GasRegsInc

Gas Regs Incorporated

107 Southbridge Court
Jamestown, NC 27282-9596

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Via FedEx

October 13, 2003

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

Re: Docket No. 00N-1484
Safety Reporting Requirements for Human Drug and Biological Products

Dear Sir or Madam:

The Gas Regs, Inc., provides the following comments as they relate to the proposed rule, "Safety Reporting Requirements for Human Drug and Biological Products", Docket 00N-1484, appearing in the Federal Register on March 14, 2003 at pages 12406 through 12497.

Gas Regs, Inc., is a Quality Assurance/Regulatory Affairs consulting firm dedicated to assisting companies who manufacture, fill, distribute and/or use medical or food grade gases with their quality and FDA regulatory compliance activities. Gas Regs, Inc.'s, clients include national, regional, and single site home care companies; international, national and regional industrial gas firms (e.g., air liquefaction, bulk gas manufacturing, and container filling operations); regional and single site cylinder filling operations, as well as medical gas container and equipment manufacturers. Most medical gases that are administered (primarily Oxygen USP, but also Nitrogen NF, Medical Air, USP, Nitrous Oxide, USP, Carbon Dioxide USP, Helium. USP, and some mixtures of these gases) are classified as drugs. FDA considers all firms filling these medical gases into dispensing containers as drug manufacturers. These medical gases are not the subject of New Drug Applications, and therefore manufacturers of these medical gases must comply with the requirements of 21 CFR §310.305 in the unlikely event that a medical gas is the subject of an Adverse Drug Experience. Gas Regs, Inc., has therefore limited its comments to the impact this proposed rule (proposal to change 21 CFR §310.305) will have on the medical gas industry and the resulting impact the rule may have on medical gas users.

Today 1.2 million people receive medical oxygen in the home care setting and a significant additional number of people receive medical oxygen and other medical gases in both acute care settings and in doctor/dental offices. Annually, several hundreds of thousands of patient deaths occur as a result of the patient's primary disease. As discussed in this letter, if the rule remains as proposed, medical gas manufacturers would be required to generate a report on each one of those hundreds of thousands of deaths. This would result in an insurmountable negative financial impact for medical gas manufacturers. Including

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Phone (336) 887-0510 ◆ Fax (336) 887-0511

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medical gases classified as drugs in this ruling would be of no benefit to the medical community and medical gas users. Nor would it fulfill the intended safety rule objective of reporting noxious and unintended responses to drug therapy. From our review of the studies cited in this Federal Register notice (pages 12470 through 12471, and others throughout the document), it is evident that medical gas manufacturers were not included in the primary financial data estimates provided. Ensuring that medical gas manufacturers are exempt from certain aspects of this ruling is paramount to the industry. This rule, as proposed, would potentially create a financial burden and hardship, resulting in an unsustainable industry that in turn would negatively impact medical gas users.

Gas Regs, Inc., understands and applauds the need for global harmonization. It is our understanding that the major focus outside the United States is with new drugs. Existing drugs, such as medical oxygen and other medical gases, are not subject to the same stringent reporting requirements, as are new drugs. We are similarly convinced that incorporating the recommendations detailed in this letter into the proposed changes to 21 CFR 310.305 will enhance the quality and effectiveness of the submissions and the analysis of these safety reports, thereby improving patient safety.

Gas Regs, Inc. proposes the agency:

1. Exempt cases where medical gases are ***'unlikely related'*** to the SADR or SAR, from the clarification of the definition of a SADR
2. Exempt medical gases from the expedited report (15-day alert) requirement specified in the proposed rule, if the agency does not agree with modifying its guidance toward 'unlikely related' incidents in number 1 above.
3. Expand the definition of a 'contact person' to include other medical healthcare professionals; and to allow them to be responsible for the content of post-marketing safety reports submitted to the FDA.
4. Exempt companies who fill medical gas containers, from using MedDRA to code safety reports even when medical gas usage may be indicated as a SADR or SAR.

Gas Regs, Inc. welcomes the opportunity to engage in further dialogue on this subject with the FDA.

1. **Regarding our request to "Exempt cases where medical gases are *'unlikely related'* to the SADR or SAR, from the clarification of the definition of a SADR"**

On page 12417 of the Federal Register Notice, guidance is provided as to what would be a SADR. Including those incidents where "the relationship cannot be ruled out" may cause extensive reporting when persons do not have a SADR that is "caused" by medical oxygen or other medical gases. Patients prescribed supplemental medical oxygen have some

significant disease process or abnormality. Medical oxygen therapy is typically and extensively used as an adjunct to the primary prescribed drug therapy.

Including supplemental medical oxygen therapy and other medical gases in the agency's required SADR reporting will be non-productive, non-informational, and create enormous amounts of paper flow with no benefit. In addition, if an individual expires or experiences a medical deterioration requiring medical intervention from underlying disease processes, while using medical oxygen or other medical gas, this will result in increased and unnecessary submissions of complex reports.

2. **Regarding our request to "Exempt medical gases from the expedited report (the current 15-day alert) requirement specified in the proposed rule, if the agency does not agree with modifying its guidance toward 'unlikely related' incidents in request 1 above."**

We request the agency exempt medical gases from the 15-day alert requirement where incidents of acute respiratory failure have occurred, as well as all the other listed conditions. This request would only be required if the agency does not agree with modifying its guidance in regards to 'unlikely related' incidents previously discussed in item 1 above.

For example, if a patient should experience acute respiratory failure while using medical oxygen or other medical gas, this occurrence would result in the need for the medical gas industry to perform Expedited Reporting (15-day alert). Because the guidance currently states that a SADR exists when the "relationship cannot be ruled out", the medical gas filler may need to complete the 15-day expedited report. Although a SADR associated with "acute respiratory failure" may be the most obvious example, when the adjunct use of medical oxygen is employed, most conditions listed in the Federal Register notice would also include the use of medical oxygen and perhaps other medical gases. Hence, all SADRs would cause unnecessary (perhaps more than a half million or more) expedited reports for the use of medical oxygen or other medical gas. This is especially true when one considers the other drugs for which a report would need to be generated whenever an oxygen unlikely related SADR exists.

This ruling will be extremely difficult, if not impossible, to comply with in any timeframe, let alone within 15 days. As medical gas manufacturers/fillers, we would need to have access to each patient's medical records from the healthcare facility, the patient's physician, and/or other entities (healthcare provider, coroner, Department of Health, etc.). Access to the record would not be permitted without written consent from the patient or his/her power of attorney.

3. **Regarding our request to "Expand the definition of a 'contact person' to include other medical healthcare professionals; and to allow them to be**

responsible for the content of post-marketing safety reports submitted to the FDA."

Medical gas manufacturers/fillers, including many home healthcare companies filling medical gas (medical oxygen) containers, do not typically have licensed physicians on staff, or on contract. Most home healthcare firms have healthcare professionals (e.g., Nurses, Respiratory Therapists, etc.) on staff or on contract. Most non-healthcare medical gas manufacturers do not even have these healthcare professionals in their employ. The process of manufacturing and distributing medical oxygen or other medical gases does not require the oversight of a physician or a healthcare professional. We propose that the agency permit a company representative to be responsible for the content of post-marketing safety reports submitted to the FDA. To require firms to hire a physician for the sole purpose of meeting the requirements of this proposed rule, if it is even possible to find a physician to accept such a position, will cause undue financial hardship on medical gas firms with no increased patient safety.

4. **Regarding our request to "Exempt medical gas companies, who fill medical gas containers, from using MedDRA to code safety reports even when medical gas usage may be indicated as a SADR or SAR."**

We propose that the agency exempt all medical gas fillers/manufacturers from the use of MedDRA. In the unlikely event that a medical gas is determined to be the cause of a SADR or SAR, the use of MedDRA in the medical gas arena would not be economically feasible.

Based on discussions with agency personnel, our understanding is that over fifty percent of all drug manufacturers registered with the agency are medical gas firms, and many of those would be classified as small business. The financial impact of this rule on these firms, as well as larger regional and nationwide firms, would be very significant if the requests for exemption from certain portions of the proposed rule are not granted. Contrary to the overall goal of trying to stem the increased cost of healthcare in the United States, this rule will significantly add cost to the manufacture and distribution of medical oxygen and other medical gases. Users (healthcare institutions and patients) of these medical gases would receive little or no benefit from the unnecessary reporting processes.

In conclusion, our review of the studies cited in the Federal Register notice makes it evident that medical gas fillers/manufacturers were not included in the primary data estimates provided in this document. We do not believe it was the agency's intention to include medical gas manufacturers, as the rule does not address the uniqueness of our industry. Perhaps it is for this reason that the financial data did not include medical gases. We have documented our issues in the above response with the understanding that the agency's intention was not to include medical gas manufacturers. Ensuring that medical

gas manufacturers are not included in this ruling is paramount to the industry, as the financial burden and hardship it would create would make the industry financially unsustainable.

If the agency does not concur with our arguments requesting exemption from the cited sections of the proposed rule (changes to 21 CFR §310.305), we strongly plead that the agency meet with the affected industry associations (i.e., American Association for Homecare, the Compressed Gas Association, the Gases and Welding Distributors Association) prior to issuing a final rule. The purpose of this meeting would be to discuss the degree this regulation would impact this industry and, more importantly, further discuss the minimal potential health benefit to the patient, if any, that this regulation would have on the safe administration of medical gases.

Gas Regs, Inc. appreciates the opportunity to comment on this proposed rule. If there are any questions regarding the request for exemption, please do not hesitate to contact John Willenbrock, President, Gas Regs, Inc., via e-mail at john.willenbrock@gasregs.com, or via phone at (336) 887-0510. Thank you for your consideration.

Sincerely,

John K. Willenbrock, President
Gas Regs, Inc.

cc: David Horowitz, Office of Compliance (HFD-300)
Duane Sylvia, Office of Compliance (HFD-325)