letters are part of a larger warning system that includes the sum of package inserts, Physician's Desk Reference (PDR), and visits to doctors by the sales force (detailmen). Issues relating to a manufacturer's duty to warn, specifically relevant to the sales force, are the frequency of visits of the doctor, and training of the sales force regarding the warning in question. *Mahr v. G.D. Searle* (222) illustrates the concept that the sum of all of the above methods are part of the big picture for transmitting warnings to doctors, and that the sum of all of the above methods can determine if a company is liable for insufficiently transmitting warnings to physicians. This particular case concerned pulmonary embolisms caused by birth control pills. *Mahr v. G.D. Searle* also illustrates the utility of *Dear Healthcare Professional* letters in transmitting warnings where a gray area is thought to exist, that is, where there is no compelling reason to believe that a drug caused the adverse drug reaction in question. Thus, this courtroom opinion reveals the situation where the *Dear Healthcare Professional* letter "indicated that no causal connection between oral contraceptives and thromboembolic disorders had been demonstrated," but also "requested physicians to report to the company all instances of thrombophlebitic disease" (223).

The goal of this narrative is solely to illustrate some general principles that might be learned from the courtroom case, showing how the *Dear Healthcare Professional* letter fits into the various methods for warning physicians and patients.

c. *Dear Healthcare Professional* letter regarding acne medicine

Snyder v. Hoffman-LaRoche (224) further demonstrates that providing warnings to physicians (and patients) is the sum of a variety of tools, including the *Dear Healthcare Professional* letter, consent forms, a Medication Guide for pharmacists to distribute with the drug prescriptions, and oral counseling by the physician to the patient. In this context, the consent form is administered in the course of ordinary medical practice, not as part of a clinical trial. This courtroom opinion concerned an acne drug (13-cis-retinoic acid, Accutane®) that may have the adverse drug reaction of inducing depression.

The timeline is as follows. In February 1998, the manufacturer amended the package insert to include the warning, "WARNINGS: Psychiatric Disorders: Accutane may cause depression, psychosis, and, rarely, suicidal ideation, suicide attempts, and suicide. Discontinuation of Accutane therapy may be insufficient; further evaluation may be necessary." The manufacturer provided additional warnings in the form of a "Dear Doctor" letter to physicians from February 1998, the 1999 issue of the Physician's Desk Reference, and an information brochure to physicians entitled "Important Information Concerning Your Treatment with Accutane." In January 2001, the manufacturer disseminated an Informed Consent Agreements for physicians to administer to all patients.

[222] Mahr v. G.D. Searle. 72 Ill. App. 3d 540; 390 N.E.2d 1214; 1979 Ill. App. LEXIS 2655.
[223] Mahr v. G.D. Searle. 72 Ill. App. 3d 540; 390 N.E.2d 1214; 1979 Ill. App. LEXIS 2655.
[224] Snyder v. Hoffman-LaRoche. Middle District Florida, 2008 U.S. Dist. LEXIS 92017.