Docket Management Branch (HFA-305),
Food and Drug Administration,
5630 Fishers Lane, rm. 1061,
Rockville, MD 20852.

Docket number: **Docket No. 03D-0165**, CDER 200081
Subject: cGMPs for Medical Gas

Greetings,

I'm an FDA Investigator in Seattle District. I'd like to comment on the section of the proposed regulation that reads: **Actual yields and percentages of theoretical yield must be determined at the conclusion of each appropriate phase of manufacturing, processing, packing, or holding of medical gases. Such calculations must be performed by one person and independently verified by a second person. FDA recognizes that accurate inventory records and reconciliation of use are difficult to maintain for liquefied gases...**

I may be one of the few field investigators who have actually tried to do this type of reconciliation. Eleven years ago, when I was very new, this requirement was written in the guidance. I actually wrote a firm up for not doing the reconciliation. I went through a very labor-intensive audit of incoming product, outgoing product, average loss due to venting, loss due to blow-downs, residual volumes for liquids, and other documents, trying to find a valid end-point. I found it simply wasn't possible. I spoke with my supervisor after returning from this road-trip. He told me not to do the reconciliation. It just didn't work for the gas industry.

There are many other areas in the medical gas arena that are related to safety and efficacy. Reconciliation is not. The only exception I would find is with nitrous oxide. I believe, due to diversion issues, this would be a gas where the reconciliation procedures might be valid.

If we require this, I believe we should give some guidance on acceptable limits of loss; these limits should have the concurrence of industry. One industry person told me they do a type of reconciliation simply for financial and stocking purposes but they "could drive a truck through..." the upper and

lower limits of acceptability. Her point was reconciliation, done in order to account for all gas from an FDA-safety perspective, would be extremely difficult or simply not possible.

With the exception of nitrous oxide, I really do not think this portion of the proposed guidelines would serve the purpose of protecting the public.

Stability studies:
I also question the need for stability studies by every site. For national firms, this may not be a burden. Corporate headquarters could commission one study for their entire operation. For small firms, I believe it will be a burden in terms of [1] knowledge; if they do it wrong, we write them up [2] stability study cylinder storage; a space-available consideration [3] time; time is money; is this rule truly beneficial?

If we require stability studies, I believe strongly we should also provide industry-specific guidance on what we want. Would it be every cylinder/cryo size/valve type [e.g., manufacturer] for every gas produced? The gas industry is not typically aware of stability studies. I believe we will need to do a fair amount of industry education if we choose to require this. However, I'm not sure there is any benefit to requiring stability studies due to the swiftness with which the contents of the cylinders are used.

I look forward to seeing the Final Rule. Thank you for your time.

Teres Speer

Teres Speer
Seattle District
FDA