Periodic Testing of Pharmaceutical Grade Medical Propellant Stock Tanks

Dr T J Noakes
Medical Propellants Technical Expert

John E Kirpatrick
Medical Propellants Transport Engineer

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Summary
It is a requirement in most countries of the world that large pressure vessels such as propellant stock tanks are subject to periodic inspection and testing. The frequency and degree of inspection can vary, but can consist of anything from an external inspection using ultrasonic instrumentation, through to a full internal inspection and hydraulic pressure test.

Due to the very special nature of Medical Propellants a particular approach has been adopted in many countries which will be described here, designed to minimise quality problems and in particular protect patient safety.

Conclusions

1. Medical propellants are totally non corrosive and pose no internal corrosion risk to any storage vessel.

2. As medical propellants are kept strictly dry and impurity free, there is no associated internal corrosion risk due to moisture or oxygen.

3. Both carbon steel and stainless steel stock tanks are therefore completely unaffected by these propellants, but use of stainless steel provides further ‘belt and braces’ protection.

4. Biological and moisture contamination are major hazards in medical propellant stock tanks, leading to a product and patient risk.

Recommendations

1. That medical propellant stock tanks should neither be internally inspected nor hydraulically tested during periodic pressure vessel inspection.

2. Inspection should be by means of external inspection.

3. Testing should be conducted non-invasively, using ultrasonic techniques.

Detail

1. *Refrigerant Gases used as medical propellants – could they lead to corrosion?*

   a. HFA134a and HFA 227ea.
   There are only two Hydrofluoroalkanes (HFAs), usually referred to as Hydrofluorocarbons (HFCs) when used for non-medical purposes, in medical propellant use. These are:

   HFA 134a (1,1,1,2-tetrafluoroethane, CF_3CFH_2, Bpt –26C) and
   HFA 227ea (1,1,1,2,3,3,3-heptafluoropropane, CF_3CFHCF_3, Bpt –17C).

   These are non-flammable refrigerant gases, and in their normal industrial use are employed in air conditioning units, refrigerators, and the like. The medical versions are chemically identical, but purified under strict medical controls such that they are free of any harmful contaminants such as water or oil.

   These HFAs are used as propellants in Metered Dose Inhalers (MDIs), commonly called 'asthma inhalers', and used to treat a wide range of lung disease such as asthma, bronchitis and emphysema. They have been selected for this duty in part because of their extreme chemical inertness, as this is required to make them toxicologically safe.

   These HFAs do not react or interact AT ALL with any ferrous alloy, carbon or stainless steel. In fact, to get them to do any form of chemistry at all they have to be attacked with strong chemical agents at very high temperatures (>200C). Categorically, they will not interact at all with stainless steel or carbon steel stock tanks.

   b. Specifications – purity and dryness.

   Both these HFAs can dissolve a limited amount of water (up to around 1000ppm) and therefore at first sight normal aqueous corrosion should be considered. In the case of stainless steel this is still not a concern, but limited rust blooming has been seen inside some carbon steel stock tanks. However, medical grade HFA propellant HAS to be supplied and kept completely dry, otherwise it is not suitable for use. Its moisture content is tightly controlled both at production, delivery and end use to be <10ppm.

   Therefore there are no associated moisture based corrosion factors to consider.

2. *Risks to propellants.*

   These propellants have rigorous quality in handling requirements, and extreme steps must be taken to comply with international requirements in the maintenance of their integrity [1]. The Metered Dose inhalers (MDIs) – such as asthma aerosols- filled from these are inhaled on a daily basis straight into the lung. Not only is this a delicate and diseased organ in its own right, but in many cases inhaling something is equivalent to a direct injection into the bloodstream.

   Therefore medical guidelines lay great stress on the purity of the propellant used, and the steps to be taken in protecting patients from contamination. Broadly speaking, the following classes of contamination should be considered when considering periodic inspection/testing of stock tanks:

   a. Biological contamination. Any ingress or pressure testing with non-sterile media (eg water) can result in biological contamination of the stock tanks. This can then pose risk for respiratory products, with pulmonary infections such as Legionnaire's disease a risk.

   b. Moisture contamination. The respiratory medications made with these propellants are extremely water sensitive. A 'total dryness' spec of <10ppm is, in fact, a feature of the propellant supply and control. Any attempt to hydraulically test such stock tanks would, in addition to posing severe biological contamination problems, create a major problem to dry and clean the tank out again before it could be charged with propellant.

3. *Tank cleaning after Inspection/testing. Propellant stock tanks*

   Maintaining cleanliness of these tanks has become much more difficult since Jan 2010. Prior to this time, whilst is has always been viewed as very undesirable to interfere with their medically validated status in any way, there were solvents available to facilitate the later stages of post entry cleaning. Bearing in mind that the only pulmonary approved solvents are sterile water and CFC 11 (and water cannot be used in this context for reasons given above) the only tank 'final clean' solvent that can be used before 134a used to be CFC 11.

   Unfortunately from 1/1/2010 use or sale of this is banned worldwide as it is a substance banned under the Montreal Protocol, so recommissioning stock tanks without this 'final wash and dry' material will be very difficult.

4. *Non invasive testing techniques.*[2]

   For all these reasons it is most strongly recommended that, as the media stored is totally non corrosive, and interference with the tank will seriously compromise its ability to store medical propellants, that inspection should be confined to external inspection, and testing should be non-invasive.

   a. Visual Inspection

      The simplest and easiest technique to apply and often called by the generic term 'inspection' on process plant.
      It is able to detect surface damage and distortion. However, access to the surface is required and the capability relies on the illumination and the eyesight of the inspector.
      Many aids are available for visual inspection ranging from a magnifying glass through endoscopes and boroscopes which allow viewing of surfaces inaccessible to the eye alone, to fully remote computerised video systems. In the latter case as 'seeing is believing' care needs to be taken to ensure that the signal processing of the image does not hide any defects.

   b. Thickness Measurement

      The commonest damage found on process plant is corrosion and so techniques which allow remaining wall thickness to be measured are widely applied.
      Ultrasonics (high frequency sound) provides an accurate point measurement of wall thickness.

      Ultrasonics is the use of high frequency sound waves in a similar manner to sonar or radar: sound pulses are reflected from interfaces or discontinuities.

      In thickness checking the reflections from the wall surfaces are measured. In defect detection reflections from cracks, voids and inclusions are detected and assessed.

      The transfer of sound from the ultrasonic probe to the component requires a coupling medium, which is usually water or gel. The condition of the interface determines how much sound is transferred into the component, how much is scattered and how much noise is produced.

      Ultrasonics requires a relatively good surface finish.

      Manual application over a large area is relatively slow and the technique needs to be tailored to the defects requiring detection. However, ultrasonics is able to provide both length and through wall size information.

The surface on which the transducer is placed needs to be clean and, as it provides a point measurement, the measurement positions need to be selected with consideration of the type of corrosion damage so that the minimum wall thickness can be detected. When using a grid to survey a large surface area, the pitch of the grid needs to be selected so that it will detect the damage of concern.

Care needs to be taken when taking measurements on plant which is painted or coated to ensure that the measurement is just that of the remaining wall.

Other thickness techniques include:
Flash Radiography, Magnetic Flux Leakage, Pulsed Eddy Currents. These techniques are more limited in their application by material type, accuracy of measurement, wall thickness or geometry than ultrasonics but offer other advantages such as speed of application or the ability to inspect under insulation.

c. Common Trade Names

Fleximat
This is a thin flexible strip containing an array of ultrasonic transducers which can be permanently bonded to a component to provide continuous corrosion monitoring of fixed locations.

Internal Rotary Inspection System - IRIS
An ultrasonic technique for the NDT of boiler and heat exchanger tubes consisting of a high frequency ultrasonic immersion probe inside a rotating test head. The system provides coverage of the full circumference and full wall thickness as the probe is scanned axially along the tube. The head can be modified for defect detection if required.

LORUS
This is an ultrasonic technique which relies on bulk waves and was designed specifically for interrogating the plate under the shell on the annular ring of an above ground storage tank. The probe does not need to be scanned backwards and forwards and so is suitable for use on the restricted surface available on the annular ring.

The sound floods the plate as it travels and is reflected from corrosion defects on the top or bottom surface. The working range is about 1 m but as the plate is flooded with sound it is unable to discriminate between top and bottom defects.

Note: Although the acronym, LORUS, is derived from Long Range Ultrasonic System, when compared to more recent techniques referred to as long-range ultrasonics, the LORUS technique can only be considered medium range (typically up to 1m).

Saturation Low Frequency Eddy Current - SLOFEC
The (SLOFECÔ) technique is very similar to the magnetic flux leakage technique. However, instead of detecting the flux leakage with a passive coil or a hall effect sensor, the SLOFEC technique has an eddy current sensor.

The fact that the eddy currents are used to sense the distortion of the magnetic field in a layer close to the surface of the component means that this NDT system is able to inspect a greater wall thickness and also able to cope with thicker non-magnetic coatings than the magnetic flux leakage NDT system.

When the equipment is used on non-magnetic stainless steels the detection technique becomes solely an eddy current NDT technique.

Small Controlled Area Radiography - SCAR
This is a proprietary radiographic system which operates in a more controlled manner and hence a much smaller area than traditional radiography. Proper application of the system will reduce the controlled area to typically within 3 metres of the emission point. This has the advantages of minimal disruption to adjacent work areas and of reduced dose rates to classified workers.

References
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b. UK version:
http://www.mhra.gov.uk/Publications/Regulatoryguidance/Medicines/CON2030291
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Mexichem UK Limited, The Heath Business and Technical Park,
Runcorn, Cheshire, WA7 4QX
Tel: +44 (0) 1928 514840
e-mail: zephexsales@mexichem.com
www.mexichemfluor.com