reviewer's comments were reasonable in that they left open the possibility of "sudden incapacitation" related to the study drug.

d. Everolimus for Preventing Rejection of Kidney Transplants

This is from a clinical trial for *everolimus*, a drug for preventing rejection of kidney transplants. The information is from NDA 21560, from Jan. 2015 on FDA's website. A male study subject died as a result of a motor vehicle accident where, according to the FDA reviewer, the "real cause of death ... is the motor vehicle accident." The reviewer states that the subject remained alive for 13 days following the accident, and that, "the final event causing the death ... might have been pulmonary emboli occurring 13 days after" the accident. The take-home lesson is that, where an accident is the initiating event that results in death, safety reporting should include the final event most closely associated with the death.

e. Tavaborole for Fungal Infections

The example of *tavaborole* is from NDA 204427, at Jan. 2015 on the FDA's website. The study drug, tavaborole, took the form of a topical solution for applying directly to toenails infected with fungus. Please note the remote nature of a drug that is applied topically, and to possible causes of falling down. The *Medical Review* described one death, writing that, "[t]he subject was 61 years old female ... [s]he was treated with tavaborole ... from July 26, 2006 until November 6, 2006 ... she fell down and, according to the death certificate, died of head trauma." Although reasons were not expressly stated, the FDA reviewer stated that the trauma "was not considered by investigators as related to the treatment ... I agree with the investigator's assessment that event was not likely related to the drug."

XIV. POSTMARKETING REPORTING OF ADVERSE EVENTS

a. Introduction

After regulatory approval of a drug, there is continued surveillance of drug safety. Healthcare professionals, as well as the general public, can submit drug safety reports to the FDA by way of a MedWatch form. There are two different versions of the MedWatch form, one of which is used by pharmaceutical companies, and the other by consumers in the postmarketing context.

The MedWatch form provides a rapid way to communicate SAEs to the FDA. This form is used for any SAE, especially those that might not be listed on the package insert, including fatalities, hospitalization, and other medically significant events. The FDA welcomes the use of MedWatch forms to report therapeutic failures, for example, if a patient needed to switch to another brand of the same drug, to report errors in the dosing instructions, and to report suspected counterfeit drugs or contaminated drugs. In the context of postapproval reporting, Nebeker et al. (326), stated that, "the FDA is interested in receiving reports on serious, unexpected adverse drug reactions (not adverse drug events) from marketed drugs. Unexpected reactions are those whose nature or severity is not consistent with the product label."

The MedWatch form finds use by physicians who treat members of the general public (not clinical trial subjects), as demonstrated by this example. Injuries to patients resulted from

[326]Nebeker JR, Barach P, Samore MH. Clarifying adverse drug events: a clinician's guide to terminology, documentation, and reporting. Ann. Intern. Med. 2004;140:795–801.