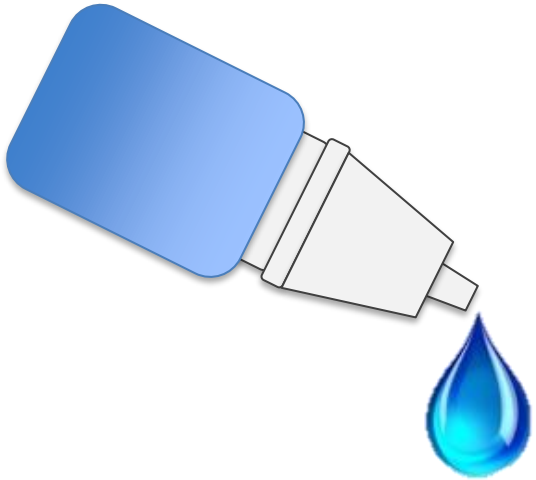
"Unfair trade/business practice"

in violation of State consumer protection laws



Courts cannot do what Ps request: isolate and change one economic variable while assuming no downstream changes.

Requires court to speculate about the decisions of independent actors.



“Unfair trade/business practice”

in violation of State consumer protection laws

Eike v. Allergan

3-0

Article III Standing

Cottrell v. Alcon Labs

2-1

Satisfies FRCP 8

[Rhrg En Banc Denied:]

3-3

Courts cannot do what Ps request: isolate and change one economic variable while assuming no downstream changes.

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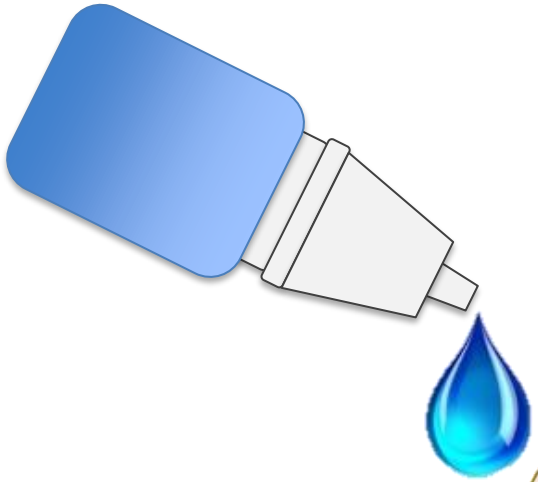
“Unfair trade/business practice”

in violation of State consumer protection laws



Eike v. Allergan

Cottrell v. Alcon Labs

China Agritech, Inc. v. Resh

U.S. Supreme Court – No. 17-432
Oral Argument: March 26, 2018

Equitable Tolling *and* Class Actions

Following dismissal, can an individual class member invoke equitable tolling to attempt another class action, or only to file an individual claim?

Top Cases: Sandoz v. Amgen

Erika Lietzan

University of Missouri School of Law

The Patent Dance

- PHSA 351(l) and 35 U.S.C. 271 contain mechanism that allows innovator & biosimilar company to litigate patent issues before biosimilar launch
- Exchange of information + generate list of patents for litigation + choose some for immediate suit

Nine Provisions

- **¶ 2: biosimilar company (BC) "shall provide" application & manufacturing info to innovator (IN)**
- ¶ 3: process by which BC & IN generate master list of relevant patents
- ¶ ¶ 4, 5: process by which BC & IN identify a subset for first phase of litigation

- ¶ 6: IN has 30 days to bring suit for first phase of litigation
- ¶ 7: process for adding patents to master list
- ¶ 8: BC must provide notice to IN no later than 180 days before commercial launch

- ¶ 9 – Limitation on Declaratory Judgment Action:
  - (A): if BC provides application under ¶ 2, then neither company can bring DJ on phase 2 patents until notice of launch
  - (B): if BC fails to complete an action under ¶ ¶ 3, 5, 6, 7, 8, then IN can bring DJ for phase 1 patents, and BC cannot.
  - **(C): if BC fails to provide application under ¶ 2, then IN can bring DJ for <u>any</u> patent that claims the product, but BC cannot.**

Theory that "Optional"

- (A): if BC provides application under ¶ 2, then . . . can bring DJ on phase 2 patents 180 days before launch
- (C): if BC fails to provide application under ¶ 2, then . . . cannot bring DJ.

Sandoz v. Amgen

- Amgen: BLA for Neupogen (filgrastim)
- Sandoz: biosimilar application, notifies Amgen that it won't be providing a copy of its application
- Amgen: petitions FDA ("make companies certify compliance") and sues Sandoz

Amgen Complaint

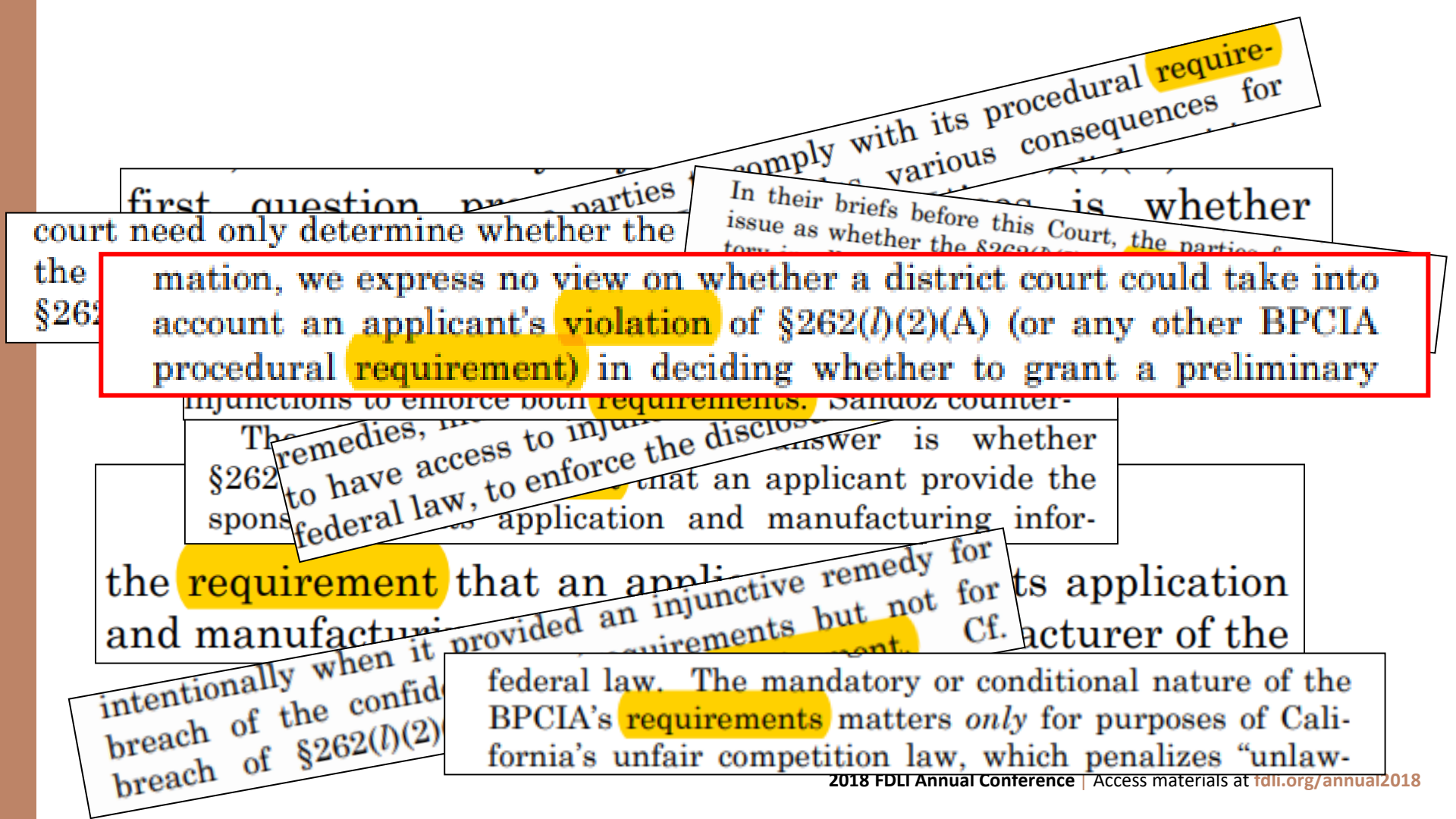
- Unfair competition under California law.
  - Order Sandoz to provide its application.
- Conversion.
  - Stop review of application until Sandoz receives permission from Amgen to cite its license.
- Patent infringement.

Top Line:
You Can Dance if You Want To 

"The first question presented by these cases is whether the requirement that an applicant provide its application and manufacturing information to the manufacturer of the biologic is enforceable by injunction. **We conclude that an injunction is not available under federal law**, but we remand for the court below to decide whether an injunction is available under state law."

But . . . Two Things to Think About

1) Justice Thomas's use of the word "required"
2) Justice Breyer's citation of *Brand X*


comply with its procedural require-
various consequences for
first question
court need only determine whether the
In their briefs before this Court, the
issue as whether the
is whether
the
§26
mation, we express no view on whether a district court could take into account an applicant's violation of §262(*l*)(2)(A) (or any other BPCIA procedural requirement) in deciding whether to grant a preliminary
injunctions to enforce both requirements. Sandoz counter-
remedies,
to have access to
federal law, to enforce the
§262
spons
answer is whether
that an applicant provide the
application and manufacturing infor-
the requirement that an
and manufacturi
ts application
acturer of the
intentionally when it
breach of the confid
breach of §262(*l*)(2)
provided an injunctive remedy for
requirements but not for
Cf.
federal law. The mandatory or conditional nature of the BPCIA's requirements matters *only* for purposes of California's unfair competition law, which penalizes "unlaw-

Remand

- “We decline to resolve this particular dispute definitively because it does not present a question of federal law.”
- “On remand, the Federal Circuit should determine whether California law would treat noncompliance with § 262(l)(2)(A) as ‘unlawful.’”
- “If the answer is yes, then the court should proceed to determine whether the BPCIA preempts any additional remedy available under state law …”
- **“The court is also of course free to address the pre-emption question first by assuming that a remedy under state law exists.”**

Conflict Preemption

- Geier v. American Honda Motor (cited in USG brief): DC law requiring airbag frustrates objective of US law (choice among passive restraint systems)

PHSA § 351, 42 U.S.C. § 262

(f) Penalties for offenses

Any person who shall violate, or aid or abet in violating, any of the provisions of this section shall be punished upon conviction by a fine not exceeding $500 or by imprisonment not exceeding one year, or by both such fine and imprisonment, in the discretion of the court.

mation, we express no view on whether a district court could take into account an applicant's violation of §262(*l*)(2)(A) (or any other BPCIA procedural requirement) in deciding whether to grant a preliminary

- Fed Cir: Federal statute provides a choice.
- Amgen: SCOTUS, is providing application required?
- SCOTUS: The requi :eable by injunction. We decline to say i on is mandatory or condition precede levant to whether violation is unfair c ate law. Federal Circuit, take the fir
- Fed Cir: We decline ation is unfair competition under state law. State law would be preempted anyway, because it conflicts with the point of the federal statute . . . to provide a choice.

JUSTICE BREYER, concurring.

The Court's interpretation of the statutory terms before us is a reasonable interpretation, and I join its opinion. In my view, Congress implicitly delegated to the Food and Drug Administration authority to interpret those same terms. That being so, if that agency, after greater experience administering this statute, determines that a different interpretation would better serve the statute's objectives, it may well have authority to depart from, or to modify, today's interpretation, see *National Cable & Telecommunications Assn.* v. *Brand X Internet Services*, 545 U. S. 967, 982–984 (2005), though we need not now decide any such matter.

Brand X (Thomas, J.)

> A court's prior judicial construction of a statute trumps an agency construction otherwise entitled to *Chevron* deference only if the prior court decision holds that its construction follows from the unambiguous terms of the statute and thus leaves no room for agency discretion.

> blank slate: Only a judicial precedent holding that the statute unambiguously forecloses the agency's interpretation, and therefore contains no gap for the agency to fill, displaces a conflicting agency construction.

Case to W… …ll States

Overtaken by events

Ruling (April 24, 2018)

- Inter partes review (IPR) does not violate Article III or the 7th Amendment.

- Explicitly (see p. 16-17) not a ruling on:
  - Whether IPR would be constitutional without judicial review
  - Constitutionality of retroactive application of IPR
  - Due process challenge of IPR
- "Finally, our decision should not be misconstrued as suggesting that patents are not property for purposes of the Due Process Clause or the Takings Clause. See, e.g., Florida Prepaid Postsecondary Ed. Expense Bd. v. College Savings Bank, 527 U. S. 627, 642 (1999); James v. Campbell, 104 U. S. 356, 358 (1882)."

Landscape in Flux

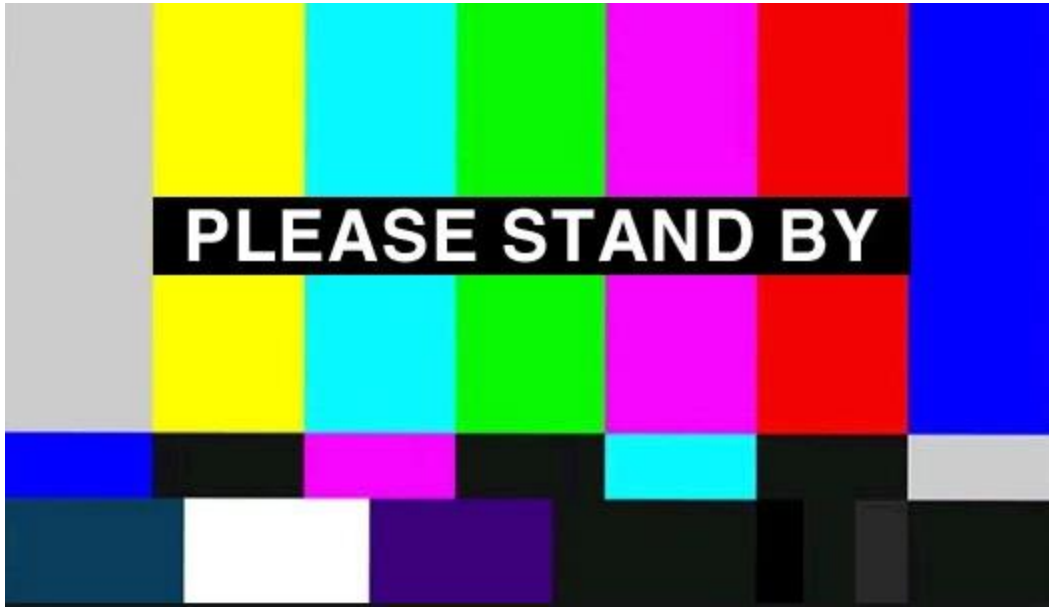
- Obligation to provide "other information that describes the process or processes used to manufacture" the biosimilar: how much is required? What if it's not enough for innovator to explain basis for claim of infringement?
- Can biosimilar company still bring DJ suit in this situation, so long as it provided its application?

Landscape in Flux

- "You can dance if you want to"
- Anyone can bring IPR (no standing rules)
- But complications:
  - Biosimilar company cannot file IPR on a patent more than one year after being served with a complaint on that patent.
  - Biosimilar company cannot file IPR if it has brought a DJ on the same patent.

Landscape in Flux

- If written decision from PTAB upholds the challenged patent, can biosimilar company seek review in the Federal Circuit even if it hasn't filed a biosimilar application yet?
- SCOTUS in SAS Institute: if PTO institutes IPR, it must decide patentability of all claims challenged
  - Implications for estoppel
  - Impact on biopharmaceutical landscape
- As a practical matter: seek IPR before application filed, then file application, to appeal IPR? File application, decline to dance, and then file IPR?


PLEASE STAND BY

Top Cases in Food and Drug Law

August Horvath

FOLEY HOAG LLP

Top Case of 2017

- *Singleton v. Fifth Generation, Inc.*, 5:15-CV-474 (BKS/TWD) (N.D.N.Y. Sept. 27, 2017).

FOLEY HOAG LLP

Product Claims

- Express claim:
  - "Handmade"
  - "Crafted in an old fashioned pot still"
- Allegedly implied claim:
  - Made in small batches
- Class injury alleged:
  - Price premium **actually** paid by consumers for perceived higher quality associated with direct human involvement and small-batch distilling

Key Issue

- Under *Comcast*, to satisfy Rule 23(b)(3) predominance requirement for class certification, plaintiff must proffer damages model estimating damages for all members of class, using common method, that matches theory of liability.
- Did plaintiff's proffered damages model satisfy this requirement?

Plaintiff's Damages Model

- Three approaches proposed.
- (1) Industry expert proposed to compare Tito's with other vodkas comparable on quality and other measures, and opine as to the premium charged for the contested claims.

Plaintiff's Damages Model

- (2) Conjoint analysis in which a specialized survey, asking subjects to select from sets of hypothetical vodkas varying as to contested claims, price and other characteristics, is analyzed to arrive at willingness-to-pay value for contested claims.

Plaintiff's Damages Model

- (3) Hedonic regression analysis, in which marketplace sales and pricing data are used to predict the impact on price of the contested claims, using features of actual vodkas as independent variables to explain their prices.

Court's Analysis

- (1) Industry expert's comparison analysis was rejected because the expert did not show a robust and systematic method of comparing the features.
- In particular the court was not satisfied with his operationalization of "quality."

Court's Analysis

- (2) Unlike some courts, this court did not reject the conjoint analysis because it measures only willingness to pay and not premium actually paid.
- Instead, court objected that "a conjoint analysis with two hypothetical products is too detached from the facts of the case to measure damages tied to Plaintiff's theory of liability."

Court's Analysis

- (3) Hedonic regression was rejected as not clearly specified. The expert made "little attempt to specify a relevant set of product attributes" to include.
- Again, in particular, there was no operationalization of vodka quality.

Result

- Class certification was denied for lack of showing of predominance of class issues.
- Case settled in late March.
- Several other courts in food advertising class actions are considering similar issues.

Case to Watch in 2018

- *Federal Trade Commission and People of the State of New York v. Quincy Bioscience Holding Corp.*, 17-3745 (2d Cir.).

Product Claims

- “Improves memory”
- “Supports healthy brain function”
- “Supports sharper mind”
- “Supports clearer thinking”

Substantiation

- One double-blind, placebo-controlled human clinical study using objective outcome measures of human cognitive function (N=218).
- Significant differences found in 2 of 8 subgroups in 3 of 9 tasks in post hoc analysis.

Decision

- Court granted Quincy's motion to dismiss.
- FTC's argument that exploratory, post-hoc subgroup analysis was likely to yield false positive significant results by chance only raised "possibility," not "plausibility," that the study does not substantiate the claims.

Appeal

- Standard of review is *de novo*.
- FTC and NY filed briefs Feb. 28.
- Quincy's appellee brief is due May 30.