



December 22, 2010

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*Regulations.gov*

Docket No. DEA-338

Drug Enforcement Administration

Attention: DEA Federal Register Representative/ODL

8701 Morrissette Drive

Springfield, VA 22152

**RE: Docket No. DEA-338; Proposed Rule: Schedules of Controlled Substances: Placement of Propofol Into Schedule IV; 75 Fed. Reg. 66195 (October 27, 2010).**

Dear Sir or Madam:

The American Veterinary Distributors (AVDA) appreciates this opportunity to provide public comments on the Drug Enforcement Administration's (DEA) Federal Register notice of proposed rulemaking: *Schedules of Controlled Substances: Placement of Propofol Into Schedule IV* ("proposed rule" or "proposal") 75 Fed. Reg. 66195 (Oct. 27, 2010).

AVDA, a not-for-profit corporation, was established in 1976 as the national trade organization for businesses engaged in the distribution of animal health products. Our members distribute animal health supplies to some 60,000 veterinarians practicing in approximately 30,000 animal health clinics throughout the United States. AVDA distributor members distribute supplies exclusively to animal health entities and annual sales of these supplies are estimated at \$5 billion. Those products include pharmaceuticals, biologicals, white goods, instruments and equipment, and pet foods. In addition, some AVDA member companies also serve the OTC market, made up of farm and feedlot operations, poultry producers, farm stores, etc. For more information about AVDA, visit [www.avda.net](http://www.avda.net).

## **BACKGROUND**

AVDA would like to echo the comments and recommendations of the Healthcare Distribution Management Association (HDMA - filing ID DEA-2010-0022-0039) and those of the American Veterinary Medical Association (AVMA - filing ID DEA-2010-0022-0037) filed on December 21, 2010.

AVDA recognizes DEA's concerns with propofol's abuse potential, its health effects and the underlying reasons for this action. While we understand the importance of controlling the use of any drug with high abuse potential, we also have concerns that adding propofol as a Schedule IV controlled substance may result in decreased use of this important anesthetic by some veterinarians associated with the additional registration and recordkeeping requirements in accordance with DEA rules. Propofol is an important drug in veterinary medicine and is supplied to veterinarians and animal health clinics by our distributor members. Propofol is administered to dogs, cats and many non-domestic animals for anesthesia induction and for maintenance.

However, once a drug is placed into Schedule IV, wholesale distributors must store the product according to the requirements set forth in 21 C.F.R. §1301.72(b). Among AVDA's wholesale distributor members, the most common approach to complying with Schedule IV storage security requirements is to place Schedule III-V products into cages within the wholesaler's warehouses. Wholesale distributors are subject to such additional measures for scheduled drugs as inventory management, reporting and recordkeeping.

Because of the Schedule IV drug storage requirements, AVDA believes that the nature of propofol's abuse profile and the consequences of a final rule are critically important factors in determining how to regulate this product. In our comments below, we will emphasize these points because placement of propofol into Schedule IV will result in an unintended security risk.

## **AVDA COMMENTS**

### ***Propofol's Abuse Profile Does not Implicate Wholesale Distribution Warehouses or Employees***

The preamble describes propofol as "... *an ultra-short acting intravenous (i.v.) anesthetic, under the commercial name of Diprivan.*" It is also used for the initiation and maintenance of Monitored Anesthesia Care (MAC) and Intensive Care Unit (ICU) sedation. [75 Fed. Reg. 66195 (October 27, 2010) 66196 col. 3.] Thus, this product has very specific, and limited, indications for use. It is our understanding that propofol is intended to be administered as an injectable emulsion, likely a key reason for propofol's current abuse profile as described in the preamble: ... *propofol ... is abused by medical professionals since they have access to the drug in medical facilities which perform anesthesia...*

Further, ...*in 96 percent of these cases, the abusers were health care providers or were in training programs to become health care professionals.* [75 Fed. Reg. 66195 (October 27, 2010) 66197 col. 1. ]

The very high mortality rate noted in the original petition to schedule propofol, filed in 2008, [75 Fed. Reg. 66195 (October 27, 2010) 66196 col. 3] is likely an additional reason why "*Medical professionals are the predominant population who are abusers of propofol.*" [75 Fed. Reg. 66195 (October 27, 2010) 66197 col. 2.] Moreover, the preamble indicates that the medical

professionals described as meeting the abuse profiles access propofol in “...*medical facilities which perform anesthesia...*” [75 Fed. Reg. 66195 (October 27, 2010) 66197 col. 1.]

AVDA’s members do not operate medical facilities, do not perform anesthesia, nor do they typically employ medical professionals in their warehouses. When reviewing recent theft incidents, AVDA’s members found that such incidents are extremely low to nonexistent for propofol in the vast majority of AVDA’s members’ warehouses.

AVDA notes that neither the proposed rule’s preamble nor the background materials on the rulemaking docket shed light on whether there is a problem of theft or diversion within wholesale distribution warehouses that warrants placement in cages. Non-medical facilities and non-medical employees are not included in the abuse profile, in the preamble or in the other rulemaking documentation. Similarly, there is no discussion of where or why current warehouse storage practices are inadequate, or reference to wholesale distribution warehouse security as a means of reducing propofol’s abuse potential.

Thus, virtually none of the products obtained by abusers are acquired through thefts or diversion directly occurring within warehouses. However, even though those who abuse this product obtain it from locations other than wholesale distribution warehouses, once scheduled, wholesale distributors must store the product into areas meeting Schedule III – V security requirements (cages). At the least, we believe an analysis is warranted to demonstrate whether the greater volumes of products stocked in warehouses not associated with propofol’s abuse profile would result in wholesale distributors bearing a greater share of the regulatory burden under a final rule than what the medical facilities in which abuse and access are clearly of concern will experience.

### ***Scheduling Will Likely Increase Warehouse Security Risks***

If more products are stored in Schedule III – V cages, there will be an increase in the number of employees granted access to the cages and/or the frequency of employee access. This is because of the increase in the number of times products will be placed into the cages or retrieved from them to fill orders. However, more frequent trips into and out of the cages result in more frequent employee access to other, more likely abused and diverted controlled substances.

To explain further, other products stored in the same cages include hydrocodone combination products, other Schedule III drugs and benzodiazepine Schedule IV drugs. These drugs have an even greater abuse potential and/or are far more attractive as a target for theft or diversion. They are often much easier to administer -- swallow a pill vs. inject/administer propofol intravenously. They are also much more readily sold “on the street” because no other medical equipment is needed. Thus, AVDA’s greatest concern is that in solving a non-existent problem, i.e., abuse directly associated with theft or diversion of propofol from within warehouses, the proposal introduces a much greater risk of theft or diversion of other products.

AVDA’s members go to great lengths to screen employees prior to employment. They also monitor employee activities both within and outside of cages, and will continue to do so particularly for anyone handling controlled substances. However, such efforts to prevent theft

and diversion are strongly supported by keeping employee access to the absolute minimum necessary to conduct operations within these restricted areas. Scheduling propofol will undermine this security approach.

### ***Construction and Operational Costs and Considerations***

There will also be costs associated with construction and other operational changes within warehouses in order to store propofol in the required secure areas. Wholesale distributors stock a large enough volume of propofol that in certain instances, the current cages in wholesalers' warehouses will need to be expanded to hold the usual levels of product kept in stock. Further, propofol has unique storage temperature requirements. According the package insert, the most commonly sold brand of propofol, Diprivan®, must be stored according at the manufacturer's specified temperature range of 4° to 22°C (40° to 72°F). (See the Diprivan® package insert at: <http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=13234>.)

This is an unusual temperature for drug product storage and means that propofol is held at temperatures cooler than warehouses' room temperature, but warmer than typical refrigerators. Space within the cages will need to accommodate not only the additional products, but also the equipment or other features needed to cool the product (e.g. dedicated refrigeration units). AVDA also points out that requirements for following the storage temperature specifications found on the drug's labeling are explicitly included in the Food and Drug Administration's (FDA) Guidelines for state licensing of wholesale prescription drug distributors, under the minimum requirements for the storage and handling of prescription drugs (21 C.F.R. § 205.50(c)). Therefore, wholesale distributors must be certain to comply.

## **RECOMMENDATIONS**

### ***Recommendation 1***

With no information to support a decision that would impose burdens on a large segment of the pharmaceutical supply chain, i.e., non-medical facilities, and no information demonstrating that controls for warehouses will prevent, or at least reduce, propofol's abuse, scheduling is inappropriate. AVDA strongly recommends that DEA withdraw the proposal to schedule propofol.

### ***Recommendation 2***

If, during the notice and comment process, DEA obtains information suggesting that placement of propofol into wholesale distribution storage areas defined under 21 C.F.R. §1301.72(b) will decrease the abuse of propofol, AVDA recommends that DEA place the new information on the docket and reopen the public comment period prior to issuing a final rule. This would allow wholesale distributors an opportunity to review and comment on the new information not currently available for public examination.

### ***Recommendation 3***

If DEA eventually determines that adequately addressing propofol's abuse must include placement into Schedule IV, AVDA recommends that DEA provide an exemption for wholesale

distributors from the security and other regulatory requirements for Schedule IV products, including 21 C.F.R. §1301.72(b)'s storage specifications.

AVDA recognizes that this is a unique recommendation. No other drug has received equivalent treatment. However, the abuse profile of this drug is also unique. The lack of demonstrated warehouse theft or diversion concerns, and the increased security risk scheduling will create further support this exemption request.

#### ***Recommendation 4***

If DEA eventually reaches a decision to issue a final rule placing propofol into Schedule IV, and does not provide wholesale distributors with an exemption from the storage requirements, it is imperative that the agency allow sufficient time for wholesale distributors to conduct the following measures:

1. Prepare for storage, including designing and building storage facilities that meet the physical storage requirements of both 21 C.F.R. § 1301.72(b) *and* of the propofol package inserts. Preparation also includes:
  - o develop extra procedural steps to separate inventory upon receipt at the loading dock,
  - o reconfigure the warehouse “flow” to ensure appropriate product storage and retrieval,
  - o revise existing or write new warehouse procedures including stocking, picking and packing,
  - o train warehouse staff on the new procedures,
  - o establish separate management monitoring to ensure employee comprehension and compliance with the procedures,
  - o establish separate/additional stock controls,
  - o establish separate procedures and space for recalls, returns and product quarantines,
  - o purchase additional equipment potentially including refrigeration, racking, shelving, computers, printers, work stations, packing materials, totes, etc.,
  - o perform computer programming, and
  - o perform background checks and hire additional staff, if needed, to perform these and other operational and compliance functions.
2. Establish recordkeeping and perform the inventory required by 21 C.F.R. §§ 1304.03, 1304.04, and 1304.11;
3. Distribution of existing stocks of propofol that are not labeled as Schedule IV controlled substances, *i.e.*, “CIV” or, in the alternative, permit the shipment of such existing stocks back to the manufacturer or other source for relabeling or other disposition. (To ensure no gaps in providing this product to patients in medical facilities, wholesale distributors must maintain an adequate stock of propofol not labeled as CIV until such time as the manufacturers are able to complete packaging and labeling changes required for schedule IV products. Thus, most of this step could not begin until the newly labeled/packaged products are available.); and

4. Physically move stock to secure areas in accordance with 21 CFR §§ 1301.71 (security requirements generally), 1301.72(b), (c), and (d) (physical security controls), 1301.74 (other security procedures), and 1301.77 (freight forwarding facilities), as appropriate.

5. Revise systems to meet requirements under 21 C.F.R. § 1301.74(b) for suspicious order monitoring. Systems will need to track ordering, develop criteria for determining unusual

patterns, procedures for investigations if an “order of interest” is identified and for reporting if the order is “suspicious”.

As can be seen from the steps listed above, the regulatory requirements will have additional spill-over effects not specified in the regulations, but wholesalers must nevertheless undertake. For example, in addition to development, inventory and other recordkeeping systems must be validated. Scheduling propofol will also require readjustment of product stocking from current storage areas into cooled areas within cages and potentially moving/restocking products already stored within the cages.

Wholesale distributor registrants must be given adequate opportunity to carry out such operations. Given the steps noted above, AVDA believes that an effective date of 18 months from the final rule’s publication is appropriate. This time frame is needed to enable distributors’ to comply with minimal disruption to patient care.

AVDA thanks DEA for this opportunity to comment. If you have any questions or if AVDA can provide further information, please do not hesitate to contact me at 443-640-1040 or at [jackie@ksgroup.org](mailto:jackie@ksgroup.org)

Sincerely Yours,



Jackie King  
Executive Director