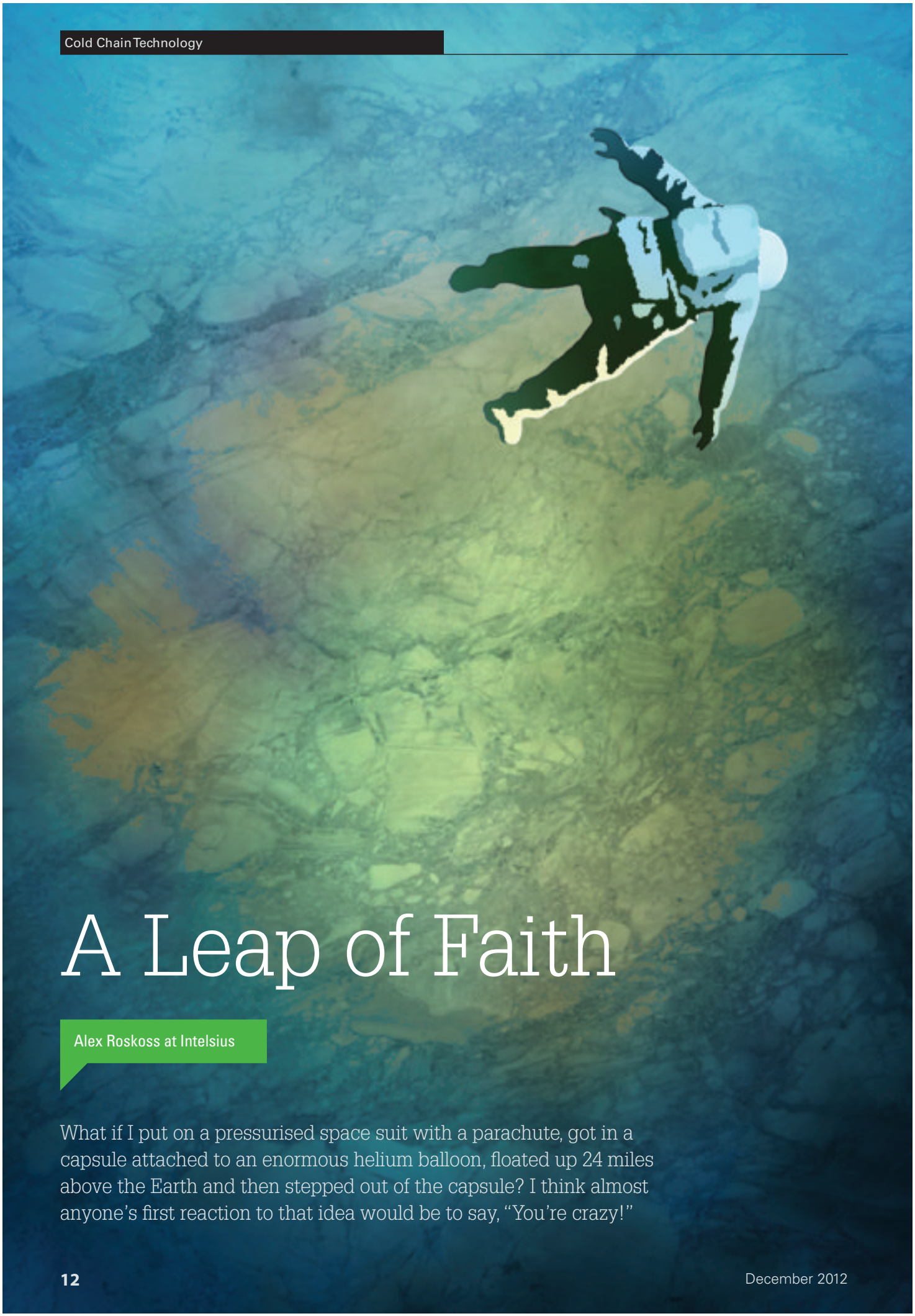


A Leap of Faith

Alex Roskoss at Intelsius

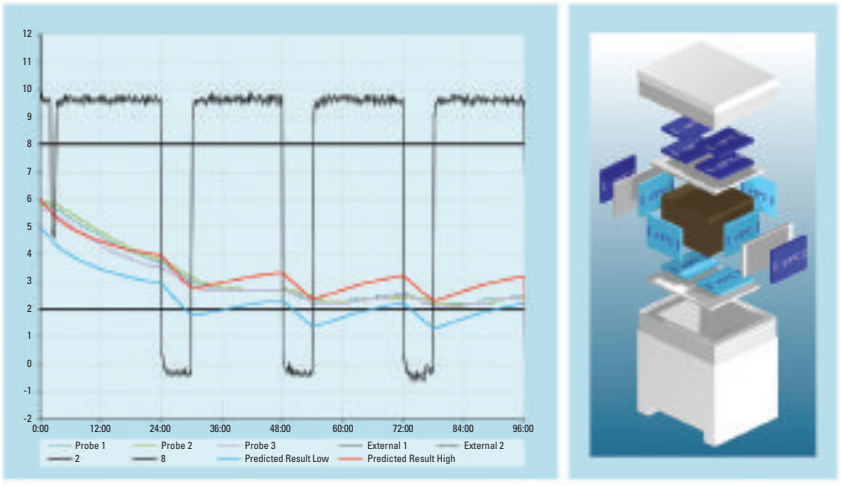
What if I put on a pressurised space suit with a parachute, got in a capsule attached to an enormous helium balloon, floated up 24 miles above the Earth and then stepped out of the capsule? I think almost anyone's first reaction to that idea would be to say, "You're crazy!"

You'd have to live under a rock to have missed that is exactly what Austrian daredevil Felix Baumgartner did on Sunday 14th October. There are striking similarities between the intense planning that went into his experiment and the value and effort Big Pharma companies invest in maintaining the appropriate temperature for their products in transit.

Understanding the effects of temperature and altitude on the capsule (shipping container) and Baumgartner's body (payload) is where the team began the five-year long process from inception to completion. Along the way, based on scientific understanding, they were reasonably able to predict what components they would need to be successful. However, unlike most finished pharmaceuticals, it only took Baumgartner two hours to reach his destination.

Scientists knew that at an altitude of 24 miles, the temperature outside the capsule would be approximately -57°C and Baumgartner's blood would vaporise if not properly protected. Temperature-related damage to drugs is not readily visible and can occur at any point in the supply chain. By modelling the thermal challenges drugs face in a dynamic global supply chain – and designing transportation solutions to meet those challenges – temperature-sensitive pharmaceuticals will be better protected. Temperature excursions are responsible for the degradation of up to 35 per cent of the world's vaccines (1). In many instances the excursions occur because the vaccines are stored improperly. However, how many of the pharmaceuticals made it to their destination at the appropriate temperature in the first place? How serious are temperature excursions? At best, they can leave a vaccine or other life-saving treatment with little to no efficacy; at worst, they can be deadly. An article in July 2011, showed that patient deaths attributed to failures in the cold chain were on the rise (2).

Figure 1: Predicted and experimental results of the configeration (below)



Source: Intelsius Technical Services

Thermal Protection

With $140 billion spent on biopharmaceuticals in 2011, and with eight out of 10 products needing temperature control, the need for reliable thermal protection is crucial (3). In addition, with the ever increasing numbers of clinical trials taking place all over the world, it's critical to get patient samples, investigational medicinal products (IMPs) and finished pharmaceuticals to their destinations at the appropriate temperature. These trials are increasingly being conducted in diverse and challenging areas; there are currently an estimated 134,000 studies taking place in 180 countries from Afghanistan to Zimbabwe (4).

If a pharmaceutical product is being shipped from Switzerland to Kabul or Harare and needs to maintain a temperature of 2-8˚C during the journey, how should it be packed? The challenges faced by a small package travelling to Brussels are very different to those faced by a pallet travelling to Johannesburg. Utilising thousands of temperature profiles created from field tests and product testing over the years, the types of thermal exposure these different routes face can be identified and packaging developed to meet these needs.

Innovate to Insulate

Software has been developed which can simulate thermal exposure by analysing thermal flows into and between the components of a packaging system. This can help to determine the performance characteristics of the proposed solution and whether the protection selected is sufficient to meet the expected challenges. An analytical modelling software can save up to 70 per cent in packaging development time and costs when bringing a new drug to market, moving drugs through a new route, or preparing for a new trial.

The thermal modelling software uses dynamic isothermal surface

“With $140 billion spent on biopharmaceuticals in 2011, and with eight out of 10 products needing temperature control, the need for reliable thermal protection is crucial”

mapping to generate a complex picture of the temperatures and heat flows in the simulated system for each time step. These calculations are derived from real experimental baseline data taken from years of thermal packaging development. The result is a step-by-step temperature against time graph showing key durations above or below thresholds, as well as mean temperature data. The temperature accuracy has been confirmed by validation testing and found to be within ±5 per cent duration to fail, across a range of system sizes, durations and exposures between -20°C and +60°C. This validation included hundreds of hours of comparison testing in calibrated thermal chambers to provide the complete semi-empirical baseline data on which the model depends.

By using thermal modelling software, a protective packaging system can be tested against multiple exposures with a wide range of thermal challenges in very quick durations. The simulation results from four to five days can be generated in minutes, rather than in over 120 hours of experimental chamber time. This increases the number of challenges you can test a system against in a limited time period and saves the energy costs of running test chambers for these repeated, long thermal exposures. These time and energy savings are in addition to the increased information obtained about the performance of the packaging system.

The high quality of the simulation data allows for confidence in system performance when facing exposures beyond the original environmental chamber testing. The speed and ease of the simulation allows for a large range of systems to be placed against the new challenge and answers on suitability quickly determined. Improving the configurations through simulation allows for less time consuming chamber testing. This reduces time to a qualification, time to system use, as well as cutting costs by saving time and energy in the testing process.

Calculated Risks

The simulation of any system is never as reliable as the data taken in the field from real trials and real exposures. This data is invaluable in ensuring your system choice has been correct, however it can be costly and time consuming to gather. The advantage in simulation is that you can present challenges to a system that may only rarely be encountered in the field. By building up a large portfolio of simulations, you can increase confidence in the behaviour of a packaging system to handle adverse thermal events. When your compounds or their diluents are subject to cold exposure, the ice formation can denature the molecules

and drastically reduce the efficacy of the medication. When exposed to high temperatures denaturing occurs at increasing rates. Keeping the drug at the right temperature increases the chance of patients seeing the positive effects intended.

Using simulation methods in addition to real world testing, provides more confidence in the solutions you have chosen to work as you intended and keep the product in the state intended from manufacturing to patient. Relying only on traditional methods could cost a company more than money – it may cause long-term damage to its reputation. But if you do it right in the first place, not just one or two people may benefit from a product – it could be valuable to the whole world one day. Like Baumgartner, whose idea seemed crazy at the beginning, the benefits to mankind of one risk-taker may mean extraordinary scientific discoveries that could be the difference between life and death. He took a calculated risk and 39,000m later landed on his feet.

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About the author

Alex Roskoss worked as an instrument developer with a large defense contractor before moving into product development at Intelsius. He oversees new product development, assesses new marketplace technologies, assists with technical sales inquiries and manages the ISTA-certified testing laboratory. Alex has helped patent of a number of new technologies at Intelsius. He holds a PhD in experimental physics and recently co-authored an article that appeared in *Healthcare Packaging* magazine. He has authored numerous papers and has been published in the *Review of Scientific Instruments*, *Pharmaceutical & Medical Packaging News* as well as *Pharmaceutical Manufacturing and Packing Sourcer* (*PMPS*).

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