Airgas Healthcare
an Air Liquide company

Medical GMP Nitrogen for Open Mouth Dewar Fills

THIS DOCUMENT IS FOR EXTERNAL PUBLICATION

August 2018
Customer Presentation

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Overview

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- **The Food & Drug Association (FDA) is enforcing new packaging and processing requirements for liquid nitrogen filled into open mouth dewars for medical applications that will require Airgas to launch a new product to meet these requirements**
  - The new product requires material changes in packaging, fill process and traceability to meet the FDA requirements and therefore will be substantially more costly to produce and deliver to our customers.
  - The FDA requirements applies to units filled at both our facilities and filled on customer locations
  - Displaces prior FDA and CGA Guidance

Overview

- **The product we will provide to comply with the FDA requirements will be a new product labeled as "Medical GMP Nitrogen NF". It will fully meet all of the applicable requirements and will be the only product available for sell for these applications**
  - As a result of the sizable additional costs, this product will have new selling prices to our customers
- **The prior product was sold pursuant to a device use interpretation for which the FDA did not require device labelling; under the current FDA requirements the product is required to be considered a drug. As a drug it must be strictly labelled and named only as a drug.**

Overview

- **Airgas has identified the branch and plant locations that will have the capabilities to provide the new product.**
  - We are implementing the necessary process changes and training to equip these branches to provide Medical GMP Nitrogen NF
  - We have committed to the FDA that we will complete all implementations by the end of October, 2018
    - The implementation schedule for your servicing branch could be earlier
  - Once the implementations are complete, the former NF part numbers will be discontinued
- **Airgas will only transact and invoice Medical GMP Nitrogen NF dewar fills as complete dewars as part of a full service. (*For example, if Airgas fills your 10 liter dewar we will invoice you as NI GMPDEWARFILL10L with a unit of measure CL*)**
- **Please contact your local Airgas branch or account manager for questions or more information**

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What are the requirements?

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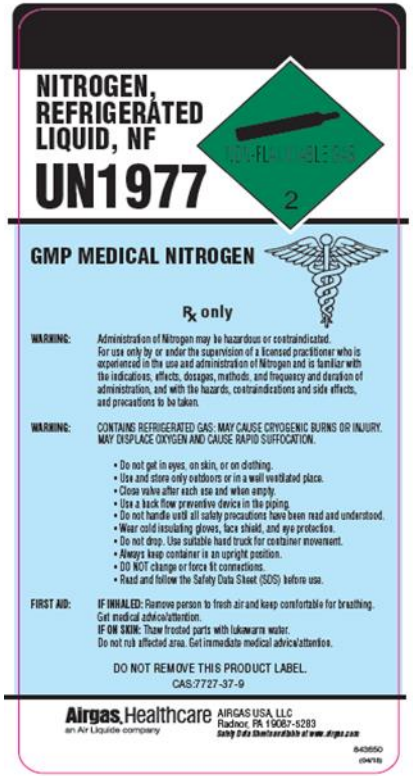
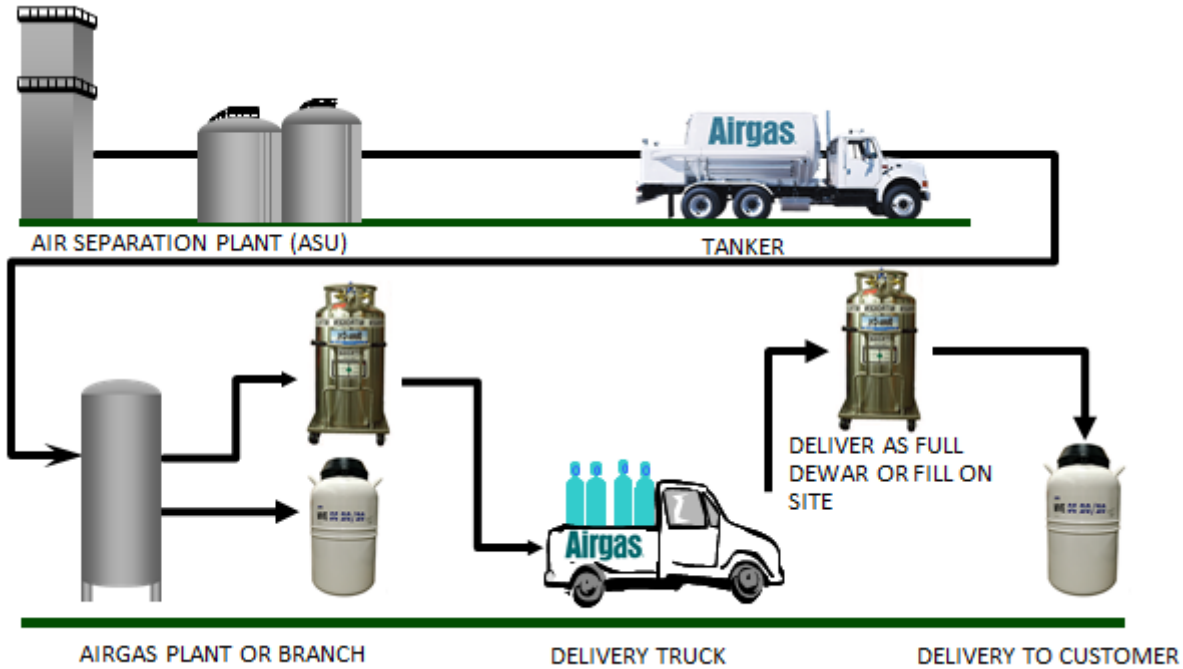
- **Any facility providing Medical GMP Nitrogen NF for dewar fill medical applications must be registered as a Drug Manufacturer with the FDA**
  - The facility must also be registered as a Drug Manufacturer with their respective State as required
- **Each time an open mouth dewar is filled with Medical GMP Nitrogen NF:**
  - The dewar must be labeled as **Medical GMP Nitrogen NF**
  - A lot number will be applied to the dewar
  - A Production Control Record (PCR) will be created
  - These requirements are necessary for dewars for medical applications to be filled at Airgas branches and plants or at customer locations
- **Customers purchasing the new product will be required to provide their medical license information to Airgas**



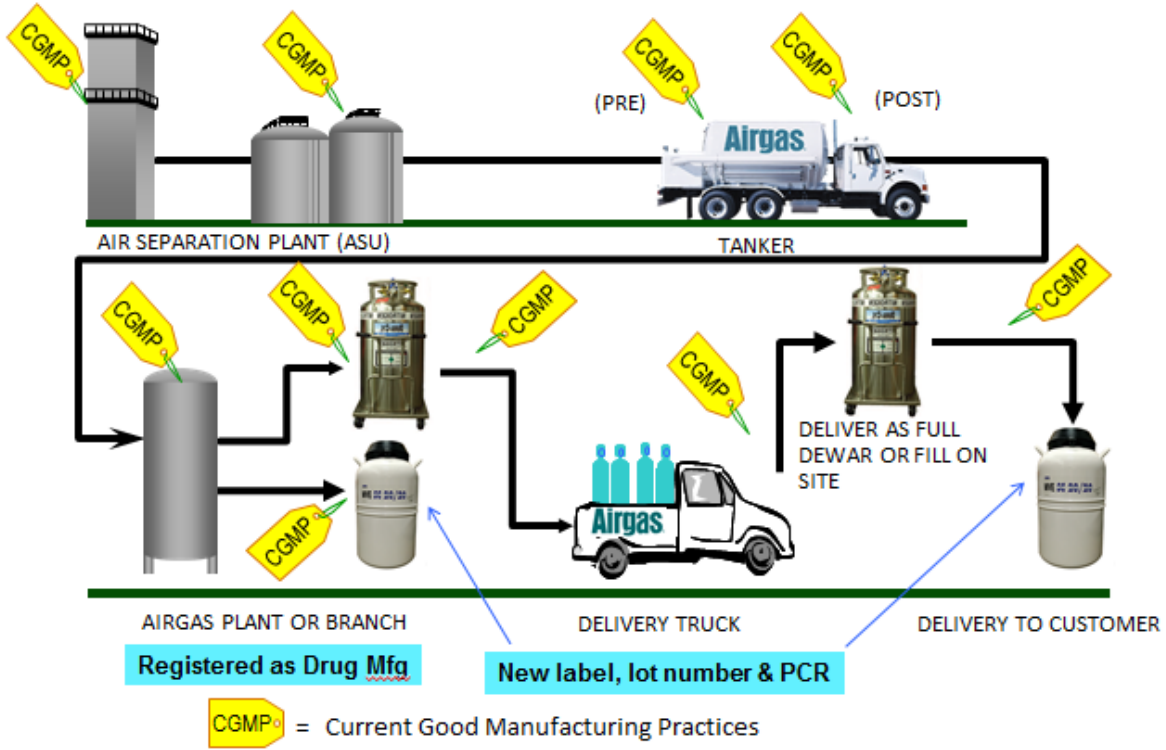
Medical GMP Nitrogen NF vs. Industrial Nitrogen

- **Liquid nitrogen filled into an open mouth dewar for medical applications must follow Current Good Manufacturing Practices as specified by the FDA**
  - These standards provide for both manufacturing process controls and testing at every stage of the process to insure the medical nitrogen chain of custody.
  - Conducting the product testing at every point in the custody transfer, along with the record keeping requirements adds substantial cost to the fill process
- **Nitrogen filled into an open mouth dewar for non-medical applications meets the Airgas Industrial Nitrogen specifications, which do not require the process, testing and chain of custody controls**
- **The following slides depict the process flow for each product**

Industrial Nitrogen Fill Process



Medical GMP Nitrogen NF Fill Process



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Frequently asked questions

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- **What is driving this change?**
  - In response to questions raised by Airgas, the FDA issued a letter of interpretation which in clarifying prior guidance announced the additional requirements and an intention to enforce the same.
- **Why is Airgas creating new part numbers?**
  - The new FDA requirements dramatically change the packaging, processing, documentation and label requirements for the filling of open mouth dewars. The new part numbers are being created to clearly distinguish this product and avoid any confusion with products used for non-medical applications.
- **Can I still order the NF Nitrogen for open mouth dewars?**
  - No, only **Medical GMP Nitrogen NF** or Industrial Nitrogen will be available for purchase

Frequently asked questions

- **What product is available to customers who require a nitrogen dewar fill, but do not have a medical application?**
  - It is the customer's responsibility to select the product appropriate for their application. However, if the customer does not have a medical license, the only product available for open mouth nitrogen dewar fills is Industrial Nitrogen
- **Does a customer have any specific requirements to purchase the new Medical GMP Nitrogen NF product?**
  - A customer may be required to purchase the new product depending upon their use and the application of relevant FDA regulation and other quality requirements. Customers purchasing the new product must provide their medical license information, similar to Medical Grade Oxygen.

Frequently asked questions

- **Can I purchase Medical GMP Nitrogen NF if I do not have a medical license to purchase?**
  - Generally no. However, there are a small number of states that allow an end user to apply for and be granted a waiver of the license requirement. Please contact your Airgas medical specialist for more information
- **I want to purchase the Medical GMP Nitrogen NF in a VGL and transfill my open mouth dewars internally. Do I need to follow the same fill process as Airgas?**
  - You should consult all regulations and quality control requirements applicable to your operations.
- **Can Airgas FDA documentation that supports the change?**
  - Yes, there are two documents that are available to share. The first is the FDA Final Guidance document and the second is the Federal Register publication announcing the guidance. Please contact your local Airgas representative if you wish to obtain copies.

Thank you