



# Cold Chains Are Hot!

Mastering The Challenges Of  
Temperature-Sensitive Distribution  
In Supply Chains

***RFID in Life Science Series: Part 1***

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### **About ChainLink Research**

ChainLink Research, Inc. is a Supply Chain research organization dedicated to helping executives improve business performance and competitiveness through an understanding of real-world implications, obstacles and results for supply-chain practices, processes, and technologies. The ChainLink Inter-Enterprise Model is the basis for our research; a unique, real-world framework that describes the multi-dimensional aspect of links between supply chain partners.

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## Executive Summary

### COLD CHAINS TAKE CENTER STAGE

Tsunami, hurricane, landslides – in responding to the needs of the victims of these natural disasters, the effective delivery of food, pharmaceuticals and life saving products are now in the spotlight. Supply challenges related to transportation, infrastructure and other issues require careful planning and coordination. And then there is another element – the need to ensure that these products are carefully handled and maintained at the correct temperature. Variations are not an option – product purity is at stake. These are the challenges of the Cold Chain – a critical subset of supply chain management.

### WHEN CUSTOMERS LOSE, COMPANIES LOSE

And even in normal circumstances this “extreme” supply chain needs careful attention. Variations in temperature, humidity, altitude – all factors that can transform modern medical miracles into useless materials! Billions of dollars spent in research; manufacturing and FDA approval are at risk as these products move through the global chain of custody from supply to demand. The stakes are high – brand integrity, customer confidence and market share are all at risk in the fragile Cold Chain.

### EMERGING TECHNOLOGIES CREATE NEW OPPORTUNITIES

Securing the Cold Chain requires innovation, collaboration and communication, ensuring that each of the critical links in the chain understands product storage and handling requirements. Advanced technologies, to include sensors, RFID, wireless and wired networks are all potential components of a Future Forward model that will ensure an ongoing ‘portable record’ of each product throughout its lifecycle. Information related to the ‘state’ of the product is critical – remedy and control are required to ensure that product is not compromised or contaminated.

### USING '3Pe' TO GUIDE YOUR PATH AHEAD

The combination of enhanced Policy, Process, Performance and Enablers provides the key to success for Cold Chain management. Leveraging technologies that have been pioneered in the Food industry, it is possible to create a Cold Chain infrastructure that understands and prepares for the constraints of Cold Chain distribution.

The case for action is compelling – lives are at stake! The ROI proposition is straightforward.





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( Photo element of cover graphic—courtesy of MedPro RX )



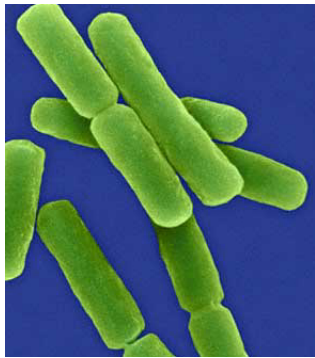


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## Introduction

### ANTHRAX AND OTHER 'NASTIES'

Bio-Terrorism.



The headlines strike fear in us all. With tensions heightened after September 11<sup>th</sup>, incidents like the Anthrax virus contamination of the mail put this threat in the national spotlight. The uninitiated learned to their horror that this was not merely a disease contracted by animals, or found in remote and under-developed locales; the modern manufactured version was deadly. The resultant lack of adequate response by the government highlighted the fact that the antibiotics required to treat the disease were in short supply. A chilling thought – the United States of America was not in a position to defend its citizens from a potential killer!

But bio-terrorism is just a new front in an ongoing battle between humans and micro-organisms trying to coexist on this planet. Natural disasters, hurricanes, floods and resultant contamination of water sources create a fertile breeding ground for typhoid, cholera and other potential killers. The horrors of the thousands swept away in the Tsunami of December 2004 filled global television screens for weeks. As the death tolls increased daily, there was an even greater fear – contamination of food, water and the eruption of cholera, typhoid and other epidemics. Infection can be deadly if not treated immediately, the key is to have rapid access to antibiotics and other biological life-science products.

While events like natural disasters grab headlines, there are other fronts in this battle that are less obvious, but nevertheless, demand constant vigilance. Virtually eliminated in the United States by a combination of modern sewage and water treatment, Cholera is still prevalent in many parts of Latin America, Africa and Asia. Travelers have brought contaminated seafood back into the United States causing food borne outbreaks. There are other virally contracted diseases like Polio that are still rampant in many parts of the world. Despite a goal of eradicating Polio globally by the year 2003, Polio is once again ravaging parts of Africa and other third world nations. As a result of inadequate health services, reduction or suspension of immunization activities, Polio once again threatens to arise as a potential epidemic.

### HEROES OF THE COLD CHAIN

Responding to the call, millions of vaccinators and volunteers are traveling with their precious cargo across the affected areas. Armed with coolers filled with polio vaccine, these



good Samaritans travel on foot, on horseback, by motor cycle and bicycle, boat or helicopter – their shared goal to reach and immunize every child at risk. They are the heroes of the Cold Chain – working in the front lines of the complicated process of delivering life saving drugs and vaccines across global boundaries.

But all their effort is in vain if these medicines are rendered useless when it reaches the patient – the customer at the end of the Cold Chain. Unlike food products, where degradation is visually apparent to the potential user, pharmaceutical and life science products in many cases can be compromised without any visual effect. Variations in temperature can transform a modern miracle into an innocuous solution with no more effect than distilled water. Undetected, this can be life threatening, since the recipient believes they are protected from a fatal disease, when in fact they are not.

The everyday challenges related to the Cold Chain cannot be under estimated – even when moving product through formalized distribution channels. Everyday, millions of people around the globe eat food, apply cosmetics or take their prescribed drugs, depending on the purity and quality of the product. And any negative outcome due to mishandling of the product throughout the chain can be damaging to the bottom line and brand equity.

So what exactly is the Cold Chain? Why is it becoming so important? What are the rules of play, the referees and the coaches? And what are the emerging supply chain best practices and technologies that hold promise for improving the Cold Chain?

We will explore this subject in greater detail in the following pages.

## Understanding the Cold Chain

### WHAT IS A COLD CHAIN?

Cold Chain refers to a subset of the total supply chain involving the production, storage and distribution of products that require some level of temperature control in order to retain their key characteristics and associated value.

The term Cold Chain originates from the terminology for the ‘chain of custody’ in the production, packaging, distribution and control of temperature sensitive product. This includes the traditional areas of supply chain, to include raw material acquisition, transformation and manufacturing process, packaging and product protection, storage and distribution.

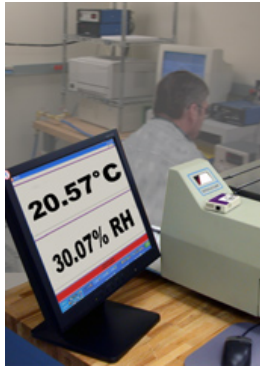


### COOL VS. COLD: WHAT’S THE DIFFERENCE?

The Cold Chain comprises the storage and distribution of products that are chemically and physically stable based on the following parameters (which should be indicated on all product packaging and documentation).

Category	International Storage and shipping requirements (stated in Celsius and Fahrenheit)
Frozen	- 25° and -10° C (-13 and 14° F)
Cold	Any temperature not exceeding 8° C (46°F)
Cool	Between 8° and 15° C (46° and 59° F)
Temperature controlled	Thermostatically controlled temperature of 20° to 25° C (68° to 77° F)
Room temperature	Temperature prevailing in a working area; not thermostatically controlled
Warm	Between 30° and 40° C (86° and 104° F)
Excessive heat	Above 40° C (104° F)

Table 1: Variables to Consider in Cold Chain Compliance



As is evident, there are many variations in terms of 'Cold Chain' compliance – it is imperative to ensure that each specific product characteristic is known and clearly communicated. A further warning relates to the measurement of all temperature in Celsius often without indicating "C" – Celsius is common in most parts of the world bar the United States!

The implications of this are extensive – storing something at 30 degrees Fahrenheit would destroy the product.

Although the term Cold Chain is used to describe products that require special handling, both in transit and at rest, these products are sensitive to all variations in temperature – too cold being as damaging as too hot! In addition, several products that fall into the category of Cold Chain are sensitive to variations in humidity and light. As such, it is appropriate to include all products sensitive to deviations from recommended storage and handling conditions in the category of 'Cold Chain'<sup>1</sup>. Thus ensuring that items requiring special handling are identified and distributed appropriately. Other considerations include variations in altitude, something that can be easily overlooked, especially when the entities involved in the logistics process are outsource partners who are unaware of product characteristics.



### THE NEED FOR A 'PORTABLE SYSTEM OF RECORD'

Extended supply chains include many players, all of whom need to have a clear understanding of the products that they are handling, specific requirements and remedy in the event of a problem.



*NOTE: Consider what happened to a shipment of blood product as a result of unclear process and procedures. There was a shortage of the plasma that was a component for a specific product and the logistics personnel at the origin location in the USA decided that instead of transporting it by ocean, as was the normal procedure, they would use airfreight. When the product arrived at the destination in Japan, the laboratory tests revealed that the product was damaged and should be destroyed. This was as a result of exposure to variations in temperature – a layover in Anchorage in extremely cold weather had frozen the product. In addition, this product was sensitive to altitude and was unsuited to air cargo. The lack of clear communication between the manufacturer and the distribution organization resulted in a loss of many millions of dollars and global shortage of a critical product.*

[1] In view of the increased globalization of the Cold Chain, it is therefore important to ensure that all labels and documentation clearly indicates the temperature in both Fahrenheit and Centigrade.

This example highlights the need to apply different measurements when moving Cold Chain products. One of the primary differences between the monitoring and control of products that fall into the category of Cold Chain is the need to establish and record the 'condition' of the product as it changes hand and state. Also to communicate product storage and handling requirements to all players at the supply linkage points, monitoring the movement of the product to ensure that these are adhered to. This is in addition to basic requirements of supply chain management – item level visibility – both in-transit and at rest. Technologies used to track and trace mainstream products capture timely data related to transactions, time and location as products are moved through the trans-shipment and interchange points.

Although this has enabled many better practices in terms of inventory management and control, there is a need to enhance these capabilities in the case of Cold Chain product to include identification of deviations in temperature, providing alerts through appropriate mechanisms. This is an area where the evolving sensor technologies play a key role in addressing some of these issues (more on this later!)



## The Food Industry: Learning from Cold Chain's Early Adopters

### DISCERNING CUSTOMERS; PERISHABLE PROFITS

Cold Chain management and control is a relatively mature process within the food industry – high volumes of refrigerated and frozen products are carefully packed, stored and shipped to ensure that they reach the market in good condition. In the case of the seafood industry, product is literally 'quick frozen' at sea, ensuring the freshness and safety of a product that has in many cases been the cause of major food related epidemics. Large 'factory ships' are equipped to clean, freeze and pack, resulting in product that is shelf ready as soon as it reaches the shore! Discerning buyers are reassured that the product they are buying is fit for consumption – expiration labels, temperature sensitive tags and other labeling technology alerting consumers to product



that is no longer suitable for sale. In the case of fresh products, potential damage and spoilage is apparent from the external appearance of the product. The old adage of the one rotten apple contaminating the bunch is a true one, and many a bushel has ended up in the dumpster due to careless handling!

The impact of food spoilage has other implications, even greater than the financial loss. Consider some of the health concerns:

- Safety risks increase in the food chain over time and distance.
- All food is infected with low levels of numerous types of bacteria.
- By 2000, 2/3 of all food borne illness was the result of temperature abuse. In 2001 there were 77 million cases, according to the CDC.
- Raw and ready-to-eat products cause the majority of food born illness, and uncooked products are the source of cross contamination.
- Food borne illness consistently follows the weather or outdoor temperature. Food's greatest exposure to the outdoor temperature comes from local and regional transportation.
- Therefore, infection is primarily the result of bacteria growing exponentially in transportation and supply chain processes!

Table 2: Cold Chain Considerations in the Food Industry

### TECHNOLOGY ENABLERS IN THE FOOD COLD CHAIN

Here we discuss technologies that are unique to the Cold Chain besides the usual enablers that are required in a typical supply chain.

## Sensors

Temperature monitoring devices are available to ensure that the storage locations are maintained at the correct temperature. Located in key areas, they monitor variations in temperature, humidity and other factors that could impact the quality of the product they store and protect. In addition, tags and monitoring devices are available to place at the item level, fluctuations in temperature triggering changes in label color, for example. These devices are also available for transportation equipment – the options are many and varied, ensuring that food products are handled in the optimal manner.



## Transportation

There are many transportation, storage and logistics providers who have specialized equipment and operations designed to optimize the flow of frozen, refrigerated and other food products that require special handling. In many cases, whole storage facilities are designed for frozen, cooler or other temperature requirements. These facilities are able to handle large quantities of food products, ensuring that they are received, stored and shipped at the correct temperature. In fact, most of the technology that has been developed for 'Cold Chain' logistics finds its roots in the food industry.



## Warehousing

Specialized warehouse management systems and technologies have been designed and developed to handle the challenges of temperature controlled storage facilities. Modern technology requires special consideration if it is to co-exist with some of the constraints of Cold Chain storage! Computers are not designed to operate at sub zero temperatures and need to be housed in protected areas; printers malfunction when exposed to humidity – a phenomenon created when condensation occurs each time storage areas are opened to enable product to move from a cool to a warmer environment – and need to be located to take into account both operations efficiency and technical requirements. In addition, the physical process of order fulfillment is more difficult when workers need to dress for the harsh environment. For example, there are many challenges related to order picking in a frozen or cooler environment, especially when workers are required to use hand held devices for task direction and data entry when updating warehouse management systems.

### Other considerations

In addition to the inability of RF readers to function well under sub-zero conditions, challenges include clumsiness of protective clothing (gloves are not conducive to keyboard entry) and the impact of insulated and metal walls on successful radio frequency transmission. One of the solutions is to include voice recognition as part of the order picking technology. In this manner it is not necessary for workers to enter data – they merely respond to verbal prompts and confirm actions via spoken word.

Temperature controlled warehousing is expensive. As such, it is necessary to ensure that product is slotted in the optimal configurations, while taking into account the need to have 'air space' to facilitate the temperature control.



Despite the many challenges, the maturity of the food processing and distribution industry, as well as the fact that temperature controlled products are normally manufactured and distributed in large quantities, has created an environment where the handling, packaging, storage and transportation of these products is relatively well controlled.

This is not the case for many pharmaceutical and life sciences products. These items tend to be distributed in relatively small shipments, in many cases in combination with other products. For example, vaccines could be packed in a single temperature controlled container that is shipped in a consolidated consignment with pallets or cases of product that has no Cold Chain requirements. This can lead to product damage when the Cold Chain product is handled in a manner appropriate for the bulk of the consignment, but inappropriate for this sensitive item.



## Life Sciences & Pharmaceuticals: Cold Chain's New Frontier

### HIGHER PRODUCT VALUE; HIGHER STAKES

Cold Chain is increasing in importance for those enterprises engaged in the discovery, manufacture and distribution of pharmaceuticals and other health care products that are impacted by variations in temperature. These include products used in treating human diseases as well as in animal health. In fact, health care for animals is a critical area. The concern is equal, whether the animals are destined for consumption or are part of a home or homestead.

Many of these products are relatively unstable, comprising biological and other components that become inactive or contaminated if handled incorrectly. Vaccines in particular need to be maintained at the correct temperature – not always an easy task when transporting or administering these to humans and animals in remote locations. The careful handling of these products is critical, especially as there is a global shortage of some vaccines – as evidenced recently in the United States, with the resultant rationing of Flu vaccines to 'at risk' elements within the community.



### COLD CHAIN'S WEAKEST LINK: OVERLOOKING THE 'LAST MILE'

These Cold Chain products, literally the lifeblood of the healthcare industry, in many cases have a long manufacturing cycle time. Years can pass from the initial discovery process, to extended and controlled clinical trials, to the final FDA approval. It is estimated that each new drug that passes approval incurs costs of literally billions of dollars.

In addition, especially with respect to some active ingredients that are undergoing clinical trials, there are only a couple of batches manufactured each year, with long and complex processes involved. Added to which certain of these products have a single source and limited supply, as in the case of some oncology and Aids drugs. The proposition is compelling – if it takes years to make a product, the yield is low and the costs are high, why take a risk in the 'last mile' of the supply chain, ruining product through careless handling?

The 'last mile', in the case of these products, is the point of consumption such as a hospital, doctor's office, or home. There are many horror stories of products that have been carefully stored and transported, only to find their way into home environments that are less than conducive to quality control. As such it falls on the doctor or





pharmacist to ensure that the patient is familiar with storage and handling requirements for these Cold Chain products. Most pharmacies include a product leaflet with each new prescription – in many cases these are not read or even understood. Better practice would include patient counseling in terms of risks of poor product storage and handling. Potentially an automated control could include the use of sensor devices to monitor the product once the patient takes it home. For high value health care products, the use of RFID technology has potential value through monitoring the lifecycle of pharmaceutical products in the same manner as proposed for electronic and other consumer products.

Ensuring the integrity and potency of the product has implications beyond those related to financial issues – the social issues and human health consequences of product degradation cannot be under rated. Lives are at stake!

*NOTE: One product that is notoriously unstable is insulin – a problem for an item that is normally self-administered by the patient. The storage and handling of this product is critical – the potency is immediately compromised by variations in temperature, shaking or other poor handling. As such, this is a candidate for better control than is currently the norm. One of the common problems with regard to this product relates to home delivery by expedited carriers and mail service. In many cases the product is handled incorrectly, is shaken or otherwise compromised. Damage is not apparent and the patient is only aware of problems when they do not achieve a predictable response to the Insulin. This is a real threat to children, who are not always able to communicate that there is a problem.*

## UNDERSTANDING THE CHALLENGES

There are 80 million shipments of life sciences Cold Chain product distributed on a global basis annually, broken into the following areas:

- Vaccines and injectables
- High value biologicals
- Blood products – including whole, blood, plasma and platelets
- Diagnostic products – including reagents and test kits
- Veterinary products
- Medical devices

Statistical data related to Cold Chain, as percentage of life sciences distribution, is hard to find, as sometimes the product is Cold Chain sensitive at different periods in the

lifecycle. For example, the materials used in R&D and clinical trials are normally temperature sensitive, but the approved and manufactured product can vary in requirements based on the dispensing form. One thing that is clear however is that biologicals are becoming more prevalent and the associated percentage of Cold Chain requirements is growing.

In the case of the pharmaceutical industry, every drug has stability data that dictates its required temperature storage range. The FDA requires that these products be stored under appropriate temperatures so that their identity, strength, quality, effectiveness and purity are not affected. However, many variables impact temperatures within a facility, including airflow, facility layout, traffic patterns and seasonal extremes.

### PRODUCT SEGMENTATION: ONE APPROACH DOES NOT FIT ALL!

*NOTE: The 2004 presidential election ran the gamut of predictable topics – from the state of the US economy, the war in Iraq, to a series of debates on values, moral standing and other controversial topics. A rather surprising topic however was the shortage of flu vaccine, in preparation for the winter of 2004/2005. Irrespective of the political implications, the inclusion of this subject highlighted one of the Achilles heels of the health care industry – on a global basis.*

All Cold Chain products are not the same. Consider one of the most critical of global healthcare products – vaccines. These products are increasingly being manufactured in dispersed locations, outsourced to lower cost producers once they achieve 'generic' status. This in turn creates supply chain issues, resulting in product shortages, exacerbated by the potential of product being damaged in transit.

Vaccines are manufactured by a limited number of companies – liability and other issues making this critical preventative less attractive from a manufacturing and distribution perspective than some of the other pharmaceutical products. And this is not limited to flu vaccines. Vaccines that have created the promise of eradicating Polio, controlling outbreaks of Cholera, Smallpox and other life threatening diseases, are in relatively short supply. This highlights the fact that the Cold Chain that is responsible for distributing these products needs to be secure and reliable. Added to which, vaccines are extremely susceptible to variations in temperature – high and low. As such, it is worth spending a little time on the specifics of Cold Chain as they relate to vaccines and biologicals.



<p>Products at risk from freezing</p> <ul style="list-style-type: none"> <li>• Vaccines, insulins, biotech products, blood products</li> <li>• Products that are physically unstable – for example, some emulsion systems</li> </ul> <p>Products at risk from elevated temperatures</p> <ul style="list-style-type: none"> <li>• Vaccines, insulins, biotech products, blood products</li> <li>• Products that are physically unstable</li> <li>• Products that are chemically unstable at elevated temperatures – e.g., chloramphenicol eye drops</li> <li>• Some semi-solid products – for example, fatty-based suppositories</li> </ul>
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**Table 3: Products at risk from freezing or elevated temperatures**

The result of variations of temperature outside of the ranges defined for the controlled storage and movement of temperature sensitive product causes physical and chemical changes as shown in the following Table 4.

What can happen when products with a recommended temperature range of 15°–25°C are exposed to	
POSSIBLE PHYSICAL CHANGES	POSSIBLE CHEMICAL CHANGES
Separation of emulsion systems	Increased rate of degradation resulting in reduction of shelf life
Sedimentation of active ingredients in suspensions and semi-solids	Increased rate of production of possibly toxic degradation products
Loss of 'volatile' components such as chloroform and flavoring agents from oral liquids	Increased rate of interaction with direct contact packaging materials – for example, the absorption of preservatives by plastic or rubber components
Changes in crystalline structure in fatty bases and active ingredients resulting in changes in melting time and bio-availability	Increased risk of interaction of components in aqueous solutions

**Table 4: Result of Variations of Temperature Outside of the Ranges Defined**

**TEMPERATURE CONSTRAINTS: TOO COLD IS AS BAD AS TOO HOT**

It is important to ensure that the correct temperature is maintained at all times – variations above and below the recommended range can have equally disastrous consequences.



Consider the following example:

**Temperature too low:** A shipment of vaccine destined for an immunization session at a school in the UK was packed in an insulated container with an ice pack. The pack came into contact with the vaccine, freezing the contents and destroying the valuable product. Investigations revealed the following:

*Inadequate records had been maintained from origin to arrival in the UK, and it was not possible to determine if the correct temperature had been maintained in transit.*

*The manufacturer had not validated the effectiveness of the distribution practices used for this product – to include the packaging materials. In this instance, the pharmaceutical wholesaler responsible for the distribution of the product suffered adverse licensing action as well as a product recall due to failure to satisfactorily demonstrate adequate temperature controlled conditions for Cold Chain product!*

As is apparent, the shipment of vaccines requires great attention to detail, to ensure that the quality of the product is not compromised. Of additional concern is the global application of metric standard for temperature, weight and quantity – this can easily create confusion in the United States. The difference between 10 degrees Celsius and 10 degrees Fahrenheit can result in destroyed product!

And these variations are applicable in the food industry as well as shown in the following example:



**NOTE:** A shipment of cocoa beans arrived at the factory in a frozen state – versus the room temperature required. During the manufacturing process it was not possible to achieve the required viscosity without adding more fat – changing the recipe – and increasing the cost to manufacture the end product!

## Who's Writing the Rules? Who's Enforcing Them?

Although by its nature the Cold Chain is truly global, there are differences in levels of control in different parts of the world. However, all authorities share the common goal of ensuring the stability and quality of temperature controlled pharmaceuticals, vaccines and other healthcare products as they are moved through the chain of custody. These authorities are also concerned about the handling and distribution of food products, monitoring these with the same concern as life science commodities. As such, regulations and controls implemented for the food industry are also applicable to life sciences products.

### REGULATORY AGENCIES: THE GUARDIANS OF COLD CHAIN

An example of some of the regulatory agencies, together with their areas of focus and jurisdiction are outlined below:

- **US Pharmacopoeia (USA):** Makes recommendations for the manufacturing, packaging and distribution of pharmaceutical products. Once approved, these become enforceable by law and create a framework for the FDA validation.
- **Food and Drug Administration – FDA (USA):** Responsible for validating compliance and control across the Cold Chain.
- **Medical & Healthcare Products Regulatory Agency – MHRA (Europe):** Formerly Medicine Controls Agency. Responsible for monitoring and enforcing regulations in Europe.
- **The World Health Organization – WHO (Global):** Provides global leadership in terms of defining packaging, storage and handling requirements for Cold Chain products.

*WHO/UNICEF requires all vaccines purchased through their agencies to apply a HEATmarker™ VVM (Vaccine Vial Monitors) to every vial/tube/ampoule/flip-off cap/auto-disable syringe packaging of vaccine. To date, more than 750 million VVMs have been sold to vaccine suppliers such as GlaxoSmithKline, Aventis Pasteur, Chiron, P.T. Bio Farma, Panacea Biotec and GreenCrossVaccine Corp.*

(For more detail related to each of these authorities, refer to Appendix A)

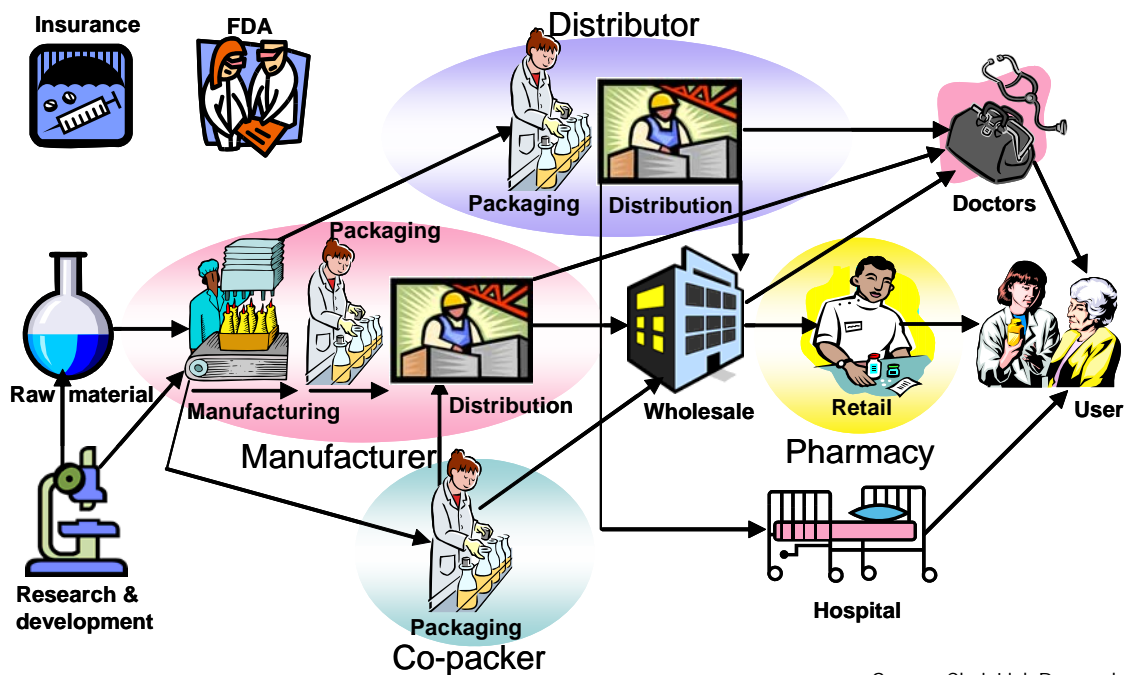
In addition, within the manufacturing entity, it is necessary to ensure that key personnel are aware of product characteristics and are kept up to date with changes to storage and handling requirements at the item level. This applies to outsource partners as well – particularly in the area of global distribution.



## Connecting the Dots: Who Does What?

### THE PLAYERS IN THE SUPPLY CHAIN

The global manufacturing, storage and distribution of Cold Chain products are a sub-set of the pharmaceutical supply chain. As such, the same processes, players and performance criteria apply – the primary difference is that the Cold Chain products have minimal tolerance for variation when it comes to the correct packaging, storage and transportation.



Source: ChainLink Research

Figure A: Holistic View of Pharmaceutical and Life Sciences Cold Chain

*The Pharmaceutical and Life Sciences Cold Chain includes many different potential configurations, with certain functions – for example, packaging and distribution being performed by outsource partners. In addition, product distribution has many variables, some product shipped from manufacturers to large Pharmacy Retailers, and other items distributed through a global network of wholesalers and distributors. As identified earlier, the 'state' of the product is critical – temperature variations resulting in loss of product, revenue, and potentially even penalties.*

## Charting the Course Ahead with '3Pe'

### CHAINLINK'S 3Pe MODEL

3Pe (which is the acronym for Performance, Policy, Process, and Enablers), is ChainLink's framework for enabling supply chain excellence. It is an effective and flexible model for analyzing a supply chain and developing a roadmap across many different industry or geographic environments. The following figure B illustrates how 3Pe accomplishes this:

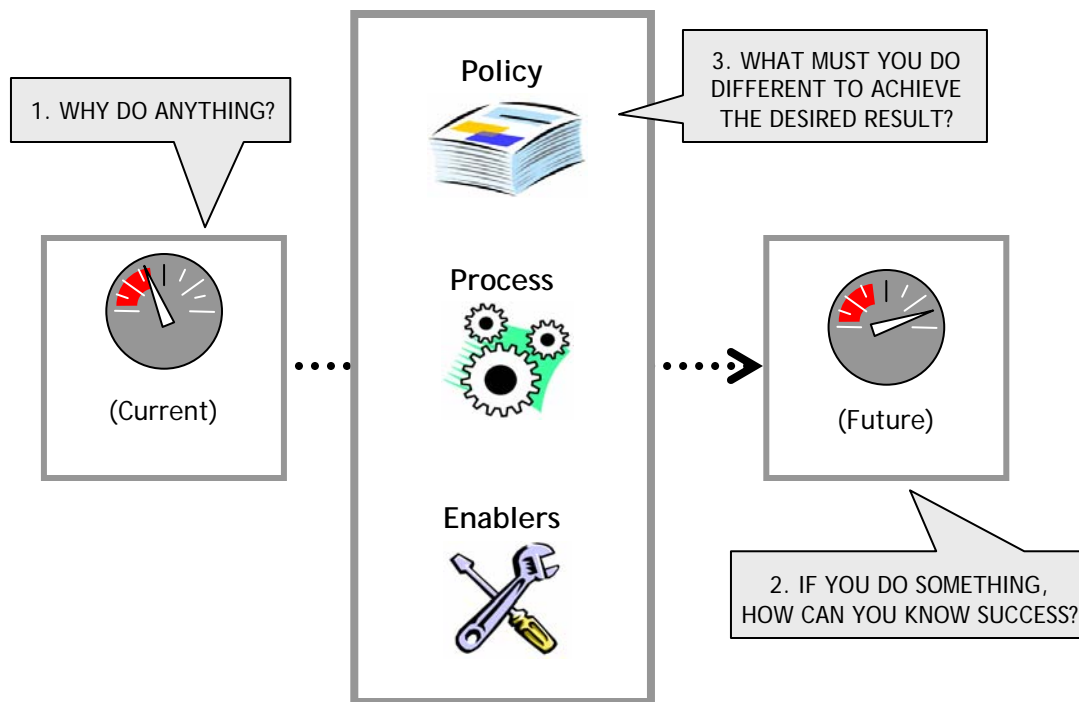


Figure B: How 3Pe Acts as a 'Compass' Towards Improved Supply Chain Performance

### UNDERSTANDING WHERE YOU ARE TODAY

Things change, new products are introduced, new markets are penetrated, and new trading partners become part of the enterprise landscape. As such it is important to take time to review the status quo. It requires understanding how the current supply chain components relate to each other – as well as areas of potential risk, ensuring that each of the players has a clear understanding of the expectation in terms of their performance. This includes service level agreements, defining roles, responsibility, remedy and metrics for the whole supply chain, that must be shared and agreed between all parties. This creates a baseline framework to understand the current structure of the Cold Chain network, as shown in the following Table.5.

<b>Key Players in the Global Cold Chain</b>		
Partner Profile	Responsibilities	Performance Measurement Criteria
Manufacturer	<ul style="list-style-type: none"> <li>• Research and Development</li> <li>• Define product characteristics, parameters, etc.</li> <li>• Document all quality control and handling requirements across the Cold Chain, from production all the way through to consumption</li> <li>• FDA compliance</li> </ul>	<ul style="list-style-type: none"> <li>• Consistent processes</li> <li>• Ensure Quality and control of product from design to consumption</li> <li>• Outsource partners measured and monitored</li> <li>• FDA compliance – (number of recalls per product/ year)</li> </ul>
Wholesaler/ Distributor	<ul style="list-style-type: none"> <li>• Market Development</li> <li>• Product Storage and distribution</li> <li>• Order fulfillment</li> <li>• Quality control</li> <li>• FDA compliance</li> </ul>	<ul style="list-style-type: none"> <li>• Expiration control</li> <li>• Product quality control (% of recalled and destroyed product)</li> <li>• Product Security/non-tampering</li> <li>• Selection of qualified and trained third party distribution partners</li> <li>• FDA compliance (violations per year)</li> </ul>
Hospital/ Doctor	Prescribing and administering Cold Chain pharmaceutical products	<ul style="list-style-type: none"> <li>• Product stored at correct temperature (noncompliance incidents per year reflected in product returns and identified damage)</li> <li>• Notification to patient of handling requirements</li> <li>• Cold Chain products monitored to eliminate expiration or damage (accurate records to enforce)</li> <li>• FIFO discipline in product usage</li> </ul>
Pharmacies	Dispensing Cold Chain products to end users	<ul style="list-style-type: none"> <li>• Patient notified of proper handling and storage requirements for Cold Chain products</li> <li>• Counseling and questioning included at time of dispensing to ensure patient understands criticality and understands the procedures</li> </ul>

**Table 5: Roles, Responsibilities and Performance Measurement - cont. next page**



<b>Key Players in the Global Cold Chain (continued)</b>		
Partner Profile	Responsibilities	Performance Measurement Criteria
3rd Party Logistics Providers	<ul style="list-style-type: none"> <li>• Outsourced Distribution Process</li> <li>• Storage</li> <li>• Pick, pack and ship</li> <li>• Transportation</li> <li>• Product quality</li> <li>• FDA compliance</li> </ul>	<ul style="list-style-type: none"> <li>• Product Delivered on time and in good order</li> <li>• Damage and returns identified and communicated throughout the Chain</li> <li>• Monitor product throughout process to ensure that there are no deviations from temperature control</li> </ul>
Regulatory and Control Agencies	<ul style="list-style-type: none"> <li>• Provide guidelines for the packaging, storage and handling</li> <li>• Monitor and Control</li> </ul>	<ul style="list-style-type: none"> <li>• Product Quality</li> <li>• Batch and lot control</li> <li>• Product recalls and destruction</li> </ul>
Insurance Providers	<ul style="list-style-type: none"> <li>• Compensation for loss or damage</li> <li>• Monitor to ensure responsible product handling environment</li> </ul>	<ul style="list-style-type: none"> <li>• Claims handling</li> <li>• Monitor and control</li> <li>• Loss avoidance</li> </ul>

Cont. Table 5: Roles, Responsibilities and Performance Measurement



### **WHERE DO YOU NEED TO GO?**

Once you have assessed the current situation in terms of your performance relative to your position in the Cold Chain, the next question is where do you need to be? Based on industry research, ChainLink develops a vision document which we call the 'Future Forward' model. And in keeping with the **3Pe** framework, the Future Forward model articulates an end-state in terms of target performance metrics and the underlying recommendations for Policy, Process, and technology Enabler changes to achieve this goal.

### **Adopting the Cold Chain Future Forward Model**

As companies become aware of the need to think and plan for Cold Chain products independently from mainstream items, it is possible to move from 'state of the industry' as reflected in current good practices to best practices as illustrated in the following Figure C.

(Detailed briefings on the Cold Chain Future Forward model are available for ChainLink clients. Please contact ChainLink to arrange a discussion. Throughout 2005, ChainLink will also be holding a series of web conferences to get into various sub-topics on Cold Chain.)

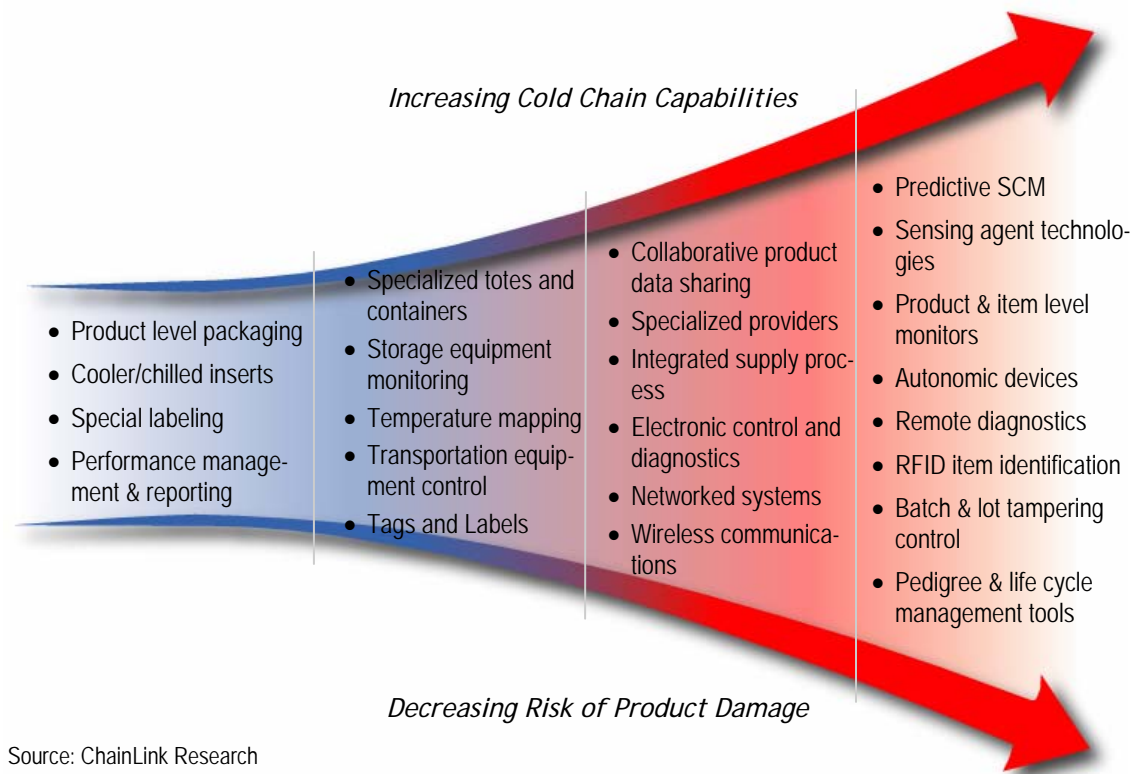


Figure C: Progression of Cold Chain Practices from Current to Best Practice (Future Forward)

### **BARRIERS TO OVERCOME: THE PRINCIPLES OF 3Pe**

After deciding upon a set of Future Forward objectives and performance targets, the next step is to understand the obstacles using the **3Pe** framework.

### **Policy: Ensuring Alignment Across the Cold Chain**

Working together, the key players have a critical role to play, adopting best practices in their functional areas as follows:

- *Manufacturers* – embrace a sustainable model that includes end-to-end accountability, shared product information and total lifecycle management. Ultimately the manufacturer, as the brand owner, must take responsibility for ensuring that all the other Cold Chain players, all the way to the point of consumption, understand what is needed and are doing their job.
- *Wholesalers* – protect the Cold Chain from manufacturer to storage at point of consumption – through temperature control and distribution monitoring.
- *Hospitals/Healthcare Providers* – understand the storage and handling requirements of each product, ensuring that this is communicated to all patients and care givers.

- *Pharmacies* – integrate Cold Chain requirements into dispensing process and procedures, with automated patient follow up for special products.
- *Insurance Providers* – create incentives and audits to ensure that true Cold Chain best practices are adopted across a global supply chain.

### **Processes – It’s all About Managing the Links!**

A clear understanding of the links and node level activities that take place through the Cold Chain process – from discovery to ultimate consumption – will enable all players to work collaboratively and ensure an optimal delivery model. However, as with all dynamic processes, constant vigilance is required to ensure that best practices at all levels are consistently applied. (These link processes are listed in Table 6 below.)

### **Enablers – Making the Business Case for Cold Chain Technologies**

There are many products that have been developed for the food industry Cold Chain that are applicable for use in the life sciences Cold Chain. A path forward includes evaluating storage, packaging and other items that are available, replacing outdated technologies with products that are tried and true in the food industry. The transition from better to best practices, adopted by all players in the Cold Chain, and adoption of state of the art technologies will ensure that Cold Chain products are distributed with the same level of care as the manufacturing processes that ensure quality and consistency.

The convergence of storage, packaging and sensor technologies with the growing world of mobile computing, will enable a level of monitoring and control only dreamed of as little as a year ago. Added to which, the more mainstream adoption of RFID has benefits for Cold Chain products as well. Many tags are now available (across a series of cost thresholds) that are able to capture data related to temperature and condition as product is moved across the Cold Chain. However, as with other technologies, the key is to ensure that data is available in ‘near real time’ and that actions required to remedy problems are well communicated across the supply chain community. This combination of improved Policy, Process, Performance and technology enablers will enable all players in this critical supply chain to achieve incremental improvement. \*\*\* (Refer to Appendix B for details of available suppliers and products).

### **Performance**

The ultimate goal is to move from current to best practice, ensuring that each of the Cold Chain components is operating at optimal performance. As such, it is important to define the desired outcomes and facilitating and monitoring this based on agreed metrics. There are many discussions related to the potential return on investment for RFID and other technology components – the following Table 6 highlights the immediate and measurable benefits of these technologies. This creates a compelling case for action that cannot be ignored!



Link Processes	Supply/Market	Collaborative Attributes	Active Metrics	Technology Enablers
<ul style="list-style-type: none"> <li>●Sales/Marketing relationship management</li> <li>●Terms and Conditions of Sale</li> <li>●Cold Chain risk assessment and distribution planning</li> </ul>	<ul style="list-style-type: none"> <li>●Roles &amp; Responsibilities</li> <li>●Product Item Master</li> <li>●Nature of the products – solids, semi-solids, liquids</li> <li>●Maximum and minimum temperatures that may be experienced by the product</li> <li>●Exposure to fluctuating temperatures</li> <li>●Number and nature of stages in the chain</li> <li>●Number of drop off points in the delivery chain</li> <li>●Written and agreed process and procedures</li> </ul>	<ul style="list-style-type: none"> <li>●Collaborative planning process</li> <li>●Compliance to standards for packaging, labeling and product handling</li> <li>●Plan for constraints such as shortages &amp; lateness/temperature issues and remedy</li> <li>●Understand product level requirements</li> </ul>	<ul style="list-style-type: none"> <li>●Risk against plan</li> <li>●SKU level damage</li> <li>●Returns and destruction</li> <li>●Product lifecycle management</li> </ul>	<ul style="list-style-type: none"> <li>●Collaborative planning systems</li> <li>●EDI or XML platforms</li> <li>●RFID as part of product</li> <li>●Pedigree control</li> <li>●Counterfeit protection</li> </ul>
<ul style="list-style-type: none"> <li>●Order Fulfillment</li> <li>●Inventory management, warehouse mgmt, distribution, pick/pack/ship</li> </ul>	<ul style="list-style-type: none"> <li>●Labeled storage requirements and associated warnings</li> <li>●Sensitivity of product to extremes of temperature</li> <li>●Likely period of exposure to temperatures outside the labeled storage requirements</li> <li>●Customize packaging</li> <li>●Special handling requirements</li> <li>●Special labeling</li> <li>●Special notification</li> <li>●Language to include all links in the chain</li> </ul>	<ul style="list-style-type: none"> <li>●Distributed order fulfillment</li> <li>●Plan shipment to ensure product protection and control</li> <li>●Inventory tracking</li> <li>●Cross docking</li> <li>●Drill through labeling</li> <li>●Unique packaging, labeling, etc.</li> <li>●Inbound/Outbound coordination w. 3<sup>rd</sup> parties, customers, etc.</li> <li>●Compliance/electronic transactions (ASNs)</li> </ul>	<ul style="list-style-type: none"> <li>●On-time</li> <li>●Cost</li> <li>●Correct temperature</li> <li>●Correct packaging</li> <li>●Correct documentation</li> <li>●Correct transportation mode defined on documentation and packaging</li> <li>●Correct labeling</li> </ul>	<ul style="list-style-type: none"> <li>●Online product level data sheets to include Cold Chain requirements</li> <li>●Temperature monitoring and tracking devices</li> <li>●RFID</li> <li>●WMS</li> <li>●Network optimizations</li> <li>●EDI or XML</li> <li>●Web-based integration to ordering systems</li> <li>●Integration to trade systems</li> <li>●Sensors and tracking devices</li> <li>●Temperature mapping in storage locations</li> </ul>

Table 6: Benefits of Applying the 3Pe Principles - cont, next page



Link Processes	Supply/Market	Collaborative Attributes	Active Metrics	Technology Enablers
<ul style="list-style-type: none"> <li>•Distribution Process/Logistics</li> <li>•Network infrastructure, trade mgmt, transportation mgmt, inbound and out-bound</li> <li>•Equipment control and monitoring</li> </ul>	<ul style="list-style-type: none"> <li>•Knowledge and experience of potential contract personnel who are responsible for receiving product at various stages in the chain</li> <li>•Monitoring devices and location</li> <li>•Temperature monitoring records</li> <li>•Controlled use of cooling elements</li> <li>•Uncertain audit trail</li> <li>•Temperature mapping (trailers)</li> <li>•Contract transport and audit</li> </ul>	<ul style="list-style-type: none"> <li>•In-transit merge</li> <li>•Cross-docking</li> <li>•Inter-model coordination</li> <li>•Rapid payments of freight settlement and reconciliation</li> </ul>	<ul style="list-style-type: none"> <li>•Current time metrics</li> <li>•ROA</li> <li>•Trace &amp; Track</li> <li>•Information cycle time</li> </ul>	<ul style="list-style-type: none"> <li>•TMS and manifesting tools</li> <li>•Track and trace event management</li> <li>•Sensors and tracking devices</li> <li>•Temperature mapping in transportation equipment locations</li> <li>•Web-based integration with shipper and customers</li> </ul>
<ul style="list-style-type: none"> <li>•Product Lifecycle Management</li> <li>•Returns, destruction</li> <li>•Batch and lot level tracking</li> <li>•Quality control</li> </ul>	<ul style="list-style-type: none"> <li>•Batch and lot control</li> <li>•Define correct temp control parameters</li> <li>•Training – warehouse personnel – drivers etc</li> <li>•Written procedures</li> <li>•Calibration of temperature monitoring devices</li> <li>•Returns of Cold Chain goods</li> </ul>	<ul style="list-style-type: none"> <li>•Optimized reverse logistics</li> <li>•Standardized returns, destruction process and procedures</li> <li>•Shared view of inventory levels with expiration and status of product</li> </ul>	<ul style="list-style-type: none"> <li>•Minimal product loss</li> <li>•No product diversions</li> <li>•Limited expiration</li> <li>•Inventory visibility</li> </ul>	<ul style="list-style-type: none"> <li>•RFID</li> <li>•Inventory control systems</li> <li>•Online product management tools</li> <li>•Shared data repository</li> </ul>

Cont. Table 6: Benefits of Applying the 3Pe Principles



## ROADMAP CONSIDERATIONS

A potential roadmap for this journey includes the evaluation and implementation of the following:

### Step 1 – Enhanced Process and Control

- Performance Monitoring and Reporting. Key process and procedures should be agreed upon in service level agreement that is carefully monitored to ensure compliance.
- Product Level Packaging/Cooler-Chiller Inserts. Ensure that the packaging components that include cooler and chiller inserts take into account product requirements, versus merely putting all Cold Chain product into 'Dry Ice'.
- Specialized Labeling. This includes the adoption of temperature sensitive labels, as well as color-coded labels to identify Cold Chain product.

### Step 2 – Material Handling and Monitoring Devices

- Evaluate and include the following in the Cold Chain for the storage and movement of product:
- Specialized totes and containers.
- Transportation equipment control/temperature mapping.
- Storage equipment monitoring and temperature mapping.

### Step 3 – Integrated and Collaborative Cold Chain

- Collaborative product data sharing.
- Appointment and training of specialized providers throughout the Cold Chain.
- Convergence of wired and wireless technologies/networks for real time data sharing.

### Step 4 – Autonomic Supply Chain Model

- Create autonomous environment where the combination of RFID tags, readers, sensors and other advanced technologies enable the tracking, tracing and monitoring of item level Cold Chain distribution throughout the product lifecycle, without human intervention.
- This should include the adoption of software and other technologies to create a product 'Pedigree'.
- An additional advantage of this approach is the potential reduction in product diversion and counterfeit.



## ENSURING COMPLIANCE

It is critical that all supply chain partners are aware of the expectation related to their role in ensuring compliance. This has requirements in:

### Documentation and Communication

Detailed shipment tracking data should be available to all parties, accessible through a shared medium. Documentation is critical to ensure that the correct packaging, storage and handling procedures are consistently applied. This should be compliant with manufacturing specifications, and all documentation that accompanies products should take into account the language of each of the parties that will be engaged in the movement of the product from source to consumption.

### Labeling



Processes and procedures should be defined to ensure that appropriate labels are used to define temperature, humidity, and other restrictions that apply. Color codes should also be used to identify the temperature sensitive items. Although product is usually labeled correctly, in many cases instructions are ignored or else the language is incorrect for the extended Cold Chain. For example, in the US there are many Spanish-speaking warehouse workers, but most products are labeled in English. Best practice includes utilization of RFID

sensors to monitor which items have Cold Chain requirements – eliminating the human error. However, to date this is not a common practice.

### Training and Auditing

As with most products that are now manufactured globally, these Cold Chain products are subject to both vertically integrated processes as well as outsourcing for certain elements. For example, in many cases vaccines and antibiotics are manufactured under license, based on costs and other drivers. These parties are subject to the same stringent controls as the Brand owner. Other areas that are frequently outsourced include packaging, sample distribution and control, and more traditional distribution. As with most pharmaceutical products, sales forces employed by the Brand owners perform a primarily educational role, visiting doctors, hospitals and health care providers to update them in terms of product prescription and control. This is one of the potential weak links in this Cold Chain – in some cases, the samples that are distributed by sales personnel could be compromised if they are not stored and transported correctly. In addition, although sales personnel are diligent in sharing information related to the prescribing and use of the drugs, there is a possible oversight with regard to educating healthcare givers in the correct storage and handling of sensitive products.

As wholesalers distribute many of these products, it is important to ensure that each of the links in the chain is well versed in the correct process and procedures. (An example is McKesson, who provide a wide range of healthcare products to pharmacies and hospitals.) Although stringent records are maintained for certain class of drugs, for example, in many cases the level of audit and control is not enforced for Cold Chain products. This weak link is a potential area of opportunity for wholesalers and providers.

### **Remedy and Reward**

It is all-important to ensure that members of the extended Cold Chain are well versed in terms of what to do if the product has been compromised and spoiled. For example, what indicators should be monitored and how should damaged product be handled? This should be clearly outlined in service level agreements between all players in this critical supply chain. The other side of this coin would be to incorporate incentive programs for service providers, ensuring that they are aware of the financial impact of poor housekeeping and material handling practices.





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## In Conclusion

Globalization and the explosive development of new manufacturing locales and third party partners has resulted in many phenomena – not the least of which is the exposure to previously unknown bio hazards. Water and food sources are in many cases suspect, and the challenges faced by the nomadic workforce now include potential health risks. These cannot be under rated, and in addition to geopolitical factors it is necessary to understand threats to our global population. Scares like the SARS epidemic highlight the need to take precautions, as well as to protect corporate brand and reputation from these inherent risks. The investment in improved process and technology will enable multiple benefits across the chain of custody – throughout the product lifecycle! The key is an understanding and sharing of the following:

- Policy – key issues and philosophies?
- Process – interaction of the links in the chain
- Performance – service level agreements – metrics and controls
- Enablers – RFID, Tags, sensors, networks, packaging and storage technologies

Ensuring that global economic growth is supported by enhanced quality of life – to include a better healthcare environment for the populations of the nations that are part of the global economic community is critical. From birth to death, pharmaceuticals and simple biologicals provide the lifeline that binds us together. Let us remember how fragile each of the links in this Cold Chain is, strengthening them through vigilance and the adoption of appropriate technology.

To the good of all humankind!



## Appendix A:

### GLOBAL REGULATORY AND CONTROL ENTITIES

The roles and jurisdiction of various industry level regulatory bodies varies – an example of which is highlighted below:

#### Medical and Healthcare Products Regulatory Agency – MHRA

This entity was formerly known as the Medicines Control Agency – its primary charter is to review and monitor the enforcement of regulations in Europe. Some areas of concern for MHRA, identified in inspections of Cold Chain related product distribution:

- 52 percent of all critical and major deficiencies recorded by MHRA GDP inspectors during 2002/2003 related to the monitoring of storage and transportation temperatures.
- 6 inspections resulted in consideration of adverse licensing action pending resolution of critical deficiencies. (See Tables 7 and 8 below.)

General Supply Chain Deficiencies		
Description	Number	%
General Storage—temperature control and monitoring	66	32.2
Lack of/or inadequate written procedures	45	21.4
Cold Storage—temperature control and monitoring	34	16.6
Premises, equipment and calibration	17	8.3
Housekeeping and pest control	8	3.9
Quality system and duties of responsible party	7	3.4
Cold Chain transportation	7	3.4
Self-inspection	6	2.9
Stock rotation and control	5	2.4
Record of transactions	2	1.0

Table 7: General Supply Chain Deficiencies



Serious GDP Deficiencies	
Description	Incidence
Temperature control & monitoring in general storage areas	25.1 %
During 'ambient' temperature transportation	7.1 %
Of Cold Stores	16.6%
During Cold Chain transportation	3.4%

Table 8: Serious GDP Deficiencies

### US Pharmacopoeia

Not for Profit private entity whose charter is to define correct storage, handling and shipment procedures for pharmaceutical products. Once approved, these become legally enforceable common standards for storage and shipment in the distribution system, such that the integrity of the item is maintained until received by the patient. Provides definitions relative to:

- Preservation
- Storage
- Packaging
- Labeling

More recently has focused on Cold Chain distribution and has provided recommendations for this area as well.

### Food and Drug Administration

US Government Agency responsible for validating compliance and control across the Cold Chain:

- Main area of focus is on the biologic products – this includes protein and polypeptide products that are produced from cell culture systems.
- Issues related to therapeutic proteins – sensitivity to temperature, humidity, oxidation, light ionic content and shear.
- Stability is an issue – the need to ensure consistency in storage conditions throughout the Cold Chain. This includes the many stages in the product lifecycle. Variability needs to be managed – at rest and in transit. Changes can affect the potency, the quality and efficacy of the product.



### World Health Organization - WHO

The World Health Organization (WHO) is the leader in terms of defining packaging, storage and handling requirements. Multiple publications have been distributed to the appropriate entities. However, in many cases the main issue relates to that complex segment of the logistics supply chain – the last mile – or final segment of the chain before patient administration. Countries most in need of life saving vaccines and biologics are in many cases the least prepared to safeguard these commodities. Refrigeration, specifically in warm countries in Africa, Asia and the Middle East, is not always available. As such, it is important to consider temperature controlled packaging and transportation totes, with associated monitoring and control devices.



## Appendix B: Storage, Handling and Labeling/ Packaging Requirements

An overview of the guidelines developed by WHO and endorsed by UNICEF is summarized below. (Detailed documentation is available directly from WHO – vaccines@who.int)

### PACKAGING FOR VACCINES

Table 9 – Classification of packaging required for currently used vaccines

Packaging Class	Type of Vaccine
A	Oral poliomyelitis
B	BCG DTP DTP-HepB DTP-HepB+Hib freeze-dried Hib Liquid Hib freeze-dried Measles freeze-dried Measles rubella combined freeze-dried Measles mumps rubella combined freeze-dried
C	DT Hepatitis B Td TT

### INSULATED PACKAGING STANDARDS

#### Class A Packaging

- Prior to and at time of packing must be kept at storage temperature recommended by manufacturer.
- Must be packed to ensure that warmest storage temperature of vaccine does not rise above +8 degrees centigrade while in continuous outside ambient temperatures of +43% for a period of at least 48 hours.

- One WHO validated Cold Chain monitor or manufacturer validated temperature monitoring device must be packed in each shipping carton of vaccine.

### **Class B Packaging**

- Prior to and at time of packing must be kept at storage temperature recommended by manufacturer.
- Must be packed to ensure warmest storage temperature of vaccine does not rise above +30 degrees centigrade in continuous outside ambient temperatures of +43% for a period of at least 48 hours.
- For vaccines sensitive to freezing only (DTP, DTP-HepB, HepB, Hib liquid, DT, Td, TT), the coolest storage temperature of the vaccine must not fall below -2 degrees centigrade in continuous external temperatures of -5 degrees centigrade for a period of at least 48 hours.
- Dilutants for freeze-dried vaccines must be included with the vaccine shipment in matching quantities to vaccines, but do not require temperature controlled packing.
- One WHO validated Cold Chain monitor or manufacturer validated temperature monitoring device must be packed in each shipping carton of vaccine. For the freeze-sensitive vaccines, a 'freeze watch' indicator must be packed in each shipping carton of vaccine.

### **Class C Packaging**

- The vaccine must be packed according to the manufacturer's instructions. At the discretion of the manufacturer, vaccines requiring this category of packaging do not need to be packed in insulated cartons with an active cooling medium for international air transportation.
- The coolest temperature of the vaccine must not fall below +2 degrees centigrade in continuous external temperatures of -5 degrees centigrade for a period of at least 48 hours.
- One WHO validated irreversible temperature threshold indicator or a manufacturer validated temperature monitoring device and a 'freeze watch' indicator must be packed in each shipping carton of vaccine.

### **STORAGE VOLUME STANDARDS**

Manufacturers must state storage volumes occupied per infant/patient dose of vaccine. This information must also be included in tender documents and trade literature.

### **LABELING AND PACKAGING**

- The external surface of vaccine packaging must be white.



- A label must be affixed to each outside face of every vaccine package in a language appropriate for the country of destination – for example,
  - French – Vaccin Urgent
  - Spanish – Vacuna Urgente
  - German – Impstoff Eilt
- Shipments of DTP/DT/Td/TT, liquid Hib and hepatitis B vaccines, or combinations thereof, require a 'do not freeze' sticker on each vaccine package.
- Labels must be attached with water-resistant adhesive; the expiry date must be printed in indelible ink on the vial or label. Note: format used for indicating expiry date should be DD/month/YY. Roman style numbering and abbreviations are not acceptable.
- All vials and ampoules must have an appropriate vaccine vial monitor (VVM) attached.



### STANDARD SHIPPING PROCEDURES

Vaccines must always travel on the most direct route. In the case where this is not possible, the journey should be planned for trans-shipment in countries with temperate climates and through airports that have cold storage facilities. Shipments must be scheduled to arrive on a business day in the destination country.

- Advance notification
  - Vaccine consignments must be booked well in advance of date of departure.
  - At least 7 days before the date of dispatch, a fax or e-mail must be sent to the consignee and to the local WHO or UNICEF office with the following information:
    - Type of vaccine
    - Total number of vials and number of doses per vial in the shipment
    - Number of cartons
    - Gross weight (in kgs.)
    - Value of the shipment (in US\$)
    - Flight number, dated and ETA at final destination
    - Airwaybill (AWB) number
    - Instructions for collection and handling



- Documents to accompany the shipment (actual document)
  - The original airwaybill (detailed information required)
  - A copy of the invoice, with detailed packing list
  - The release certificate(s) from the national regulatory authority of the country of manufacture
  - A copy of the vaccine arrival report (VAR)



These documents are usually sent inside the vaccine shipment, in the box labeled number 1. This box should be clearly labeled 'containing vaccine shipping documents'.



## Appendix C: Monitoring and Control Technology

An example of the diversity and scope of some of the products available is highlighted below:

Cold Chain Technologies ([www.coldchaintechnologies.com](http://www.coldchaintechnologies.com))

- Hobo Series - Temperature loggers.
- Monitor In-Transit Temperature Recorder - Temperature strip chart recorder.

DeltaTRAK ([www.deltatrak.com](http://www.deltatrak.com))

- FlashLink Series - Range of reusable data loggers for retail and transit application.
- FlashCheck Digital Pocket Check Thermometers - Core temperature probes.
- ThermoTrace Non-contact Infrared thermometers - Check temperature with an infrared beam.

Escort Data Logging Systems ([www.escortdls.com](http://www.escortdls.com))

- Intelligent logger family - Cool down logger.
- Transport and storage monitoring of temperature/humidity.

Fourier Systems ([www.fouriersystems.com](http://www.fouriersystems.com))

- MicroLog - Temperature and external sensor and data logger. Relative humidity option available.

FreshLoc Technologies ([www.freshloc.com](http://www.freshloc.com))

- FreshLoc - Continuous automatic monitoring through wireless sensor array. Internet-based monitoring and support.
- FreshSync - Automatic wireless logger for transport. Internet-based monitoring and support.

Gemini ([www.geminidataloggers.com](http://www.geminidataloggers.com))

- TinyTag eXtra Data Logger - Data logger with download option.

Intermec Technologies ([www.intermec.com](http://www.intermec.com))

- Handheld scanners - Barcode, omni-directional and/or 2D imaging, CCD or laser versions.
- Handheld computers - Keypad or notepad.



Marathon Products Inc. ([www.marathonproducts.com](http://www.marathonproducts.com))

- Temperature Data Loggers - Series of electronic data loggers.
- TempCheck - Strip chart temperature recorder.

Sensitech ([www.sensitech.com](http://www.sensitech.com))

- Ryan HAT - Humidity and temperature monitor.
- Ryan RL100 - Waterproof temperature monitor.
- Ryan UTI, EZT and Universal K Analog Recorders - Strip chart recorders.
- TempTale Series - Logs humidity and ambient temperature. Probe attachment available for core temperature measurements.
- TagAlert - Disposable electronic temperature monitor with digital display.

Stream Peak International, PTE. LTD. ([www.streampeak.com.sg](http://www.streampeak.com.sg))

- Shock and tilt indicators/detectors.
- Temperature, humidity, pressure and vibration indicators/recorders.

Symbol Technologies ([www.symbol.com](http://www.symbol.com))

- Handheld, hands free, and wearable scanners and computer systems.

Veriteq ([www.veriteq.com](http://www.veriteq.com))

- VL-series precision humidity and temperature mapping system.
- Networked data logger system.

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