October 14, 2003

U.S. Public Health Service
Food and Drug Administration
Dockets Management Branch (HFA-305)
Rm. 1061
5630 Fishers Lane
Rockville, MD 20852

RE: 21 CFR Parts 310, 312, et al., Safety Reporting Requirements for Human Drug and Biologic products; Proposed Rule

Dear Sir or Madam:

Introduction/Overview

Air Liquide America L.P. (Air Liquide) incorporates by reference all comments to the referenced Proposed Rule submitted by the Compressed Gas Association (CGA). In addition, ALA includes in this letter numerous comments to the referenced Proposed Rule. Our comments are organized in two (2) parts. In Part I, we address General Concepts. In Part II, we point out specific areas of the Proposed Rule that neither enhance public safety, nor add value to manufacturing or safety of medical gas products. Where feasible, and for brevity, we've consolidated our comments. Our comments are linked to the Proposed Rule, as published.

Air Liquide America also requests an exemption for Oxygen (USP) and Nitrogen (NF) medical gas products from certain sections of the proposed rule regarding safety reporting requirements for human drugs as published in the Federal Register on March 14, 2003. Our reasons for this exemption request are provided below in the body of text. The sections of the proposed rule from which exemption is requested are:

- 310.305 (c)(1)(iii)(C) - Minimum information for potential medication error reports
- 310.305 (c)(2)(v)(B) - Potential medication errors
- 310.305 (c)(2)(viii)(A) - Supporting documents; Autopsy or death certificate
- 310.305 (d)(4) – Responsible physician

I. General Concepts:

We fully support the intent of the proposed rule with respect to patient safety. As an international company, Air Liquide applauds the efforts to harmonize global processes and expectations for acquisition, evaluation and submission of safety information for

marketed drugs. However, for the reasons explained below, Air Liquide believes strongly that several of the requirements specified in the proposed regulation, as applied to medical gas products (i.e., Oxygen USP, Nitrogen NF), would not advance the stated goals of the proposal or impact in a positive manner public safety or health. Additionally, the costs for compliance, as defined in section V (D) of the introduction to the proposed rule, do not reasonably anticipate the costs associated with the increased number of reports of medication errors associated with medical gases. We request that these new and important distinctions pertaining to medical gases be factored into the request that those products be exempt from the proposed rule requirements as specified above.

Another major concern we have with the proposed rule is the apparent requirement of the proposed rule that manufacturers disregard protection of patient privacy rights as specified in the Health Insurance Portability and Accountability Act (HIPPA).

HIPAA became law in 1996. The purpose of HIPPA is to improve the Medicare program under title XVIII of the Social Security Act ("Act"), the Medicaid program under title XIX of the Act, and the efficiency and effectiveness of the health care system, by mandating the development of standards and requirements to enable the electronic exchange of certain health information. Section 262 of subtitle F added a new Part C to Title XI of the Act. Part C (42 U.S.C. 1320d - 1320d-8) requires the Secretary to adopt national standards for certain financial and administrative transactions and various data elements to be used in those transactions, such as code sets and certain unique health identifiers. Recognizing that the industry trend toward computerizing health information, which HIPAA encourages, may increase the access to that information, the statute also requires national standards to protect the security and privacy of the information. The HIPAA provisions, by statute, apply only to the following persons:

1. A health plan.
2. A health care clearinghouse.
3. A health care provider who transmits any health information in electronic form in connection with a transaction referred to in section 1320d-2(a)(1) of this title.

Collectively, these entities are known as "covered entities."

Sections 310.305 (c)(1)(iii)(C), and 310.305 (c)(2)(viii)(A), of the proposed rule require that medical gas manufacturers obtain, submit, and maintain patient sensitive data, records and other information protected by HIPPA. However, nowhere in the proposed rule are manufacturers either exempted from the predicate HIPPA Act, nor are they provided lawful status as “covered entities” under the proposed rule or under HIPPA. Air Liquide believes these again, to be significant reasons for granting exemption to medical gas manufacturers from the above sections of the proposed rule.

Finally, we request that certain procedural protections be applied to the medical gas industry as part of this rulemaking process in the event that the agency does not concur with our requested exemption.

Therefore, Air Liquide requests exemption for medical gas manufacturers from the following proposed rule sections:

310.305 (c)(1)(iii)(C) - Minimum information for potential medication error reports

310.305 (c)(2)(v)(B) - Potential medication errors

310.305 (c)(2)(viii)(A) - Supporting documents; Autopsy or death certificate

II. Aspects of the Proposed Rule of Particular Concern

A. Data Collection and Review Requirements

Medical oxygen represents approximately 90% of all medical gas applications. Reports of adverse incidents for this product over the years have been extremely rare as compared to other conventional drug products. As noted in the Agency's proposal, there may be as many as 98,000 fatalities per year due to medication errors from more traditional drug products.

Air Liquide America fully supports that any investigation of significant adverse events requires thorough efforts to determine root causes of problems. With traditional pharmacological agents, investigations necessarily involve the full array of clinical issues present with a given patient and therapeutic regimen (e.g., the expected or unexpected adverse effect profile of a given pharmacological agent; the underlying disease condition(s) of a patient; concomitant medications; medical care and error; and related factors). By contrast, for medical gases, root cause investigations are more straightforward and focus primarily on the actions of involved parties (those who distribute or administer the drug) to determine the cause of the mix-up or related use concerns. Thus, the extensive need for medical evaluation, including active querying of adjunctive medical issues, and a review of the data by a licensed physician, brings no apparent value when considering our industry's historical product safety issues.

The proposed rule appears to require significant new reporting for medical gas companies. Active querying and physician review obligations in this context run the risk of masking, or even potentially delaying the review of, legitimate incidents and analysis to identify root cause concerns. We support general concepts and intent of active querying to ensure that appropriate information is aggressively procured and that qualified individuals undertake investigations. For medical gas products, we believe that these goals would be best served through a focus on manufacture, distribution and administration factors as opposed to extensive gathering of medical information.

Therefore, Air Liquide proposes that medical gas manufacturers be exempt from section 310.305 (d)(4) – Responsible physician review.

Conclusion:

Based on careful review of the proposal and its stated intentions, we have concluded that an exemption from specific portions of the proposed rule is appropriate for Medical Gas manufacturers and products. We would welcome an opportunity to review the issue of safety reporting with the Agency to identify ways that might improve safety reporting with consideration for the unique nature of our industry.

If the Agency does not agree with our request that medical gas product be exempt from the proposed rule, we request a meeting between Agency officials and Air Liquide prior to any rule implementation. The purpose of the requested meeting would be two-fold: (1) to discuss the degree to which this regulation would impact the medical gas industry; and (2) to assess how risk modeling should be applied so that the rule extends only to legitimate medical gas product safety concerns.

We appreciate the opportunity to comment on this proposed rule. If there are any questions regarding the proposed recommendations for exemption and clarification, please do not hesitate to contact Harold Jones, Director CGA-FDA Liaison, at the address below, or phone 713-402-2174.

Thank you for your consideration.

Harold F. Jones

for Walter Mason, Ph.D.

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