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NEWSLETTER

THE OFFICIAL JOURNAL OF THE ANESTHESIA PATIENT SAFETY FOUNDATION

CITATION: Thomas B. Off-label low-flow sevoflurane: regulatory red herring or liability landmine?. *APSF Newsletter*. 2022;372:57–58.

Off-Label Low-Flow Sevoflurane: Regulatory Red Herring or Liability Landmine?

by Brian Thomas, JD

Administration of sevoflurane at low-flow rates remains a controversial practice due to the low-flow limits described in the Food and Drug Administration's (FDA) required labeling. Specifically, the labeling in the United States requires no less than 1 L/min for up to 2 Minimum Alveolar Concentration (MAC)-Hours and no less than 2 L/min during longer exposures.¹ While there is substantial evidence that Compound A is not toxic to humans and many carbon dioxide absorbents do not produce Compound A, the language in the labeling continues to influence practice.² Labeling requirements create confusion about whether or not prescribing or administering a drug in an "off-label" manner (e.g., for a purpose not approved by the FDA) is safe and meets the standard of care.* This article will address whether administering sevoflurane at off-label low-flow rates increases anesthesia professionals' potential liability exposure in the event of an adverse outcome.

FDA APPROVAL AND OFF-LABEL USE

The FDA "plays a role in almost every aspect of the approval, marketing, labeling, advertising, and promotion of both over-the-counter and prescription drugs."³ To approve a drug, the FDA must obtain sufficient information based on clinical testing to determine: 1) if the drug is safe and effective for the proposed use(s) and whether the benefits of the drug outweigh its risks; 2) whether the proposed labeling is appropriate and what (if anything) should be changed; and 3) whether the methods used in manufacturing the drug and the controls used to maintain its quality are adequate.⁴

Once a drug is approved for a specific purpose, the drug can be used for any treatment even if the FDA did not approve that treatment. Using the drug for a purpose not indicated on its FDA-approved label is called an "off-label" practice.⁵ Off-label use is allowed by law in the context of therapy, but not allowed for research. The distinction between off-label use and research is important as the FDA closely regulates the development and clinical investigation



(i.e., "research") of new drugs. The FDA does not, however, regulate the practice of medicine, and anesthesia professionals are allowed to prescribe approved drugs for off-label use if such prescriptions do not qualify as "research."⁶

POTENTIAL MALPRACTICE LIABILITY

The most likely cause of action against an anesthesia professional who prescribes or administers a drug for an allegedly improper off-label use is the lack of informed consent.[†]

INFORMED CONSENT

In the United States, the doctrine of informed consent generally requires an anesthesia professional to provide the patient or their legal surrogate with material information regarding the proposed treatment, the alternatives to treatment (including no treatment), the risks and potential benefits of the proposed treatment and alternatives. Given that information, the patient or their legal surrogate must be allowed to determine whether to consent to the proposed or alternative treatment. Most states apply the "reasonable anesthesia professional" standard when determining whether an

adequate informed consent discussion was provided. This standard requires a determination by the jury or judge whether a reasonable anesthesia professional would have provided the material information necessary for the patient to make an informed decision.

In applying the doctrine of informed consent to off-label drug prescription or administration, many state courts have held that anesthesia professionals and other health care providers do not have to disclose to patients that a proposed use is off-label. For example, in one seminal appellate case, the court held:

"The decision whether or not to use a drug for an off-label purpose is a matter of medical judgment, not of regulatory approval. By analogy, the off-label use of a medical device is also a matter of medical judgment, and as such, subjects an [anesthesia professional] to professional liability for exercising professional medical judgment. Off-label use of a medical device is not a material risk inherently involved in a proposed therapy which an [anesthesia professional] should have disclosed to a patient prior to the therapy."⁷

Most states' informed consent laws limit an anesthesia professional's duty to providing medical information. In those states, the courts have held as a matter of law that there is no duty obligating an anesthesia professional to discuss the FDA regulatory status of drugs or products being used for a particular treatment, nor does a drug or product's legal status (e.g., FDA-approved or off-label) affect the nature of the treatment.⁸

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* "Medical standard of care" is a legal term that is generally defined as the level and type of care that a reasonably competent and skilled anesthesia professional, with a similar background and in the same medical community (specialty), would have provided under the same or similar circumstances.

† If informed consent is not obtained, an anesthesia professional can be exposed to civil liability. Performing an invasive procedure without a patient's consent is battery, an intentional tort, for which monetary damages may be awarded. If an anesthesia professional failed to inform a patient about risks of a procedure and alternative treatments, he or she may be liable for negligence if the patient is injured as a result of the treatment.

Anesthesia Professionals Are Allowed to Administer “Off Label” Drugs If Such Drugs Do Not Qualify As “Research”

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However, a minority of states apply a “reasonable patient or person” standard of review for informed consent. That is, would a reasonable patient or person have considered the fact that a drug or medical device was going to be administered or used in an off-label manner material information for purposes of consenting to the treatment? Even in those states, the plaintiff would still need to prove that had the patient known the drug prescribed or administered was off-label, the patient would have refused the treatment.⁹

Plaintiff attorneys continue to file lack of informed consent cases based on the fact that an anesthesia professional did not inform his or her client that the drug was administered in an off-label manner. A layperson on a jury could give great deference to the fact the FDA did not approve the use for which the anesthesia professional prescribed or administered the drug, even though such use may be widely accepted.¹⁰ Additionally, plaintiff attorneys will have little difficulty identifying anesthesiology experts to testify that the administration of sevoflurane off-label for low-flow anesthesia is below the standard of care based, at least in part, on the manufacturer’s and FDA’s warning label recommending against fresh flow rates < 1 L/min. However, if the anesthesia professional’s care was appropriate, most of these cases are defensible and do not result in settlement or ever make it to trial.

CONCLUSION

Anesthesia professionals have safely prescribed and administered a multitude of drugs off-label for decades. A review of Preferred Physicians Medical’s 4,594 anesthesia closed claim files from 1987 to March 10, 2022, did not identify any claims with allegations of patient injury or death involving low-flow sevoflurane anesthesia. The FDA does not regulate the practice of medicine, and anesthesia professionals are allowed to prescribe and administer drugs for off-label uses if such drugs do not qualify as “research.” Like all medical judgments, a decision to administer a drug “off-label” becomes a risk-benefit decision. While the off-label use of a drug may potentially increase the risk of liability, that risk may be mitigated by an adequate informed consent process and adherence to the standard of care. In summary, litigation involving allegations of negligence due to off-label administration of drugs is uncommon and, in most cases, defensible on behalf of anesthesia professionals.

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The author has no conflicts of interest.

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