There They Go Again

Thursday, October 20, 2011

A lot of people think that Ronald Reagan won the presidency in 1980 in his first debate when he replied jokingly "there you go again" to then-President Carter's attempt to portray him as some sort of rightwing nut intent upon destroying accepted government programs like Medicare.

Whether one believes that President Reagan's election was a good thing or a bad thing, there's no denying that his disarming line was effective in dispelling his opponent's attempt to sow fear of his then unknown policies.

We've confronted similar situations ourselves as, periodically, some law review article or another decides to tilt at the windmill of FDA regulatory informed consent claims in off-label use cases. Bexis dealt with that topic in a law review article he wrote long before he wised up and started blogging. Beck & Azari, "FDA, Off-Label Use, and Informed Consent: Debunking Myths and Misconceptions," 53 Food & Drug L.J. 71 (1998) (available here).

Here on the blog, we addressed this topic back in 2007, critiquing an article that advocated informed consent suits against doctors for not discussing the non-FDA-approved status of off-label use, essentially as a means of indirectly punishing drug companies for allegedly promoting such uses too effectively.

We're pleased to say that nothing came of that 2007 article. The law is still as we stated back then. Legal information, like whether a 50 mg dose is FDA approved but a 75 mg dose isn't, remains beyond the pale of informed consent. Only the actual medical risks/benefits/alternatives of, say, our hypothetical 50 mg (on-label) versus 75 mg (off-label) are relevant to informed consent:

"[T]he FDA labels given to a medical device do not speak directly to the medical issues surrounding a particular surgery. The category into which the FDA places the device for marketing and labeling purposes simply does not enlighten the patient as to the nature or seriousness of the proposed operation, the organs of the body involved, the disease sought to be cured, or the possible results. The FDA administrative label does not constitute a material fact, risk, complication or alternative to a surgical procedure. It follows that a

physician need not disclose a device's FDA classification to the patient in order to ensure that the patient has been fully informed."

Southard v. Temple University Hospital, 781 A.2d 101, 107 (Pa. 2001) (Bexis' case); accord, Earle v. Ratliff, 998 S.W.2d 882, 891-92 (Tex. 1999); Hansen v. Universal Health Services, 974 P.2d 1158, 1159-60 (Nev. 1999); Packard v. Razza, 927 So.2d 529, 534 (La. App. 2006); Blazoski v. Cook, 787 A.2d 910 (N.J. Super. A.D. 2002) (Bexis' case); Alvarez v. Smith, 714 So. 2d 652, 654 (Fla. App. 1998); Osburn v. Danek Medical, Inc., 520 S.E.2d 88, 92 (N.C. App. 1999), aff'd mem., 530 S.E.2d 54 (N.C. 2000) (Bexis' case); Klein v. Biscup, 673 N.E.2d 225, 231 (Ohio App. 1996) (Bexis's case); Balderston v. Medtronic Sofamor Danek, Inc., 285 F.3d 238, 239 n.2 (3d Cir. 2002) (applying Pennsylvania law) (Bexis's case); Bogle v. Sofamor Danek Group, Inc., 1999 WL 1132313 *7 (S.D. Fla. April 9, 1999) (Bexis's case); In re Orthopedic Bone Screw Products Liability Litigation, 1996 WL 107556 (E.D. Pa. March 8, 1996), reconsideration denied, 1996 WL 900351 (E.D. Pa. May 21, 1996) (Bexis's case); cf. Daum v. Spinecare Medical Group, 61 Cal. Rptr.2d 260, 271-73 (Cal. App. 1997) (FDA regulatory status outside common law informed consent; discussion of status only required where FDA regulations say so).

Since 2007, the only contrary authority that we know of was a rogue South Dakota federal court, predicting (in blatant violation of Erie principles) that South Dakota, uniquely, would allow a regulatory informed consent claim. We excoriated DeNeui v. Wellman, 2009 WL 4847086 (D.S.D. Dec. 9, 2009), here. Even in DeNeui, however, the regulatory informed consent claim proved to be a lousy theory. The plaintiff lost at trial, proving that at least sometimes juries have more sense than judges.

On the good side of the ledger, Maryland's highest court agreed, in University of Maryland Medical System Corp. v. Waldt, 983 A.2d 112 (Md. 2009), that purported informed consent "expert" testimony, solely on the point that off-label use is not FDA "approved," was excludable as not "material" in an informed consent case:

"[Plaintiffs] proffer was that [their expert] would testify about the approved uses of the neuroform stent. . . . The intermediate appellate court explained . . . that the only proffered (albeit vaguely) substantive testimony of [plaintiffs'] expert] was that the neuroform stent device was not approved for use on [the patient's] type of [condition]. This is not a proffer of a risk inherent to the procedure that [the patient] underwent. . . . We

agree with the intermediate court that no testimony was proffered concerning the material risks of the procedure that would make out a prima facie case for informed consent."

Id. at 129-30 (partially quoting lower appellate court). Thus now, as in 2007, there is no appellate authority, either in federal or state court, supporting a claim for FDA regulatory informed consent anywhere in the country.

But now, here they go again – trying to scare us that off-label use "may not be safe or effective," and therefore, if doctors don't use the magic word "unapproved" they should be liable for breach of informed consent. We've just read a (relatively) new article, Rosoff & Coleman, "The Case For Legal Regulation Of Physicians' Off-Label Prescribing," 86 Notre Dame L. Rev. 649 (2011), also available online here, that once again attempts to resurrect claims for FDA regulatory informed consent.

The Rosoff article relies on statistics that "[m]ost physicians don't keep track of FDA-approved uses of drugs," p. 652 n.13, and advocates forcing these "ignorant," id., doctors to learn the FDA regulatory status of all the drugs they use so they can regurgitate that information to their patient. We don't think that's a good use of scarce physician time. We'd much rather that doctors spend whatever time they have left for education brushing up on the medical risks and benefits of their therapies. That's what doctors are trained to do. Tracking the ins and outs of drug approvals on the FDA's website should be left to us lawyers.

But leaving well enough alone would mean less litigation, and Rosoff and company can't have that. They perceive a need – not presently being met – for the law to "micromanage medical practice." Article at 675. After all, more litigation means more jobs for lawyers. More jobs for lawyers means that law students might find more jobs. Ultimately, that might mean more jobs (or at least not fewer jobs) for law professors and law review editors (at least to an economic determinist). The Rosoff article would require doctors to learn the FDA regulatory status of hundreds of drugs and medical devices and then, on threat of being sued, doctors would have to describe standard of care medical treatments (which many off-label uses are) as "unapproved" so patients will be scared away from such treatments.

At least the Rosoff article recognizes that there are various types of off-label use. It classifies them as: (1) "OLU justified by high-quality evidence"; (2) "OLU justified by some but not high-quality evidence"; (3) "OLU justified by the need or desire to innovate"; and (4) what they call "unjustified" (we'd say "experimental") off-label use. Article at 652. Indeed, there are literally

hundreds of well-accepted off-label uses listed in compendia such as the United States Pharmacopeial Drug Information, and the American Hospital Formulary Service Drug Information for which federal government programs provide reimbursement notwithstanding their off-label status. Alternatively, the Physicians Desk reference also lists "routine" off-label uses for hundreds of "specific medical problems." PDR at "forward."

So what's the fuss? Why should doctors have to go beyond their well-established duties of discussing medical risks and benefits (such as that "experimental" off-label use isn't backed by any medical evidence that it will be safe or effective) and discuss FDA regulatory status as well?

The Rosoff article counters by stating "it is difficult to imagine that there is not a more material fact than that a proposed treatment's – in this case, an OLU's – safety and efficacy have not been established." Article at 654. That sort of argument stuffs the rabbit deep in the hat.

Established by whom?

There are many drugs – typically generics – and many medical conditions – chiefly uncommon ones – as to which the effectiveness of treatment has been established by decades of clinical experience. Running the sort of clinical trials that the FDA requires for approval is expensive as all get out (a technical term). If there's no patent protection, or only a small market, there won't be FDA approval no matter how safe or effective the use is. Again, we're economic determinists.

Or maybe there is FDA approval. Suppose a company is pushing a new drug use through FDA channels, which can take years. On date X the use is off-label, even though a bunch of published studies have been run and the material is being considered by the FDA. On date X +1, the FDA approves the use. Why should the informed consent discussion be different on date X, as opposed to date X +2, when every scrap of medical information is identical? Why should doctors have to keep track of FDA approvals?

We say they shouldn't.

Whether safety of effectiveness of a particular drug use is "established" for purposes of medical treatment (as opposed to FDA regulatory purposes) depends on the quality of the medical information on which the treatment is based. That's what doctors are trained to

evaluate. That's all we think they should be legally required to discuss with their patients in informed consent discussions.

The Rosoff article runs away at high speed from these situations. No, they say, we're worried only about "problematic" off-label use:

> "It is antithetical to patient welfare to prescribe such products because they may be affirmatively harmful. Even if they are not, they preclude alternative approaches with a proven track record of effectiveness. Prescribing problematic OLU is anachronistic medical ethics because modern ethics call for evidence-based medical practice and, correspondingly, preclude experimentation outside of formalized trials with built-in safeguards to protect patient-subject health and decisional autonomy. By definition, problematic OLU are the opposite of evidence-based medical practice. And by definition, they are experimental, albeit with more or less of a basis for trusting in the outcome of the experiment depending on the degree of evidentiary support at issue. On the latter point, it has been well over fifty years since Nuremberg, when societies around the world – including the United States – rejected the notion that experimenting with patients, even ostensibly in their own interests, was permissible in the absence of consent for the experiment."

Rosoff article at 680. So "problematic' off-label use is what the Nazis did. Let's break out our "definitions" and define it as "non-evidence based" and "experimental" (Rosoff has a philosophy degree, so he knows that he who defines the terms, wins the argument). That's what needs greater "regulation" (but they advocate lawsuits, not real regulation), not the well established stuff. Article at 656-67. Sorry, we don't buy that, either. Who is going to define what's "problematic" and what's not?

Lawyers whose sole financial interest is in bringing lawsuits, that's who. The Rosoff article's primary – indeed only – concrete recommendation is to resurrect regulatory informed consent as a cause of action. Article at 682-84.

That means we get inevitable litigation creep. Lawyers certainly can't be trusted to sue only over something truly "problematic." Look at what the food fascists sue over in California, one timely example that comes immediately to mind. Or see our prior post about plaintiffs arguing that doctors have some sort of informed consent duty to tell patients about preemption. No legal doctrine safe from abuse – certainly not one as malleable as "informed consent." Doctors are by and large litigation averse people, and if they weren't, their insurers are. Allow a pure

regulatory informed consent claim anywhere, and doctors will be forced to subscribe to the Code of Federal Regulations everywhere. There's a big camel behind that nose.

And as a practical matter, the claim is totally unnecessary, because doctors already have a duty to be informed about the medical basis of the treatments they prescribe. It's called "evidence based medicine." We're in favor of it and we discussed it at some length here. If treatment A is reasonably effective, and treatment B is based on a wing and a prayer, we don't need any new cause of action to enforce safe medical practice. Patients should get the comparative medical evidence, and if they don't there's already a cause of action for that, traditional informed consent.

Conversely, if there's really no well established alternative to an off label use, then what good does it do, after the doctor has said "you've got six months to live but a few case reports suggest that treatment X might help," to add – "oh, by the way, the FDA hasn't approved it either."

None. Nada. Zilch. Zip.

You don't have to believe our pro-defense blather to demonstrate the strong potential for litigation creep. It's visible, plain as day, in the Rosoff article itself. Check out page 672, where the article describes a "pedicle screw used off-label as an 'internal fixation device' in the context of spinal fusion surgery" as a form of "experimental OLU" to which its proposed remedies would apply. The article's discussing bone screws, and we happen to know a little about bone screws. And the truth about bone screws is that they're about as far from "experimental" or "problematic" as you can get.

Rather, pedicle screw fixation was, and is, the medical standard of care – so much so that the FDA itself was unable to organize the usual clinical trials, precisely because it would have been unethical to withhold standard of care treatement. Rather, the FDA had to resort to a retrospective cohort study to resolve the labeling issue and get the approved labeling for bone screws caught up to medical reality. Again, don't believe us (if you don't want to). It's all laid out in the Federal Register by the FDA itself. See 63 Fed. Reg. 40025-41 (FDA Jul. 27, 1998).

In that Federal Register publication – not cited in any of the Rosoff article's 139 footnotes – the FDA "confirmed" that bone screws used for pedicle fixation raise "no new issues relating to

the[ir] safety or effectiveness." Id. at 40027. Over four years of FDA analysis, and a huge cohort study, determined:

- The data "reviewed as a whole . . . demonstrate[d] the safety and effectiveness of pedicle screw spinal systems." Id. at 40028 (item 2).
- "[P]edicle screw spinal systems exhibit adequate mechanical strength, rigidity, and fatigue resistance." Id. at 40033 (item 17).
- The "incidence" of "adverse outcomes is no greater when a pedicle screw spinal system is used." Id. at 40031 (item 4).
- "[P]remarket approval is not necessary to provide reasonable assurance of safety and effectiveness." Id. at 40034 (item 22).

So please excuse us when we scoff at the Rosoff article's claim to limit its proposal to "problematic" off-label uses. That's a tissue-paper thin pretext that vanished when the article itself asserts that a use that the FDA **actually did approve** was nonetheless "experimental." If Rosoff *et al.* couldn't do their homework well enough to avoid branding well-established (no longer) off-label uses as "experimental," we have zero confidence that, in practice, lawyers litigating cases (or judges adjudicating them) would be any more careful. Make no mistake about it, whatever legal restrictions the Rosoff article aims at "problematic" off-label used would also be asserted against all other off-label uses – probably without even a decent period for plausible deniability.

There are, however, a lot of good reasons for off-label use, even of the "problematic variety. One is the lack of good alternatives. Take Alzheimers, for example. We saw a story not too long ago in the *Science News* (about the limit of our capacity to digest technical issues) about some scientific evidence (a mouse study and anecdotal brain scan results) suggesting that certain antidepressants may reduce the plaques that are characteristic of the disease. That's certainly not enough for FDA approval, but with no good treatment alternative, what's unethical about trying it? We assume that current informed consent – involving medical risks, benefits, and alternatives – is given. Why is anything more, particularly the fact that the FDA hasn't approved these drugs for that use, needed? Why would the Rosoff article equate such a thing with Nazi experiments? Their home state of North Carolina (article at 665) certainly wouldn't. There is no "per se rule requiring the jury to be instructed that a health care provider in every

instance has a duty to inform a patient of the experimental nature of a proposed treatment procedure." Osburn, 520 S.E.2d at 92.

The Rosoff article also bases its proposals to litigate FDA regulatory status on an assertion, admittedly not based on any "empirical" data, that "most patients erroneously believe that the drugs their doctors prescribe for them have been determined – somehow, by someone – to be safe and effective for the uses to which they will be put." Article at 673. It then goes on to argue, based on nothing more than personal prejudices, that doctors have some duty to correct that misconception. See Id. at 683 ("since it appears that most patients mistakenly believe that FDA approval codes for safety and efficacy . . . FDA status is medically material information"). Well, poll after poll after poll (that's actual "empirical" data) has shown that a majority of Americans believe in angels. Heaven help us if Rosoff's argument was applied to the clergy.

But more to the point, there's no precedent in creating a duty to warn based upon a admittedly "mistaken" belief. Doctors (or anybody) cannot be held liable for not clearing up a public misconception that they had no part in creating. The law is (and always has been) that there is no duty to rescue someone from a peril not of the defendant's own making. E.g.:

> "We know of no principle of law by which a person is liable in an action of tort for mere nonfeasance by reason of his neglect to provide means to obviate or ameliorate the consequences of the act of God, or mere accident, or the negligence or misconduct of one for whose acts towards the party suffering he is not responsible. If such a liability could exist, it would be difficult, if not impossible, to fix any limit to it."

Estate of Cilley v. Lane, 985 A.2d 481, 489 (Me. 2009); see generally Restatement (Second) of Torts §314 (1965) ("that the actor realizes or should realize that action on his part is necessary for another's aid or protection does not of itself impose upon him a duty to take such action"). This isn't to say that pro-liability law professors haven't tried to create such a duty, e.g., Weinrib, "The Case for a Duty to Rescue," 90 Yale L.J. 247 (1980), but the law has had too much common sense to adopt such nebulous liability. The Rosoff article is, plain and simple, an attempt to create a duty to rescue in the particular area of off-label use.

Nowhere is the Rosoff article's disrespect, bordering on contempt, for the medical profession more apparent than it's blowing off the argument (as "specious") that it's onerous to force doctors to learn, and then discuss with their patients the FDA regulatory status of anything and

everything that's used off-label. These are the guys, after all, who couldn't be bothered to learn the correct FDA regulatory status of bone screws before condemning them as "experimental" when in fact that use has been approved by the FDA since 1998. The pace of medical advance is high and increasing. So are the numbers of patients a lot of doctors have to see in this era of managed care. There's less time to talk to patients, so the quality of discussion has to go up, not be diverted into legalisms. Meanwhile the FDA is being starved of necessary resources (see Wyeth v. Levine, 129 S. Ct. 1187, 1203 n.11 (2009) (collecting data)). Thus, the gap between what doctors can do therapeutically for their patients and what the FDA can do gets ever larger. We don't know where Rosoff *et al.* expect doctors to get all this additional time to look up FDA regulatory information every time they propose what may be an off-label use, see Article at 685, but we'd hope that instead doctors would educate themselves about new medical information. That's real "evidence-based medicine" – not using absence of FDA approval as some sort of "proxy" for the real thing. Article at 683.

Nor is it correct to say, as the Rosoff article does, that if we don't allow regulation by lawsuit, there's no regulation of informed consent with respect to FDA regulatory status. While the FDCA precludes the FDA from regulating off-label use, informed consent practices relating to off-label use (and anything else) are subject to state regulation if the state cares to do so. Cf. Cordray v. Planned Parenthood Cincinnati Region, 911 N.E.2d 871 (Ohio 2009) (describing state regulation of off-label use of abortifacient drug). **No state anywhere has chosen to adopt – legislatively or regulatorily – a informed consent requirement that physicians discuss FDA regulatory status of off-label uses.** The Rosoff article laments the lack of actual state-law regulation, even by medical malpractice:

> "The best indication of the ineffectiveness of medical malpractice law as a tool to regulate OLU is probably the dearth of published cases, either reported (useful as precedent in future cases) or unreported (officially unavailable as precedent) in which off-label use by a medical provider was a focus of the plaintiff's case. Furthermore, the substance of the published decisions reinforces the suggestion from the numbers that off-label prescribing is a weak basis for finding liability against a physician."

Article at 666. Actually, the approach of the states to off-label use goes beyond what the Rosoff article cares to admit. Most state regulation of off-label use is exactly the opposite of the "cut off reimbursement" philosophy of the article (pp. 688-89, advocating non-reimbursement by both government programs and private insurers), and instead has sought to **increase** reimbursement of off-label uses. E.g., N.J. Stat. §26:1A-36.9(c).

We draw a different conclusion than the Rosoff article from the consensus of state laws. We think that this uniform lack of action by any of the the fifty states is telling. If no state has chosen to impose a regime of regulatory informed consent, that tells us: (1) that the supposed "problem" to which the Rosoff article seeks a an admittedly "new" and "controversial" solution (Article at 659), isn't really that much of a problem, and (2) the prevailing common law, limiting informed consent to medical risks and benefits, has gotten it right. If it ain't broke, don't fix it.

Thus, we think that the Rosoff article combines the worst attributes tort triumphalism (a belief that lawsuits can solve anything), with a chilling disrespect for science and medicine – especially the ability of doctors to exercise their professional judgment independently in the best interests of their patients.

Doctors deserve more credit than that. They're highly trained professionals. If an off-label use is prevalent, that's usually because it works better than the alternatives. Indeed, that's one (of many) reasons that third-party payer cases based on off-label use have almost uniformly failed – because the TPPs can't allege, let alone prove, that off-label uses for which they seek recovery don't help patients. See Our Third-Party Payer posts here. Thus, in the great majority of cases, the new/old FDA regulatory informed consent cause of action the Rosoff article advocates could serve only to harm to patient treatment – by deterring patients from receiving standard of care medicine (as we showed above, it would be impossible to limit the claim to "problematic" uses) in the mistaken belief that, because the FDA hasn't passed on the treatment, there must be something wrong with it. This cause of action would only encourage more lawsuits, and higher costs for everything, without increasing patient safety one iota, since existing informed consent already requires discussions of actual medical risks and benefits – just not the through-a-glass-darkly "proxy" of FDA regulatory status.

Our bottom line is this. There are good reasons why appellate court in the country that's considered whether to expand informed consent to include FDA approval status has said "no." There are good reasons why no state statute or regulation requires anything of the sort. The law of informed consent already requires patients to be told about medical risks and benefits – regardless of FDA regulatory status. If the situation is so dire that some experimental treatment with unknown risks is indicated, then patients should be told about that medical uncertainty. Do off-label uses have medical risks? Absolutely, but so do all prescription drugs, which is why they require prescriptions in the first place. In both on- and off-label use situations, patients should be (and legally are required to be) told about those medical risks

directly. They should not be bothered with an FDA legal status that often means only that research into new drugs is more profitable than research into drugs with little or no patent protection left.

The only people who profit from injecting legal information such as FDA regulatory status into medical informed consent discussions are lawyers. For anyone actually needing medical care, as opposed to needing a legal job after graduating from law school, we think that's a truly lousy idea.