Make your medical microbulk deliveries meet full compliance

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Delivery of cryogenic medical gases from microbulk units to smaller healthcare facilities such as nursing homes and surgical centers is increasing in popularity as a mode of medical gases delivery. It appears that the entire spectrum of company size, from small to large are taking the plunge and adding medical microbulk units to their fleet.

Dedicated units not required

The processes, equipment, and personnel associated with the delivery of bulk cryogenic liquid medical gases are all subject to FDA requirements and the regulations in Title 21 of the Code of Federal Regulations. The key concept microbulk operators need to keep in mind is that the distinction between medical and industrial gases is the paperwork that documents the manufacturing and delivery processes – not the actual manufacturing processes, or the purity of the gases themselves.

If the paperwork pedigree of the product in the microbulk unit is incomplete or missing then it cannot be called medical grade product. Standard industry practice is to use the same equipment for deliveries to medical and industrial customers on the same delivery run and FDA currently permits this as an acceptable practice.

Contrary to a persistent industry urban legend, dedication of delivery equipment to medical service is not a requirement in today's regulatory environment. Morever, we do not anticipate this changing in the foreseeable future. Any firm today that is operating a dedicated medical fleet is doing so based entirely on its business portfolio – not any regulatory requirement.

Qualifications: medical is never industrial

Product delivered and sold as medical grade product must have originally been manufactured as medical product. It is absolutely un-acceptable to fill a delivery unit with industrial grade product, test the product in the delivery unit, and then sell it as medical grade.

Photo courtesy of Chart

The FDA defines the filling of delivery units with medical gases as drug manufacturing. ASU's that ship medical grade product, as well as firms that fill medical delivery units from a bulk

storage vessel at their site, must first register with the FDA as a drug manufacturer. They also need to comply with applicable state registration requirements that are no different than what is required for filling high-pressure cylinders.

Paperwork pedigree

Determining if a delivery unit is in medical or industrial service is predominantly a function of its paperwork pedigree. Units that have industrial grade documentation are considered in industrial service. Conversely, units with USP/NF grade documentation are classified as in medical service. This remains true even if a unit in medical service only makes deliveries to industrial customers.

Industrial service units moving into medical service must first go through a qualification process. The same holds true for new delivery units, unless the unit's manufacturer can provide appropriate documentation that shows the unit is already qualified for medical service. There are a number of techniques to qualify units for medical service but the key point to remember now is that you cannot simply perform testing on an industrial unit and call it medical – there must be some activity which cleans/qualifies the microbulk unit for medical service.

Continuity is critical

Once medically qualified a delivery unit is considered a medical unit provided it is re-loaded with medical product, and the unit's documented medical pedigree remains un-broken. The exception to this is if a "qualifying event" occurs. A couple of examples of qualifying events include:

A unit in medical service experienced a total loss of pressure due to a bursting disk failure, and the contents are potentially exposed to atmospheric air.

There was a backflow of product into the delivery unit from the bulk tank being filled.

A two-hose delivery system is used, thereby allowing product from the customer vessel to be returned to the delivery unit. (This is common in many CO_2 and N_2O deliveries).

The unit was loaded at a facility not registered with the FDA. This could be either an ASU or a location with a bulk vessel used to load delivery units.

In each of these instances the delivery unit would likely need to undergo the re-qualification process prior to being re-loaded with medical grade product.

Filling and delivery operations

Prior to loading a delivery unit already in medical service, a pre-fill analysis must be performed on the residual product in the delivery vessel. Once filled, each unit must be tested for all required USP/NF tests, and each unit must be assigned a unique lot number for that load of product.

In some areas of the country firms have their bulk supplier fill their delivery units directly from the bulk tanker at the same time they fill their bulk supply vessel. This is acceptable, provided the firms procedures adequately ensure a pre-fill analysis is performed, and the delivery units are

held in quarantine until they are analyzed and released by the QC Unit for distribution.

Most firms elect to use the same procedures for both medical and industrial, deliveries, opting to use one process for both types of deliveries. However, the documentation required for medical loads is typically not kept for industrial deliveries. There are some key provisions associated with making medical product deliveries. Drivers must have documented training, including basic cGMP training. For example, all medical delivery processes must be performed in accordance with written standard operating procedures. The key steps of the loading and delivery processes must also be documented.

The biggie

But the most important provision is maintaining a delivery unit's medical pedigree by preventing any potential backflow from the customer vessel into the delivery unit. FDA's position on backflow is that even a minimal amount is un-acceptable, and breaks the delivery unit's medical pedigree. Across the industry there is a wide variety of backflow prevention practices, ranging from engineering controls such as installing a validated spring-loaded check valve in the delivery pump outlet line, to procedure-based controls such as having the driver monitor and record delivery unit and vessel pressures, thereby documenting no backflow occurred from the customer vessel during the delivery.

A final issue concerns the delivery hose itself. Hoses that are not kept capped and protected from the elements between deliveries can potentially introduce significant levels of contaminants into the customer vessel during product deliveries. The delivery firms procedures should stipulate that hose caps must be used religiously between deliveries, and driver training should reinforce that requirement.

Documentation requirements

In pharmaceutical manufacturing, the documentation processes and the diligence a company applies to them are essential to ensuring compliance to FDA requirements, and this absolutely applies to making microbulk medical deliveries. Some of the issues specific to bulk delivery units, that firms need to focus on include:

Documentation of the key steps in the delivery unit re-loading process

Documentation of the key steps in the customer delivery process

Documentation of delivery unit qualification activities

Documentation of delivery unit maintenance activities – both preventative & repairs

Maintenance of the delivery unit's medical paperwork pedigree

Customers receiving medical product must be provided a certificate of analysis for each load/delivery of product. The bulk product COA, like the drug product label applied to cylinders, serves to identify the product and its quality attributes. When making night deliveries it is common for the driver to leave the COA document in a box or container near the vessel, rather than hand it directly to the customer. While not mandatory, many companies want a customer

signature on the delivery paperwork as confirmation that the delivery was made correctly.

One area where we have seen companies run afoul of FDA regulations is to permit the delivery unit, once filled, to leave the facility before the documentation has been reviewed and approved by the QC Unit. Firms that permit this practice violate one of FDA's cardinal rules and risk severe FDA sanctions on their business.

Finally, many firms are moving to remote release of bulk product, especially in delivery operations that run 24/7. There are a number of key requirements involved in setting up a program to perform the remote release of product, but since virtually every operation is different, it is best to discuss your specific issues with a compliance expert to develop a customized solution for your operation.

Medical microbulk deliveries offer increased operational efficiencies over the more traditional method of supplying cryogenic medical gases to healthcare facilities in portable liquid cryogenic cylinders. In our opinion, the smaller healthcare facilities will continue to migrate away from cylinders and to microbulk to take advantage of these efficiencies, not to mention the convenience factor of not having to move large heavy cylinders around the facility.

B&R Compliance has developed a special FDA compliance program just for medical microbulk deliveries. It includes all the necessary procedures and forms for managing and documenting every step of the process. If you have questions about microbulk medical deliveries or FDA compliance in general just call us for assistance.

About the author

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