Regulatory Compliance: *Global Edition*

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- ✓ Pharmaceutical and medical device companies operate globally.
- ✓ Global operations involve overlapping, and at times inconsistent, regulatory schemes.
- ✓ Foreign and domestic regulatory evidence provide dangers and opportunities at trial.

Plaintiffs' themes:

- The product is unsafe.
- Company put profits over patient safety.
- Jury is the only safeguard to protect patients and the community.

In virtually every case, plaintiffs will find regulatory evidence that requires explanation.

Our Job:

First, consider how best to keep jury's focus on individual plaintiff and causation in most cases.

Then:

- Limit admissibility of adverse regulatory evidence.
- Provide context for the regulatory evidence that comes in.
- Where helpful, use regulatory evidence affirmatively to show company's efforts and reasonableness.

- ✓ Essential to learn the drug or device's regulatory story with both the FDA and foreign regulatory agencies.
- ✓ Evaluate what regulatory evidence is likely to come in, and how negative evidence can be explained.

Agenda

FDA Evidence

- Devices: 510(k) clearance is hotly contested.
- Drugs: Usually admissible but outliers remain.
- Trial strategies.

Foreign Regulatory Evidence

- What are plaintiffs looking for?
- Inadmissibility: Irrelevance, confusion, and prejudice.
- Context at trial.

FDA

- Steps taken by a defendant to comply with FDA regulations can be a powerful counter to plaintiffs' "no one is watching the baby" mantra.

- Post-market surveillance, studies conducted with regulatory input, and label interactions with the FDA may also be useful affirmative evidence.

Before Trial: Admissibility

FDA

- Plaintiffs recognize the increasing effectiveness of FDA evidence for the defense, and in many cases are now moving to exclude regulatory evidence at trial.
- Generally, this argument is made in litigation involving devices cleared under the 510(k) process.

510(k) Devices: Clearance Excluded

Why (per plaintiffs)?

- FDA clearance is not “approval.”
- FDA clearance “does not speak to [the device’s] safety or efficacy.”
- FDA clearance does not show a company’s reasonableness in bringing the device to market.

510(k) Devices: Clearance Excluded

Judge Goodwin has repeatedly excluded clearance and other FDA evidence in mesh MDLs.

- *Lewis v. Johnson & Johnson*, 991 F. Supp. 2d 748 (S.D.W. Va. 2014)
- *Wise v. C.R. Bard, Inc.*, No. 2:12-CV-01378, 2015 WL 541933 (S.D.W. Va. Feb. 10, 2015)
- *Eghnayem v. Boston Scientific Corp.*, No. 2:13-cv-07965, 2014 WL 5461991 (S.D.W. Va. Oct. 27, 2014)
- *Tyree v. Boston Scientific Corp.*, No. 2:12-cv-08633, 2014 WL 5320566 (S.D.W. Va. Oct. 17, 2014)

510(k) Devices: Clearance Excluded

Metal-on-metal hip litigation:

> THE FACT THAT THE F.D.A. GAVE CLEARANCE TO THE DEVICE IS OF MARGINAL RELEVANCE AND MAYBE UNDULY PREJUDICE AND CONSUME AN IMMEASURABLE AMOUNT OF TIME -- AN UNREASONABLE AMOUNT OF TIME.
>
> DEFENDANT SAYS THAT THEY WILL NOT MISUSE THE CLEARANCE STATUS AS AN APPROVAL STATUS. HOWEVER, DEFENDANTS' OPPOSITION REALLY SEEMS TO SUGGEST THAT THAT IS WHAT THEIR PURPOSE IS.
>
> THERE IS A DIFFERENCE BETWEEN CLEARANCE, WHICH REQUIRES ONLY A DEMONSTRATION OF EQUIVALENCY TO A PREDICATE DEVICE, AND APPROVAL, WHICH REQUIRES A MUCH MORE THOROUGH EVALUATION OF EFFECTIVENESS AND SAFETY.
>
> IN ORDER TO PUT A -- IN ORDER TO PUT CLEARANCE INTO CONTEXT WOULD REQUIRE A FULL DESCRIPTION OF THE DIFFERENCES BETWEEN THE TWO AND TAKE AN EXTENSIVE AMOUNT OF TIME.

Kransky v. DePuy Orthopaedics, Inc., No. BC456086, Hearing Tr. at 5-6 (Cal. Sup. Ct. Jan. 18, 2013).

510(k) Devices: Clearance Excluded

Metal-on-metal hip litigation:

Oklahoma state court: Excluded all communications from the FDA to defendants, including clearance, but permitted evidence of the defendant's communications to the FDA.

Smith v. DePuy Orthopaedics, Inc., No. CJ-2011-5804, Trial Tr. at 15-16 (Okla. Dist. Jan. 14, 2015)

510(k) Devices: Clearance Admitted

Metal-on-metal hip litigation

Same product—different result.

> The Court is persuaded that Defendants are entitled to present evidence of the 510(k) clearance as it represents the process by which the device came to be on the market and is, therefore, relevant. Despite Plaintiff's protestations, the probative value outweighs the danger of unfair prejudice or jury confusion and this evidence will also be subject to a special jury instruction. Therefore, Plaintiff's motion to exclude evidence of 510(k) clearance is denied.¶

McCracken v. DePuy Orthopaedics, Inc., No. 11 dp 20485, Slip Op. at 9 (N.D. Ohio July 26, 2013).

510(k) Devices: Clearance Admitted

Metal-on-metal hip litigation

So, we hear -- everybody in this jury is going to say what did the FDA say about this because that's the world we live in. They want to know. You all are going to have to make your arguments concerning what it means what the FDA said.

Here you're saying to DePuy you didn't act as a reasonably careful company. That's your negligence claim. In the punitive claim you're saying more than that. You weren't just negligent, that you were in fact willful and wanton. So, based on that they get to defend themselves.

So, since there is no rule that keeps it out, I don't -- I think the jury is going to wonder, what about the FDA. And then it's going to be your job, both of your jobs, to convince them what that means.

Strum v. DePuy Orthopaedics, Inc., No. 2011 L 009352, (Ill. Cir. Ct. March 1, 2013)

Admissibility of FDA clearance evidence remains a hotly contested, unresolved issue.

Appeals pending:

- Fourth Circuit (*Cisson*)
- California Court of Appeal (*Kransky*)

Drugs

- ✓ Courts are less likely to exclude FDA drug approval evidence, because approval involves a “safe and effective” finding by the FDA through the NDA process.
- ✓ But there are outliers.

Drugs

Excluded:

- FDA approval of labeling and safety communications.
- Compliance with FDA regulations.

Why?

- FDA standards differ from Nevada standards.
- FDA compliance not a complete defense to punitive damages.
- Preemption barred under *Wyeth v. Levine*.

Drugs

Zometa court's response to defense challenge to plaintiffs' regulatory expert: *exclude regulatory evidence altogether*.

> Plaintiff cannot have her cake and eat it too; she cannot bring common law claims not grounded in FDA regulations only to present an expert to opine on whether defendant violated those regulations. By the same token, the Court will not permit defendant to litigate the case in the shadow of the FDA.

Hogan v. Novartis Pharm. Corp., No. 06-CIV-0260, 2011 WL 1533467 (E.D.N.Y. Apr. 24, 2011)

Drugs

Regulatory Evidence Irrelevant:

- No federal claim or fraud-on-FDA claim.
- No complete defense based on federal law (preemption or compliance).
- "[E]vidence that reveals nothing more than responsiveness to the FDA is irrelevant."
- Corporate conduct not at issue because punitive damages not sought.

Hogan v. Novartis Pharm. Corp., No. 06-CIV-0260, 2011 WL 1533467 (E.D.N.Y. Apr. 24, 2011)

Drugs

Regulatory Evidence Prejudicial:

- Evidence of compliance or non-compliance "has all kinds of danger, [and] prejudicial impact."

Hogan v. Novartis Pharm. Corp., No. 06-CIV-0260, 2011 WL 1533467 (E.D.N.Y. Apr. 24, 2011)

Drugs

I am mindful that without Dr. Parisian and defendant's mention of its efforts to cooperate with the FDA, the jury will be operating in a universe that is devoid of the heavy regulatory framework that affects the development and marketing of pharmaceutical products. Nevertheless, I find that the benefits of excluding this evidence outweighs its costs; the Court's review of the submitted exhibits and Dr. Parisian's report reveal that some of the battlegrounds the parties have chosen are simply not the ones pled in the complaint or stated in the JPTO. And as the parties seem to agree at the Conference, even if the FDA's role in this litigation were properly described, it would be a side show; if the Court allowed Dr. Parisian to testify, the side show would turn into the main event. Thus, the jury's task will be a narrow one and involve the application of state law only.

Hogan v. Novartis Pharm. Corp., No. 06-CIV-0260, 2011 WL 1533467 (E.D.N.Y. Apr. 24, 2011)

Drugs

Both courts excluding FDA evidence:

- Reasoned that because federal law did not provide a complete defense, FDA approval or compliance had *no* relevance.
- Were concerned that FDA issues would displace state tort law at trial.

At Trial

At Trial: If FDA Evidence Is *Admitted*

Plaintiffs will criticize the company's FDA disclosures and interactions:

- Information company gives to the FDA is incorrect, selective, or "massaged."
- Information company does not give to the FDA makes submissions misleading.
- Interactions with the FDA are improper, including fighting label changes or offering alternative explanations for troubling data.

At Trial: If FDA Evidence Is *Admitted*

Legal objection to attacks on FDA submissions

Buckman: "State-law fraud-on-the-FDA claims inevitably conflict with the FDA's responsibility to police fraud consistent with [its] judgment and objectives."

Buckman Co. v. Plaintiffs' Legal Committee, 531 U.S. 341 (2001).

Lofton: State-law warnings claims based on fraud-on-the-FDA are also barred.

Lofton v. McNeil Consumer & Specialty Pharm., 672 F.3d 372 (5th Cir. 2012).

At Trial: If FDA Evidence Is *Admitted*

Does *Buckman* bar evidence? Courts are split.

- ***Yes***: Trasylol MDL excluded withholding-from-FDA arguments as requiring "speculation and second-guessing" FDA's response, violating "the principles laid out in *Buckman*."
  In re Trasylol Prods. Liab. Litig., 763 F. Supp. 2d 1312 (S.D. Fla. 2010).

- ***No***: Yasmin/Yaz MDL allowed withholding-from-FDA arguments; *Buckman* "is a claim preemption case . . . not an evidence preemption case."
  In re Yasmin & YAZ, No. 3:09-MD-02100, 2011 WL 6301625 (S.D. Ill. Dec. 16, 2011).

At Trial: If FDA Evidence Is *Admitted*

Countering withholding-from-FDA attacks

- **FDA is sophisticated and powerful.**
  - Expertise.
  - Access to information.
  - Mechanisms to punish and deter.
- **FDA is focused on particular types of information.**
  - Safety or efficacy data and analyses.
  - *Not* emails and speculation.
- **FDA had the information needed in this case.**
  - Outcome unchanged.

At Trial: If FDA Evidence Is *Excluded*

- Offer industry standard testimony instead.
- Stay vigilant for plaintiffs opening the door.
- Preserve the record.

Agenda

FDA Evidence

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Foreign Regulatory Evidence

- What are plaintiffs looking for?
- Inadmissibility: Irrelevance, confusion, and prejudice.
- Context at trial.


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JAPAN
CFDA China Food and Drug Administration
CDSCO
TGA Health Safety Regulation

Foreign regulatory evidence includes:

- Safety and labeling communications
- Adverse event reports and databases
- Calls for additional studies, testing, and data
- Adverse health and safety determinations
- Safety alerts and warning letters
- Recalls and withdrawals—voluntary or mandated

Foreign Regulatory Evidence

"I have not seen a single regulatory decision that was fully consistent across regulatory agencies."

. . .

"There are increasing regulatory differences across the regions."

Head of Research, Sanofi (France), March 18, 2015

Foreign Regulatory Evidence

Attacking the Product: Design and Safety

- Denial of approval in other markets.
- Safety and adverse event data from expanded patient population.
- Recall or withdrawal from a foreign market.

Foreign Regulatory Evidence

Attacking the Product: Warnings

- Different information in foreign labels.
- Regulatory investigations of label's accuracy.
- Foreign study commitments.
- Warning letters for promotional materials.

Foreign Regulatory Evidence

Attacking the Product: Manufacturing

- Criticisms of manufacturing facilities and quality procedures.
- Product complaints and related company investigations.

Foreign Regulatory Evidence

Attacking the Company

- Label is updated abroad but not in U.S.
- Response abroad appears motivated by protecting profits and U.S. sales.
- Sales halted in other countries but continue in U.S.

Before Trial: Admissibility

Foreign Regulatory Evidence

Plaintiffs argue admissibility based on:

- Notice of safety issues.
- Defendant's state of mind or reasonableness.

Foreign Regulatory Evidence

Defendants argue inadmissibility based on:

- Irrelevant.
- Confusing to jury and prejudicial.
- Time-consuming mini-trials needed to put foreign regulatory actions or statements into context.

Foreign Regulatory Evidence

Plaintiffs argue relevance based on:

- Notice of safety issues.
- Defendant's state of mind or reasonableness.

Foreign Regulatory Evidence

Excluded as Irrelevant

"The Court finds that ***any*** **discussion of foreign regulatory actions is irrelevant** to the current litigation and should therefore be excluded."

In re Viagra Prods. Liab. Litig.,
658 F. Supp. 2d 950, 965 (D. Minn. 2009)

Foreign Regulatory Evidence

Admissible for Notice or Motive

"The probative value of McNeil's and its subsidiaries and sister companies' foreign labeling, as it relates to **Defendants' knowledge of the risks** and **willfulness in not sharing certain of those risks on its American OTC label**, is not substantially outweighed..."

Newman v. McNeil Consumer Healthcare, No. 10 C 1541, 2013 WL 4460011 (N.D. Ill. Mar. 29, 2013)

Foreign Regulatory Evidence

Admissible for Notice or Motive

"[T]he plaintiffs are not presenting final regulatory action to which a jury might defer out of confusion. Rather they are presenting only preliminary actions in Europe, in conjunction with defendants' responses which were **intended to limit the impact potential regulatory action in Europe might have on the U.S. market** for the drug."

In re Levaquin Prods. Liab. Litig., No. 08-1943, 2010 WL 4676973 (D. Minn. Nov. 9, 2010)

Foreign Regulatory Evidence

Rebutting Notice Arguments

Underlying Information → Notice

Regulatory *Response* → Not Notice

"[N]otice is not dependent on government action."

In re Baycol Prods. Liab. Litig.,
495 F. Supp. 2d 977 (2007)

Foreign Regulatory Evidence

Rebutting Notice Arguments

In re Seroquel:

- Excluded foreign label changes and foreign approval status.
- Regulatory *actions* are distinct from underlying *information*.
  - But limited evidence of information communicated by regulators to company may be admissible for notice.

Foreign Regulatory Evidence

Rebutting Notice Arguments

"After all, **what AstraZeneca was being told** by foreign regulators about the safety of Seroquel is more probative of issues of notice, knowledge and scienter than **what the foreign agencies decided to do—or required AstraZeneca to do**—in the face of that information."

In re Seroquel Prods. Liab. Litig.,
601 F. Supp. 2d 1313 (M.D. Fla. 2009)

Foreign Regulatory Evidence

Rebutting Notice Arguments

- Confusion
- Prejudice
- Waste of Time

Foreign Regulatory Evidence

Finding Confusion and Prejudice

"[A] lay juror would have difficulty distinguishing that the term 'causality assessment,' as the term relates to safety surveillance, is not the same as 'causation.' In fact, **it is highly probable that a juror would perceive the company's "yes" response in the causality assessment field as an admission** by Defendants' physicians that Accutane did in fact cause the adverse events reported."

In re Accutane Prods. Liab., No. 804-MD-2523T-30TBM, 2007 WL 1288354 (M.D. Fla. May 2, 2007)

Foreign Regulatory Evidence

Finding Confusion and Prejudice

"To admit evidence about the foreign regulators' actions regarding Seroquel without providing context . . . would **strip the jury of any framework** within which to evaluate the meaning of that evidence. Absent such background and context, **a jury might be more inclined to abdicate its responsibilities and defer to the negative decisions of three foreign regulators** regarding Seroquel's safety."

In re Seroquel Prods. Liab. Litig.,
601 F. Supp. 2d 1313 (M.D. Fla. 2009)

Foreign Regulatory Evidence

Finding Waste of Time

"On the other hand, allowing AstraZeneca to introduce this evidence would result in **a series of "mini-trials"** regarding the grounds for the decisions and the regulatory schemes of the three foreign countries involved. **This would confuse the jury and waste everyone's time.**"

In re Seroquel Prods. Liab. Litig.,
601 F. Supp. 2d 1313 (M.D. Fla. 2009)

Foreign Regulatory Evidence

Other Arguments for Exclusion

Role of Experts

Rezulin MDL: "[T]he challenged testimony focuses on a set of non-technical factual allegations . . . that plaintiffs would use as springboards for arguments about Warner-Lambert's conduct in the United States. **None of it qualifies as 'scientific, technical or other specialized knowledge.'"**

In re Rezulin Prods. Liab. Litig.,
309 F. Supp. 2d 531 (S.D.N.Y. 2004)

Foreign Regulatory Evidence

Other Arguments for Exclusion

Role of Experts

Trasylol MDL: Suzanne Parisian "**merely summarizes and restates the findings of the foreign Inspection Reports and the proposed change** for Trasylol's EU label, and thus her testimony can not be considered expert testimony that would be helpful to the trier of fact."

In re Trasylol Prods. Liab. Litig., 709 F. Supp. 2d 1323 (S.D. Fla. 2010).

At Trial

Be Prepared

- Regulatory story is complex.
- *Global* regulatory story even more so.
- Locating admissible foreign evidence can be challenging and take time.

Issues Requiring Explanation

- **Criticism of adverse event reporting.**
  - What needs to be reported and when varies between jurisdictions.
- **Preliminary safety reports.**
  - Preliminary regulator concerns may later be proven inconsequential.

Issues Requiring Explanation

- **Outlier regulatory decisions.**
  - Driven by issues other than science?
  - May be minimized by weight of authority from other jurisdictions.
- **Withdrawal from a foreign market.**
  - May be a business decision driven by differing patient populations, competitor products, or other non-safety issues.

Affirmative Evidence

- Positive reviews or statements by a foreign regulatory body.
- Labeling discussions with a foreign agency.
- Guidance from foreign agencies on responding to safety data.
- Internal company safety reviews and analyses of foreign regulatory data.


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Thank you.