



AMERICAN SOCIETY OF ANESTHESIOLOGISTS

Office of Governmental Affairs

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BY MESSENGER

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Docket Number 2005P-0267; Comments Opposing Citizen Petition Requesting Change in Propofol Labeling

Attention: Dr. Robert Rappaport
Center for Drug Evaluation and Research

Dear Dr. Rappaport:

The American Society of Anesthesiologists (ASA) is pleased to have this opportunity to submit comments in response to the above-captioned petition submitted by the American College of Gastroenterologists (ACG) seeking the removal of warning language from the package insert for propofol (Diprivan®). The language in question states: "For general anesthesia or monitored anesthesia care (MAC) sedation, DIPRIVAN Injectable Emulsion should be administered only by persons trained in the administration of general anesthesia and not involved in the conduct of the surgical/diagnostic procedure." It is apparent that what we can call the current "anesthesia training warning" has two components: first, propofol should be administered only by those trained in the administration of general anesthesia, and second, that such individuals not be engaged in the conduct of the surgical or diagnostic procedure involved so that their full attention can be devoted to the state of the patient. The safety considerations that led the FDA to support this warning are still valid and the warning should remain in place. Moreover, FDA lacks the legal authority to unilaterally change a warning in a way that might reduce patient safety. ASA therefore respectfully requests that the Commissioner reject the ACG petition.

By way of background, ASA, founded in 1905, is the national educational, research and scientific association of physicians organized to raise and maintain the standards of the medical practice of anesthesiology and improve the care of the patient. For our 40,000 member physicians, patient safety is paramount. Propofol is a powerful anesthetic agent with all of the risks of general anesthesia. Most important is the risk that patients, whose responses to propofol are unpredictable, may enter a state of general anesthesia even if only moderate sedation was

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intended. Fully anesthetized patients may face a number of life-threatening complications. Individuals not trained and experienced in the administration of general anesthesia may not be able to restore breathing or normal cardiac activity in time to prevent a catastrophe. ASA and its members strongly believe that the requested change is ill-advised. It is not supported by sound clinical data and is not in the best interests of patient safety.

1. The ACG Petition Does Not Provide Sufficient Legal or Policy Grounds to Support the Requested Labeling Change

ACG's Petition fails to provide sufficient grounds to justify the requested action. Although styled as being submitted pursuant to 21 C.F.R. § 10.30, the Petition fails to include the required detailed discussion "of the factual and legal grounds on which the petitioner relies" 21 C.F.R. § 10.30(b) (underlining added).¹ Instead, it is simply a summary of numerous published scientific articles designed to support an economic objective. It is far from clear that FDA has the unilateral authority to require the deletion of the "anesthesia training warning" statement in response to a petition such as the one submitted by ACG. In any event, such action would be inconsistent with FDA's past practice, and contrary to the interests of patient safety.

The Petition's silence with respect to the legal basis for FDA to act as requested is not surprising. The Agency's authority to require changes to drug products after they have been approved is extremely limited under the Federal Food, Drug, and Cosmetic Act (FDC Act). For example, FDA can require the addition of so-called "black box" warnings to address serious safety issues that arise after approval.² However, there is no authority for FDA to require a labeling change in the absence of a safety or effectiveness concern (especially where, as in this case, the removal of a statement designed to assure patient safety is being requested rather than the addition of new safety information or warnings designed to address adverse clinical experience). The Agency may seek to "encourage" a drug company to change its labeling under threat of withdrawing its approval on the grounds of evidence that becomes available showing that the drug is unsafe or ineffective under its approved conditions of use. FDC Act § 505(e). However, this does not permit FDA to act to change the approved labeling if the manufacturer declines.

More important in this case, nothing in the ACG Petition suggests that propofol is unsafe or ineffective with the current "anesthesia training warning" in the labeling. The fact that FDA approved the labeling with this statement is *prima facie* evidence that FDA believed such warning was necessary for the safe and effective use of the drug. The ACG Petition does not claim to show any evidence to the contrary. Rather, ACG's argument is simply that there may

¹ The one attempt at a legal justification appears to be a citation to various hortatory statements from Executive Order 12866 concerning the need for agencies to evaluate costs and benefits when promulgating regulations. Exec. Order No. 1,866, Regulatory Planning and Review, (58 *Fed. Reg.* 51735 (October 4, 1993)), cited in ACG's Petition at 8. However, FDA does not approve New Drug Applications (NDAs) like the ones for propofol via "regulations," and such approval actions are not covered by the Executive Order.

² "The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved. . . . Special problems, particularly those that may lead to death or serious injury, may be required by [FDA] to be placed in a prominently displayed box." 21 C.F.R. § 201.57(e).

be other circumstances under which propofol may safely be used that allegedly would result in lower economic costs³. Even if these points are correct, however, they do not provide a legal basis for FDA to unilaterally change the product's labeling, since FDA's mandate is to protect public health.

Even assuming, *arguendo*, that FDA has the legal authority to take the requested action (without conceding that it does), there is no legitimate policy reason for it to do so here. In past cases where labeling questions have arisen, FDA has worked with the drug manufacturer to address the issues, and this is in fact FDA's stated policy:

After approval, the Agency continues to monitor information bearing on the safety and effectiveness of the drug and, where appropriate, works with the sponsor to update the labeling. We note, as have many courts, that "The FDA is the agency charged with implementing the [FDC Act]. [The Agency's] judgments as to what is required to ascertain the safety and efficacy of drugs falls squarely within the ambit of the FDA's expertise." (underlining added) (citation omitted).⁴

For example, in 2001, a company asserted that a comparative statement in the labeling of a competitor's drug was literally false.⁵ After reviewing the petition, FDA concluded that the disputed statement was "not supported by any data" in the product's NDA. FDA "requested that [the sponsor] remove the statement from the [product's] labeling. [The sponsor] complied with FDA's request and submitted a labeling supplement to remove the sentence from its labeling."⁶ Despite the fact that the information in question was false, FDA did not purport to change the labeling on its own. In the case of propofol, there is no suggestion that the current labeling is somehow inaccurate, much less false or misleading. Thus, it would be especially inappropriate for FDA to act unilaterally.⁷

In summary, from a legal standpoint, the ACG Petition does not provide sufficient legal or policy bases for FDA to take the requested action. Even if such authority existed, however, the scientific evidence cited in the Petition shows that patient safety will not be adequately protected if the "anesthesia training warning" is deleted from the labeling. The scientific issues are addressed in the following section.

³ As these comments will show in the next section, the studies cited in ACG's Petition fail to, in fact, support the claim that patient safety would not be adversely affected.

⁴ FDA Docket No. 2002P-0244 (FDA denial of Citizen Petition requesting "black box" warnings for concerning the interaction of statin drug products and CoQ10) (dated March 4, 2005)

⁵ FDA Docket No. 01P-0122 (Citizen Petition concerning "Transderm Scop®") (dated March 7, 2001)

⁶ FDA Docket No. 01P-0122 (FDA response granting petition) (dated May 10, 2002)

⁷ ASA does not know what position, if any, AstraZeneca (the holder of the approved NDA for Diprivan®) has with respect to the claims in the ACG Petition.

2. Patient Safety Requires Extensive Training to Use Propofol

Propofol is a powerful anesthetic agent that can produce unpredictable levels of sedation along the continuum from sedation to general anesthesia. It is efficacious and safe when administered by physicians with the appropriate training and appropriate monitoring technology. Because sedation is a continuum, it is not always possible to predict how an individual patient will respond. The extremely rapid action and high potency of propofol make it difficult to quickly attain the desired level of sedation and make it easy to induce an unintended state of general anesthesia within as little as 30 seconds of a single intravenous dose. Patients differ widely in their individual reactions to a standard dose, and there is an approximately 20-fold variation in the rate of metabolism of propofol.

There are no antagonist or reversal medications for propofol. This is an important factor that distinguishes propofol from other sedatives, such as benzodiazepines and narcotics, currently used by non-anesthesiologist physicians. Due to the potential for rapid, profound changes in sedative/anesthetic depth and the lack of antagonist medications, agents such as propofol require special attention. Even if moderate sedation is intended, patients receiving propofol should receive care consistent with that required for deep sedation. This means that the clinician administering propofol must be competent to recognize a state of general anesthesia and rescue a patient experiencing any of the complications of general anesthesia.

General anesthesia frequently entails the loss of the ability to maintain ventilatory function, and patients often need assistance in maintaining a patent airway. Positive airway pressure may be required because of depressed spontaneous ventilation or drug-induced dependence of neuromuscular function. A patient under general anesthesia is at risk for life-threatening respiratory and cardiovascular changes, including hypoxia, hypoventilation, bradycardia, tachycardia, hypotension and hypertension.

Because patients may readily enter a state of general anesthesia even if a lower level of sedation was planned, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) requires that clinicians intending to administer deep sedation be qualified to rescue patients from general anesthesia and be competent to manage an unstable cardiovascular system as well as a compromised airway and inadequate oxygenation and ventilation. ASA believes that the involvement of an anesthesiologist in the care of every patient undergoing anesthesia is optimal. If this is not possible, however, we have stated that “non-anesthesia personnel who administer propofol should be qualified to rescue patients whose level of sedation becomes deeper than initially intended and who enter, if briefly, a state of general anesthesia.”⁸

To be qualified to rescue patients from general anesthesia, the physician responsible for the use of propofol should have the education and training to manage the potential medical complications of sedation and anesthesia. “The physician should be proficient in airway management, have advanced life support skills appropriate for the patient population, and

⁸ Statement on Safe Use of Propofol approved by ASA House of Delegates October 27, 2004

understand the pharmacology of the drugs used.”⁹ The physician should be proficient in recognizing the sometimes subtle signs of adverse respiratory or cardiac events and should have the knowledge and technical skills (e.g. rapid intubation) to manage cardiovascular events and compromised airways.

It is possible for non-anesthesiologist physicians to have the requisite training and experience to manage deep sedation. Privileges to administer general anesthesia awarded by the facility in which a physician practices would be the best indicator of adequate training. Removal of the warning label from the propofol package insert may encourage the use of propofol by practitioners with inadequate training and experience in non-accredited facilities where credentialing is not required, such as private offices. We note that almost 20% of procedures are now being performed in private offices, and the proportion is expected to grow.

In 1999, the Institute of Medicine (IOM) identified ASA as the sole exception to its observation that “few professional societies or groups have demonstrated a visible commitment to reducing errors in health care and improving patient safety.”¹⁰ As an organization long committed to improving the quality and safety of patient care, ASA is very concerned with the adequacy of some of the anesthesia and sedation training offered to other medical specialties. For example, attached is a copy of a brochure for a forthcoming symposium, sponsored principally by the American College of Gastroenterology, on “Endoscopic Sedation: Preparing for the Future.” We question the seriousness or sophistication of a section on “Maximizing Patient Safety” that dedicates just 20 minutes to a lecture entitled “Airway Management for Dummies.”

Gastroenterologists are concerned with “the troublesome and increasing problem of undertrained endoscopists,” attributed to the propensity of hospitals to replace subspecialty-trained endoscopists with less costly generalists.¹¹ If undertrained endoscopists lack proficiency in endoscopy, it is difficult to imagine that they have the requisite education and experience in anesthesiology.

3. The Literature on Gastroenterologists’ Use of Propofol Does Not Establish the Safety of the Practice

To understand the evidence summarized in the ACG Petition, we asked the Methodology Group of the ASA Committee on Practice Parameters to analyze the 31 studies cited, using standard techniques for assessing the strength of literature for the preparation of evidence-based practice parameters. The methodologists found that the literature did not provide sufficient statistical or meta-analytical evidence to address the two major safety concerns: 1. Use of propofol by non-anesthesiologists and 2. The involvement of the physician responsible for the sedation in the conduct of the surgical/diagnostic procedure (physician involvement is discussed below). Only

⁹ *Id.*

¹⁰ Wall Street Journal, June 21, 2005.

¹¹ Rex DK. Three Challenges: Propofol, Colonoscopy by Undertrained Physicians, and CT Colonography. *Am. J. Gastroenterol* 2004; 3:100; 510-513

one of the studies sufficiently addressed the administration of propofol by anesthesiologists compared to non-anesthesiologists.¹² In a recent abstract of this study, the investigators concluded that administration of propofol by anesthesiologists is associated with a reduced adjusted relative risk of cardiopulmonary complications compared to its administration by non-anesthesiologists. The list below identifies some of the complications occurring with the use of propofol by non-anesthesiologists as reported in this literature:

Selected interventions and corresponding outcomes

Propofol (single agent) - observational and noncomparative studies

Oxygen saturation < 90%:	7 studies	Range = 0.55% to 6.5% of patients
Oxygen saturation < 85%:	3 studies	Range = 0.1% to 0.6% of patients
Blood pressure decline > 25%:	3 studies	Range = 26.7% to 33.1% of patients
HR decline > 20% or < 50 bpm:	4 studies	Range = 1.7% to 10.9% of patients

Propofol (combined with other agents) - observational and noncomparative studies

Oxygen saturation < 90%:	1 study	9% of patients
BP decline > 20 mm Hg:	1 study	27% of patients
BP decline > 50 mm Hg:	1 study	7.3% of patients
Heart rate < 50 bpm:	1 study	3.3% of patients

A spreadsheet listing each of the 31 studies referenced by the ACG and comparing their designs and data, or stating the reason for their rejection by the methodologists, is appended to the electronic version of this letter.

The most that can be said for the literature offered in support of the ACG petition is that no long-term or major adverse outcomes were reported in the two larger studies cited.¹³ Given that the anesthesia mortality rate in healthy patients is only 1:300,000, this is not surprising. The two studies in question were conducted in hospitals or ambulatory surgical centers (ASCs) with high-volume endoscopy practices that followed protocols for training, education and propofol monitoring. They are not necessarily representative of what might happen in facilities that perform fewer endoscopies, including private offices. Failure to rescue has consistently been reported in the gastroenterology literature as a prominent cause of poor outcomes. In particular, that literature shows greater rates of complications among patients with imperfect health and

¹² Vargo JJ, Eisen GM, Faigel DO, Holub J, Lieberman DA. Anesthesiologist or non-anesthesiologist-administered propofol and cardiopulmonary complications for endoscopy: which is safer? [abstract]. *Gastrointest Endosc* 2004; 59:AB93

¹³ Walker JA, McIntyre RD, Schleinitz PF, Jacobson KN, Haulk AA, Adesman P, Tolleson S, Parent R, Donnelly R, Rex DK: Nurse-administered propofol sedation without anesthesia specialists in 9152 endoscopic cases in an ambulatory surgery center. *Am J Gastroenterol* 2003; 98:1744-1750; Rex DK, Overley C, Kinser K, Coates M, Lee A, Goodwine BW, Strahl E, Lemler S, Sipe B, Rahmani E, Helper D: Safety of propofol administered by registered nurses with gastroenterologist supervision in 2000 endoscopic cases. *Am J Gastroenterol* 2002; 97:1159-1163

patients who are older than 50 years of age.¹⁴ Some state health agencies are also aware of the threat to patient safety. Between 2001 and 2004, no fewer than 38 deaths related to the performance of endoscopies in ASCs were reported to the Florida Health Care Administration Board of Medicine.¹⁵

Even more important, there is reason to believe that the number of complications can be greater yet in the hands of other non-anesthesiologists who use propofol. Emergency physicians face particular risks since their patients are not usually fasting and thus can be expected to have a higher incidence of aspiration. Even though emergency physicians are trained and generally qualified to administer deep sedation, their literature reports unacceptable rates of respiratory depression.¹⁶ The difficulty of titrating propofol to the right level is more pronounced for pediatricians.¹⁷ Removing the warning label from propofol would encourage its use by non-anesthesiologists in settings where proficiency in administering and rescuing from anesthesia is truly critical, and the individual administering it is also responsible for the conduct of often delicate procedures that demand his or her full attention.

4. Patient Safety Requires the Right Staffing and the Right Facility

A. The right staffing

The current labeling for Propofol includes the precaution that the individual who administers the drug should “not [be] involved in the conduct of the surgical/diagnostic procedure.” This reflects the well-established principle that there must be an independent practitioner whose sole responsibility is administering propofol and monitoring the patient to assess level of consciousness and to identify early signs of hypotension, bradycardia, apnea, airway obstruction and/or oxygen desaturation.¹⁸ The corollary benefit to patient safety, of course, is that a practitioner conducting a surgical/diagnostic procedure during which propofol is administered is free to devote his full attention to the procedure, secure in the knowledge that an expert in anesthesia is devoting his full attention to monitoring the patient’s response to the drug.

The ACG has petitioned for the discontinuance of the portion of the propofol package insert requiring both administration by a clinician trained in general anesthesia and the non-

¹⁴ Vargo JJ, Eisen GM, Faigel DO, Holub J, Lieberman DA. Cardiopulmonary complications with non-anesthesiologist-administered propofol vs. standard sedation: the CORI experience [abstract] *Gastrointest Endosc.* 2004; 59: AB 132

¹⁵ Florida Board of Medicine: Surgical Care Committee Report, 2004.

¹⁶ Green SM, Kraus B: Propofol in Emergency Medicine: Pushing the Sedation Frontier, *Ann. Emerg Med* 2003; 42(6): 792-7

¹⁷ Barbi E, Gerarduzzi T, Marchetti F, Neri E, Verucci E, Bruno I, Martellosi S, Zanazzo G, Sarti A, Ventura A. Deep sedation with propofol by nonanesthesiologists: a prospective pediatric experience. *Arch. Pediatr Adolesc Med* 2003; 157(11):1097-1103

¹⁸ Statement on Safe Use of Propofol approved by ASA House of Delegates October 27, 2004; ASA Practice Guidelines for Sedation and Analgesia by Non-Anesthesiologists. *Anesthesiology* 2002; 96: 1004-17

involvement of the physician performing the procedure. It appears that the ACG may be seeking to make the use of a second practitioner optional.

This may be because their members do not believe the services of an anesthesiologist or even a certified registered nurse anesthetist (CRNA) to be necessary. As the ACG states in its petition, a professional fee is associated with the services of qualified anesthesia providers, and they argue that this is sufficient reason to eliminate the warning label. There is no separate fee for sedation administered and/or monitored instead by a registered nurse without advanced training, but RNs are not always available or willing to perform these functions.

In some 13 states, the Nurse Practice Act explicitly prohibits nurse-administered propofol sedation.¹⁹ In numerous others, the legal status of nurses administering anesthesia with propofol is ambiguous. The large majority of hospitals and ambulatory surgical centers across the United States do not allow this practice either and do not credential RNs to provide deep sedation with propofol.

The July 2003 issue of *Outpatient Surgery* magazine reported 74.8% of respondents in an on-line reader survey felt that propofol administration by RNs was a patient-safety risk and 71.2% believed administering anesthesia with propofol to be outside of an RN's scope of practice.²⁰ According to the article, many RNs are uncomfortable using propofol, feeling that unpredictable and instantaneous patient reactions such as loss of an airway render administration and monitoring of the drug beyond their competence. In 2002, ruling on a petition filed by registered nurses, the Florida Board of Nursing declared the administration of propofol to be beyond the scope of practice of an RN, even if an anesthesiologist were supervising. The challenges to nurses administering anesthesia with propofol include the greater risk of respiratory or cardiovascular complications presented by growing number of obese or other patients, as well as the multitasking expected of RNs but not of anesthesiologists or CRNAs whose only responsibility is to the patient, as discussed in an editorial in the August 2005 issue of the same magazine calling upon the FDA to reject the ACG petition.

The American Association for the Accreditation of Ambulatory Surgical Facilities (AAAASF) has explicitly taken the position that propofol, unlike other intravenous sedation, may not be administered by a registered nurse.

If RNs are not permitted or available to administer propofol, the import of the ACG proposal to eliminate the current warning statement is that the endoscopist could personally administer the drug and conduct the procedure, resulting in divided attention to these two separate tasks. Yet not one of the 31 articles cited in support of the petition to eliminate the label addresses the safety of allowing the physician who is performing the surgical/diagnostic procedure to

¹⁹ Meltzer B. RNs Pushing Propofol. *Outpatient Surgery* (July 2003)

http://www.outpatientsurgery.net/2003/os07/rns_pushing_propofol.php (accessed October 11, 2005)

²⁰ *Id.*

administer propofol. Without any evidence that safety would not be compromised, the Agency should not deny the petition.

B. The right facility

One additional reason why the patients in the two largest studies referenced in the petition had no enduring complications is that they were all performed on healthy patients in hospitals with full anesthesia or emergency medicine backup and the anesthesia equipment necessary for monitoring and intervention, as noted above.

Had there not been personnel trained in general anesthesia, monitoring equipment, supplemental oxygen, devices for assisted ventilation, atropine to treat bradycardia, and equipment to perform endotracheal intubation and general anesthesia mid-procedure or to provide emergency care to hypoxic patients who did not respond adequately to increased oxygen, there might easily have been major sequelae or even death attributable to the use of propofol. The warning label on propofol itself contains a second sentence, not challenged in the ACG petition, stating that "Patients should be continuously monitored, and facilities for maintenance of a patent airway, artificial ventilation, and oxygen enrichment and circulatory resuscitation must be immediately available."

Organizations that accredit hospitals, such as JCAHO,²¹ and ambulatory surgical facilities, such as the Accreditation Association for Ambulatory Health Care (AAAHC) and the American Association for the Accreditation of Ambulatory Surgical Facilities [AAAASF], require the immediate availability of staff expert in airway management and advanced cardiopulmonary resuscitation, as well as immediate access to emergency equipment. The AAAASF, as noted above, allows anesthesiologists and CRNAs to administer propofol.

It is unlikely that every office-based endoscopy suite is properly staffed and equipped for deep sedation and general anesthesia. Only 12 states require accreditation of office-based surgical facilities and some 30 states do not regulate such facilities at all. Again, from a patient safety standpoint, the critical needs include having 1) the personnel on hand who can ensure continuous monitoring and proper care, including emergency care, of a patient under general anesthesia, and 2) the appropriate tools and equipment to do so.

Furthermore, office-based endoscopy suites may be far from hospital or ambulatory facilities that do have the necessary personnel and equipment for resuscitation of patients who experience respiratory or cardiovascular emergencies. Irreversible brain damage may occur within 4 minutes of the cessation of oxygen flow. Some endoscopy offices use 911 for their emergency backup, but 911 response times are almost always greater than a few minutes.

²¹ Planning the Administration of Moderate or Deep Sedation or Anesthesia. Joint Commission: The Source, October, 2005.

Discontinuing the package insert warning, as requested by the American College of Gastroenterology, would remove inhibitions on the administration of propofol not just in hospitals and ambulatory surgery centers and on the physicians credentialed to perform deep sedation by those facilities, but also on physicians with minimal anesthesia training working in under-staffed and under-equipped offices that might be quite remote from the nearest emergency medical care.

5. The Decision on the Petition Must be Based on Safety, Not on Economics

We are unaware of any FDA decision based on the ability to lower procedure costs by eliminating practitioner training and monitoring requirements. The Agency's focus must remain centered on patient health. This means that the Agency must consider safety and efficacy of the products that it regulates, not costs to third party payors.

The ACG petition gives only two grounds why the Agency should change the labeling for propofol: (1) that the change "will eliminate the need for an anesthesiologist or nurse anesthetist to participate in endoscopic procedures involving propofol sedation, and thus will reduce the cost to payors of those procedures," and (2) that it "also will eliminate an unneeded restriction on the practice of gastroenterologists."

As it is, many payers already refuse to cover the services of anesthesiologists or nurse anesthetists in routine endoscopies, claiming that only endoscopist-administered moderate sedation is needed for healthy patients undergoing such procedures. Endoscopists who believe that the use of propofol is important to their practice have the option of obtaining the appropriate training and credentialing for its use. They also have available a number of safe, effective sedating agents and do not need to use propofol. Indeed, a joint statement by a working group of members of the ACG, the American Gastroenterological Association (AGA) and the American Society for Gastrointestinal Endoscopy (ASGE) includes the assertions that "Clinically important benefits over standard sedatives [over propofol] have not been consistently demonstrated in average-risk patients undergoing standard routine upper and lower endoscopy. Further randomized clinical trials are needed in this setting."²²

Many gastroenterologists who do use anesthesia providers apparently are unwilling to sacrifice patient safety for the sake of incrementally higher profit margins. For that reason, some members oppose the ACG's stance on propofol and the ACG's immediate past president has said he believes "that this is the most internally divisive issue in clinical gastroenterology at this time."²³

²² A Joint Statement of a Working group from the American College of Gastroenterology (ACG), the American Gastroenterological Association (ASGE) and the American Society for Gastrointestinal Endoscopy (ASGE), March 8, 2004. <http://www.asg.gi.org/physicians/nataffairs/trisociety.asp>. (accessed October 16, 2005).

²³.Rex, DK "Three Challenges," *supra*.

Given the totally inconclusive research on the safety of propofol administration, with or without continuous monitoring of the patient, by non-anesthesiologists – including emergency and pediatric specialists -- and the irrelevance of gastroenterologists' practice preferences or economic concerns -- the FDA should not change the warning label on propofol.

For the reasons discussed above, FDA must deny the Petition because the action requested falls outside of the Agency's legal authority and would be inconsistent with its past practice. In addition, and more important, the information provided with the Petition does not support the conclusion that patient safety will be protected. For decades, ASA's members' primary interest and responsibility has been to assure best possible care for the patients who entrust their lives and well-being to them. Without clear evidence to show that patient safety will be protected by ACG's proposed labeling modification, FDA must deny the Petition.

Thank you for your consideration.

Sincerely,



Eugene P. Sinclair, M.D.
President
American Society of Anesthesiologists

Attachments:

1. ASA Statement on Safe Use of Propofol
2. ASA Practice Guidelines for Sedation and Analgesia by Non-Anesthesiologists
3. Table analyzing studies cited in ACG Petition
(Excel file attached to as a diskette)