

asymptote

2014 European Cryopreservation
Technology Innovation Leadership Award



FROST & SULLIVAN



50 Years of Growth, Innovation & Leadership

Technology Innovation Leadership Award Cryopreservation Europe, 2014

Frost & Sullivan's Global Research Platform

Frost & Sullivan is in its 50th year in business with a global research organization of 1,800 analysts and consultants who monitor more than 300 industries and 250,000 companies. The company's research philosophy originates with the CEO's 360-Degree Perspective™, which serves as the foundation of its TEAM Research™ methodology. This unique approach enables us to determine how best-in-class companies worldwide manage growth, innovation and leadership. Based on the findings of this Best Practices research, Frost & Sullivan is proud to present the 2014 European Technology Innovation Leadership Award in Cryopreservation to Asymptote Limited (hereafter referred to Asymptote).

Significance of the Technology Innovation Leadership Award

Key Industry Challenges Addressed by Asymptote Limited

Cryopreservation plays a critical role in the manufacturing and clinical delivery of cell therapies. Well-preserved living organisms are essential for conducting successful investigations in life sciences research and biotechnology for research programmes, industrial processes, and training courses. The Current Good Manufacturing Practices (CGMPs), which enable the long-term and stable storage of living organisms, demands validated, reproducible, and safe methods of generation and preservation of cells and tissues. This guarantee is essential to the final user, not only in terms of sample freezing, but also with regard to the entire cold chain.

Cryopreservation processes should preserve the integrity of constructs and maintain high levels of cell viability and cell functions after cryopreservation. Similarly, if stem cells are involved, then cell proliferation and differentiation ability, as well as cell-to-cell interaction, constitute key capabilities to be diligently preserved.

To achieve high viability of cells, protective compounds, so called cryoprotective additives need to be added to the cells and the rate of cooling from ambient temperature to the storage temperature must be controlled in an accurate manner. The optimum cooling rate is known to vary with different cell types. At cooling rates faster than the optimum damaging intracellular ice can form, whilst at rates lower than the optimum the cells are damaged by exposure to the high levels of cryoprotective agents for extended periods.

Key Benchmarking Criteria for Technology Innovation Leadership Award

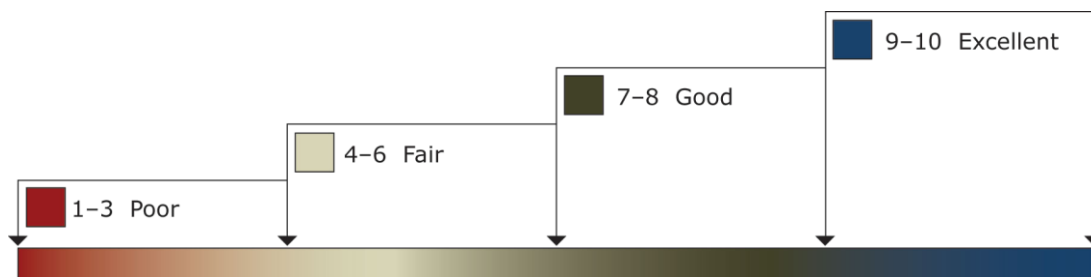
For the Technology Innovation Leadership Award, the following criteria were used to benchmark Asymptote's performance against key competitors:

- Uniqueness of Technology
- Impact on New Products/Applications
- Impact on Functionality
- Impact on Customer Value
- Relevance of Innovation to Industry

Decision Support Matrix and Measurement Criteria

To support its evaluation of best practices across multiple business performance categories, Frost & Sullivan employs a customized Decision Support Matrix (DSM). The DSM is an analytical tool that compares companies' performance relative to each other with an integration of quantitative and qualitative metrics. The DSM features criteria unique to each Award category and ranks importance by assigning weights to each criterion. The relative weighting reflects current market conditions and illustrates the associated importance of each criterion according to Frost & Sullivan. Fundamentally, each DSM is distinct for each market and Award category. The DSM allows our research and consulting teams to objectively analyze each company's performance on each criterion relative to its top competitors and assign performance ratings on that basis. The DSM follows a 10-point scale that allows for nuances in performance evaluation; ratings guidelines are shown in Chart 1.

Chart 1: Performance-Based Ratings for Decision Support Matrix



This exercise encompasses all criteria, leading to a weighted average ranking of each company. Researchers can then easily identify the company with the highest ranking. As a final step, the research team confirms the veracity of the model by ensuring that small changes to the ratings for a specific criterion do not lead to a significant change in the overall relative rankings of the companies.

Chart 2: Frost & Sullivan’s 10-Step Process for Identifying Award Recipients



Best Practice Award Analysis for Asymptote Limited

The Decision Support Matrix, shown in Chart 3, illustrates the relative importance of each criterion for the Technology Innovation Leadership Award and the ratings for each company under evaluation. To remain unbiased while also protecting the interests of the other organizations reviewed, we have chosen to refer to the other key players as Competitor 1 and Competitor 2.

Chart 3: Decision Support Matrix for Technology Innovation Leadership Award

<i>Measurement of 1-10 (1 = lowest; 10 = highest)</i>	Award Criteria					Weighted Rating
	Uniqueness of Technology	Impact on New Products/Applications	Impact on Functionality	Impact on Customer Value	Relevance of Innovation to Industry	
Relative Weight (%)	20%	20%	20%	20%	20%	100%
Asymptote Limited	9.6	9.8	9.7	9.5	9.7	9.7
Competitor 1	5.5	6.0	5.5	5.0	5.4	5.5
Competitor 2	4.9	4.5	4.3	4.8	4.1	4.5

Criterion 1: Uniqueness of Technology

From cell therapy to the food and pharmaceutical industries, Asymptote has excelled in the development of products and process technologies that are adapted to its customers' requirements. Committed to providing novel, effective, and environmental-friendly solutions, Asymptote aims to produce a liquid, nitrogen-free, good manufacturing practices (GMP)-compliant cold chain that comprises end-to-end cryopreservation, shipping, and thawing of material under strictly controlled regulatory standards. The EF600-controlled rate freezer consists of a low-cost, ultra-portable, liquid nitrogen-free cryocooler. Most specifically designed for the cryopreservation of stem cells, embryos, and spermatozoa, this small volume-controlled rate freezer has demonstrated excellent results in other laboratory and portable cryopreservation applications. Among its principal features, the balance between its cooling rate control accuracy and its simplicity and ease-of-handling is of note. Furthermore, the EF600 supports numerous sample formats and allows one to work with linear and non-linear cooling profiles. The seeding process, which is also called ice nucleation, does not require liquid nitrogen. Consequently, the running costs are significantly diminished and are estimated to be one per cent of liquid nitrogen controlled rate freezing. The EF600 is suitable for use in Grade B clean rooms.

The VIA Freeze range of controlled rate freezers, on the other hand, are large-volume liquid nitrogen-free, controlled rate freezers developed by Asymptote for easy adaptation to clean rooms. This product allows end users to easily program and upload cooling profiles for further validation and report generation. The last prototype was developed as a part of a Technology Strategy Board (TSB)-funded project. Designed to minimise temperature gradients, the VIA Freeze enables the achievement of a highly accurate control of the cooling rate and the temperature.

The company has also developed a novel active nucleation biocompatible material named IceStart™ that helps to reduce the damage caused by supercooling during the cryopreservation process. The IceStart acts as an ice nucleant during the cooling of aqueous solutions. Compared to other products on the market, the use of IceStart induces ice nucleation that is closer to the melting point of the solution. This results in an important reduction in the number of samples that are subjected to extreme undercooling. Consequently, the number of cells recovered and their viability are substantially increased.

Criterion 2: Impact on New Products/Applications

Suited to a variety of requirements, Asymptote's liquid nitrogen-free cryogenic solutions are aligned with most of the cutting-edge technologies in the fields of regenerative medicine, stem cells, tissue transplantation, and biobanking, among many others. Most of the aforementioned fields of research require strict handling and manipulation. Asymptote's GMP cold chain technology provides novel solutions for the life sciences and biomedical industries. Customers' feedback strongly validates this fact.

The EF600 can ideally be exploited primarily in life sciences research applications, while the VIA Freeze equipment is better suited for manufacturing processes in clinical applications. The EF600 can be adapted for use in operating rooms for the optimised cryopreservation of source material for autologous treatments in biopsy, cell therapy, and tissue transplantation. On the other hand, the VIA Freeze allows for the cryopreservation of large volumes of materials, thus enabling the cryopreservation of cells in different formats, such as cryovials, cryobags, or cassettes. With a capacity of 250 cryovials, the VIA Freeze represents the best option for the creation of seed cell banks (SCBs) and master cell banks (MCBs), which require validated, reproducible, and safe methods of freezing cells during their creation. The temperature, cryoprotectant medium, and freezing technique should be reproducible during the manipulation of clinical-grade cells in clean room facilities under CGMP guidance. Cryobags contain 200 ml of cells in suspension (T cells) and alginate encapsulated cells (hepatocytes). Cassettes can be cryopreserved as large volumes (up to 1500 ml) of alginate-encapsulated hepatocytes for use as a bioartificial liver. Society for Biomolecular Sciences (SBS) formats are being designed for the development of new tools for cell-based assays that use stem cell-derived cell lines.

Criterion 3: Impact on Functionality

With outstanding Cambridge-based cryopreservation specialists on board, Asymptote has obtained a grant from the Technology Strategy Board (TSB) for its project in portable, self-charging, cryogenic solutions to improve the storage of live vaccines in developing nations. Asymptote has excelled in developing ultra-low-temperature storage equipment that helps to prevent the discarding of vaccines due to thermal stabilisation problems.

The company, which is innovatively using electrically powered Stirling cryocoolers in cryopreservation equipment, expects to significantly impact the cryopreservation market through the distribution of live vaccines in territories where liquid nitrogen is not readily available and the supply of electricity is unreliable.

Criterion 4: Impact on Customer Value

With 20 years of experience in the field of cryopreservation, Asymptote works in close collaboration with its customers in order to provide tailored solutions for each particular case. The company also offers consultation programs to achieve an in-depth understanding of cryopreservation, freeze drying, scale control, and process optimisation.

Criterion 5: Relevance of Innovation to Industry

Asymptote is leading its investigations based on five principal projects: 1) the development of a GMP cryogenic cold chain for the clinical delivery of regenerative medicine therapeutics; 2) the development of coatings that induce ice nucleation; 3) an improved method of freeze drying; 4) the development of a portable, self-charging cryogenic vessel for the shipment and short-term storage of cryopreserved material; and 5) the development and testing of

technology for the cryopreservation of hepatocytes in microtiter plates for subsequent screening applications. These projects are carried out in collaboration with its customers, in order to continuously improve their results and guarantee that their needs are met.

The company is currently proposing the development of the first GMP-compliant cryogenic cold chain for the clinical delivery of regenerative medicine therapeutics. The \$2.3 million project is being carried out in collaboration with four research centres that specialise in different cell therapies.

Long-term stabilisation of biological materials is crucial for their utilisation in medicine and science. Asymptote is developing an ice-nucleating coating for the inside of vessels that are used for cryopreservation, which will overcome the problems caused by random ice nucleation and improve cell recovery upon thawing.

New solidification processes to improve the outcome of freeze-drying technologies are also required. The company expects to determine the real impact of these new developments in the market, as well as their disruption capability for improving an existing solution or for the creation of new products.

Portable, self-charging, cryogenic solutions are ideal for making it possible to utilise live vaccines in developing countries. Asymptote's newly proposed concept of cryopreservation deals with the discharge of vaccines due to thermal damage associated with failures in the cold chain.

Asymptote is collaborating with a life sciences company to generate high fidelity, cryopreserved human hepatocytes for research purposes. In partnership, Asymptote is developing a consistent, highly functional and biologically robust technology for the cryopreservation of cells in microtiter plates. The main goal of the project is to develop novel tools for drug screening applications, including drug safety and metabolic response in pharmaceutical research.

Conclusion

Based in Cambridge, UK, Asymptote Limited is excelling in the development of products and processes that are adapted to its customers' requirements. Aiming to provide novel, effective, and environment friendly solutions and having on board laureate cryopreservation specialists, Asymptote is focused on the development of a liquid nitrogen-free, GMP-compliant cold chain that comprises end-to-end cryopreservation and the shipping and thawing of material under strictly controlled regulatory standards. Recognizing the innovative capabilities of Asymptote's technologies and its commitment to addressing major global health concerns, Frost & Sullivan is proud to present the 2014 European Technology Innovation Leadership Award in Cryopreservation to Asymptote Limited.

Critical Importance of TEAM Research

Frost & Sullivan's TEAM Research methodology represents the analytical rigor of our research process. It offers a 360-degree view of industry challenges, trends, and issues by integrating all seven of Frost & Sullivan's research methodologies. Our experience has shown over the years that companies too often make important growth decisions based on a narrow understanding of their environment, leading to errors of both omission and commission. Frost & Sullivan contends that successful growth strategies are founded on a thorough understanding of market, technical, economic, financial, customer, best practices, and demographic analyses. In that vein, the letters T, E, A and M reflect our core technical, economic, applied (financial and best practices) and market analyses. The integration of these research disciplines into the TEAM Research methodology provides an evaluation platform for benchmarking industry players and for creating high-potential growth strategies for our clients.

Chart 4: Benchmarking Performance with TEAM Research



About Frost & Sullivan

Frost & Sullivan, the Growth Partnership Company, enables clients to accelerate growth and achieve best-in-class positions in growth, innovation and leadership. The company's Growth Partnership Service provides the CEO and the CEO's Growth Team with disciplined research and best-practice models to drive the generation, evaluation and implementation of powerful growth strategies. Frost & Sullivan leverages 50 years of experience in partnering with Global 1000 companies, emerging businesses and the investment community from more than 40 offices on six continents. To join our Growth Partnership, please visit <http://www.frost.com>.