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Activity, ICT, and Material Infrastructure in Complex Multi-Organisational Settings: An assessment of innovation potential for pharmaceutical cold chain transport and handling

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Abstract

What are the infrastructural possibilities for introducing novel ICT based services in the international multi-modal logistics environment? The specific case of nascent real-time reporting potentials for cold chain transport and handling in a hybrid data carrier environment is explored and an infrastructural analysis indicates the technical suitability of a GSM telemetry. Activities and technology-in-use were also observed and our analysis suggests that a socio-organisational infrastructure of uniform or standard practices, policies, procedures and software is infeasible and may in fact be undesirable in complex, international, multi-organisational settings.

Keywords: cold-chain, inter-organisational system, network innovation, real-time

1 Introduction

How might members of organisations attempt to introduce innovative technologies in complex, international, multi-organisational, multi-modal and multi-systems environments? More generally, how can organisational actors experiment, develop and

learn to use open-ended, multi-faceted and interdependent innovations such as package and container security, tracking devices, electronic invoices or data pools in real world settings? This case study attempts to illuminate the potentials and problems of such inter-organisational innovation in the pharmaceutical industry. Specifically, the goal was to assess the feasibility of better securing the distribution channel by enhancing electronic documentation through cold chain telemetry.

Biologics[1] and vaccines (a rapidly expanding area in life sciences innovation) pose greater challenges (typically) for handling than traditional pharmaceuticals due to the greater fragility and sensitivity of biologic molecules. These compounds place new and stringent demands on supply chains; demands which impact product handling, storage, packaging, and transport. Product life and viability may be impacted by exposure to environmental extremes, time spent in certain temperature ranges, humidity, agitation, light exposure, etc. (Isom, 2006).

Manufacturers have an obligation to control medicines and their ingredients in transit; this implies an overlap between good distribution practice and good manufacturing practice. One consequence is that product pedigree regulations may expand the remit of pharmaceutical inspection to include the logistics and supply chain within the scope of product audits (Brady and Wright, 2007). The effective management of temperature controlled logistics – the cold chain – is one important competence for a safer life sciences supply chain and an important area for research and innovation. However workplace competencies and technical infrastructures may be underdeveloped, incomplete, or have not achieved levels of reliability expected for realistic cold chain scenarios (Estrada-Flores, 2008).

Addressing this area is complex as it involves technical (lack of standards, challenges of physical environment) and legal issues (absent, compatible and/or inconsistent regulatory environment), resource limitations (cost of roll-out, capabilities at distance), social/organisational concerns (ROI and uncertain business cases, new skills, specialist knowledge), and work practices. That the problems remain largely unresolved may be viewed as a kind of market failure, perhaps due to coordination costs, incentive misalignments, cost/benefit challenges, international regulatory incompatibilities, or other mechanisms.

1.1 Cold chain challenges

A cold chain may be chilled (>+1°C), frozen (-20 to -40°C e.g. frozen carbon dioxide refrigerant), or cryogenic (<-160°C e.g. liquid nitrogen refrigerant). A cold chain is defined, for the purpose of this paper, as a logistics environment (covering storage, handling, and transport) maintained within specified temperature ranges, for example between +2 to +8°C.

We know that pharmaceutical and life-sciences products are sensitive to handling, shipping and storage conditions. Vaccine viability for example may be affected during

[1] Biologics are (typically) large, complex, molecular structures manufactured for medicinal and therapeutic use. In this paper we use the term 'biopharma products' to refer to temperature sensitive biologics, vaccines and pharmaceuticals.

transport and storage if exposed to extremes in temperature. While conditions at the end of the supply chain, in clinics, is the factor most frequently cited affecting vaccine viability, upstream control of bulk vaccine shipment prior to packaging or post processing is ultimately more significant due to its impact on whole product batches. Exposure to environmental extremes isn't just a problem for clinical delivery; it can also affect APIs[2], intermediate product and bulk product shipment between sites. Something as mundane as a delayed flight or a truck breakdown, adding a 24 hour delay to a cold-chain shipment, may reduce a products shelf life, or worse, spoil an entire batch, if measures aren't taken to manage a situation. In situations like these there is usually a 'plan B' but timing is critical and timely information enables the most effective response.

Empirical evidence of cold-chain performance for transport of perishable goods and pharmaceuticals (Brady and Wright, 2007) indicates that temperature control in shipping or transport may be inconsistent. One study reports, that in the case of vaccine cold chain control, 90% of incidents occur at medical service provider sites, 9% during transport to surgery or clinic, and 1% during transport between upstream service providers (Nayda, 2002)[3]. These figures echo the findings of an extensive body of research into the problem of vaccine cold chain control, concluding that refrigeration at the clinic setting is the most prevalent problem area (Lugosi and Battersby, 1990). Clinical cold chain management is now addressed through standard cold chain instructions and training at primary care settings (e.g. Chapman and Butt, 2006). However, while cold chain events (CCEs) during transport are a relatively small source of vaccine cold chain breakdowns, upstream transport and storage remains a concern and one which is amplified by virtue of the greater loss or risk potentials of bulk product movements.

Cold chain systems rely heavily on protective insulated containers for the shipment of temperature sensitive supplies and products. Hence protective package design[4] and control is a significant determinant of cold chain performance, but what happens when supporting systems breakdown or the unexpected comes into play? For example, weather extremes, accidents, hold-ups, or delays. Package level temperature control defines the time window for transport but it cannot adapt to changing conditions. It has been argued that industry is over-reliant on protective containers for temperature protection, and in turn that a reliance on protective containers results in reduced operator training and support, in fewer or less informative instructions on containers detailing handling or remedial actions (Lovell, 2004). Even if standard operating procedures are set out under service level agreements, which type of contingencies should be planned for and addressed? For example, should standing reserves of dry ice

[2] API: Active Pharmaceutical Ingredient, precursors or ingredients for end products.

[3] This report summarizes vaccine cold chain events (CCE) in the state of South Australia which were notified to the regulatory agency. Over the study period 159 CCEs occurred at clinical sites of which 21 CCEs occurred during transport.

[4] Packaging design and validation is addressed by ISTA (International Safe Transit Association) packaging guidelines (ISTA, 2007).

be made available, is refrigerated warehousing accessible from the breakdown or hold-up location, are local operators able to access the inside of a package, to restock perhaps with dry ice? Emerging situations are often unique and singularly situated at a certain location in time and place. Having timely or near real-time information is the key to managing these emerging situations in a measured and responsible manner.

2 Research Case Study

This case study was established to assess the feasibility of employing off the shelf technological components in novel configurations to address the cold chain requirements of an actual biopharma products supply chain. Case studies are indicated when studying complex ill defined situations which in turn require multiple analytical lenses and methodological approaches (Yin, 2003). We employed a case study research design to facilitate the development of theory grounded in actual field data (Eisenhardt, 1989). The case study was designed to explore a paradigmatic situation (Flyvbjerg, 2001); i.e. to construct an understanding of the practical reality of servicing the cold chain shipping process. Selection and refinement of the locus of research follows the idea of 'theoretical sampling,' where research narrows onto concepts which emerge from the data, after the procedures of grounded theory (Strauss and Corbin, 1998). Interpretive data gathering was employed consisting of observation, interview, and document analysis; the lines of enquiry were delineated as follows:

- Identify involved actors
- Record and assess the practical operation of SOPs (Standard Operating Procedures)
- Ask actors to explain their understanding of SOPs and other processes
- Identify the technologies and tools used (e.g. forms, screens, sensors etc)
- Observe technologies and tools in use, query actor sense-making of technology
- Note control and exchange points between organisations
- Assess the physical or operational environments encountered

The case study considered multiple stakeholders: a multinational biopharma manufacturer, secondary processing facilities, storage & distribution operators, and carriers. A particular concern was to access temperature data and to identify opportunities to correlate cold chain information with existing documentation, both electronic and paper based. We were interested in how documents and messages were generated, their target audiences and interfaces between organisations including regulatory agencies.

Researchers undertook a 'follow the actors' strategy (Law, 1991) for the 'as-is' study. Three field methods were employed to gather this data: direct observation, document analysis and interview. The activities and events surrounding and constituting a shipment along its supply chain were observed (e.g. pick and pack; retrieval from cold storage, package assembly, loading, transport, receiving, repacking, ground handling, receipt etc.). Interviews and informal conversations with involved actors were carried out in parallel with observational studies. Researcher's checked their interpretation of

events against actor's understandings and gradually built up a rich description of the background, history and day to day operation of cold chain shipments.

The following description of the case site reuses a constellation of institutional actors described in an earlier study not directly related to the current case (Kavanagh and Kelly, 2002)[5]. The logic behind this device is threefold; the cases bear a strong similarity, the research design and theoretical grounding of both cases is sympathetic and closely aligned, and the approach reinforces the anonymity of the corporations and individuals involved.

3 GTA Garrydaniel Factory 1 and Fortunestown Factory 2

> *"GTA is the production arm and a wholly owned subsidiary of the pharmaceutical giant Groight and Co. In 1973 GTA build a pharmaceutical plant in Garrydaniel, a townland in Kilkenny, Ireland…" (Kavanagh and Kelly, 2002)*

The Garrydaniel Factory 1[6] plant manufactures of a number of specialised biopharma products including Anvoir, a flu vaccine. Anvoir in liquid form must be stored at 5±2°C. If Anvoir freezes it precipitates and looses potency. Higher temperatures have less impact on potency but will significantly shorten the product shelf life.

GTA Garrydaniel Factory 1 ships Anvoir in bulk to its sister plant in Denver, CO for filling and packing to market. The Denver plant, known as Fortunestown Factory 2, receives up to two shipments a week from Garrydaniel Factory 1 to supply Anvoir for the Americas market. The production/shipping schedule is planned months in advance with up to 300 litres of Anvoir a week being supplied. The product from Garrydaniel Factory 1 is shipped by refrigerated trailer to Dublin airport where it joins a PAE (Penguin Air Express) cargo flight to London Stansted. From Stansted the container is transferred to PAE's heavy freight partner, KHA (Kanga Heavy AirCargo), on one of its bi-weekly flights from London to Atlanta, GA. The shipment then joins a connecting flight to Dallas, TX whereupon it is driven (under Customs bond) by refrigerated trailer to Denver, CO. The shipment is then Customs cleared in Denver and driven to GTA Fortunestown Factory 2 when it is 'received' back into GTA's systems and physical possession.

3.1 Cold Chain Possibilities

Our research team had been interacting with the Garrydaniel shipping group on a related study when an opportunity to research the process for intra-firm cold-chain shipments presented itself. Cold chain and chain of custody had become an area of growing concern for the life sciences sector generally and GTA in particular as they participated on a standards review committee for chain of custody exchange. The Garrydaniel

[5] The authors of the original GTA case were not involved in this cold chain case study, however they were contacted and their permission obtained to reuse the setting, scene and cast from Kavanagh and Kelly (2002).

[6] Pseudonyms have been used throughout to preserve the anonymity of individuals, organisations and corporations involved in this study.

shipping group wanted to follow their shipments much more closely than was currently possible. Their expectations and questions focus on information needs across the areas of temperature data, shipment disposition, package integrity, and documentation.

1. Temperature – was the product outside the approved and agreed ambient, transit temperature range?
2. Duration – did the product arrive at its final destination within the approved time schedule?
3. Physical integrity – has the product and packing been dropped, or tampered with, where is it stored, in what environment (e.g. outside, inside, in direct sunlight, ambient temp, etc), who has access to the product or container?
4. Documentation – are the accompanying documents and labels complete, accurate and up to date, can they be improved or reduced?

Many of these questions are answered only after a shipment is completed, but some things are better to know when they happen, to take corrective action and minimise risk or avoid loss.

Observations of actual end-to-end shipments were undertaken in an 'as-is' study to highlight the key events in the physical movement and data flows of a cold chain biopharma shipment. Key actors included: warehouse personnel, truck drivers, express/freight forwarder executives, division heads for carriers, air cargo load managers, ground personnel, and customs clearance operators. Researchers accompanied the product container on road movements by refrigerated trailer from Garrydaniel to Dublin Airport. They observed and recorded procedures for readying the container for air handling (ULD/air pallet) and observed boarding procedures. Arrival, warehouse, and transfer handing processes airside at Stansted Airport were observed for two shipments. The container was also met during the final road transport leg from Dallas to Denver. Customs and agency clearing was observed followed by end receipt at Fortunestown Factory 2. Road-air movement of bulk product appears, superficially at least, to be a relatively straight forward process. SOPs require that carriers follow agreed instructions, i.e. drive specified routes, target departure and arrival times, and co-shipment restrictions. SOP service levels are also designed to allow the flexibility to accommodate some unforeseen circumstances or events such as detours, port closure or flight cancellation.

The following sections present summary findings from the 'as-is' field study in four sections; Temperature Trails, Shipping Activities, ICT Infrastructure, and Additional Documentation.

Temperature Trails

Temperature data is recorded for all cold chain shipments. Passive temperature logging devices store sensor readings at preset intervals throughout the life of a shipment. Temperature loggers and their sensors are placed inside the actual package so that conditions in, on and surrounding the product can be measured and assessed afterwards. The data gathered is useful for a number of purposes:

1. Validating viability and shelf-life of biopharma product.

2. Complying with product pedigree or provenance requirements, particularly necessary in the case of product recalls.
3. Validating the performance of insulated temperature managed packaging.
4. Assessing cold chain risks from ambient (surrounding) conditions, usually seasonal, but also due to contingent events.

Temperature data loggers store readings in solid state memory. Loggers may be reset and recharged to be recycled for use in subsequent shipments once temperature data stored in them is uploaded.

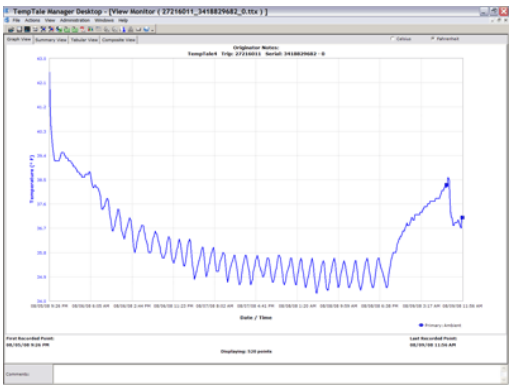

Figure 1 Graph of a package temperature sensor trip log

Temperature readings are uploaded to a computer when the shipment is received at Factory 2. These 'trip' logs are shared electronically with Factory 1 where temperature data is graphed and assessed for the occurrence of cold chain events, and then archived.

Shipping Activities

Each shipment undergoes a controlled packaging sequence in the factory to ensure the product's physical state is maintained within set parameters (temperature, orientation, durability) over the whole duration of its movement between the manufacturing plants. In this case, product prepared at one factory is shipped to another to undergo value added processing. The Anvoir bulk shipment is post processed at Fortunestown Factory 2 for filling, and final packaging. The generic shipping activity sequence is represented in Figure 2.

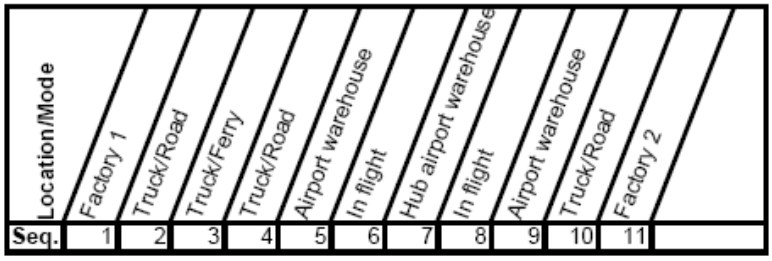

Figure 2 Generic shipping sequence

Shipments are prepared as follows:

a) Bulk factory vessel: For example stainless steel tanks, plastic drums or bags for handling/holding within refrigerated environments in a manufacturing plant.

b) Package assembly: Packing of bulk factory vessels in box, foam, wrap, refrigerant (e.g. dry ice) to create a temperature controlled environment for the vessel.

Thermal control of the packed materials is established when the package is 'capped.' Complete package assembly from refrigerated storage to 'ship ready' may take up to 45 minutes depending on the size and number of packs and containers used. Secondary covering (usually plastic shrink wrap) may be applied later at airside receiving to prepare the container for air cargo conditions.

c) Truck pallet: Package assembly is strapped and secured with tamper proof seals to a pallet. This enables ease of handling by forklift in shipping bays, trucks and containers.

d) Air pallet assembly: Using either ULDs[7] or flat air pallets for irregular cargos. This involves plastic wrapping, heavy load straps and air webbing to secure. Container movement in the air side container environment is managed wholly on roller bed handling equipment, from aircraft hold to dolly trailer to air side warehouse storage.

ICT Infrastructure

In this case we assessed data network infrastructures that were already present in the shipping environment. An operational environment for multi-modal internal shipments is enabled for data by the provision of various data networks. The question asked here is "what ICT or data networks are available as the package moves through the multi-modal environment?" A distinction is drawn between wireless data networks, and wired networks depending on whether a data source (e.g. temperature sensor) connects continuously or at discrete events like 'being scanned'.

Active RF[8] devices transmit and communicate independently via RF data networks whereas a wired network is activated when a data token (e.g. RFID, 2D matrix barcode) comes into proximity to a reader device. The reader node may then itself be connected to an ICT network (either wired or wireless).

Available data networks in the shipping environment were observed, for example in Factory 1 no GPS[9] signal was available within factory buildings; however GSM[10] and secure wireless local area networks were detected.

[7] ULD: Universal Load Device. Light weight air containers and pallets designed for handling shipments and packages in the air cargo environment.

[8] RF: Radio frequency.

[9] GPS: Global Positioning System. A system enabling global navigation through position determination of receivers by time/delay calculation from satellite radio signals.

Table A: Available data networks

	Wireless Networks			Wired Networks	
Environment	**LAN**	**GSM**	**GPS** *3.	**RFID**	**Barcode**
Factory 1	X	X	-	X	X
Truck/Road	-	X	*1.	-	X
Truck/Ferry	-	-	*1.	-	X
Truck/Road	-	X	*1.	-	X
Airport warehouse	X	X	-	X	X
In flight	-	-	*2.	-	-
Hub airport warehouse	X	X	-	X	X
In flight	-	-	*2.	-	-
Airport warehouse	X	X	-	X	X
Truck/Road	-	X	*1.	-	X
Factory 2	X	X	-	X	X

*1. = vehicle fitted GPS X = network available

*2. = aircraft fitted GPS - = network absent

*3. No GPS inside buildings

Factory 1 also had barcode printers and reader units available throughout the factory environment. RFID gate/reader systems were also present. The results are summarised in Table A.A process of elimination reveals that GSM networks and barcode networks are available and accessible at nearly all points along the cold chain except for conditions where meaningful intervention is impossible or improbable (i.e. in flight). GSM networks offer the possibility of being able to transmit data generated on-the-fly by devices like package temperature sensors. Static data packages such as RFID and Barcode encode fixed details or static references to external information systems. Static data packages are useful for linking with external referential information rather than for generating dynamic local information.

As we noted the presence and operation of different data networks we also observed their operation. Network use required skilled, knowledgeable operation by professions or specialisations among the key actors encountered. The data networks and more particularly, software systems running on data networks coexisted and sometimes overlapped with other services and documentation systems. None of the technological systems were autonomous; indeed all of them required active management from their own local constellations of actors; they were in a sense hybrid ‘managed infrastructure’. It was evident moreover that the entire assembly of ICT, services, work practice and knowledge was successful because it was resilient. This resilience was observed at various junctures when for example, a software service on the critical path went off-line, or a data device broke, or the network itself was unavailable, or when someone mislaid a needed document pouch. At these points, secondary duplicate systems, often paper based came into play. Knowledgeable actors (experts), who knew how to improvise in an infrastructure provided for some redundancy thereby overcoming the frailties of both human and ICT agency.

[10] GSM: Global System for Mobile communications. A communications standard for mobile telephony.

Additional Documentation

Shipping documentation is a key input for international logistics but while documentation is an enabler for trade it also adds costs, effort and complexity to the shipping process itself. The burden of documentation (often referred to as 'red tape') differs depending on whether you are importing or exporting, and whether the other party is inside or outside a common market. Accompanying documentation is physically attached to (or placed within) the shipment and documents are also handed to the lorry driver before the shipment leaves the building. Much of the documentation is generated directly from GTA's internal MRP/ERP[11] systems. Inter-organisational messages are exchanged electronically through inter-organisational system interfaces between the manufacturer, logistics partners, and other agencies in parallel with printed accompanying documentation. These organisations store messages and may use the data later to generate other messages which may in turn be used to generate documentation for the shipment or to send messages to others involved in a shipment (e.g. Customs, port authorities, forwarder, agent etc).

Table B: Manufacturer view of documentation requirements on import/export movements

	Non-EU (US)	EU
Export	16 typical, of which 9 are regulatory requirements	7 typical, of which 2 are regulatory requirements
Import	9 typical, of which 5 are regulatory requirements.	5 typical, of which 2 are regulatory requirements.

Table B summarises a general assessment of documentation requirements (Table D, Table E,

[11] MRP/ERP: Manufacturing Enterprise Resource Planning /Enterprise Resource Planning systems

Table F, Table G) presented in Appendix I. Typical figures are variable, depending on the type of shipment e.g. a biologic precursor containing animal serum, or bulk finished product etc. These tabulations are based on a comparison between GTA's view of shipping documentation and the relevant national consultation document (Forfás, 2008). Note that this analysis simply seeks to capture the manufacturer's view of the documentation requirements for each type of movement.

From an EU based manufacturer's perspective, you can export either to another EU member state or internationally, in this case the US. Likewise you can import supplies from within the EU or internationally. The case considered in this paper is for Export from an EU entity (Garrydaniel Factory 1) to a Non-EU (US) entity (Fortunestown Factory 2). In this case Garrydaniel typically produces 16 documents of which 9 are required by regulatory and government agencies. We can conclude that international exports require a considerable amount of documentation, much of it required by the country of destination. Naturally, movements to or from EU member states carry a relatively smaller documentation burden, only two documents are needed to satisfy regulatory requirements and the remainder relate to *commercial* inter-organisational or domain specific controls (e.g. accounting, quality assurance). It is noteworthy that the commercial documentation may be considered more pertinent, informative and relevant for independent regulatory reviews and audit of biopharma production and its commercial activities. We note that the document trail above indicates just the manufacturer's perspective of the paperwork; *it does not* include documentation generated by partner organisations along the supply chain servicing diverse aspects of each shipment (e.g. purchase orders, air waybills, various insurance premiums, shipping manifests, advance notices, letters of introduction, driver credentials etc). As noted during our observation of data networks and ICT infrastructure, the additional documentation serves as a kind of backup, a system of sometimes manual processes and direct interaction between the various actors which can be drawn on when something goes wrong. These secondary layers of information are available to actors to exchange, compare, to make sense of a situation, and to reconstruct or *make* the shipment *right* again.

4 Discussion

It seems inevitable that pharmaceutical pedigree regulation will expand the remit of pharmaceutical inspection to include logistics and supply chain audit. Therefore, effective management of temperature controlled logistics, the cold chain – is an important competence for a safer life sciences supply chain and an important area for research and innovation (Bishara, 2006, Brady and Wright, 2007).

Biopharma products typically have three important characteristics in extremis which impact their shipping and handling; they are compact (concentrated form), physically sensitive (e.g. limited shelf life, susceptible to temperature, humidity, light) and valuable (e.g. ethical use, high economic value). The management and execution of bulk biopharma product shipments is therefore of interest at several levels as it involves or implies; temperature sensitivity, potential for digital integration, international multi-modal logistics, open ICT standards, and flexible services (Table C).

Each challenge poses one or more requirements, each of which may be addressed as indicated.

The requirement for remote temperature monitoring suggests the desirability of real-time and/or periodic live updates of event records to ascertain product viability (e.g. core and ambient temperature, location, tamper, custody). Cold chain event messages broadcast by RF telemetry devices would be an innovative solution to this requirement.

The potential for digital integration is desirable for any innovation in inter-modal logistics, particular for international movements. While Auto-ID technologies may be claimed as technical innovations, significant benefits arise more through how they are used than in their simple technical function. Therefore reporting and analytics tools should be intuitive and accessible for operators and customers; they can also provide web service integration with EPCIS[12] and product historian data. Web services should be interoperable as required with other web services such as Customs messaging or other regulatory systems (e.g. Single Windows or Single Electronic Access point).

Table C Biopharma cold chain challenges

Cold chain challenge	Case site requirement	Recommendation
Temperature sensitivity	Real-time or near-real-time communication and local data storage.	Cold chain event messages broadcast by RF telemetry devices indicated
Potential for digital integration	Interfaces with other systems (e.g. Customs messages) and enhanced reporting demonstrating 'in-control.'	Reporting and analytics tools should be intuitive and accessible for operators and customers.
International multi-modal	Harsh environmental conditions.	New services should be robust, redundant, and assessable, while coexisting with other services.
Open ICT standards	Standards-based data and message formats.	Network effects indicates desirability of open standards.
Flexible services	Irregular shipment configurations are the norm for air cargo.	Technologies should be self contained and simple to operate.

International inter-modal logistics impose harsh environmental conditions on all shipments. Air cargo, road, and sea freight, may expose temperature sensitive products to challenging physical environments, e.g. extreme weather events or long-term environmental changes (ambient air temperature is variable across the globe). Technological and occupational changes must complement or enhance the extant operating environment and new services must be robust, redundant, and assessable, while coexisting with other services.

What are the infrastructural possibilities for introducing novel ICT based services for real-time or near-real-time cold chain monitoring in the international multi-modal logistics environment? One problem is the absence of a common ICT infrastructure in the multi-modal shipping environment. International movements involving multiple organisations utilise coexisting, overlapping and independent systems. Such systems employ multiple standards and proprietary approaches to constitute the operational milieu. However shared standards-based data and message formats (non-proprietary)

[12] EPCIS: Electronic Product Code Information Systems (see GS1)

facilitate commercial and regulatory interoperability among many involved parties. These multi-actor organisational and technological environments present heterogeneous computing environments and thereby create a tension between integration and independence, added to this the desire for robust and scalable systems suggest that new technologies and systems might be also be self contained and simple to operate, their operation and servicing of device should be uncomplicated and feasible in difficult working environment under worst case situations.

Infrastructure

There is an assumption that the widespread roll-out of RFID labelling and reader portals will eventually 'build out' a single standard supply chain ICT infrastructure, however earlier case studies and pilots acknowledge the installation of a complete RFID infrastructure is still some way off. Indeed older generations of marking technology seem not to have outlived their usefulness. Recent studies endorse the use of multiple modes of ICT marking and interaction, termed a '*hybrid data environment*'[13] (BRIDGE WP6, 2009). Barcode technologies have found their way into mobile applications to deliver additional valuable information and data for example; recall data, product history, ingredient lists, shelf life, loyalty, etc. (GS1 Mobile Com, 2008). We can conclude that hybrid data carrier information infrastructures are an intrinsic feature of the international multi-modal logistics environment. We expect that hybrid data environments will continue to *proliferate* due to the rapid pace of innovation of ICT in wider markets, and through differential rates of global diffusion where differing technology versions and architectures are developed, purchased and installed at different times and in different places.

Real-time or near real-time information?

What infrastructural possibilities exist for enabling real-time or near-real-time data capture as a shipment passes between factories, trucks, warehouses, and aircraft?

Extant data networks are provided by different organisations for different purposes. For example, the GSM network is provided by competing telecommunications operators for their customers; their aim is to provide complete geographic coverage of a region. LAN networks are provisioned by separate organisations (and some third parties) to enable local computer networks and internet access. Coverage is usually localised to buildings and offices. GPS is a US government satellite service which is generally available to third party reader devices; coverage is global but its use requires a clear line of sight between reader devices and satellites. Furthermore, the GPS network is not bidirectional; it sends data (much like television broadcast) but cannot be used for returning data. Networks of RFID and barcode labels carry data 'payloads' which may be read by handheld and gateway scanners. Individual actors deploy and manage their own tags and tag information systems. While coverage is 'spatial' in the sense that these

[13] A hybrid data environment would involve multiple data networks such as LAN, GSM, GPS; and multiple data carriers or packages such as GS1 Data Matrix, RFID, databases, printed labels and documents.

networks occupy space, its operation requires the relative proximity of tags or labels to reader devices which may themselves be connected to a LAN or GSM network.

Technically we have an indication that an innovative cold chain pilot or proof-of-concept technological solution can employ off-the-shelf components in a novel fashion. But cold chain also requires operator knowledge and skills cover handling methods, temperature mapping, storage, to deal with both normal and adverse events. Organisationally we have observed the inherent requirement for mindful and skilled work practice and performance; in 'making' the work of managing a cold chain, specialist knowledge and skills are necessary to manage and maintain it across complex, multi-actor, international, supply chains.

Cold chain pilot

We have identified the absence of a shared technological infrastructure for multi-modal shipping environments as a challenge to the provision of real-time end-to-end cold chain control. We posit that the absence of such a shared, end-to-end, logistics infrastructure, is one factor limiting technologically mediated innovation in complex inter-organisational supply chains. However we also note the presence of a common 'social infrastructure' along the supply chain, where those involved see themselves as shipping and logistics people. Their knowledge of shipping activities, regulation and documentation, use of systems and ICT is an unsung and hidden performance of competence and professionalism behind the largely technical description presented in this paper.

Reflecting on the contingencies and opportunities identified thus far we recommend experimenting with pilot systems, services, and work activity. A cold chain pilot might therefore be structured as both a technical and organisational exercise, an exercise designed at the outset to involve and engage workers across many countries, organisations and professions. The objective would be to learn in real life settings under actual working conditions, by taking technology out of the laboratory and put it into a 'living laboratory' to demonstrate and evaluate the feasibility, usability, and value of real-time or near real-time electronic temperature information. Pilot systems can be used to model network enabled sensor devices, device management, web services, ROI etc. but more importantly, they can used to understand sense-making by those involved, explore work practices, labour activities, and ultimately the viability of their business models.

5 Conclusion

International supply chains depend on the seamless integration of organisational interfaces, relationships, inter-organisational systems, and the delivery or exchange of material and information. Further to this, temperature control of high-value, sensitive, biopharma products by land and air cargo demands near perfect cold-chain control to ensure product life and viability.

We have observed segments or islands of control but not a chain of control. Our analysis did not support the expectation that an appropriate level of interoperability across the existing systems is achievable and would provide the required real-time monitoring ability. Technological progress and reduction of infrastructure and

component cost make the creation and maintenance of a control infrastructure a viable option. GSM messaging or telemetry devices may be used to provide real-time or near-real-time state information such as temperature/time/location for sensitive product shipments in multi-modal biopharma supply chains. Given the multi-stakeholder environment, sharing of information appears as a promising option, which might however be undermined by information ownership and transparency concerns. Moreover simply introducing more technology to the situation will be problematic without first addressing and respecting the knowledge, practice, and skilled performance of actors and technology in pre-existing socio-technical systems. It might undermine the observed resilience of the system if actors along the chain become solely dependent on a technical infrastructure, which might also fail at times.

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Appendix I. Shipper perspectives on accompanying documentation[14]

Table D. Export to Non-EU (to US) : Shipper perspective

Accompanying documentation (typical)	Doc template source	Target audience
Export QA checklist	internal	internal
Pro-forma invoice	internal	external
Packing list	internal	external
Certificate of analysis	internal	internal/external
Delivery note	internal	external
Insurance cert.	third party	internal/external
Additional accompanying documents	internal	internal
SAD	*external*	*external*
Materials handling data sheet/instructions	*internal*	*external*
US DA Memo	*internal*	*external*
TSCA Memo	*internal*	*external*
US FDA Memo	*internal*	*external*
US DTA Consignor Compliance Memo	*internal*	*external*
USHS cargo release form	*external*	*external*
US Customs declaration	*external*	*external*
Importer instruction	*internal*	*external*

Table E. Export to EU member state: Shipper perspective

Accompanying documentation (typical)	Doc template source	Target audience
Export QA checklist	internal	internal
Pro-forma invoice	internal	external
Packing list	internal	external
Certificate of analysis	internal	internal/external
Delivery note	internal	external
Dangerous goods	*external*	*external*
Animal by-products declaration EC 1774	*external*	*external*

[14] Italicized documentation name indicates a government or regulatory form. Some regulatory documentation is required even though there is no formalized template, in which case an agreed format is created (e.g. Memo).

Table F. Import from Non-EU (from US): Shipper perspective

Accompanying documentation (typical)	Doc template source	Target audience
Import QA checklist	internal	internal
Pro-forma invoice	internal	external
Packing list	internal	external
Commercial accompanying documents	internal	external
IMDG or IATA Hazardous Materials	*external*	*external*
USDA Health certificate (per consignment)	*external*	*external*
VET 16 application for import license	*external*	*external*
Import license (per consignment from VET 16)	*external*	*external*
SAD	*external*	*external*

Table G. Import from EU member state: Shipper perspective

Accompanying documentation (typical)	Doc template source	Target audience
Import QA checklist	internal	internal
Pro-forma invoice	internal	external
Packing list	internal	external
Commercial accompanying documents	internal	external
VET 1	*external*	*external*