IN THE COURT OF APPEALS OF TENNESSEE
AT NASHVILLE
March 1998 Session

CYNTHIA RICHARDSON, ET AL. v. JAMES MILLER, M.D., ET AL.

Appeal from the Circuit Court for Davidson County
No. 94C-1993 Marietta M. Shipley, Judge

No. M1997-00205-COA-R3-CV - Filed August 16, 2000

This appeal involves a medical malpractice action stemming from the use of an infusion pump to administer terbutaline sulphate subcutaneously to arrest a pregnant woman's labor. After suffering a heart attack shortly before giving birth to a healthy child, the woman and her husband filed suit in the Circuit Court for Davidson County against her attending physician, the supplier of the infusion pump, and others alleging that their negligence had caused her heart attack. The woman's medical insurance carrier intervened to assert its contractual reimbursement rights based on the payments it had advanced for the woman's medical expenses. The trial court dismissed the insurance carrier's complaint, and a jury returned a verdict for the physician and the pump supplier. Among their issues on this appeal, the woman and her husband take issue with the exclusion of evidence regarding the FDA-approved uses of terbutaline and with the trial court's refusal to give their requested missing evidence instruction. The physician and the pump supplier assert that they were entitled to a directed verdict at the close of all the proof. Finally, the medical insurance carrier takes issue with the dismissal of its reimbursement claim. While we have determined that the trial court correctly overruled the motions for directed verdict, we conclude that the trial court erred by excluding the evidence regarding the off-label use of terbutaline and by declining to give the requested instruction. The trial court also erred by dismissing the medical insurance carrier's claim. Accordingly, we vacate the judgment for the physician and manufacturer of the pump and remand the case for a new trial.

Tenn. R. App. P. 3 Appeal as of Right; Judgment of the Circuit Court Vacated and Remanded

WILLIAM C. KOCH, JR., L., delivered the opinion of the court, in which HENRY F. TODD, P.J., M.S., joined. BEN H. CANTRELL, J., filed a dissenting opinion.

Mary A. Parker and C. Michael Lawson, Nashville, Tennessee, for the appellants, Cynthia Richardson and William Richardson.

Douglas Berry, Nashville, Tennessee, for the appellant, Principal Mutual Life Insurance Company.

Thomas A. Wiseman, III, Nashville, Tennessee, for the appellee, James Miller, M.D.

Thomas Pinckney, Nashville, Tennessee, for the appellee, Tokos Medical Corporation.

OPINION

Cynthia Richardson married William Richardson in 1991. Ms. Richardson was a 26-year-old physical therapist, and Mr. Richardson was four years her junior. Ms. Richardson loved children, and the couple decided not to delay starting a family because Ms. Richardson, as she put it later, felt her "biological clock ticking." Ms. Richardson learned that she was pregnant with the couple's first child on Thanksgiving Day 1992. Her estimated due date was July 28, 1993.

Ms. Richardson sought her prenatal care from Dr. James Miller. In early January 1993, Ms. Richardson complained that she was experiencing periods of palpitations, rapid heartbeats, and shortness of breath. Dr. Miller referred her to Dr. James W. Ward, Jr., a cardiologist who had previously evaluated Ms. Richardson in 1987 for a similar complaint. Dr. Ward placed Ms. Richardson on a 24-hour heart monitor that showed only benign changes in her heart rhythm. Accordingly, Dr. Ward reported to Dr. Miller that he recommended no additions to Ms. Richardson's medical care. Ms. Richardson made no other cardiac complaints during subsequent office visits with Dr. Miller.

Ms. Richardson made her last prenatal office visit to Dr. Miller on June 23, 1993, when she was approximately thirty-five weeks pregnant. The checkup was routine and ended with the doctor's office scheduling her for a return visit the following week. Events, however, brought the parties together sooner. On the afternoon of the very next day, Ms. Richardson was admitted to Nashville Memorial Hospital in labor. Dr. Miller was immediately concerned that the labor was premature and that there could possibly be complications for the baby if born at thirty-five weeks. He ordered bed rest and hydration and tested Ms. Richardson to rule out mere uterine irritability. When the contractions showed no signs of abating, Dr. Miller opted to affirmatively retard Ms. Richardson's premature labor by tocolysis, *i.e.*, giving her medication to stop her contractions by relaxing her uterine muscles.

Dr. Miller first prescribed and administered magnesium sulfate with limited success. On June 24, 1993, when the frequency of Ms. Richardson's contractions did not decrease, Dr. Miller ordered a different tocolytic drug – terbutaline sulfate ("terbutaline"). While terbutaline had been approved by the FDA only for treating bronchial asthma, it was also being widely used as a tocolytic agent because it relaxes smooth muscles, including the muscles of the uterus.

Ms. Richardson received her first oral dose of terbutaline at approximately 8:30 p.m. on June 24 and her second dose, again by mouth, four hours later. Sometime during the early morning hours of June 25, she awoke with a "horrible pain" in her chest. Ms. Richardson had not gone back to sleep when a nurse came in at approximately 4:00 a.m. with a third oral dose of terbutaline. Ms. Richardson refused the drug, telling the nurse, as the nurse's notes reflect, that her chest hurt. Said Ms. Richardson, "I'm not taking that. . . . [M]y chest is killing me. I don't want any more of that stuff."

The next morning, the nursing staff informed Dr. Miller that Ms. Richardson had complained of chest pain and had refused to take the third dose of terbutaline. When Dr. Miller examined Ms.

Richardson, he discovered that her chest pains had subsided but that she was still in labor. At that point, Dr. Miller suggested using an infusion pump to subcutaneously infuse smaller, timed doses of terbutaline into Ms. Richardson's system. Ms. Richardson may not have understood that the pump would be used to give her the very same drug that she had earlier refused to take orally, but she understood that the whole purpose of the pump was to give her medication to retard her labor and that it was Dr. Miller's intention to stabilize her contractions and then to send her home with the infusion pump in place until her pregnancy was full term.

Dr. Miller had little prior experience with terbutaline infusion pumps other than attending a 1989 seminar, conversing with a manufacturer's representative, and reading professional articles. After completing his examination of Ms. Richardson, Dr. Miller directed the attending nurses to contact Vanderbilt University Hospital about arranging for a terbutaline pump. Nurse Gail Harris was eventually directed to Tokos Medical Corporation ("Tokos"), a California-based medical services and drug provider, who arranged to supply a tocolytic pump designed and programmed to infuse terbutaline subcutaneously in set doses. Other than deciding to start Ms. Richardson on the pump, Dr. Miller was not directly involved with installing the pump or determining the dosage of terbutaline Ms. Richardson would receive while on the pump.

On the afternoon of June 25, Christine Evans, a nurse employed by Tokos, arrived at Memorial Hospital with the infusion pump ordered by Dr. Miller. She did not confer with Dr. Miller, but instead, she reviewed Ms. Richardson's medical records, talked with Ms. Richardson, and then gave Ms. Richardson and the hospital nursing staff instructions concerning the use of the pump. After conferring with one of Tokos's staff pharmacists, Ms. Evans also established the dosage of terbutaline that Ms. Richardson would receive. The hospital staff then obtained the terbutaline from the hospital pharmacy, filled the infusion pump, inserted the needle that would deliver the medication, and activated the pump. As Ms. Richardson remembers it, "[t]hey initially set it up, and the [hospital] nurse put the needle in. And I remember that every four hours the machine would give [me a] dose [of medicine]. And before [each] time I was to check my pulse rate to see if it was in the range – I don't remember the range that they gave me."

Ms. Richardson received regular subcutaneous doses of terbutaline for approximately the next forty-eight hours. Her labor contractions did not stop immediately; however, they eventually began to decrease. By around noon on June 27, three days after their onset, the contractions stopped. Although Ms. Richardson experienced shakiness and what she characterized as a "rapid heart rate," the nurses' notes stated that Ms. Richardson's vital signs were "stable" around the time her contractions stopped.

Ms. Richardson visited with her sister at approximately 3:00 p.m. on June 27. She became upset when her sister told her that their mother's dog had died. At that time, Ms. Richardson's chest, arm, jaw, and head began hurting. When a nurse arrived, Ms. Richardson exclaimed that she was having a heart attack and insisted that she be removed from the terbutaline pump. After some confusion and hesitation, the nurses disconnected Ms. Richardson from the pump, and she was subsequently transferred to a critical care unit where an electrocardiogram confirmed that she had, in fact, experienced a heart attack.

That night Ms. Richardson gave birth to a healthy, six-pound boy. A few days later, Ms. Richardson underwent open-heart by-pass surgery to repair a tear in her coronary artery associated with her heart attack. After recuperating for several days, Ms. Richardson and her baby were discharged from Memorial Hospital.

On June 23, 1994, the Richardsons filed a medical malpractice and products liability action in the Circuit Court for Davidson County seeking $3,500,000 in compensatory and punitive damages from Dr. Miller, Tokos, and two other defendants.[1] They alleged that the administration of terbutaline during Ms. Richardson's labor caused her to suffer a heart attack resulting in permanent heart damage. Later, the Principal Mutual Life Insurance Company ("Principal Mutual"), the issuer of Ms. Richardson's employer-provided group health policy, sought to intervene as a plaintiff to recover approximately $52,000 in medical bills paid in connection with Ms. Richardson's heart attack. On Dr. Miller's motion, the trial court dismissed Principal Mutual's complaint on the ground that Tenn. Code Ann. § 29-26-119 (1980) prevented an injured plaintiff from seeking medical care expenses as damages when the plaintiff's insurance had paid those expenses.

The remaining parties, the Richardsons, Dr. Miller, and Tokos, all requested a trial by jury. In anticipation of the trial, all sides moved in limine to exclude certain evidence. Dr. Miller moved to prevent the Richardsons from introducing or using any information from both terbutaline's drug package insert and the Physicians' Desk Reference ("PDR") indicating that the drug had not been approved by the federal Food and Drug Administration for use in stopping premature labor.[2] The trial court granted Dr. Miller's motion.

When the trial commenced in June 1996, the Richardsons asked the trial court to reconsider Dr. Miller's motion in limine. Their request prompted Dr. Miller to ask for additional rulings specifically precluding any reference at trial to off-label use of terbutaline taken from the drug's package insert, the Physicians' Desk Reference, or the pretrial deposition testimony of Dr. Mario Gaudino, a Ciba-Geigy employee. The trial court, siding with Dr. Miller, prohibited all references at trial to the off-label use of terbutaline. By the time of trial in June 1996, the Richardsons had narrowed their negligence claims against Dr. Miller and Tokos. They were no longer asserting that Dr. Miller was negligent for initially attempting to use orally administered terbutaline to slow Ms. Richardson's labor. Rather, they were asserting that Dr. Miller breached the standard of care by continuing tocolysis using terbutaline after Ms. Richardson began experiencing chest pain while taking terbutaline orally and by electing to administer the terbutaline subcutaneously using an infusion pump. With regard to Tokos, the Richardsons were asserting that the company acted

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[1]The two other defendants were A+ Stat Home Care, Inc., the employer of the home health nurse who accompanied Christine Evans to the hospital on June 25, 1993, and the Ciba-Geigy Corporation, the manufacturer of terbutaline. These defendants were later dismissed from the lawsuit and play no role in this appeal.

[2]Ciba-Geigy's package insert and the parallel PDR reference state under "Usage" that terbutaline "is indicated for the prevention and reversal of bronchospasm in patients with bronchial asthma and reversible bronchospasm associated with bronchitis and emphysema." Both sources expressly warn that, "Terbutaline sulfate should not be used for tocolysis. Serious adverse reactions may occur after administration of terbutaline sulfate to women in labor. In the mother, these include increased heartrate, transient hyperglycemia, hypokalemia, cardiac arrhythmias, pulmonary edema, and myocardial ischemia."

negligently by failing to inform Dr. Miller that Ms. Richardson was not a candidate for the infusion pump under their guidelines because of the advanced stage of her pregnancy and because of her history and complaints of cardiac problems and by failing to insist on an EKG before beginning Ms. Richardson on the pump.

The jury later returned a verdict in favor of Dr. Miller and Tokos, and the trial court subsequently entered judgment on the jury's verdict. After the trial court denied their motion for new trial, the Richardsons perfected this appeal.

I.
THE EXCLUSION OF EVIDENCE REGARDING THE OFF-LABEL USE OF TERBUTALINE FOR TOCOLYSIS

The Richardsons assert that the trial court committed five errors entitling them to a new trial. We have concluded that the dispositive issue involves the trial court's decision to prevent the Richardsons from introducing evidence regarding or cross-examining Dr. Miller's or Tokos's witnesses concerning the FDA-approved uses of terbutaline, Ciba-Geigy's directions for using terbutaline, or the off-label use of terbutaline as a tocolytic agent. We have determined that this evidence is relevant and that the trial court committed reversible error by excluding it.

A.
THE FDA REGULATORY PROCESS

Any discussion of the admissibility of evidence regarding the off-label use of a prescription drug must begin with a definition of the term "off-label use." The term is an essentially regulatory concept derived from the federal Food and Drug Administration's ("FDA") regulation of prescription drugs and their labeling. *See* James M. Beck & Elizabeth D. Azari, *FDA, Off-Label Uses, and Informed Consent: Debunking Myths and Misconceptions*, 53 Food & Drug L.J. 71, 83 (1998) ("Beck & Azari"); Steven R. Salbu, *Off-Label Use, Prescription and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy*, 51 Fla. L. Rev. 181, 186 (1999) ("Salbu"). The term, as customarily used by health care providers, is medically neutral and refers to a circumstance in which a patient uses a prescribed drug or device in a manner that varies in some way from the drug's or device's FDA-approved labeling. *See* Beck & Azari, 53 Food & Drug L.J. at 85; Lucinda M. Finley, *Guarding the Gate to the Courthouse: How Trial Judges Are Using Their Evidentiary Screening Role to Remake Tort Causation Rules*, 49 DePaul L. Rev. 335, 368 (1999); Salbu, 51 Fla. L. Rev. at 188.[3] Because the term is linked so closely with the FDA's oversight of

[3]The director of the FDA's Center for Drug Evaluation and Research describes off-label use as "[u]se for indication, dosage form, dose regimen, population of other use parameter not mentioned in the approved labeling." *See* Janet Woodcock, *A Shift in the Regulatory Approach* (Presentation to DIA Montreal June 23, 1997) (<http://www.fda.gov.cder/present/diamontreal/regappr/sld003.htm>) (visited July 5, 2000); *see also Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 55 (D.D.C. 1998). As a general matter, off-label usage occurs in one of three circumstances: (1) off-label prescriptions where a physician orders a drug or device to be used in any manner that varies from the label's instructions; (2) off-label promotion or marketing where a manufacturer promotes a drug or device for purposes, to patient populations, or in combinations other than those approved by the FDA; and (3) off-label use by the (continued...)

prescription drugs, it cannot be fully understood without some basic understanding of the FDA's procedures for approving the promotion and sale of prescription drugs.

The federal Food, Drug, and Cosmetic Act ("FDCA") and its later amendments were enacted to prevent wide-spread tragedies such as those involving sulfanilamide[4] and thalidomide by improving the manufacture, testing, and labeling of prescription drugs. *See* Note, *The Drug Amendments of 1962: How Much Regulation?*, 18 Rutgers L. Rev. 101, 115 (1963). The premise of the legislation is that a federal agency is necessary to protect consumers from the products of a profit-seeking drug industry bent on increasing its sales and profits. *See* James R. Bird, *Package Inserts for Prescription Drugs as Evidence in Medical Malpractice Cases*, 44 U. Chi. L. Rev. 398, 406 (1977) ("Bird"). Under the FDCA, a manufacturer cannot market or sell a new prescription drug without first obtaining FDA approval. *See* 21 U.S.C.A. § 355(a) (West 1999).

The FDA's approval process begins when a manufacturer submits a new drug application. This application must include detailed information regarding the drug, including (1) its components, (2) its manufacturing process, (3) samples of the drug, (4) studies conducted to determine the drug's safety and efficacy for a particular use or uses, and (5) the proposed labeling for the drug. *See* 21 U.S.C.A. § 355(b)(1); 21 C.F.R. §§ 314.50, 807.87(e) (1999). The FDA's consideration of a new drug application is limited to the use or uses for which the manufacturer has conducted safety and efficacy studies. *See* 21 U.S.C.A. § 360e(d)(1)(A) (West 1999); 21 C.F.R. §§ 314.50, -.54, 807.92(a)(5), 807.100(b)(1) (1999); *see also Washington Legal Found. v. Friedman*, 13 F. Supp. 2d at 55; Salbu, 51 Fla. L. Rev. at 187.

After receiving the new drug application and the supporting data, the FDA conducts a risk-benefit analysis to ascertain the new drug's safety and therapeutic effectiveness for the intended use or uses specified by its manufacturer. *See* Margaret Gilhooley, *When Drugs Are Safe For Some But Not Others: The FDA Experience and Alternatives for Products Liability,* 36 Hous. L. Rev. 927, 928 (1999) ("Gilhooley"), *citing* FDA, U.S. Dep't of Health & Human Servs., *Managing the Risks From Medical Product Use, Creating a Management Framework*, Report to the FDA Comm'r from the Task Force on Risk Management 21 (1999); Sidney A. Shapiro, *Limiting Physician Freedom to Prescribe a Drug for Any Purpose: The Need for FDA Regulation*, 73 Nw. U.L. Rev. 801, 805 (1978) ("Shapiro"). Once the FDA determines that the new drug is safe and effective, the FDA and the drug's manufacturer negotiate the language to be included in the drug's labeling. *See* Bird, 44 U. Chi. L. Rev. at 410.

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[3](...continued)
patient that may take place without the knowledge of the manufacturer or prescribing physician. *See* Salbu, 51 Fla. L. Rev. at 188-92.

[4]The infamous "Elixir Sulfanilamide" disaster involved the deaths of over one hundred Tennesseans who were poisoned after a reckless manufacturer marketed a supposedly therapeutic potion containing the solvent diethylene glycol. *See* David F. Cavers, *The Food, Drug, and Cosmetics Act of 1938: Its Legislative History and Its Substantive Provisions*, 6 Law & Contemp. Probs. 2, 20 (1939).

The labeling[5] submitted by a drug manufacturer must be limited to the intended use or uses of the drug. Manufacturers are neither required nor expected to submit labeling reflecting all of a drug's possible uses. *See* 21 C.F.R. 807.87(e). The purpose of labeling to ensure that a drug's promotional literature contains accurate and complete information regarding the approved use or uses and known risks of the drug. *See* Lars Noah, *The Imperative to Warn: Disentangling the "Right to Know" from the "Need to Know" About Consumer Product Hazards*, 11 Yale J. on Reg. 293, 326-333 (1994). Thus, the labeling must include information necessary for the safe and effective use of the drug, such as dosage and methods of administration, as well as warnings, precautions, indications and contraindications, drug abuse and dependence, and adverse reactions. *See* 21 C.F.R. §§ 201.56, 201.57 (1999). The FDA will not approve a new drug until it finds the proposed labeling acceptable. In particular, the FDA will not approve a new drug application if the labeling contains instructions regarding uses other than those for which the drug has been shown to be safe and effective. *See* 21 U.S.C.A. § 355(d)(1); David W. Opderbeck, *How Should FDA Regulate Prescription Drug Promotion on the Internet?* 53 Food & Drug L.J. 47, 55 (1998); Salbu, 51 Fla. L. Rev. at 187; Kaspar I. Stoffelmayr, Comment, *Products Liability and "Off-Label" Uses of Prescription Drugs*, 63 U. Chi. L. Rev. 275, 276 (1996) ("Stoffelmayr").

The FDA-required labeling includes the package inserts that accompany the drug. The same information is also included in the PDR, an encyclopedia of medications written and published annually and provided to all practicing physicians. *See Spensieri v. Lasky*, 723 N.E.2d 544, 547 (N.Y. 1999); Edmund Polubinski, III, Note, *Closing the Channels of Communication: A First Amendment Analysis of the FDA's Policy on Manufacturer Promotion of "Off-Label" Use*, 83 Va. L. Rev. 991, 995 (1997). Both the drug's labeling and the parallel PDR reference are directed at the physicians who prescribe the drug rather than at the patients who will be taking it. *See* Salbu, 51 Fla. L. Rev. at 187. To comply with FDA regulations, the information in a drug's PDR reference must be the same as the information in the FDA-approved labeling and package inserts. *See* 21 C.F.R. § 201.100(d)(2) (1999).

The instructions and warnings contained in a prescription drug's labeling and its parallel PDR reference are the primary way of insuring the drug's safe use. Physicians are expected to take the information into account when prescribing the drug. *See* Gilhooley, 36 Hous. L. Rev. at 939. Package inserts, as reprinted in the PDR, are now the most frequently consulted source of information on the use of prescription drugs. At least one Congressional committee has received evidence suggesting that physicians not only consult the package inserts or the parallel PDR references but that they also rely on them when making decisions on dosage and method of administration. *See Morlino v. Medical Ctr.*, 706 A.2d 721, 729 (N.J. 1998); Bird, 44 U. Chi. L. Rev. at 416, *citing Examination of the Pharmaceutical Industry, 1973-74, Hearings on S. 3441 and S. 966 Before the Subcomm. on Health of the Sen. Comm. on Labor and Pub. Welfare*, 93rd Cong., 1st & 2d Sess., pt. 5, at 1548 (1973-74).

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[5] "Labeling" is a term of art that encompasses all written, printed, or graphic material on any of the drug's containers or wrappers accompanying the drug. *See* 21 U.S.C.A. § 321(k) & (m) (West 1999); *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d at 55. It also includes any other form of a drug company's promotional activities, including booklets, pamphlets, mailing pieces, bulletins, and all other literature that supplements, explains, or is otherwise related to the drug. *See* 21 C.F.R. § 202.1(l)(1), (2) (1999).

The FDA's approval of a new drug does not end its oversight of the drug's use. Both the FDA and the manufacturer must continue to collect positive and negative information regarding the actual safety and efficacy of the drug on patients. The FDA regulations emphasize the collection of negative information regarding the clinical experience with a prescription drug "to make or facilitate a determination of whether there are or may be grounds . . . for suspending or withdrawing approval of the application." 21 C.F.R. § 310.303(a) (1999). If the off-label use of a prescription drug becomes widespread or endangers the public health, the FDA is obligated to investigate it thoroughly and to take whatever action is warranted to protect the public. *See* Legal Status of Approved Labeling for Prescription Drugs: Prescribing for Uses Unapproved By the FDA, 37 Fed. Reg. 16,503, 16,504 (to be codified at 21 C.F.R. pt. 130) (proposed Aug. 14, 1972);[6] Stuart L. Nightengale, *Unlabeled Uses of Approved Drugs*, 26 Drug Info. J. 141, 143 (1992).[7] The FDA may withdraw approval of a drug if new information indicates that the drug is not safe and effective for use under the conditions discussed in the drug's labeling, *see* 21 C.F.R. § 314.150(a)(2)(i) (1999), or it may require the manufacturer to include statements in the drug's labeling that certain uses are contraindicated. *See* 21 C.F.R. §§ 201.57(d), 801.109 (1999).

Once the FDA has approved a prescription drug for a particular use or uses, the drug's manufacturer cannot market or promote the drug for an off-label use until it resubmits the drug for another series of clinical trials similar to those required for initial approval of a new drug application. *See* 21 C.F.R. §§ 314.54, 314.70, -.71 (1999); *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d at 55; Salbu, 51 Fla. L. Rev. at 187-88. As new uses for an already approved drug become known, the drug's manufacturer may request the FDA's approval to add new approved uses to the drug's labeling. *See* Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 Va. L. Rev. 1753, 1775 (1996) ("Merrill"); Glenn C. Smith, *Avoiding Awkward Alchemy – In the Off-Label Drug Context and Beyond: Fully Protected Independent Research Should Not Transmogrify Into Mere Commercial Speech Just Because Product Manufacturers Distribute It*, 34 Wake Forest L. Rev. 963, 969 (1999) ("Smith"). Because of the time and expense of obtaining FDA approval of new uses for an already approved drug, drug manufacturers frequently do not voluntarily request FDA approval for a new use unless the change in the labeling will pay for itself in increased profits. *See* J. Howard Beales, III, *Economic Analysis and the Regulation of Pharmaceutical Advertising*, 24 Seton Hall L. Rev. 1370, 1387, 1392-93 (1994); Bird, 44 U. Chi. L. Rev. at 412; Merrill, 82 Va. L. Rev. at 1855; Salbu, 51 Fla. L. Rev. at 188; Shapiro, 73 Nw. U.L. Rev. at 811; Stoffelmayr, 63 U. Chi. L. Rev. at 277.

B.
OFF-LABEL USE OF PRESCRIPTION DRUGS

[6] This proposed rule was never made final.

[7] Dr. Nightengale is the FDA's Associate Commissioner for Health Affairs.

The FDA's broad authority over prescription drugs and devices does not extend to a physician's decisions regarding the use of these products. *See Washington Legal Found. v. Friedman*, 13 F. Supp. 2d at 55; Beck & Azari, 53 Food & Drug L.J. at 76; Smith, 34 Wake Forest L. Rev. at 969. To avoid limiting the ability of physicians to treat their patients,[8] the lack of FDA approval of a drug or device for a particular use does not imply that using the drug or device for that use is either disapproved or improper. *See* Beck & Azari, 53 Food & Drug L.J. at 83-84.[9] Thus, physicians may use approved drugs or devices in any way that they, in their professional judgment, believe will best serve their patients, regardless of whether the FDA has approved the drug or device for that particular use. *See Washington Legal Found. v. Henney*, 202 F.3d 331, 333 (D.C. Cir. 2000); *United States v. Evers*, 643 F.2d 1043, 1048 (5th Cir. 1981); *Proctor v. Davis*, 682 N.E.2d 1203, 1206 n.1 (Ill. App. Ct. 1997); *Femrite v. Abbott Northwestern Hosp.*, 568 N.W.2d 535, 541 (Minn. Ct. App. 1997); *Klein v. Biscup*, 673 N.E.2d 225, 231 (Ohio Ct. App. 1996). This prerogative includes (1) prescribing a drug for conditions other than those for which it has been approved, (2) prescribing a drug for patient groups other than those for which it was originally approved, and (3) varying the dosage or method of administering a drug from that contained in its labeling. *See* Stoffelmayr, 63 U. Chi. L. Rev. at 277.

In the current regulatory environment, when the FDA authorizes a prescription drug or device to be marketed, it is well aware that the drug or device will likely be put to an off-label use. *See* Beck & Azari, 53 Food & Drug L.J. at 82. The FDA has acknowledged that once a drug or device is on the market, a "physician may, as part of the practice of medicine, lawfully prescribe a different dosage for his [or her] patient or may otherwise vary the conditions of use from those approved in the package insert, without informing or obtaining the approval of the Food and Drug Administration." Legal Status of Approved Labeling For Prescription Drugs: Prescribing For Uses Unapproved by the FDA, 37 Fed. Reg. 16,503, 16,504 (to be codified at 21 C.F.R. pt. 130) (proposed Aug. 14, 1972).[10] An FDA technical bulletin has recognized that the off-label use of an approved drug represents acceptable, and sometimes essential, clinical practice. *See Use of Unapproved Drugs for Unlabeled Indications*, 12 FDA Drug Bull., Apr. 1982, at 4-5, cited in 59 Fed. Reg. 59,820, 59,821 (noting that "[v]alid new uses for drugs already on the market are often first discovered

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[8] *See United States v. Algon Chem., Inc.*, 879 F.2d 1154, 1163 (3d Cir. 1989); *Chaney v. Heckler*, 718 F.2d 1174, 1180 (D.C. Cir. 1983), *rev'd on other grounds*, 470 U.S. 821 (1985).

[9] Similarly, the off-label use of a drug or device by a physician seeking an optimal treatment for his or her patient is not necessarily considered to be research or an investigational or experimental treatment when the use is customarily followed by physicians. *See Weaver v. Reagen*, 886 F.2d 194, 198-99 (8th Cir. 1989); *Salgo v. Leland Stanford, Jr. Univ. Bd. of Trustees*, 317 P.2d 170, 180 (Cal. Ct. App. 1957); *Ramon v. Farr*, 770 P.2d 131, 135 (Utah 1989); Beck & Azari, 53 Food & Drug L.J. at 83.

[10] Even though this position is found in a rule that was never made final, the FDA recently restated it. *See* Citizen Petition Regarding the FDA's Policy on Promotion of Unapproved Uses of Approved Drugs and Devices: Request for Comments, 59 Fed. Reg. 59,820, 59,821 (Nov. 18, 1994). This position remains an "important statement of agency policy." David G. Adams, *The Food and Drug Administration's Regulation of Health Care Professionals* 423, 426 (David G. Adams, et al., eds., 2d ed. 1997).

through serendipitous observation and therapeutic innovation").[11] It is also possible that the off-label uses of a drug may exceed the uses for which the drug was originally approved. *See* John Calfee, *Free Speech, FDA Regulation, and Market Effects on the Pharmaceutical Industry, reprinted in Bad Prescription for the First Amendment: FDA Censorship of Drug Advertising and Promotion* 64 (Richard T. Kaplar, ed. 1993).

Off-label prescriptions are now an integral part of the modern practice of medicine. *See Washington Legal Found. v. Henney*, 202 F.3d at 333. While estimates concerning the prevalence of off-label use varies, there is a consensus that the practice is widespread. *See* Beck & Azari, 53 Food & Drug L.J. at 80; Lars Noah, *Constraints on the Off-Label Prescription Drugs*, 16 J. Prods. & Toxics Liab. 139, 139 (1994); United States General Accounting Office, *Off-Label Drugs, Reimbursement Policies Constrain Physicians in Their Choice of Cancer Therapies*, GAO/PEMD-91-14, at 5 (Sept. 1991) ("GAO Report"). Off-label uses of approved drugs have become extremely important in specialities such as cancer,[12] pediatric medicine,[13] heart and circulatory disease,[14] AIDS,[15] and kidney disease.[16]

Recognition of the propriety of the off-label use of drugs and devices has spread beyond the medical profession. A number of state legislatures, including the Tennessee General Assembly, have recognized that off-label uses of approved drugs are appropriate ways to provide medical care at lower costs and have precluded medical insurers from declining to pay for approved drugs prescribed off-label solely because the FDA has not approved the drug for that use. *See* Tenn. Code Ann. § 56-7-2352(a)(6)-(7), -2352(c)(1); Beck & Azari, 53 Food & Drug L.J. at 76 n.56. The courts have also repeatedly recognized the legitimacy of the off-label use of approved drugs and devices. *See Rhone-*

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[11] Because the pace of medical discovery runs ahead of the FDA's regulatory machinery, the off-label use of some drugs is frequently considered to be "state-of-the-art" treatment. *See* Beck and Azari, 53 Food & Drug L.J. at 79. In some circumstances, an off-label use of a particular drug or device may even define the standard of care. *See Hartwell v. Danek Med., Inc.*, 47 F. Supp. 2d 703, 705 n.3 (W.D. Va. 1999); *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d at 56; *Proctor v. Davis*, 682 N.E.2d at 1210.

[12] The Government Accounting Office has estimated that 25% of all anti-cancer drugs are prescribed off-label and that 56% of all cancer patients receive at least one drug off-label. *See* GAO Report, at 5, 11, 13-14, 40; *see also* Tenn. Code Ann. § 56-7-2352(a)(6) (Supp. 1999) (reflecting the Tennessee General Assembly's finding that approximately fifty percent of all cancer drug treatment is for off-label indications); Smith, 34 Wake Forest L. Rev. at 971.

[13] *See* Robert Levine, *Ethics and Regulation of Clinical Research*, 241 (2d ed. 1986); Beck & Azari, 53 Food & Drug L.J. at 79-80; J.S. Jameson & M.E. Holland, *Off-Label Use of Antimicrobial Agents in Infants, Children and Adolescents: A Time for Action*, 17 Pediatric Infectious Disease J. 739, 744 (1998); Smith, 34 Wake Forest L. Rev. at 971; 143 Cong. Rec. S8165 (daily ed. July 28, 1997) (statement of Sen. Bill Frist).

[14] *See* Gregory Mundy, et al., *Current Medical Practice and the Food and Drug Administration*, 229 JAMA 1744, 1746 (1974).

[15] Forty percent of all drugs prescribed for AIDS treatment are off-label and eighty percent of AIDS patients receive at least one off-label prescription. *See* Carole Brosgart, *Off-Label Use in Human Immunodeficiency Virus Disease*, 12 J. Acquired Immune Deficiency Syndromes and Human Retrovirology 56, 57-58 (1996).

[16] *See* Beck & Azari, 53 Food & Drug L.J. at 80 n.17.

Poulenc Rorer Pharm., Inc. v. Marion Merrell Dow, Inc., 93 F.3d 511, 514 n.33 (8th Cir. 1996); *Bristol-Myers Squibb Co. v. Shalala*, 91 F.3d 1493, 1496 (D.C. Cir. 1996); *Ortho Pharm. Corp. v. Cosprophar, Inc.*, 32 F.3d 690, 692 (2d Cir. 1994); *Weaver v. Reagen*, 886 F.2d at 198; *Alvarez v. Smith*, 714 So. 2d 652, 653-54 (Fla. Dist. Ct. App. 1998); *Klein v. Biscup*, 673 N.E.2d at 231; *Southard v. Temple Univ. Hosp.*, 731 A.2d 603, 611 (Pa. Super. Ct. 1999).

The off-label use of approved drugs results in one significant complication for physicians. Because of the FDA's restrictions on the dissemination of information regarding off-label uses of approved drugs, physicians do not have readily available the same information concerning the use, dosage, and method of administration of the drug that is provided for approved uses. Neither the FDA-approved labeling nor the parallel PDR reference contain information about off-label uses. *See Washington Legal Found. v. Friedman*, 13 F. Supp. at 56.[17]

When the off-label use of a drug becomes widespread, there is an increased possibility that a physician with inadequate knowledge will prescribe it. *See* Shapiro, 73 Nw. U.L. Rev. at 826. Accordingly, physicians prescribing a drug or device off-label have a responsibility to be well-informed about the drug or device. *See Staudt v. Froedtert Mem'l Lutheran Hosp.*, 580 N.W.2d 361, 363 (Wis. Ct. App. 1998); *Femrite v. Abbott Midwestern Hosp.*, 568 N.W.2d at 542; Cynthia Starr, *A Careful Approach to Off-Label Drugs*, Patient Care (Sept. 30, 1999) (visited July 6, 2000) <http://pc.pdr.net/pc/static.htm?path=content/journals/p/data/1999/0930/offlabel.html>. In the absence of the information found in the FDA-approved labeling, physicians must obtain reliable, up-to-date information from other sources. These sources may include: (1) discussion with professional colleagues, (2) continuing medical education programs, (3) case studies in professional journals, and (4) reports of the clinical results of the use of the drug in other countries. *See Baker v. Danec Med.*, 35 F. Supp. 2d 865, 873 (N.D. Fla. 1998); *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d at 56; Shapiro, 73 Nw. U. L. Rev. at 809-10.

C.
ADMISSIBILITY OF EVIDENCE THAT A PARTICULAR USE OF A DRUG IS OFF-LABEL

The next issue to be addressed is whether a prescription drug's labeling or parallel PDR reference is admissible with regard to the standard of care for using and administering the drug. Virtually every court addressing this question has concluded that the drug's labeling and PDR reference are relevant to the standard of care issue. The primary dispute among the courts involves the weight to be given to this evidence. The great weight of authority is that a drug's labeling or its parallel PDR reference is admissible, as long as it is accompanied by other expert evidence regarding the standard of care.

A plaintiff's burden of proof in a medical malpractice case is governed by statute. As a general matter, the law will not presume that a health care provider acted negligently simply because

[17] The publisher of the PDR now publishes the "PDR Companion Guide," an 1,800-page reference augmenting the PDR. This guide includes an "Off-Label Treatment Guide" listing drugs routinely used, but never approved, for the treatment of nearly one thousand disorders. *See* Medical Economics Co., *Physicians' Desk Reference*, Foreword (54th ed. 2000).

a treatment was unsuccessful. *See* Tenn. Code Ann. § 29-26-115(c) (1980); *Roddy v. Volunteer Med. Clinic, Inc.*, 926 S.W.2d 572, 578 (Tenn. Ct. App. 1996).[18] Thus, in order to make out a prima facie case of medical negligence, a plaintiff must come forward with evidence that complies with Tenn. Code Ann. § 29-26-115(a). This statute requires the conduct of health care providers to be judged by an objective community standard. Accordingly, Tenn. Code Ann. § 29-26-115(a)(1) requires the plaintiff to present evidence of "[t]he recognized standard of acceptable professional practice in the profession and the specialty thereof . . . that the defendant practices in the community in which he [or she] practices . . . at the time the alleged injury or wrongful action occurred." Establishing this professional standard of care requires expert testimony. *See Moon v. St. Thomas Hosp.*, 983 S.W.2d 225, 229 (Tenn. 1998); *Cardwell v. Bechtol*, 724 S.W.2d 739, 742 (Tenn. 1987); *Jennings v. Case*, 10 S.W.3d 625, 627 (Tenn. Ct. App. 1999).

Plaintiffs in other medical malpractice cases have argued that the instructions in a prescription drug's FDA-approved labeling or the parallel PDR reference should be sufficient, by themselves, to establish a physician's standard of care regarding the use of the drug. Several jurisdictions, believing drug manufacturers to be uniquely knowledgeable about the proper use of their products, have held that a drug's labeling or its parallel PDR reference amounts to prima facie evidence of the standard of care as far as the use of that drug is concerned.[19] However, a majority of jurisdictions have determined that a prescription drug's labeling or parallel PDR reference is admissible to prove the standard of care, but only if the plaintiff also introduces other expert testimony regarding the standard of care. These jurisdictions have concluded that while the labeling and PDR reference provide relevant and useful information regarding the standard of care, they are not the sole determinant of the standard of care because, in any particular case, adhering to the manufacturer's recommendations and warnings in the labeling or the PDR may or may not have been within the standard of care when the alleged negligent act occurred.[20]

Four considerations support the majority view governing the admissibility of a prescription drug's labeling or parallel PDR reference in a medical malpractice case. First, permitting the labeling or the PDR reference alone to establish a physician's standard of care would be inconsistent with Tenn. Code Ann. § 29-26-115(a)(1) because it would permit the drug manufacturer, rather than the medical profession, to establish the standard of care. *See Morlino v. Medical Ctr.*, 706 A.2d at 730; *Spensieri v. Lasky*, 723 N.E.2d at 548. Second, the FDA-required labeling and parallel PDR reference may not be easily understood by the jury without expert assistance because these materials

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[18]The Tennessee Supreme Court recently recognized a narrow exception to this principle when it held that a jury could infer negligence from an unsuccessful result if an expert testifies that the result would not ordinarily have occurred in the absence of negligence. *See Seavers v. Methodist Med. Ctr.*, 9 S.W.3d 86, 96 (Tenn. 1999).

[19]*See Haught v. Macelich*, 681 F.2d 291, 303 n.12 (5th Cir. 1982); *Ohligschlager v. Proctor Community Hosp.*, 303 N.E.2d 392, 396 (Ill. 1973); *Mulder v. Parke Davis & Co.*, 181 N.W.2d 882, 887 (Minn. 1970); *Mueller v. Mueller*, 221 N.W.2d 39, 42-43 (S.D. 1974).

[20]*See Salgo v. Leland Stanford, Jr. Univ. Bd. of Trustees*, 317 P.2d at 180; *Bowman v. Songer*, 820 P.2d 1110, 1114 (Colo. 1991); *Garvey v. O'Donoghue*, 530 A.2d 1141, 1145-46 (D.C. App. 1987); *Craft v. Peebles*, 893 P.2d 138, 151 (Haw. 1995); *Thompson v. Carter*, 518 So. 2d 609, 613 (Miss. 1987); *Bissett v. Renna*, 710 A.2d 404, 408 (N.H. 1998); *Morlino v. Medical Ctr.*, 706 A.2d at 728; *Spensieri v. Lasky*, 723 N.E.2d at 548; *Grayson v. State*, 838 P.2d 546, 549 (Okla. Ct. App. 1992); *Ramon v. Farr*, 770 P.2d at 135.

are written for the medical profession, not the general public. *See Craft v. Peebles*, 893 P.2d at 151 n.17; *Morlino v. Medical Ctr.*, 706 A.2d at 729-30; *Spensieri v. Lasky*, 723 N.E.2d at 548. Third, the drug manufacturer and the FDA do not intend to establish the standard of care when they prepare a drug's labeling or PDR reference. These materials are intended to comply with the FDA's regulations, to provide advertising and promotional material, and to limit the manufacturer's liability. *See Thompson v. Carter*, 518 So. 2d at 612-13; *Morlino v. Medical Ctr.*, 706 A.2d at 729; *Spensieri v. Lasky*, 723 N.E.2d at 549; *Ramon v. Farr*, 770 P.2d at 135-36; Bird, 44 U. Chi. L. Rev. at 424. Finally, the labeling and PDR reference cannot be cross-examined. *See Spensieri v. Lasky*, 723 N.E.2d at 548.

We adopt the majority approach regarding the introduction and evidentiary weight to be given to FDA-approved drug labeling and the parallel PDR reference. Neither of these materials, by themselves, are prima facie evidence of the prescribing physician's standard of care. Thus, proof of a departure from the recommendations in a drug's labeling or PDR reference is not alone sufficient to prove a breach of the standard of care. However, the labeling and the PDR reference can provide significant assistance in identifying the standard of care. Accordingly, we find that a prescription drug's labeling or its PDR reference, when introduced along with other expert evidence on the standard of care, is admissible to assist the trier-of-fact to determine whether the drug presented an unacceptable risk to the patient.

D.
THE USE OF ADRENERGIC DRUGS FOR TOCOLYSIS

At trial, the Richardsons claimed that Dr. Miller violated the standard of care by continuing Ms. Richardson on terbutaline after she complained of severe chest pains, and by deciding to administer terbutaline to Ms. Richardson subcutaneously using an infusion pump. A survey of the evidence and other information about the off-label use of drugs like terbutaline for tocolysis provides a helpful framework for determining whether the trial court properly excluded the evidence regarding the off-label use of terbutaline for tocolysis in light of the Richardsons' claims. This information indicates that the safety and efficacy of terbutaline administered with an infusion pump for tocolysis was being debated when it was administered to Ms. Richardson and continues to be debated today.

In the early 1970's, the FDA approved the use of a beta-adrenergic drug called ritodrine hydrochloride ("ritodrine") for use in tocolysis. This drug, which could be administered orally, intravenously, or intramuscularly, was a smooth muscle relaxer that helped relax uterine contractions thus buying more time for babies to develop in their mother's womb before being delivered. At approximately the same time, a Swedish manufacturer named Astra Pharmaceuticals ("Astra") developed another beta-adrenergic drug, terbutaline, principally as a bronchodilator to relax and open the constricted airways of persons suffering from asthma. After obtaining the FDA's approval to market terbutaline as an asthma medication, Astra manufactured and sold the drug under the trade name "Bricanyl." Thereafter, Astra licensed Ciba-Geigy to manufacture and market terbutaline. Ciba-Geigy began selling terbutaline under the trade name "Brethine" using the same labeling that the FDA had approved for Bricanyl.

In the mid-1970's, physicians began to discover that terbutaline, administered intravenously, had tocolytic effects similar to those of ritodrine. *See* Fung Lam, et al., *Clinical Issues Surrounding the Use of Terbutaline Sulfate for Preterm Labor*, 53 Obstet. & Gyn. Survey S85, S86 (Supp. 1998) ("Lam"). However, in 1980 or 1981, Astra amended the FDA-approved labeling for Bricanyl to warn against the intramuscular use of terbutaline for tocolysis after it received reports of adverse reactions to the drug when it was used for that purpose. After the FDA approved Astra's changes to Bricanyl's labeling, Ciba-Geigy added the same warning to the Brethine's labeling.[21] In 1983, both Astra and Ciba-Geigy added the same wamings and precautions to their terbutaline tablets.

Despite the warnings in the drug's labeling regarding the use of terbutaline for tocolysis, the drug found increasing favor with physicians around the country as an appropriate way to prolong premature labor. The typical course of treatment, albeit off-label, involved administering terbutaline intramuscularly while the patient was hospitalized and then switching to oral medication if the drug had the effect of slowing down the patient's labor.[22] In 1986, a San Francisco physician began experimenting with an infusion pump to administer terbutaline on an out-patient basis without requiring hospitalization. *See* Lam, 53 Obstet. & Gyn. Survey at S86-S87. In 1988, the physician reported that his "Subcutaneous Terbutaline Pump Therapy" ("SQTP") produced dramatic tocolytic effects at a greatly reduced dosage level. These reports prompted various infusion pump manufacturers and others to begin heavily promoting SQTP therapy.

In October 1992, the FDA's Fertility and Maternal Health Drugs Advisory Committee concluded that oral ritodrine maintenance therapy had no place in obstetric practice because of its lack of efficacy in the presence of its known toxicity.[23] Accordingly, the FDA advised ritodrine's manufacturer to perform more studies to validate the drug's efficacy. Rather then taking on this financial burden, the manufacturer simply withdrew oral ritodrine for maintenance tocolysis from the United States market. *See* Lam, 53 Obstet. & Gyn. Survey at S91. As a result of this decision, terbutaline became the most commonly used beta-adrenergic drug for tocolysis, despite the manufacturer's warnings.

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[21] Following these changes, the labeling provided the following warning for the intavenous use of Brethine:

> Controlled clinical studies and other clinical experience have shown that Brethine, like other β-adrenergic agonists, can produce a significant cardiovascular effect in some patients, as measured by pulse rate, blood pressure, symptoms, and/or ECG changes.

The following also appeared in the "precautions" section of the labeling:

> Terbutaline sulfate should not be used for tocolysis. Serious adverse reactions may occur after administration of terbutaline sulfate to women in labor. In the mother, these include increased heart rate, transient hyperglycemia, hypokalemia, cardiac arrhythmias, pulmonary edema, and myocardial ischemia.

[22] American College of Obstetricians and Gynecologists, Technical Bulletin No. 206, *Preterm Labor* 6 (June 1995) ("ACOG Bulletin No. 206").

[23] Letter from Janet Woodcock, Director, Center for Drug Evaluation and Research, to Fung Lam, M.D., Terbutaline Strategy Group, at p. 3 (Oct. 19, 1999) (<http://www.fda.gov/ohrms/dockets/dailys/102999/pdn0001.pdf>) (visited July 6, 2000) ("Woodcock Letter").

In May 1993, the FDA's Fertility and Maternal Health Drugs Advisory Committee concluded that "terbutaline administered intravenously appeared to have an acceptable risk-benefit profile for the acute treatment of preterm labor under limited circumstances (i.e., in pregnancies of 33 weeks or less, when cervical dilation is 4 centimeters or less and there is no premature rupture of the membranes, and with careful maternal and fetal monitoring." Woodcock Letter, *supra* note 23, at 2 (citing Transcript of Fertility and Maternal Health Drugs Advisory Committee meeting, May 21, 1993, at 181-83); *see also* Lam, 53 Obstet. & Gyn. Survey at S92. After concluding that terbutaline may be effective in preventing preterm labor for a brief period of forty-eight to seventy-two hours but that evidence of its long-term effectiveness was lacking, the FDA invited supplemental new drug applications requesting approval to use terbutaline for tocolysis. The FDA also encouraged the manufacturers to review their labeling to address the need for clarification of the uses and risks of terbutaline. *See* Woodcock Letter, *supra* note 23, at 2-3, 9. Despite the FDA's invitation, terbutaline's manufacturers did not request approval to use the drug for tocolysis and did not request changes in the drug's labeling.

The debate surrounding the safety and efficacy of terbutaline as a tocolytic agent has continued since Ms. Richardson's injury. In June 1995, the American College of Obstetricians and Gynecologists ("ACOG") issued a technical bulletin regarding preterm labor.[24] While noting that tocolytic agents are commonly used, the bulletin pointed out that "no studies have convincingly demonstrated an improvement in survival or any index of long-term neonatal outcome with the use of tocolytic therapy. On the other hand, the potential damages of tocolytic therapy to the mother and the neonate is well documented."[25] With specific regard to SQTP therapy, the bulletin noted that "there is no evidence to support the efficacy of this costly and complicated approach."[26] The bulletin also observed that "[e]ach case must be judged individually by weighing the risks of continuing the pregnancy versus those of delivery" and that "most clinicians begin treatment prior to 34 weeks of gestation but approach the management of preterm labor at 34-37 weeks on an individualized basis."[27] Accordingly, ACOG concluded that "[a]lthough different forms of therapy . . . are being used to prevent prematurity, their true benefit and the proper place for their application remain to be established."[28]

In 1996, the National Women's Health Network petitioned the FDA to review the subcutaneous administration of terbutaline using an infusion pump.[29] On November 13, 1997, the FDA's Associate Commissioner for Health Affairs issued a "Dear Colleague" letter to the medical

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[24]For the purposes of the bulletin, ACOG defined "preterm labor" as "labor occurring prior to the completion of 37 weeks of gestation (less than 259 days from the last menstrual period)." ACOG Bulletin No. 206, *supra* note 22, at 1.

[25]ACOG Bulletin No. 206, *supra* note 22, at 6.

[26]ACOG Bulletin No. 206, *supra* note 22, at 6.

[27]ACOG Bulletin No. 206, supra note 22, at 4.

[28]ACOG Bulletin No. 206, *supra* note 22, at 8.

[29]*See* Woodcock Letter, *supra* note 23, at 6.

community warning physicians about the continuous subcutaneous administration of terbutaline.[30] Noting the FDA's concern over the "promotion and increasingly widespread use of subcutaneous terbutaline delivered by infusion pump for the treatment/prevention of preterm labor," the letter stated that "it is clear that the demonstrated value of tocolytics in general is limited to an initial, brief period of treatment, probably no more than 48-72 hours" and that "[n]o benefit from prolonged treatment has been documented." Thus, the FDA letter alerted "practitioners, home health care agencies, insurance carriers, and others that continuous subcutaneous administration of terbutaline sulfate has not been demonstrated to be effective and is potentially dangerous." In April 1998, the Terbutaline Strategy Group, a coalition of researchers and practicing physicians, requested the FDA to reevaluate its position regarding the use of terbutaline by subcutaneous infusion. However, on October 19, 1999, the FDA reaffirmed its concerns regarding the "prolonged, at-home use of subcutaneous terbutaline" and declined to withdraw the November 13, 1997 "Dear Colleague" letter or to require the manufacturers of terbutaline to remove the warnings in the drug's labeling against its use for the management of preterm labor or to submit a new drug application for approval of terbutaline as a tocolytic agent. *See* Woodcock Letter, *supra* note 23, at 9-12.

E.
ADMISSIBILITY OF THE RICHARDSONS' EVIDENCE THAT THE USE OF TERBUTALINE FOR TOCOLYSIS IS OFF-LABEL

While the practice of using drugs off-label is widespread and not inherently inappropriate, there are well-documented instances where an accepted and popular off-label use of a drug has ultimately proved to be harmful. *See* Beck & Azari, 53 Food & Drug L.J. at 71-72; Smith, 34 Wake Forest L. Rev. at 971.[31] Physicians may be found negligent if their decision to use a drug off-label is sufficiently careless, imprudent, or unprofessional. The Richardsons' causes of action against Dr. Miller and Tokos are not based simply on the fact that tocolysis is an off-label use of terbutaline.[32] Rather, their negligence claim rests on the following two theories:(1) Dr. Miller should have discontinued administering terbutaline for tocolysis when she began experiencing chest pain following the second oral dose and (2) Dr. Miller should not have ordered, and Tokos should not have provided, the subcutaneous administration of terbutaline using an infusion pump because the effect of using the pump was to maintain or even increase, rather than decrease, the level of terbutaline in her system.

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[30] See Letter from Stuart L. Nightengale, Associate Commissioner for Health Affairs, (visited July 6, 2000) (Nov. 13, 1997) <http://www.fda.gov/medwatch/safety/1997/terbut. htm> ("Dear Colleague Letter").

[31] The most recent, well-publicized example of the harmful effects of using prescription drugs off-label is fen-phen (the combination of fenfluramine and phentermine). Combining these drugs and using them for an extended period are off-label uses. After the use of fen-phen became widespread, it was discovered that users were suffering from cardiac valvular damage. Accordingly, the use of fen-phen was discontinued. Fenfluramine has been withdrawn from the United States market; however, phentermine remains available for the short-term treatment of obesity.

[32] We note the existence of two reported cases in which the patients alleged that their physician was negligent for failing to use terbutaline for tocolysis. *See Bell v. Maricopa Med. Ctr.*, 755 P.2d 1180, 1182 (Ariz. Ct. App. 1988); *Bridges v. Shelby Women's Clinic, P.A.*, 323 S.E.2d 372, 374-76 (N.C. Ct. App. 1984).

The Richardsons did not intend to limit their evidence regarding the applicable standard of care solely to terbutaline's FDA-approved labeling or the parallel PDR reference. They also intended to call Drs. Glen Farr, Mario Gaudino, Ronald Krone, and James Dingfelder to provide expert opinions on this issue. Dr. Gaudino, representing terbutaline's manufacturer, would have (1) authenticated the drug's FDA-approved labeling, (2) testified regarding the origin of the manufacturer's warnings and precautions against using terbutaline for tocolysis, and (3) confirmed that the labeling contained no instructions regarding the dosage or method of administering terbutaline when used for tocolysis. Dr. Farr, a pharmacologist, was prepared to testify that the absence of dosage or administration directions in terbutaline's labeling would have required physicians to rely on individual policies and standards for administering or prescribing terbutaline to retard preterm labor. This testimony, when coupled with Dr. Dingfelder's testimony that Dr. Miller should not have continued Ms. Richardson on terbutaline after she began experiencing chest pain would have been sufficient to require Dr. Miller to explain why he continued administering terbutaline after Ms. Richardson began experiencing severe chest pains, as well as the basis for his decision to use an infusion pump and how the proper dosage was determined.[33]

Decisions regarding the admissibility of evidence address themselves to the trial court's discretion, *See Seffernick v. Saint Thomas Hosp.*, 969 S.W.2d 391, 393 (Tenn. 1998); *Dockery v. Board of Prof'l Responsibility*, 937 S.W.2d 863, 866 (Tenn. 1996). While the trial courts have wide latitude in making these decisions, *see Overstreet v. Shoney's, Inc.*, 4 S.W.3d 694, 702 (Tenn. Ct. App. 1999), they must take into consideration the factual circumstances and the relevant legal principles. *See State v. Shuck*, 953 S.W.2d 662, 669 (Tenn. 1997). Accordingly, appellate courts will not overturn a trial court's evidentiary ruling unless the trial court applied an incorrect legal standard, based its decision on a clearly erroneous view of the evidence, or has reached a decision against logic and reason that caused injustice to the complaining party. *See State v. Shuck*, 953 S.W.2d at 669; *Ballard v. Herzke*, 924 S.W.2d 652, 661 (Tenn. 1996); *Overstreet v. Shoney's, Inc.*, 4 S.W.3d at 708.

Tenn. R. Evid. 402 reflects the policy that all evidence meeting Tenn. R. Evid. 401's test of relevancy is admissible unless otherwise excluded on constitutional or statutory grounds or by virtue of other provisions in the rules themselves. *See Phillips v. F.W. Woolworth Co.*, 867 S.W.2d 316, 318 (Tenn. Ct. App. 1992). Tenn. R. Evid. 403 provides one such exception to the general principles of admissibility. It authorizes the trial court to exclude otherwise relevant evidence if its probative value is outweighed by the danger of unfair prejudice, confusion, misleading the jury, or unnecessary delay. The language of Tenn. R. Evid. 403 strongly suggests that relevant evidence should be admitted if the balance between the probative value of the evidence and its prejudicial effect is close. *See* Neil P. Cohen, et al., *Tennessee Law of Evidence* § 403.3, at 152 (3d ed. 1995) ("Tennessee Law of Evidence"). Thus, excluding otherwise relevant evidence under Tenn. R. Evid. 403 is an

[33] If, for example, he asserted that using the infusion pump to administer terbutaline posed less of a danger to Ms. Richardson because lower doses were being administered, he would have been required to explain away the fact that using the infusion pump results in the same or higher levels of terbutaline in the patient's system. *See* Woodcock Letter, *supra* note 23, at 6.

extraordinary step that should be used sparingly. *See White v. Vanderbilt Univ.*, ___ S.W.3d ___, ___ (Tenn. Ct. App. 1999).[34]

As we have recently pointed out, a trial court's application of Tenn. R. Evid. 403 should proceed in two steps. The first step requires the trial court to balance the probative value of the evidence sought to be excluded against the combined weight of the countervailing factors in Tenn. R. Evid. 403. If the court determines that the countervailing factors do not outweigh the probative value of the evidence, the trial court should proceed no further and should deny the motion to exclude the evidence under Tenn. R. Evid. 403. If, however, the court determines that the countervailing factors outweigh the probative value of the evidence, it should proceed to the second step in which the court exercises its discretion to decide whether the evidence should be excluded notwithstanding its relevancy. *See White v. Vanderbilt Univ.*, ___ S.W.3d at ___.[35]

We have determined that the trial court misapplied Tenn. R. Evid. 403 in this case. The evidence regarding terbutaline's off-label usage is particularly relevant with regard to Dr. Miller's decision to continue Ms. Richardson on terbutaline after she experienced chest pain, as well as his decisions regarding the method of administration and the proper dosage. In light of the absence of the manufacturer's instructions regarding recommended dosage levels and methods of administration, pinpointing the basis for Dr. Miller's decisions regarding the use of the drug is integrally related to the Richardsons' claim that Dr. Miller should not have continued Ms. Richardson on tocolysis using terbutaline after she experienced chest pain.

In comparison, there is very little basis in the record to support the conclusion that permitting the Richardsons to introduce this evidence or to cross-examine the defendants and their experts based on this evidence would have produced any of the countervailing factors included in Tenn. R. Evid. 403. There is no arguable claim that permitting the Richardsons to use this evidence would have resulted in undue delay, waste of time, or the needless presentation of cumulative evidence. The only colorable grounds for excluding the evidence are unfair prejudice, confusion of the issues, or misleading the jury. We perceive no real danger of unfair prejudice because this evidence will not prompt the jury to decide the case based on improper considerations such as bias, sympathy, hatred, contempt, retribution, or horror. *See Buddy Lee Attractions, Inc. v. William Morris Agency, Inc.*, 13 S.W.3d 343, 352 (Tenn. Ct. App. 1999); *State v. Collins*, 986 S.W.2d 13, 20 (Tenn. Crim. App. 1998).

Likewise, we find little basis for concern that permitting the Richardsons to use the evidence that tocolysis is an off-label use of terbutaline will confuse the issues or mislead the jury. Such arguments assume that lay persons will be unable to understand that prescribing a prescription drug for an off-label use is not necessarily negligent. State and federal courts around the country have dealt with this very sort of evidence without becoming bogged down with the sorts of problems Dr. Miller and Tokos imagine. The Richardsons may very well want the jury to believe that Dr. Miller

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[34] *See White v. Vanderbilt Univ.*, No. M1997-00105-COA-R3-CV, 1999 WL 1270974, at * 8 (Tenn. Ct. App. Dec. 30, 1999), *perm. app. denied* (Tenn. June 5, 2000).

[35] *See White v. Vanderbilt Univ.*, 1999 WL 1270974, at *8.

should not have continued Ms. Richardson on terbutaline. However, if Dr. Miller's actions were consistent with the applicable standard of care, we have no doubt that he will be able to present competent expert evidence to support the propriety of his actions. Vigorous cross-examination, the presentation of contrary evidence, and proper instructions will head off any possibility that the jury will be confused or misled regarding the significance of the regulatory status of terbutaline.

Furthermore, we do not find that the status of terbutaline's FDA-approved labeling is misleading. Standing alone, it does not establish the standard of care. The trial court will no doubt make this clear to the jury in its instructions. In this case, the fact that terbutaline was put to an off-label use is simply one piece of information along with everything else for the fact-finders to sort out and consider. Based on these considerations, we find that the possible prejudice to the defendants stemming from the admission of the evidence regarding the off-label use of terbutaline for tocolysis does not outweigh the probative value of the evidence. Accordingly, the trial court had no basis for exercising its discretion to exclude this evidence or to prevent the Richardsons from cross-examining the defendants and their experts based on this evidence. We also find that the trial court's decision to exclude this evidence materially hampered the Richardsons' ability to prove their medical malpractice claims and, more probably than not, affected the outcome of the trial.

We find, therefore, that the trial court erred by granting Dr. Miller's motions to exclude the evidence regarding terbutaline's off-label use, including its labeling and the parallel PDR reference and Dr. Gaudino's testimony, as well as that of the Richardsons' other medical experts. The jury was entitled to consider this evidence along with the opinions of Ms. Richardson's experts that Dr. Miller breached the standard of care by continuing to prescribe terbutaline as a tocolytic agent after Ms. Richardson complained of cardiac-related symptoms. Accordingly, the appropriate remedy is to vacate the verdict and remand the case for a new trial.

II.
THE TOKOS - RELATED EVIDENTIARY ISSUES

The Richardsons raise two other evidentiary issues regarding Tokos. First, they assert that the trial court erred by preventing them from introducing Tokos's policy strongly suggesting an EKG before beginning terbutaline infusion therapy. Second, they take issue with the trial court's refusal to permit them to prove that Tokos did not have a license, permit, or certificate of need to operate in Tennessee. We need not dwell long on either of these issues; however, we are addressing them because the issues will likely reoccur should this case be tried again.

A.
THE TOKOS POLICY REGARDING AN EKG

The Richardsons assert that the trial court "should have allowed plaintiffs to introduce the Tokos policy regarding [the] requirement of an EKG and should have permitted the plaintiffs to cross-examine defendants about their failure to follow their own protocols." This argument is somewhat puzzling. Although the record on this point leaves much to be desired, it appears that the trial court permitted the Richardsons to make their point that Dr. Miller did not order, and the Tokos

representatives did not suggest or request, an EKG immediately before beginning the infusion pump even though the Tokos protocols recommended one.

The parties had several skirmishes both before and during trial regarding the Tokos policy requiring an EKG before starting tocolysis using an infusion pump. The Richardsons asserted that Tokos violated its own policy by not insisting on an EKG, and they were prepared to introduce the policy and to prove that no Tokos employee requested or suggested an EKG before starting the pump. For their part, Dr. Miller and Tokos argued that the policy was irrelevant, first because the failure to administer an EKG prior to using the infusion pump did not cause Ms. Richardson's injuries, and second because the Tokos policy did not apply while Ms. Richardson was hospitalized.[36]

Before empaneling the jury, the trial court held that evidence regarding the policy was admissible as a factual matter but not on the issue of causation.[37] Based on that ruling, the Richardsons introduced portions of the deposition of Bev Palmer, Tokos's zone pharmacy manager. Ms. Palmer discussed two Tokos policies during the portions of her deposition that were read to the jury. First, she acknowledged that PBH-00322 required the Tokos clinical staff "to confirm physician's orders for an EKG as part of the guidelines for initiation of tocolytic infusion therapy for a patient."[38] Second, she referred to a portion of PBH-00304 stating that "[i]t is strongly recommended that patients have a recent EKG and appropriate lab work . . .." The trial court directed that PBH-00304 be admitted and marked as Exhibit 3.[39] In addition, the following three questions and Ms. Palmer's answers were read to the jury:

> QUESTION: Well, do you know whether it was a policy of Tokos Medical Corporation for the Tokos clinical staff to confirm that a physician had ordered an EKG?

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[36] Judy Elmore, Tokos's vice president of pharmacy, undermined the latter argument when she testified that Tokos employees were expected to adhere to the company's protocols when the plan was to stabilize the patient and then send her home from the hospital with the infusion pump in place. There is no factual dispute that the defendants intended to discharge Ms. Richardson once her contractions were stopped and that they intended for her to maintain her pregnancy using the infusion pump and a uterine monitor.

[37] Specifically, the trial court stated: "First of all on the EKG, I think that's a question of whether Dr. Miller by his own decision making powers should have given an EKG. I think its also a question to discuss whether Tokos should have talked with the other nurse or talked with Dr. Miller. It is not, again, to be inferred as any causation for anything, but it is a fact that happened."

[38] PBH-00322 was never made part of the record in this case.

[39] The status of Exhibit 3 is somewhat unclear. Even though the trial court directed unequivocally that PBH-00304 containing the language "It is strongly recommended that patients have a recent EKG . . ." be admitted as Exhibit 3, the copy of Exhibit 3 containing this language is actually marked "ID only." In addition, the appellate record contains Exhibit 3A which is also a copy of PBH-00304 but from which the strong recommendation for an EKG has obviously been whited out. Other than the exhibit stamp itself, the transcript contains no indication that Exhibit 3A was ever admitted into evidence. Having no explanation concerning how Exhibit 3A came to be admitted, we will base our decision on Exhibit 3 because the transcript clearly indicates that the trial court permitted Ms. Palmer to testify regarding the very language that was whited out on Exhibit 3A.

* * *

ANSWER: The note. It is strongly recommended that patients have a recent EKG and appropriate lab work, et cetera, et cetera, et cetera. So to me the policy is that an EKG - - it is strongly recommended that patients have a recent EKG.

* * *

QUESTION: I'm asking you, from your understanding of responsibilities of an area clinical pharmacist in June of '93, would the area clinical pharmacist under Tokos policies and procedures in June of '93 have a responsibility to confirm that an EKG had been conducted prior to the initiation of a patient's tocolytic infusion therapy?

ANSWER: I believe so.

* * *

QUESTION: You do believe it was a policy for the Tokos nurse to converse with the physician in June of '93 prior to initiation of tocolytic infusion therapy?

ANSWER: I believe that was a policy.

Three other Tokos employees discussed two other Tokos policies during their testimony, but neither policy dealt directly with the necessity of an EKG before beginning tocolysis using an infusion pump.[40] In addition to introducing this testimony, the Richardsons' lawyers were permitted to cross-examine Dr. Miller and the Tokos employees regarding their failure to order an EKG before they began using the infusion pump. Likewise, one of the Richardsons' lawyers argued to the jury that the Tokos employees had failed to follow the Tokos protocol requiring a recent EKG before starting a patient on an infusion pump.

We concur with the trial court's determination that Tokos's policies regarding indications and contraindications for using the pump, its guidelines for determining which patients were candidates for using the pump, and its procedures for implementing infusion pump therapy were relevant and admissible. They were certainly relevant to the Richardsons' negligence claims against

[40] Christine Evans, the registered nurse employed by Tokos who assessed Ms. Richardson's suitability for an infusion pump, testified regarding the patient selection criteria in Tokos's "Hospital Protocol." She also testified that she decided that an EKG was not warranted based on the information she obtained from Ms. Richardson and her chart. Gail Garner, the Tokos area clinical pharmacist who consulted with Ms. McBride regarding the proper dosage level for Ms. Richardson, testified that Dr. Miller was responsible for determining whether tocolytic therapy was appropriate. Later, Judy Elmore testified regarding PBH-00301, Tokos's policy containing the guidelines for accepting patients for subcutaneous tocolytic infusion therapy.

Tokos. They were likewise relevant with regard to the Richardsons' claims against Dr. Miller. While these policies and protocols, like terbutaline's labeling and parallel PDR reference, do not, by themselves establish a physician's standard of care for determining when the infusion pump should be used, they can materially assist the trier of fact in determining whether Dr. Miller acted negligently by ordering that Ms. Richardson continue to receive terbutaline subcutaneously by infusion pump after she complained that the terbutaline she was taking orally was causing chest pain.

Considering the record as a whole, we find no basis for the Richardsons' assertion that the trial court inappropriately limited their ability to introduce and use the evidence involving Tokos's policies pertaining to obtaining EKG's prior to beginning infusion pump therapy. The record shows that the Richardsons had a fair chance to make their point about the fact that neither Dr. Miller nor any of the Tokos employees working with Ms. Richardson obtained an EKG before commencing infusion pump therapy.

B.
TOKOS LICENSURE STATUS

The Richardsons also assert that the trial court erred by excluding evidence that Tokos had not obtained a license or certificate of need from the State of Tennessee. They insist that this evidence was admissible under Tenn. R. Evid. 608 because "failure to have appropriate licensing is certainly a factor affecting the credibility of Defendant Tokos in this case." We need not reach the question of the admissibility of this sort of evidence in this case because the Richardsons have failed to demonstrate just how state law required Tokos to have either a license or a certificate of need in order to provide a prescribed medical device to a hospitalized patient on orders of her physician.

We are not dealing here with home health care even though the plan, prior to the events of June 27, 1993, had been to discharge Ms. Richardson to permit her to continue her pregnancy at home for ten to fourteen more days. Tokos entered the picture when Dr. Miller ordered an infusion pump while Ms. Richardson was hospitalized. Tokos sent a registered nurse, properly licensed in Tennessee, to the hospital to deliver the pump and to educate Ms. Richardson and the hospital staff in its use.[41] The Tokos nurse was not allowed to deliver the pump until the hospital approved her credentials. Even then, she was not allowed to touch Ms. Richardson. The insertion of the needle for the pump was performed by a registered nurse employed by the hospital, and the terbutaline was obtained from the hospital pharmacy on Dr. Miller's orders.

From this evidence, we conclude that Tokos was supplying a piece of medical equipment and providing consulting advice to Dr. Miller and the hospital staff regarding the use of its infusion pump and the proper terbutaline dosage to be administered. Ms. Richardson has pointed to no state law or regulation, and our research has failed to discover one, requiring that Tokos obtain a license or certificate of need for its activities in this case.

[41]Tokos's registered nurse was accompanied by a home health nurse employed by A+ Stat Home Care. Presumably, Ms. Richardson's care at home, had she been discharged, would have been provided through A+ Stat Home Care. No issue has been raised in this record regarding the credentialing of the home health nurse or A+ Stat Home Care.

III.
THE REQUESTED MISSING EVIDENCE INSTRUCTION

The Richardsons challenge the trial court's refusal to give their requested jury instruction regarding a missing nursing assessment form filled out by Tokos's nurse on June 25, 1993. While the trial court permitted the Richardsons' lawyer to argue to the jury that it could conclude that the contents of the missing form were adverse to Tokos, it declined to give an instruction based on Tennessee Pattern Jury Instructions T.P.I. 3-Civil 2.04 (3d ed. 1997) ("T.P.I. 3-Civil"). We have determined that the Richardsons were entitled to the instruction but that the trial court's refusal to give the instruction is not, by itself, reversible error because the trial court permitted the Richardsons' lawyer to argue the presumption to the jury. However, should this case be retried, we have concluded that the Richardsons will be entitled to the instruction if Tokos' explanation for the missing nursing assessment from and the surrounding facts remain the same.

After Dr. Miller ordered an infusion pump for Ms. Richardson, the hospital staff telephoned Tokos to request the delivery of a pump. Tokos telephoned Christine Evans, its registered nurse in the Nashville area, and instructed her to deliver a pump to the hospital for Ms. Richardson. Ms. Evans, accompanied by Jackie Harris, a nurse employed by A+ Stat Home Care, took the pump to the hospital. Upon arriving at Ms. Richardson's room, Ms. Evans reviewed Ms. Richardson's medical chart and took her medical history to determine whether Ms. Richardson met Tokos's preconditions for using the pump and to obtain the information needed to determine how much terbutaline Ms. Richardson should receive. Ms. Evans recorded her findings on two Tokos forms, a nursing assessment form and a tocolytic infusion intake form. She placed these forms in the patient's file she maintained and sent copies to Tokos's regional office in Atlanta. According to Tokos's policy, these forms would have been sent to Tokos's office in California after Ms. Richardson discontinued using the pump.

During discovery, Tokos produced a nursing assessment form and a tocolytic infusion intake form. It turned out that the nursing assessment form that Tokos produced was not the form that Christine Evans had completed on June 25, 1993. It was not even a Tokos form. Rather, it was only one page of a two-page nursing assessment form used by A+ Stat Home Care. The form was not in Christine Evans's handwriting and was signed by Lisa Evans, an employee of A+ Stat Home Care who was not present at the hospital on June 25, 1993 when Christine Evans obtained the needed medical information from Ms. Richardson.

At trial, the only explanation offered by Tokos employees for the absence of the nursing assessment form completed by Christine Evans on June 25, 1993, was that it must have been either lost in the mail or misfiled. No explanation was offered for the presence in the file of the nursing assessment form signed by Lisa Evans, who was not even at the hospital on June 25, 1993, or for the presence in the file of the tocolytic infusion intake form that would have accompanied the missing nursing assessment form. Accordingly, the Richardsons requested the trial court to give the T.P.I. 3-Civil 2.04 instruction regarding the conclusions to be drawn from a party's failure to introduce evidence that it could have produced. Noting that it had never before encountered a missing evidence issue, the trial court declined to give the requested instruction because there was no proof that Tokos had acted maliciously and because the language of the proposed instruction was "too

strong." However, the trial court permitted Ms. Richardson's lawyer to ask the jury to consider whether the missing nursing assessment form might have indicated that Ms. Evans had concluded that Ms. Richardson was not a proper candidate for the infusion pump.[42]

A trial court's instructions should be complete and accurate and should fairly reflect the parties' theories of the case. *See Ladd v. Honda Motor Co.*, 939 S.W.2d 83, 102 (Tenn. Ct. App. 1996). They must carefully consider the special instructions requested by the parties because the parties are entitled to these instructions (1) if they are supported by the evidence, (2) if they embody a theory relied on by the parties, (3) if they are correct statements of the law, and (4) if their substance is not already contained in other portions of the charge. *See Ingram v. Earthman*, 993 S.W.2d 611, 636 (Tenn. Ct. App. 1998). Based on these criteria, the Richardsons were entitled to an instruction based on T.P.I. 3-Civil 2.04.

The "missing evidence" charge in T.P.I. 3-Civil 2.04 is a nod in the direction of Sherlock Holmes' famous dog that did not bark. It is a recognition that sometimes the absence of something expected can be significant. In Tennessee, as in other jurisdictions, a party's failure to produce a document capable of shedding light on a material contested issue can give rise to a permissive inference that the missing document would have been unfavorable to the party possessing it. *See* Tennessee Law of Evidence § 401.9, at 99. Parties seeking to take advantage of this inference must demonstrate:

(1) that the party against whom the inference is sought could have introduced the evidence but failed to do so;

(2) that the document was uniquely in the possession of the party against whom the inference is sought and that party could have produced the document by exercising reasonable diligence;

(3) that the document was not equally available to the other parties;

(4) that the document would not have been cumulative to other evidence;

(5) that a reasonable person under the same or similar circumstances would have produced the document had it been favorable; and

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[42] Ms. Richardson's lawyer argued the following to the jury without objection:

> I'm not a conspiracy type person that believes the President Kennedy conspiracy and all, I really am not that kind of person. And there may not be – there's probably no conspiracy, but there's something strange about these medical records missing. That is just too coincidental. It really is.
>
> I'm not accusing anyone of potentially doing this, but the fact of the matter is the nursing assessment that's an exhibit in this case, Exhibit Number 6, was not filled out by Chris Evans. It's undated. She testified that the nursing assessment that she filled out she mailed it in and it's missing. It's something to look at.
>
> I submit it just goes along with the attitude of this company that's been throughout this whole trial. I wonder what the nursing assessment that she filled out said. I'd like to see that. I wonder what it said. Not approved for treatment? Who knows. It's not here.

(6) that the party against whom the inference is sought has not offered a reasonable excuse for failing to produce the document.

See T.P.I. 3-Civil 2.04; *State v. Jones*, 598 S.W.2d 209, 224 (Tenn. 1980), *overruled on other grounds, State v. Shropshire*, 874 S.W.2d 634, 638 (Tenn. Crim. App. 1993).

Where the missing evidence is a document, the party seeking the missing evidence instruction must demonstrate that the document existed and was in its adversary's exclusive control. *See Fares v. Fox*, 603 N.Y.S.2d 892, 893 (App. Div. 1993). The party must also demonstrate that the party possessing the document could have produced it. *See Cleveringa v. J.I. Case Co.*, 595 N.E.2d 1193, 1211 (Ill. App. Ct. 1992). To avoid a missing evidence instruction, the party failing to produce a document in its possession must give a reasonable explanation for failing to produce it. *See generally State v. Wilson*, 687 S.W.2d 720, 724 (Tenn. Crim. App. 1984).

Evidence that the party failing to introduce a document was acting maliciously is not required. Seldom will parties be able to prove that their adversary maliciously destroyed or secreted a missing document. Courts should consider giving the missing evidence instruction where the missing evidence is shown to be unavailable due to questionable negligence, *see DeLaughter v. Lawrence County Hosp.*, 601 So. 2d 818, 822 (Miss. 1992), or dubious mishandling. *See Sacramona v. Bridgestone/Firestone, Inc.*, 106 F.3d 444, 447 (1st Cir. 1997).

A jury issue is created when the party seeking the missing evidence instruction puts on evidence showing (1) that the document exists, (2) that the document is relevant, and (3) that the opposing party had exclusive control of the document and the party possessing the document proffers an explanation for not producing it. *See Beers v. Bayliner Marine Corp.*, 675 A.2d 829, 831-33 (Conn. 1996); *DeLaughter v. Lawrence County Hosp.*, 601 So. 2d at 821-22. When the party failing to produce a document claims that it has been innocently lost, the jury should decide the matter for itself when the evidence, viewed as a whole, colorably creates a credibility issue about whether the document was lost or not. *See Bihum v. AT&T Info. Sys., Inc.*, 16 Cal. Rptr. 2d 787, 794-97 (Ct. App. 1993); *see generally Rogers v. State*, 2 Tenn. Crim. 491, 502-03, 455 S.W.2d 182, 187 (1970).

Juries should judge credibility issues. *See Kinney v. Yazoo & M.V.R.R.*, 116 Tenn. 450, 453, 92 S.W. 1116, 1116 (1906); *Lorentz v. Deardan*, 834 S.W.2d 316, 320 (Tenn. Ct. App. 1992). If a jury concludes that a missing document was genuinely lost and that the document's absence is not brought about by manipulation, then the jury should draw no inference against the non-producing party that the document would have been unfavorable. *See Brewer v. Quaker State Oil Ref. Corp.*, 72 F.3d 326, 334 (3rd Cir. 1995).

The circumstances surrounding the missing nursing assessment form created a jury issue. The missing nursing assessment form was solely under Tokos's control and was not equally available to the Richardsons. In light of the evidence regarding Tokos's record keeping practices, Tokos should have been able to produce the document without much difficulty. In the face of the Richardsons' negligence claims, Tokos can reasonably be expected to introduce the nursing assessment form because it would have supported its claim that Christine Evans made a careful and

complete medical assessment of Ms. Richardson before beginning her on the infusion pump. The document would not have been cumulative to other evidence because it would have been the only written evidence, prepared contemporaneously with the other relevant events, of the information Christine Evans used to assess Ms. Richardson's suitability and to determine the dosage of terbutaline she would receive.

Whether this form was innocently lost in the mail or misplaced in Tokos's files is a jury question in light of two facts. First, Tokos was able to produce the tocolytic infusion intake form that Christine Evans completed at the same time she completed the missing nursing assessment form, and Tokos offered no explanation how it could have lost one form but not the other. Second, Tokos offered no explanation for the presence in its file of the undated nursing assessment form apparently completed and signed by a person who was not a Tokos employee and who was not even present at the hospital on June 25, 1993. Based on this evidence, a jury could conclude that the missing nursing assessment form contained information indicating that Ms. Richardson did not meet Tokos's own patient selection criteria. A jury could also conclude that Tokos could not produce the missing nursing assessment form because, in reality, Ms. Evans never completed one. Either conclusion has a direct bearing on Tokos's defense that it conducted a careful medical assessment before determining that Ms. Richardson was a candidate for tocolysis using the infusion pump and setting the dosage amounts of terbutaline the pump would administer.

The Richardsons were entitled to jury instructions on every factual and legal issue raised by their pleadings and put in issue by their evidence. However, what the trial court took away with one hand, it gave back with the other when it permitted the Richardsons' lawyer to argue the missing evidence presumption to the jury. Because the trial court permitted the Richardsons' lawyer to make rhetorical use of the presumption in closing, we do not find that declining to give the requested instruction, in and of itself, affected the outcome of the trial. Assuming, however, that the facts surrounding the missing nursing assessment form remain the same, the trial court on retrial should give an instruction based on T.P.I. 3 - Civil 2.04 if the Richardsons request it. The jury should be permitted to decide for itself whether the missing nursing assessment form, if produced, would be adverse to Tokos.

IV.
THE MOTIONS FOR DIRECTED VERDICT

Dr. Miller and Tokos assert that the trial court should have granted their motions for directed verdict at the close of all the proof. Obviously, were we to affirm the jury's verdict for the defendants, the trial court's failure to direct a verdict for the defendants would be a non-issue. However, because we have vacated the verdict based on the trial court's erroneous exclusion of relevant evidence, we must address Dr. Miller's and Tokos's arguments that they were entitled to a directed verdict.

A.

To avoid a directed verdict under Tenn. R. Civ. P. 50, the non-moving party must present some evidence on every element of its case — enough evidence to establish at least a prima facie

case. *See Harrogate Corp. v. System Sales Corp.*, 915 S.W.2d 812, 818 (Tenn. Ct. App. 1995). Normally, a directed verdict is proper only where no material evidence exists on one or more elements that the non-moving party must prove. *See generally Conatser v. Clarksville Coca-Cola Bottling Co.*, 920 S.W.2d 646, 647 (Tenn. 1995). Whether the trial court should have directed a verdict presents us with the legal question of whether material evidence was introduced on every element sufficient to create a jury issue. *See Lazy Seven Coal Sales v. Stone & Hinds*, 813 S.W.2d 400, 403 (Tenn. 1991); *Underwood v. HCA Health Servs. of Tenn., Inc.*, 892 S.W.2d 423, 425 (Tenn. Ct. App. 1994). *Dickson v. Stephens*, 20 Tenn. App. 195, 211, 96 S.W.2d 201, 211-12 (1935).

When reviewing a trial court's disposition of a motion for directed verdict, appellate courts do not resolve disputes in the evidence, weigh the evidence, *see Conatser v. Clarksville Coca-Cola Bottling Co.*, 920 S.W.2d at 647, or evaluate the credibility of the witnesses. *See Benson v. Tennessee Valley Elec. Coop.*, 868 S.W.2d 630, 638-39 (Tenn. Ct. App. 1993). Instead, we review the evidence most favorably to the party against whom the motion is made, give that party the benefit of all reasonable inferences from the evidence, and disregard all evidence contrary to that party's position. *See Eaton v. McClain*, 891 S.W.2d 587, 590 (Tenn. 1994); *Gann v. International Harvester Co.*, 712 S.W.2d 100, 105 (Tenn. 1986).

Directed verdicts are appropriate only when reasonable minds can reach one conclusion. *See Williams v. Brown*, 860 S.W.2d 854, 857 (Tenn. 1993); *Crosslin v. Alsup*, 594 S.W.2d 379, 380 (Tenn. 1980). A case should go to the jury, even if the facts are undisputed, when reasonable persons could draw conflicting conclusions from the facts. *See Gulf, M. & O.R.R. v. Underwood*, 182 Tenn. 467, 474, 187 S.W.2d 777, 779 (1945); *Pettus v. Hurst*, 882 S.W.2d 783, 788 (Tenn. Ct. App. 1993). These conclusion, however, must be based on more than speculation, conjecture, and guesswork. *See Daniels v. White Consol. Indus., Inc.*, 692 S.W.2d 422, 425 (Tenn. Ct. App. 1985).

B.

Both Dr. Miller and Tokos assert that the trial court should have directed a verdict in their favor at the close of all the proof because the Richardsons' evidence failed to establish causation. Ms. Richardson had the burden to prove at trial that she suffered injuries she would not otherwise have suffered as a proximate result of Dr. Miller's and Tokos's negligence. *See* Tenn. Code Ann. § 29-26-115(a)(3); *Kilpatrick v. Bryant*, 868 S.W.2d 594, 598 (Tenn. 1993). Dr. Miller and Tokos maintain that Ms. Richardson's evidence did not show that the administration of terbutaline proximately caused her coronary artery dissection and heart attack.

The Richardsons sought to prove the causal link between the terbutaline she was taking and her coronary artery dissection with the testimony of Dr. Ronald Krone, a Missouri cardiologist, and Dr. James Dingfelder, a North Carolina obstetrician and gynecologist. Dr. Krone saw Ms. Richardson approximately a year after her heart attack. In addition to examining Ms. Richardson himself, he reviewed her hospital records. Based on his medical experience and his knowledge of the plaintiff, Dr. Krone testified sure-footedly that Ms. Richardson's heart damage was caused by the splitting of an artery serving her heart. When asked for his professional opinion of what caused the arterial splitting that led to the heart attack, he answered that terbutaline, in his opinion, increased

the risk of heart attacks in pregnant women and the administration of terbutaline is what caused Ms. Richardson's heart attack.[43]

In addition, Dr. Dingfelder gave the following opinion with regard to causation:

> I believe after looking at all of the alternative explanations for this patient's injury which have been put forward and which I have considered, including shock at hearing bad news, and something that she was born with, a congenital anomaly, these, in my opinion, pale in significance to the obvious known effects of terbutaline.
>
> I mean, this patient has already manifested chest pain from terbutaline to begin with. So it's perfect medical logic, in my opinion, that terbutaline is the cause.

Dr. Miller and Tokos attack Dr. Dingfelder's testimony as contradicting his prior deposition testimony and as being medically weak because Dr. Dingfelder was not a cardiologist. Dr. Dingfelder's testimony may very well be subject to attack on these grounds. However, this court is charged with viewing the challenged testimony in the strongest possible light favoring the Richardsons. Weighing the evidence is the jury's task. When we view both physicians' testimony favorably, and we discard everything that would lessen its weight, we cannot say that Dr. Krone's and Dr. Dingfelder's testimony provided no material evidence on causation. Weak or strong, their testimony at least created a jury question on causation, and therefore the trial court did not err in refusing to direct a verdict on that ground.

V.
THE DISMISSAL OF PRINCIPAL MUTUAL LIFE INSURANCE COMPANY

The final issue involves the trial court's dismissal of Principal Mutual's intervening complaint. Ms. Richardson had employer-provided, non-contributory group health insurance underwritten by Principal Mutual. Her policy contained a provision stating that "where allowed by law" an insured who receives benefits for sickness or injury and who has "a lawful claim" against third parties for damages related to that sickness or injury must reimburse the insurance company for payments made on the insured's behalf out of any recovery the insured receives from a third-party wrongdoer.[44]

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[43] During his cross-examination, Tokos's lawyer got Dr. Krone to admit that he could not medically rule out the possibility that Ms. Richardson could have had the heart attack due merely to the stress of pre-delivery labor. However, Dr. Krone never said that in his professional opinion the heart attack *was due only* to Ms. Richardson's labor. In any event, Dr. Krone's concession on cross-examination went to the weight of his testimony, which was for the jury to determine.

[44] Although Principal Mutual characterizes its claim as one for subrogation, it is more in the nature of a claim for reimbursement. The policy provision on which Principal Mutual relies allows it to recoup payments made to its own insured. *See generally York v. Sevier County Ambulance Auth.*, 8 S.W.3d 616, 619 (Tenn. 1999).

Following Ms. Richardson's heart attack, Principal Mutual paid $52,434.54 in medical bills. After the Richardsons filed suit against Dr. Miller, Tokos, and others, Principal Mutual sought to intervene based on its contractual right to reimbursement and sought reimbursement out of any recovery Ms. Richardson may obtain in her malpractice action. The trial court dismissed Principal Mutual's complaint evidently on the theory that Tenn. Code Ann. § 29-26-119 prohibited Ms. Richardson from recovering any medical expenses that had been paid by Principal Mutual.

Tenn. Code Ann. § 29-26-119 states that a medical malpractice plaintiff may not recover for the cost of medical care if that cost was indemnified in whole or in part by employer-provided insurance. The statute seeks to prohibit injured parties from making a double recovery by reducing a plaintiff's recovery by the amount of benefits paid by employer-provided insurance. *See Nance v. Westside Hosp.*, 750 S.W.2d 740, 742 (Tenn. 1988). Excluded, however, from the statute's general operation are collateral payments made where the collateral payor has subrogation rights. *See Nance v. Westside Hosp.*, 750 S.W.2d at 743. Where the injured insured must repay the insurer out of any damages recovered, the insured gets no double recovery. Stated another way, where a right of subrogation exists or where the tort victim has a legal obligation to repay the collateral source payor, then the victim's losses have not been "replaced or indemnified" for purposes of Tenn. Code Ann. § 29-26-119. *See Nance v. Westside Hosp.*, 750 S.W.2d at 743; *Hughlett v. Shelby County Health Care Corp.*, 940 S.W.2d 571, 574 (Tenn. Ct. App. 1996).

In this case, Ms. Richardson's legal obligation to repay the approximately $52,000 of covered medical expenses is contractual. As part of her health coverage, she has contractually agreed to reimburse Principal Mutual for medical benefits paid on her behalf if she subsequently receives those amounts from third parties responsible for her injury. Contractual provisions like Principal Mutual's are enforceable to the extent that an insured has received full compensation and has been made whole for his or her losses. *See York v. Sevier County Ambulance Auth.*, 8 S.W.3d at 621; *Board of Trustees v. Graves*, No. M1997-00069-COA-R3-CV, 1999 WL 1086454, at *2 n.4 (Tenn. Ct. App. Dec. 3, 1999) (No Tenn. R. App. P. 11 application filed).[45] As a matter of contract law, Principal Mutual may legitimately seek reimbursement from Ms. Richardson. Consequently, her losses have not been "replaced or indemnified" by her own health insurance, and Tenn. Code Ann. § 29-26-119 does not prevent her from pursuing recovery of those medical expenses against Dr. Miller and Tokos. For that reason, the trial court should not have dismissed Principal Mutual's intervening complaint.

VI.

Based on the foregoing, we reverse the judgment dismissing the Richardsons' claims against Dr. Miller and Tokos and remand the case for a new trial consistent with this opinion. We tax the costs of this appeal in equal proportions to James Miller, M.D. and to Tokos Medical Corporation for which execution, if necessary, may issue.

WILLIAM C. KOCH, JR., JUDGE

[45] Of course, any question about whether Ms. Richardson has been made whole in this case remains to be litigated on remand.