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 Feb. 1998, the 1999 issue of the PDR, an information brochure to physicians entitled "Important Information Concerning Your Treatment with Accutane." In Jan. 2001, the manufacturer disseminated an Informed Consent Agreement for physicans to administer to all patients. The Informed Consent (to be read by patients) included the language, "I understand that some patients, while taking Accutane or soon after stopping Accutane, have become depressed or developed other serious mental problems. Signs of these problems include feelings of sadness, irritability, unusual tiredness, trouble concentrating, and loss of appetite." The Informed Consent also read, "Once I start taking Accutane, I agree to stop using Accutane and tell my provider right away if any of the following happen. I start to feel sad or have crying spells, lose interest in my usual activities,. . ."

On or about Feb. 2000, the physician first prescribed the drug to Mr Snyder for treating acne. Treatment was continued until Sep. 2003. But in Feb. 2005, the patient (Mr Snyder) committed suicide.

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

f. *Dear Healthcare Professional* Letter Regarding Appetite Suppressants

In re Brisco et al. (376) provides one more illustration of a *Dear Healthcare Professional* letter, this time, where the goal is to inform physicians that a drug was withdrawn from the market. As in the above examples, the *Dear Healthcare Professional* letter was used in combination with other methods for warning physicians and patients. To quote from this courtroom opinion, "The publicity began on September 15, 1997. At 5:00 p.m., the Houston CBS news affiliate started the broadcast with a report that . . . diet drugs had been pulled from the market, announcing that the Food and Drug Administration is urging millions of dieters to stop taking them as they have been linked to serious heart problems. Similar newscasts kicked off the five o'clock news for both the ABC and NBC affiliate station in the Houston area . . . furthermore, [the manufacturer] sent a *Dear Health Care Provider Letter* to approximately 450,000 physicians and pharmacists in which it informed them of the withdrawal of the drugs from the market and of the potential association between use of the drugs and instances of valvular heart disease" (377).

The purpose of this narrative is solely to reveal general principles that can be learned regarding how *Dear Healthcare Professional* letters fit into the array of available methods for warning physicians and patients.

XVI. FDA'S DECISION-MAKING PROCESS IN EVALUATING RISK MINIMIZATION TOOLS

a. Introduction

The comments from FDA reviewers provide concrete guidance to all Sponsors regarding the content of their draft REMS, and whether they should submit any REMS with their NDA or BLA.

[376]In re Brisco, et al. 448 F.3d 201, U.S. Court of Appeals, 3rd Circuit, 2006 U.S. App. LEXIS 11990.

[377]In re Brisco, et al. 448 F.3d 201, U.S. Court of Appeals, 3rd Circuit, 2006 U.S. App. LEXIS 11990.