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Life sciences equipment

By Rhea Healy

Cryogenic storage and freezing demands have demonstrated continual and incremental growth over the years due to healthcare advances, improved quality of life, and longer lifespans, with the majority of samples in medical and pharmaceutical applications passing through the cold chain and typically requiring cold storage and cryogenic freezing at some point.

As Andy Pazahanick, General Manager of Worthington Industries’ CryoScience product line, points out, “According to a 2014 study by Visiongain, it’s estimated that there are 1.3 billion bio samples in the life sciences market worldwide – and it is growing by 100 million bio samples each year. These samples are extracted, processed, analysed, stored and shipped in the cold storage chain.”

So how is cryogenic freezing and cold storage in the cold chain advancing, and what new products are being developed to keep up with its expanding demand capacity? This month’s In Focus… explores the growth drivers in the sector and the new technologies that companies are implementing to freeze out their competition.

Joint forces

When Worthington acquired the assets of Taylor-Wharton’s global CryoScience business in December 2015, the US business also acquired the entirety of its cryogenic storage and freezing product line. As a result, Worthington now manufactures cold chain storage and transport vessels and equipment, providing critically reliable transportation of biological samples and an entry into this thriving market.

Through this acquisition, Worthington now offers complete solutions for cold storage in the life sciences market; from liquid nitrogen dewars and shippers for sample storage and transportation, to microbulk and bulk tanks for on-site storage. Its LABS and K-Series freezer solutions are extensively used for medical universities, hospitals, laboratories and biorepositories, as they use liquid nitrogen to securely store irreplaceable specimens for IVF, cancer treatments and other life-saving research.

Despite the product reinforcement that the $33.25m acquisition provided, however, Pazahanick revealed that there are always equipment improvements to be made. He explained, “Currently, we’re working to develop new technologies for hybrid liquid nitrogen freezers that are more efficient, decrease operating cost, increase sample security, and provide a broader temperature range for cold storage requirements.”

“We’re expanding our cryogenics offering beyond packaged gas and bulk products to include a complete liquid nitrogen portfolio of cold storage and transportation solutions to global industrial gas and life sciences markets,” he continued. “We’ve added expert bench strength in life sciences, increased our product portfolio with cryo refrigerators and freezers, microbulk and large engineered tanks, and grown our global manufacturing footprint to better serve our markets.”

Pazahanick indicated that the precision medicine, cell therapy and pharmaceuticals for cancer research industries are current growth drivers for the company’s technological advances, propelled by “an ageing population, increased pharma research and development (R&D) for more effective clinical treatments, and global demand for better healthcare.” This provides a knock-on effect for the industrial gases market in the form of increased demand for liquid nitrogen usage through freezers, dewars and shippers.

But in terms of current technological trends, he stressed that there is still room for innovation and revealed Worthington’s current developments. “We see a market for liquid nitrogen freezers that do a better job at cryopreservation than today’s standard freezers,” Pazahanick confirmed. “By designing a next generation hybrid liquid nitrogen freezer, we intend to create a much better user experience while ensuring the security of the samples inside. We’re also considering solutions for the integrated biorepository, where data on all cold chain equipment is centrally monitored online for anytime, anywhere access.”

Opportunities

The ongoing and emerging opportunities in this sector are abundant; from the rising growth of bio-banking applications to general global healthcare necessities, several factors are presenting promising opportunities for both gas suppliers and equipment manufacturers in cold storage and cryogenic freezing innovations.

For one such freezing equipment manufacturer, Dohmeyer, these opportunities lie in a different way of processing samples in the cold chain. “The cold chain itself is not always guaranteed due to manipulated,” Director Fabian Van Dammme explained. “In our opinion, the missing factor is thawing – when you thaw the product back to ambient temperatures you pass the same latent heat plateau. We believe thawing curves are just as important as freezing curves.”

Dohmeyer became a government recognised R&D centre in 2011, and has since shifted its focus towards the cryogenic freezing of biological materials, biochemical products and pharmaceutical products. Today, Dohmeyer turns over approximately 40% of its revenue in the pharmaceutical and biomedical sector and has even created a separate entity for its life science products due to the immense growth witnessed in the sector.

The company creates custom cabinet freezers designed to operate at temperatures of -60°C, for liquid carbon dioxide injection, or -110°C for liquid nitrogen, and uses control rate (CR) freezing to freeze blood products and a variety of other important samples. Van Dammme clarified, “We freeze – bringing the temperature down from ambient to storage using programmable freezing curves. We master the flow of air (velocity) and temperature. In this way, we manage the control of the freezing process.”

“We manufacture freezers that are different as we do not work based solely on temperatures – that is just one parameter,” he continued. “When you want to control the freezing, you need to manage the cold transfer to the product. Cold transfer is temperature and air velocity and air velocity is more important than temperature – that is why our freezers work differently.”

“Commercial use of semen for cattle and animals is a big industry for us and is still growing. Further, we see more and more use of cryogenics in drug production: vaccines, ODT tablets and so on,” he specified.

Promising pelleting

Another company focused on the freezing side of applications in the life sciences sector is an area in which we are very active on the processing side. Often a system from CES is a unique and efficient combination between proven technology and individual solutions reflecting the customer’s needs.”

But he went on to reveal that the company’s latest breakthroughs have incorporated cryogenic pelletising. “Cryogenic pelletising is now already extensively used in the bio-industry, in particular for the production of fermentation. We observed that cryogenic pelleting of pharmaceutical products is practiced to a lesser extent, but CES has built the pharmaceutical pelletiser with the largest capacity for the industry. For example, we have just finalised a cryogenic freezer that is followed by a non-cryogenic carousel type cold storage for a major Swiss pharmaceutical company.”

The company considers cryogenic freezing to be the most suitable technology for the biopharmaceutical industry due to the flexibility of the equipment and the properties of liquid nitrogen. “It allows continued operation at temperatures down to -150°C, which is particularly useful when controlled freezing rates are required for the quality of the product,” he explained. But in terms of future technological advancements, Vanackere believes that pelletising holds the most promise. “Cryogenic pelleting of bio-products in particular, but also pharma-products in some cases will be driving growth…”

“Extremely low temperatures before they are placed into cold storage, but CES is also focusing on a different form of freezing – cryogenic pelletising.”

CES produces a number of standard cryogenic freezing cabinets designed for use in biopharmaceutical plants, with CEO Hans Vanackere confirming, “The life sciences sector is an area in which we are very active on the processing side. Often a system from CES is a unique and efficient combination between proven technology and individual solutions reflecting the customer’s needs.”

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“At this time, the low temperature buffering required or temporary storage...
for fast frozen biopharmaceutical products could be illuminated or reduced to a much smaller space, which would only be used in equipment breakdown situations,” he continued. “Further developments in the use of a continuous lyophilisation process would require continuous freezing systems instead of batch freezing systems or cabinet freezers that are frequently being used now.”

“The main feature of our technology is safety – realised by means of our product series BIOSAFE®. Under this turnkey solution, Cryotherm develops and supplies a complete product range from the rack system for vials, freezing bags and straws through sample management system software, to liquid nitrogen supply from special supply containers or super-insulated transfer piping to networked control and monitoring devices – including temperature, data and management software.

Anticipated growth
There is little doubt that future demands for cold storage and cryogenic freezing will continue to expand rapidly, with the further growth anticipated in the life sciences sector enhancing future manufacturing opportunities.

But what emerging technologies and trends will shape the future of cold storage and cryogenic freezing? According to Flohr, the potential lies in optimisation.

"Standard systems optimised from a technical-economical viewpoint expanded upwards with large and extremely large storage containers in connection with an increasing realisation of closed cooling chains,” he said.

And of course, the technological advancements of cryogenic freezing and cold storage of life sciences samples cannot escape the impact of worldwide digitalisation. Pazahanick alluded that, "Data management is becoming a trend in the industry as repositories and labs are not staffed around the clock, yet they need to be aware if and when samples are in jeopardy of falling below critical cryogenic temperatures and immediately track that data.”

"Today, many repositories and labs are locally monitored via audible or visual alarms on individual units. In the future, the entire biobank will be integrated and monitored remotely in the cloud, 24/7.”

But Vanackere believes that the industry can look to other sectors that use the cold chain for technological inspiration. He concluded, “A worldwide growth of the requirement for fast freezing of biopharmaceutical products is expected, but the lyophilisation for the production of dry powders in the biopharmaceutical industry is not yet a continuous process, whereas continuous lyophilisation is already widely used in the food industry.”

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Today’s solution, tomorrow’s advance: Besides different processes such as thawing and pelleting proving to be propitious avenues, what other technological trends are driving growth?

Wolfgang Flohr, Product Development at specialist cryogenics company Cryotherm, proffered, “Today; networked control and monitoring devices for level control, temperature control and logging, as well as data and management software. Tomorrow; cold chain process and supporting technology in automation.”

With this in mind, Flohr unveiled a new product to be released by the German company at the end of this year – the ‘Cryotherm Cold Chain Tracking Tool.’ He stressed, “It has become adequately apparent from specialist literature that fluctuations in temperature have a negative effect on the quality of frozen samples. As the quality of each sample has to be the highest possible objective, all individual component parts of a cryobank are optimised to that goal and their development is constantly being driven forward through cooperation with science and industry.”

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© Cryotherm | BIOSAFE® System from Cryotherm.

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gasworld.com/specialfeatures
Sample storage and control

Nitrogen and biosafe storage

By Cryotherm

Deep cold liquefied (cryogenic) gases like nitrogen, oxygen, argon, hydrogen and helium are used in industry – for example in the fields of chemistry, aerospace – as well as in medicine and research. In order to store and apply them, insulated vessels and piping is required to reduce evaporation losses.

The long-term storage of medical, biological and ecological samples at temperatures of approximately -130°C in the gas phase in so-called cryobanks has been state-of-the-art technology for some time. The goal is to store valuable samples for a long time and to keep them unchanged. Due to its inert character, liquid nitrogen (boiling point -196°C at ambient pressure) serves as a cooling agent. For larger sample quantities, vacuum super-insulated storage vessels are amalgamated to a cryobank.

In order to fulfil the high requirements of this application area Cryotherm offers the system series BIOSAFE®-MD® and -SC®. BIOSAFE®-Systems with the addition MD® are medical products of class II2a according to the EU-directive, the addition SC® designates the standard version. Storage systems always have to be medical products when the samples stored are intended for re-introduction to human beings (for example with blood or sperm).

“For safe, long-term storage the liquid nitrogen level of vessels has to be constantly within pre-set values”

Due to vacuum super-insulation, vessels which made of stainless steel possess high thermic quality at extremely low rates of evaporation. As the wall thickness reduces, the effectivity of the insulation increases, BIOSAFE®-Systems possess high storage capacity and can be erected especially to save space.

For safe, long-term storage of samples the liquid nitrogen level of vessels has to be constantly within the pre-set threshold values. It is the only way to ensure that the temperature of the samples is permanently under -130°C. In addition, liquid nitrogen has to be refilled accordingly to compensate for the losses due to evaporation.

BIOSAFE-Control® ß unifies these two essential functions in one package and works according to tried and trusted measuring principles: Regulation of the levels is executed by means of a level adjustable temperature measuring sensor (measuring range -200°C to 50°C) protected against manipulation. The liquid level is flexible from zero (gas phase) to 100% adjustable. The vessel status is easy to recognise at any time. Alarm signals in plain text are set off in case the selected filling level goes undercut or overshot, as well as each time the maximum vessel temperature, lid opening time and filling tile are exceeded. Monitoring minimum and maximum alarm signals takes place redundantly and independent of processors.

In a cryobank with more than one storage system, the administration of alarm signals is executed in a central location and the messages forwarded to the computer. Up to 32 systems can be connected to one network. As an optional an I/O-Box for certain functions such as management of a main valve, common alarm, or device error is available. The computer will not only visualize the status of a vessel; in addition, all the vessel parameters can be set up in clearly arranged and password protected pop-up windows. With the help of the software, all the data of a cryobank can be documented completely.

Safety

There has to be an equal focus on human safety. The deep cold of liquid nitrogen is needed to stop any biological action and using mechanical type refrigerators, even very cold ones, is not feasible in the field of cryobiology. Many of the cells needed for medicine are difficult to freeze and are then transferred to liquid nitrogen storage tanks.

Cryogenic storage at such low temperatures is presumed to provide an indefinite, if not near infinite, longevity to cells – but it also means that cautionary measures have to be observed for personal protection when dealing with deep cold nitrogen. Dangers can arise through the extreme cold and the oxygen displacement characteristics of nitrogen. For this reason, the cryobank in a container is equipped with a warning device triggered in events of oxygen displacement. Furthermore, the system has a built-in active ventilation system; if the oxygen content of the air in the container falls below a pre-set threshold value, there is an automatic alarm signal and the active ventilation system is triggered. The existing nitrogen in the interior is immediately replaced with fresh air from the outside.

All vessels and piping is fitted with vacuum super-insulation in order to avoid danger from the extremely low temperature of deep cold liquefied nitrogen. An impermissible rise in pressure due to evaporating nitrogen in rooms that can be locked is prevented by the use of full lift safety valves.