Maintaining food and medical grade gas quality

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The quality specifications for food and beverage grade and medical grade gases are very different. However, each of these different grades of gas depends on one thing – the paperwork pedigree – to distinguish them from common industrial grades of the same gas. At the same time, new Federal and state regulatory agencies are turning their focus to the prevention of prescription drug counterfeiting through the implementation of new rules and regulations requiring something called a 'prescription drug product fingerprint'.

This article will look at recent changes in some parts of the US, what are these new requirements, and what can gas producers look forward to in the coming months.

Differing product specifications

The specification for product assay of medical grade gases in the US is typically only 99 percent, while in other parts of the globe, such as Europe and Asia, for common medical gases such as oxygen and nitrogen, the assay specification is typically 99.5 percent. In the US, the United States Pharmacopeia (USP) established these assay specifications early in the last century. They were based on the manufacturing processes used by industry then and the limited analytical capabilities of that era. In those days, a 99 percent pure product was a high standard to achieve. Nowadays, with our ultra modern air separation facilities and digital analyzer systems capable of measuring impurities to a single part per million (ppm) and better, 99 percent pure medical gas is a much easier threshold to achieve.

At this point you are probably wondering, over the last half century why hasn't the USP raised the purity specification for medical gases? In actuality this issue does periodically come up for review and discussion. Virtually every study ever performed on this issue has shown that there is no additional therapeutic benefit to a patient to be gained by raising the purity specification from 99 percent to say 99.5 percent; however the increase in cost to the gases industry, and ultimately the patient, would be very significant. As a result of the lack of benefit for such a significant potential investment, we do not see the purity specification for medical gases changing in the US anytime soon.

For food grade gases it is a different issue. There are two groups promulgating purity specifications for food and beverage grade gases today. They are the Food Chemical Codex (FCC) and the International

Society of Beverage Technologists (ISBT). While the FCC standards have quasi regulatory authority (just like the USP), the ISBT is different. ISBT requirements are industry consensus standards, and represent more of a best practice approach to product specifications. While they have no authority under law, they have a significant influence in the landscape of the beverage grade gas industry nonetheless. When large food and beverage manufacturers adopt these types of standards, and make compliance with them a mandatory condition of doing business, that kind of supply chain pressure is just as powerful as the pressure regulatory authorities can exert.

Under FCC, the typical assay specification for common gases like nitrogen and carbon dioxide supplied to the food industry is 99 percent, just like medical gases. However, for the same gases supplied to food and beverage firms under the ISBT standard, the assay specification rises to 99.9 percent. Companies supplying food and beverage grade gases need to make sure they are aware which assay standard their customers expect them to meet when they are supplying product.

Medical gas pedigree

Paperwork pedigrees for medical gases are nothing new and in fact date back to the 1970s, when the good manufacturing practices regulations contained in 21 CFR § 210 & 211 were first introduced and determined to be applicable to medical gases. The importance of this pedigree cannot be understated, as the only discernable difference between an industrial gas and a medical gas is the documentation created and maintained to attest that a batch of product is in fact a medical gas. If that paperwork trail is incomplete or missing, then the product can no longer be considered a medical grade product, even if the product meets or exceeds all medical product purity specifications.

For independent manufacturers the pedigree process usually starts with a certificate of analysis. When a medical gas firm receives product from their supplier, the FDA allows that activity to be performed in accordance with one of three possible scenarios. Scenario one involves someone from the firm receiving the product actually witnessing the testing of the product they are receiving. The act of witnessing that testing must be documented, and there must be training records that the witness has been trained in the supplier's current and most recent analytical procedures and methods.

Scenario two involves the receiving firm quarantining the delivery vessel and conducting full USP testing on the tanker before the product is unloaded into their tank. The receiving firm's QC Unit must release the tanker product before unloading. Scenario three, which is by far and away the most common method, is for the customer to receive a valid Certificate of Analysis (COA) from their supplier, and then analyze the co-mingled product in their tank once the load has been delivered. When using scenario three, under FDA regulations, each load must be accompanied by a valid COA. It is not acceptable to get an annual letter from your supplier stating they will only deliver USP product. A promise letter from your supplier is not sufficient to meet the FDA's pedigree requirement, as without a COA you have no documentation that you actually did receive medical grade product.

The additional elements of a medical gas pedigree are, or should be, very familiar to independent manufacturers. In addition to the COA, this will include things like fill logs, calibration logs, training and qualification records, lot distribution records, complaint files, corrective and preventative actions, laboratory and analytical records, label and labelling records, and annual program review records. While all of these different documents often do not reside in a single file, collectively they constitute the paperwork pedigree that must be created and maintained for each batch of medical gases the company processes. Miss one piece of this paperwork matrix and to the FDA the pedigree falls apart – making the product something other than a medical gas.

Medical gas fingerprinting

While the FDA is still talking about a national pharmaceutical fingerprint regulation, many of the individual states have taken the initiative and forged ahead with implementing their own set of pharmaceutical fingerprint requirements.

These fingerprint regulations are an outgrowth of efforts in America to control and eradicate counterfeiting of prescription pharmaceuticals, and are another example of medical gases being pulled along with well meaning efforts to stem a legitimate issue. Unfortunately product counterfeiting is not an issue that currently affects, or is ever likely to affect, the gases industry. While there is a brisk trade in counterfeit erectile dysfunction drugs, the bottom line regarding medical gases is not as attractive. When the container is worth much more than the drug it contains, as is typical with a high pressure cylinder of medical oxygen, there is simply no financial incentive to counterfeit medical gases.

Unfortunately, that has not deterred a number of states such as California, Nebraska, and Florida from putting fingerprint regulations on the books and making them applicable to all prescription drugs. All of these states are now enforcing their fingerprint regulations against medical gas companies. Some states, such as Florida, are aggressively enforcing these regulations, and issuing significant monetary fines to companies who are not in full compliance. In the current economic climate some states are finding that pharmaceutical inspections have the potential to generate additional revenues to state coffers.

Basically, the fingerprint process requires firms to track the product from its initial manufacture, through the different steps and product transfers within the supply chain, and all the way down to the end-user. This would include the different product transfers from the primary manufacturer, to a cylinder fill facility, to a home care firm or a health care facility, and then to the patient. In some states the fingerprint file accompanies the product down the supply chain, and is added to by each entity that handles or uses the product.

B&R has already established and is providing our customers a special module for those firms that need to comply with these new regulations. The procedures, forms, and tools we provide equips our customers to meet the documentation requirements for each batch/lot of product they produce, which includes:

- Name, address, and registration information/state license number of the product manufacturer.
- Name, address, and registration information/state license number of the firm receiving and selling the product.
- Name, strength, dosage, and quantity of each of the prescription drugs.
- Distribution records of the drugs to customers, including in some states putting the customer's current registration/license information on the shipping papers.
- If product is sold directly to patients this would potentially include prescription files.
- Applicable financial information as required by state regulations. This can include shipping papers, invoices, certificates of analysis, and other such documentation.

I think you can see that fingerprinting requirements are different from pedigree requirements and are intended to address different regulatory concerns. However, some states are using the two terms interchangeably, which can lead to some confusion. Medical gases pedigrees are about the ability to verify, through documentation, that a medical gas has actually been produced and distributed in accordance with all applicable manufacturing regulations. Medical Gas Fingerprinting is about the ability to verify that a medical gas product has not been counterfeited somewhere along the supply chain, and that as the product moves down through the supply chain there is documentation that every individual or company the product passes though is a legitimate entity entitled to participate in the buying/selling/end-use of a pedigreed medical gas product.

Food grade pedigrees and fingerprints

At this point there are no regulatory requirements for food and beverage gas fingerprints or pedigrees. But things are about to change on that front.

In January 2011 the Food Modernization and Safety Act (FMSA) was signed into law. We are still waiting for the FDA to begin the rule making process, which will usher in what they are calling a sweeping reform of the good manufacturing practices for food. Early indications are that product traceability through the supply chain will be one of several key considerations under development by the agency.

We expect that many of the pedigree requirements implemented by the FDA for medical gases will be the template for food and beverage grade gases down the road. While these new requirements are still in the future, we are encouraging our customers to begin the planning process now, and consider how to improve their management of incoming and outgoing product traceability of food and beverage grade gases. It is our opinion that the pedigree requirements of medical gases and food and beverage gases will probably not be all that different at some point in the near future.

As regards to fingerprinting of food and beverage grade gases, hopefully common sense will prevail and those requirements will not be applied, at least in the gases industry.