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Decentralised manufacturing of cell and gene therapies

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EXPERT INSIGHT

DECENTRALISED MANUFACTURING OF CELL AND GENE THERAPIES

DECENTRALISED MANUFACTURING OF CELL AND GENE THERAPIES

A discussion with Richard Harrison¹, Loughborough University, September 2017

Reg Harris There has been a resurgence of interest in the concept of decentralised manufacturing (DCM) of health products including some cell and gene therapies (CGTs). The relative merits of traditional, essentially centralised, manufacturing and delivery of CGTs and the decentralised alternative(s) have been at the heart of the debate. A significant driver of activity is the growing call from the marketplace for efficacious, safe and **personalised** therapies. Richard Harrison, Nicholas Medcalf², Steven Ruck³ and Qasim Rafiq⁴, in one of a suite of papers addressing *Decentralised Manufacturing of Cell and Gene Therapy Products* address the benefits, barriers and potential solutions for implementing DCM.

So Rich, could you outline the concept of DCM?

Richard Harrison Centralised manufacturing has been the dominant means for creation of goods and products since the industrial revolution. As workers migrated towards factories and assembly lines were established in the early 'Fordist' factories in the US and elsewhere, economies of scale were able to be realised. This had the effect of dramatically reducing manufacturing costs and reducing variability. For these reasons many production strategies revolve around centralised production. Decentralised (or re-distributed) manufacturing in essence does quite the opposite, moving parts of a production cycle back into geographically separated regions. In doing so, the product being produced could be increasingly customised towards the localised requirements.

Reg Harris In your suite of papers you highlighted how this manufacturing network may function in a UK or European context. What characteristics make the UK such an interesting prospect for decentralised manufacturing?

Richard Harrison In many ways the UK is an exciting test-bed for rolling out a decentralised manufacturing network. First, the UK has a strong academic base working in the field of Regenerative Medicine. This is backed by a strong agglomeration effect of academics, companies and financiers in the 'Golden Triangle' between Cambridge and London which can be thought of as a mini-version of Boston in the USA. In addition to this, Central Government is committed to Regenerative Medicine manufacturing and, with the *National Health Service (NHS)* as a single-payer healthcare service, stands to simplify the reimbursement landscape. Finally, with the *Cell and Gene Therapy Catapult* and the *Fisher CryoHub*, there has been, recently, a notable investment in logistics and distribution.

Reg Harris Now let's look at how the UK/European template might apply in a small jurisdiction such as New Zealand. Transposed to New Zealand, while keeping an eye on demographics, medical centre disposition, logistic capability and economics [etc], a **centralised** manufacturing programme might feature manufacturing hubs in Auckland, Wellington and Christchurch which then serve the local population either in clinics or in an adjacent treatment centre. Conversely a **decentralised** network could involve multiple small manufacturing sites across the country which function in parallel with a centralised hub, yet are not fully dependent upon it. These potential networks are detailed in **Figure 1**.

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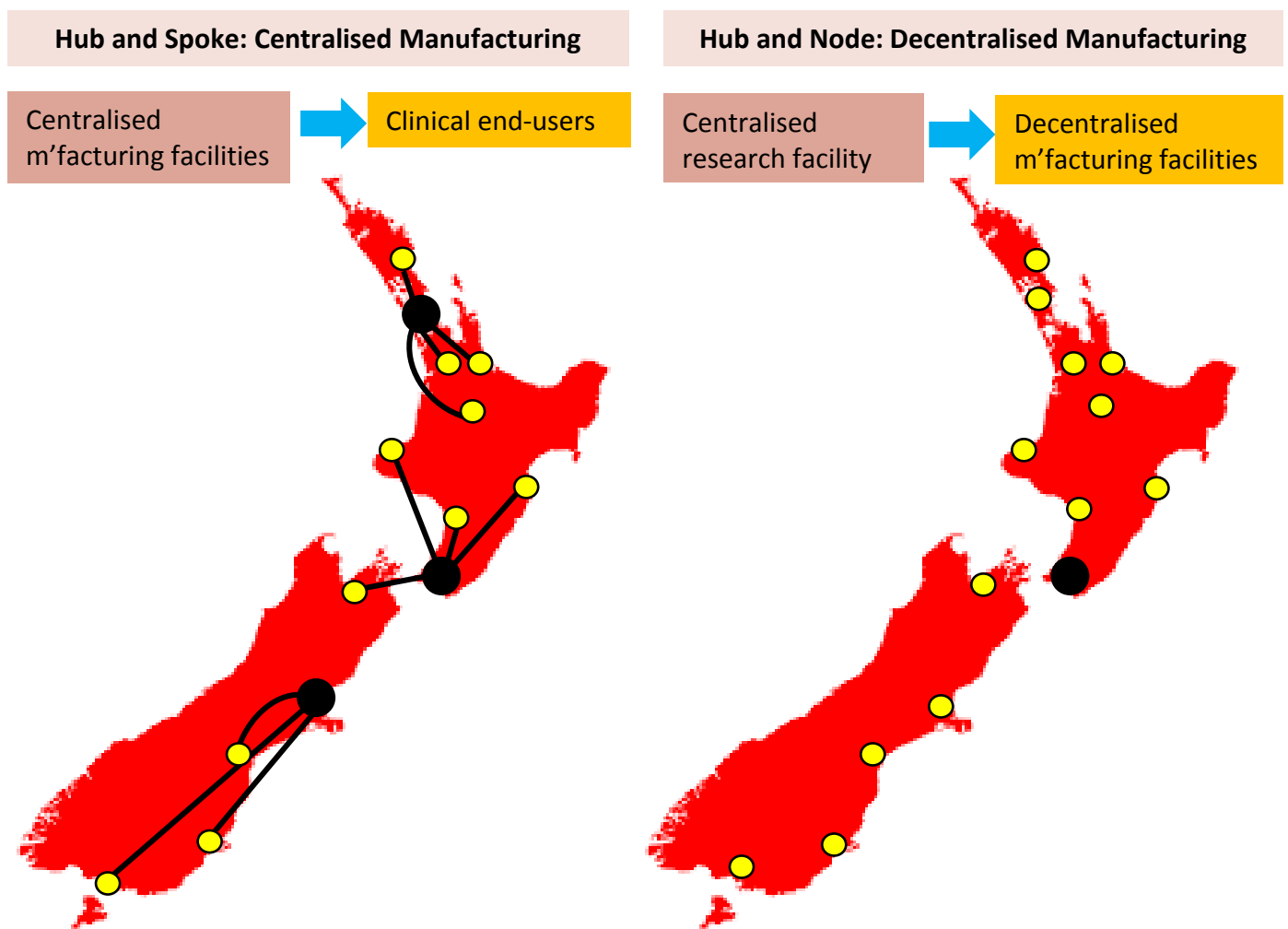


Figure 1: Overview of centralised and decentralised manufacturing networks as they might apply in New Zealand

So in the **centralised** model each of the three hubs [black spots] would perform production and oversight and carry with them the probability of 'lower' manufacturing costs. But they would be burdened with challenging point-to-point logistics of the final product as well as being the single points of failure for their respective networks. In the **decentralised** model the hub may produce some materials and support production logistics. Manufacturing costs may be 'higher' but offset by simpler logistics for final product i.e. a short straightforward hop from local manufacturer to clinic and patient. Importantly the network would stand to be less interdependent and more resilient in the face of market shifts.

Richard Harrison Yes, exactly, one of the key pressures driving decentralisation is the high logistical burden associated with a product with a very limited shelf life personalised to a specific patient. It isn't just a question of finishing the production run, bottling it, loading it into a protective carton and shipping it *via* same-day courier to the clinic. The clinical facility, clinical staff and patient all need to be ready at the correct time as well. This might be simpler for a patient who is receiving a cell-based treatment for arthritis of the knee, but gets significantly more complicated for a patient in a poor state of health.

Reg Harris New Zealand is a long and relatively narrow country with two main islands and a small population (4.7 million), three quarters of which is concentrated in the twenty largest urban areas. Logistical and distribution assets can be generally classed as 'modern' and well suited to the collection, storage, transport and delivery of most industrial and primary products. Would these characteristics be advantageous in establishing decentralised manufacturing of CGT products?

Richard Harrison Perhaps. Previously we investigated the concept of a cell **microfactory**. This can be imagined as a self-contained unit able to reliably and autonomously produce clinical products with very little oversight. We currently lack the technology to make this a reality, but a real-life decentralised manufacturing facility might not be too far-fetched. This facility, which is able to operate independently irrespective of the efficacy of distribution and supply networks, would certainly be advantageous in a country where geography complicates those supply lines.

The exemplar country I often imagine as being able to benefit hugely from a decentralised production network is Indonesia *viz* many islands and within those islands a poor transport infrastructure.

Reg Harris DCM represents a radical shift in the industry away from the current preponderance of ‘off-the-shelf’ healthcare solutions to customised therapies. You stated in your papers that ‘perhaps.....the radical changes needed to gain wider **societal acceptance** of decentralised manufacturing amount to a greater challenge than those for meeting technical requirements’. Could you articulate briefly why you feel so strongly that these non-technical barriers are so challenging to overcome?

Richard Harrison The simple answer is that it will necessitate a rethinking by all players, including chief executives, marketing and financial strategists, logistics specialists, engineers, technologists, academics and clinicians. All of these have some skin in the game and some have a significant amount of money riding on specific projects or products. What is best for one stakeholder may not be best for another and this creates challenges. In short, the industry requires national or even global coordination between these stakeholders and an ability to look at individual challenges as part of the whole.

Reg Harris So, to continue on this thread, industry must understand that in order to meet the demand for personalised therapies successfully centralised manufacturing is unsuited, and that business models bringing manufacturing close to the patients and responding quickly and effectively to their singular needs will constitute a key *modus operandi* in the foreseeable future. Clearly a prerequisite for wider societal acceptance is for industry to have ‘the right attitude’. Yes?

Richard Harrison Yes, I think that sums it up well.

Reg Harris There are possibly at this point, for many countries, no fully developed national ‘strategies’ for fostering this attitude in an industry-wide co-ordinated manner. Perhaps this leaves the way for industry itself to address the task, with or without the support of academia, which has invested significant intellectual effort in defining, describing, inter-relating and communicating the multitude of challenges.

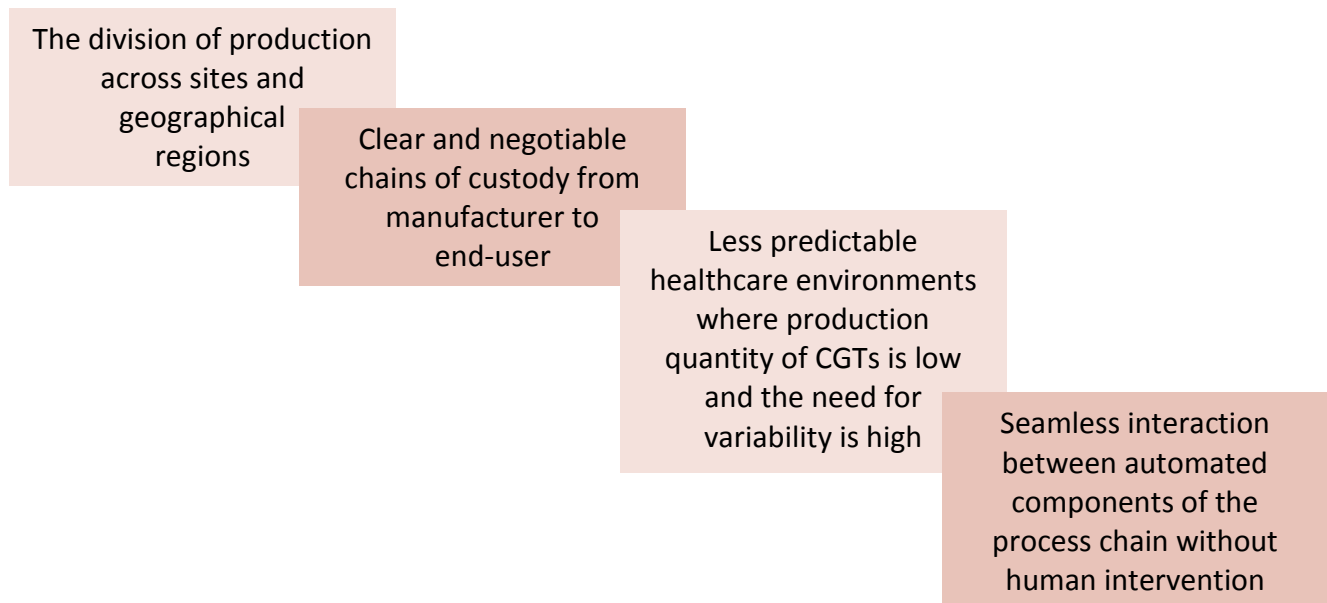
Richard Harrison Although it has had set-backs in global coordination voting for Brexit, the UK has established its Regenerative Medicine national strategy well. It has a strong academic base and the *Cell and Gene Therapy Catapult*⁵ is set up to help catalyse the translation of these academic breakthroughs to industry. It is also very lucky to have a strong background in regulation. These factors, working together, definitely encourage stakeholders to get on the same page. Canada with the *Canada Centre for Regenerative Medicine* is in a similar position attempting to establish its national strategy. Whilst these programmes are certainly useful, I don’t believe that a nationally focussed agenda on its own is enough. Cooperation needs to be cross-border.

Reg Harris Cross-border co-operation, yes. But, with or without deliberate national or global strategies aimed at promoting DCM it might reasonably be envisioned that at a fundamental level a new ‘**landscape of decentrality**’ in producing CGTs will emerge, driven by basics such as economics, competition and business opportunities.

⁵The CGTC was established in 2012 as a centre of excellence to bridge the gap between scientific research and full scale commercialisation, and to accelerate the growth of the Regenerative Medicine industry in the UK.

Richard Harrison We believe so! Because of the substantial costs involved for development and production of CGTs, it makes sense for decentralisation to be a global trend. One way or another it will happen.

Reg Harris Yes, and I would see this trend as being characterised by four factors:



Also, I would envisage that ultimately the ability to deliver customised healthcare to patients would become the norm rather than off-the-shelf generic solutions offered by remote central facilities.

Richard Harrison Yes, this would be the case for certain therapies. Off-the-shelf products certainly have their place. Hip implants, or indeed other bone implants, have been instrumental in treating patients for decades, yet there is still an emerging demand for customised printed bone replacements. We see this demand for customised therapeutics transposing to bio-printing and cell and gene therapies. The most important differentiator is that it is ‘agile’ manufacturing, as opposed to ‘lean’ manufacturing, and thus able to respond to rapidly changing patient requirements in a way a centralised production process simply couldn’t match.

Reg Harris The **internet of things (IoT)** is a central concept pervading consideration of all forms of modern interconnected industrial environments ranging from telecommunications and healthcare to transport and manufacturing. How do you see it fitting into DCM?

Richard Harrison We touched on the IoT when discussing DCM and our view is that it is likely to become a key component of DCM. Indeed interconnected ‘smart devices’ are going to feature in manufacturing more generally. *IBM* has termed these ‘Smart Factories’, *GE* the ‘Industrial Internet’ and *Airbus* ‘The Factory of the Future’. These companies are masters of advanced manufacturing, logistics and supply chain management and IoT will help in all these respects. In DCM however, the company is geographically distributed and far more vulnerable to standardisation drift and site-to-site variability issues.

Reg Harris So you see the IoT as beneficial to advanced manufacturing as a whole, but of critical importance to DCM to maintain acceptable standards across the network?

Richard Harrison Yes, exactly, removing human operators from the equation through automation is a step towards minimising variability, but this is only one component. Processes at one site need to match the tolerances established across the network, equipment has to be calibrated across the network to ensure results are replicable. Increasing and enhancing the interconnectivity and reporting are steps towards achieving this.

Reg Harris My understanding is that the IoT is the means to facilitate and maintain interconnectivity between automated components of the process chain. Subsequently it would be an enabler for the efficient management, co-ordination, monitoring and control of all operations from manufacturer to clinic.

Richard Harrison Yes, critically, by removing communication and distance as an obstacle, it would allow manufacturing replicability within the network of ‘smart factories’ for CGTs in hospital clinical sites and specialist medical centres, manufacturing facilities in academic sites and other clinical centres of excellence (the nodes in Figure 1). In simple terms, the IoT helps to lock down a set of parameters which the ‘smart factories’ and their human operators can work within to produce therapies which are personalised, but personalised only to the tolerances allowed by the framework.

Reg Harris In any deliberate moves CGT manufacturers make towards decentralisation, they stand to learn lessons from **other healthcare sectors** either going, or having gone, through a similar transformation. You address this in one of your papers and highlight a number of sectors which you believe share commonalities with the CGT sector. Could you touch on those examples?

Richard Harrison We examined this first in respect to automation of DCM and then further in its own stand-alone paper⁶. The four fields examined were nuclear medicine, total parenteral nutrition, blood products supply and anti-cancer medicines. Key factors considered were cost of infrastructure, product stability, transport window, risk of product loss owing to supply chain failure, and degree of product customisation. All fields are found to share similarities to some degree with personalised CGT therapies.

Table 1 summarises the outcomes.

	Nuclear medicine	Total parenteral nutrition	Blood product supply	Anti-cancer medicines
Cost of infrastructure	High	Low	Medium	Low-Medium
Product stability	Low	Medium-High	Medium	High
Transport window	Hours-Days	Days	Hours-Days	Days
Risk of product loss ex supply chain failure	Medium-High	Low	Medium-High	Low
Degree of product customisation	Medium	Low-High	Medium-High	Low-Medium

Table 1 Some key characteristics of health sectors selected as reference paradigms for CGT product manufacturing and delivery

⁶ Automating decentralised manufacturing of cell and gene therapy products: Cell and gene therapy insights. Richard Harrison, Qasim Rafiq and Nick Medcalf, 2016

Reg Harris There is an element of ‘swings and roundabouts’ in judging which field has the edge over the others in respect of relevance to CGT product delivery. In my mind, however, the top ranking for **blood products** in customised [read: personalised] therapies tips the balance. Would that be an accurate assessment?

Richard Harrison Blood certainly has a lot of overlap with CGT and a lot to offer. Part of this stems from the fact that they are inherently similar biological products. Tissues are harvested from donors, checked, purified, stored and allocated as required. Blood and its products have the advantage of being very well characterised and simple to store with current technologies. But this hasn’t always been the case; we have been working on getting blood to patients since at least the 1960s. The CGT field in comparison is very young and we have a way to go before it becomes as mature as the blood field.

Reg Harris I wonder if it could be feasible for CGT manufacture, in decentralised mode, to ‘piggy-back’ on a country’s established blood collection services to minimise doubling up on capacity which already exists?

Richard Harrison This is certainly a possibility and one which would make financial sense from a big-picture perspective. This attitude is one which is probably easier to implement in a single-payer healthcare system where large strategic level decisions can be made for the whole country. In the UK, the *NHS Blood and Transplant* service comprises 23 permanent blood donation venues (approximately one for every 2.4 million people), augmented by community-based venues, situated in towns and cities across England. As a part of this network there are 88 mobile blood collection teams running about 23,000 blood collection sessions a year in communities across England. This translates to a wide and deep reach into almost all communities and the ability to interact closely with individual donors.

Reg Harris In New Zealand⁷ the *New Zealand Blood Service* has nine Donor Centres [one for every 522,000 people] and runs over 300 mobile blood drives each year. The Donor Centres are in Auckland, Hamilton, Tauranga, Palmerston North, Wellington, Christchurch and Dunedin. Mobile blood drives take place in community halls, education centres and workplaces. Whole blood donors can donate at a mobile blood drive or any of the nine Donor Centres. Plasma and platelet donations require an apheresis machine [for extracorporeal therapy] and can be made at eight of the nine Donor Centres.

It seems to me that these extensive networks could accept and even support operations such as biological material harvesting (biopsy), storage and preservation, transport, and the use of some facilities able to cater for the processing of adherent cells and associated tissues in addition to blood and its products.

Richard Harrison Whilst the network is there, it should probably be thought of as more of a blueprint which would require further investment at specific points. A phlebotomist is not necessarily trained in the skill that harvest protocol requires, the mobile facilities don’t contain the required equipment, and the supply chain is not rapid enough for the product being collected. It is also important to point out that the physical infrastructure around blood supply is not the only important factor. Decades of theoretical frameworks and models which help predict the interaction between supply and demand are perfect starting points for modelling a similar CGT-focused framework.

Reg Harris Yes, and note also that I would not expect that CGT operations could or would simply use the array of blood product technology and methods; rather, they would introduce their own and use them within the supply chain network. Consider transport, for instance. Road transport by courier or other delivery vehicles had been assumed by researchers at *Loughborough University* to have a deleterious impact on the safety and integrity of cells. Accordingly, vehicle and package-resonant vibrations as well as rough-road vibrations were investigated in a ‘stacked green box experiment’ by Nikolaev *et al* and reported

⁷ New Zealand has approximately 8.6% of the population of England

on in their paper ‘The sensitivity of human mesenchymal stem cells to vibration and cold storage conditions representative of cold transportation’⁸.

Their conclusions were twofold. The *first* was that the sensitivity of human mesenchymal stem cells (hMSCs) to different vibrations within the mechanical system was different to that observed for human dermal fibroblasts and in both cases the strongest effect was observed for a frequency of 25Hz; vibrations at 25Hz resulted in dramatic reduction in cell number. The *second* was that long cold storage makes hMSCs significantly susceptible to mechanical vibrations of 50Hz, peak acceleration 140m/s² and peak displacement 1.4mm.

It is this type of investigation that would lead to the design of suitable packaging for the storage and transport of CGTs within the blood supply chain network. Likewise other pieces of research might be needed before CGT operations can fit neatly with the practical requirements and limitations of the network.

Richard Harrison Transit trials would be required to validate the shipping conditions of the product. This becomes slightly more challenging when for many CGTs we are unsure what exactly the best markers of efficacy are. Chimeric antigen receptor T-cells (CAR-Ts) could lead the way in this as they have a very clearly defined mechanism of action relative to many cellular therapies. Simply, we know what we are looking for in a ‘good’ therapy. Thus, as they move through a DCM network calculating relative efficacy is simpler.

Reg Harris Another perspective on decentralised manufacturing of CGTs working in concert with blood supply networks can be gained by considering **Figure 2** (I recrafted this from a paper depicting alternative routes for the manufacture, distribution and delivery of small-scale more-than-minimally-manipulated autologous cell therapy products⁹). The red flashes added to the basic chart represent points at which blood supply assets, primarily vehicular transport under some strict contractual arrangement, might be used for moving cellular products between various sites. As a ‘fall back’ when blood supply assets are stretched, standard commercial couriers that meet stringent criteria for cell material transport might be called in. Conveyance by air might be necessary in some instances.

The framework could be incorporated in its entirety within any one of the DCM clusters represented by yellow dots in Figure 1. That would be tidy. It is not unlikely, though, that factors such as ‘market’ demand for therapy, specialist and facilities availability, patient waiting times and clinical urgency will necessitate mutual support and **load sharing** between clusters.

Could this work?

Richard Harrison Whilst load sharing isn’t something we’ve covered in our current manuscripts, it is definitely something we have been discussing. This is another example of a case where the blood supply chain has lessons applicable to the CGT supply chain. Models have been developed which predict supply and demand as well as extrinsic factors affecting them.

As the field develops and we have a clearer idea on the transport and logistical constraints of a given therapy, I believe this will dictate the extent to which facilities are able to support each other. Certainly, in an ideal world, a DCM network will be both resilient and reconfigurable. In simple terms, it could tolerate being cut off (in a limited capacity) from the network and production lines can adapt to fulfil changing needs.

⁸ Journal of the Royal Society Interface published online 23 May 2012

⁹ Regulatory challenges for the manufacture and scale-out of autologous cell therapies: Paul Hourd, Amit Chandra, Nick Medcalf, David J. Williams; March 2014 StemBook (Internet)

In the meantime there is no reason to believe that the use of specialised vehicular assets for cell transport (etc) could not become a reality in some, even all, of the spaces marked by the red flashes.

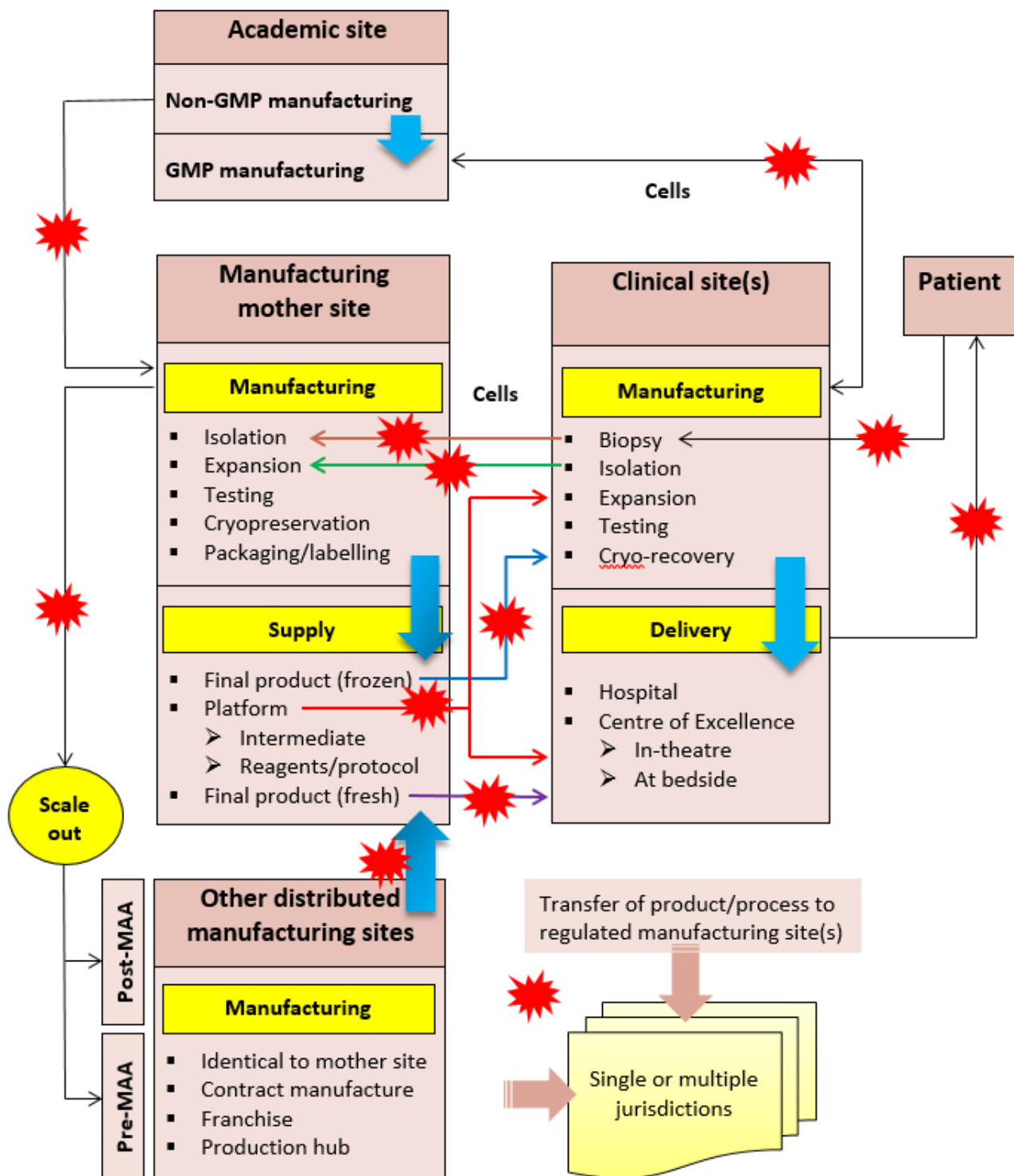


Figure 2: Alternative routes for the manufacture, distribution and delivery of small-scale more-than-minimally-manipulated autologous cell therapy products, with red flashes indicating places where specialised blood supply chain assets might be used

Reg Harris In the administration of **autologous therapies** cells are harvested from a patient and the culture expanded *ex vivo* to large quantities over many weeks and then returned to the patient i.e. 'one for one'. Would you surmise that this constitutes the biological platform for DCM?

Richard Harrison This is certainly one way to see it. An alternative would be an off-the-shelf cell product with a **late personalisation step**. Bio-printing could be an example of this, using generic biological material with a personalised printing process. Such therapies come at a high cost per patient *vis-à-vis* allogeneic therapies ('one for many') but with clever thinking the economic complexion could change considerably i.e. expensive treatment but only one-off, with no immune rejection, thus lower overall cumulative cost by elimination of the need for continuing reimbursements from [ultimately] the taxpayer.

Reg Harris This would necessitate the development of innovative new **regulatory mechanisms** that recognise and accept such a one-off investment in the future health of the patient based on an officially recognised treatment of a specified condition. What are the obstacles to be overcome in reaching this challenge?

Richard Harrison There is a limited pharmaceutical precedent similar to the curative potential of Regenerative Medicine. The closest analogues are *Sovaldi* and subsequently *Harvoni* which offer curative treatments for hepatitis C. These have an extremely high price tag and haven't been commercially successful. Rather, these products have been branded as priced too high even though from a cost effectiveness perspective they are merit-worthy. The set-backs experienced with persuading consumers and their advocates of the cost justification for these therapeutics is not reassuring when we consider we have to achieve this for Regenerative Medicine.

Reg Harris So, commercially, the reimbursement is a hard-sell. How is the picture for the regulatory space, specifically for Regenerative Medicine.

Richard Harrison There is no regulatory precedent for DCM and it will require a collaborative effort between technology suppliers, product manufacturers and regulators to establish a framework which enables DCM to succeed. The position paper produced by Hourd *et al*¹⁰ discusses 3D bio-printing in detail and many of the challenges discussed there are equally applicable to DCM of CGTs.

Reg Harris The challenge of developing effective **inventory management systems** is an immediate one and underlines the need for close-to-clinic manufacturing. I see the mantra of DCM as one of striving to deliver 'fresh' product to the clinic. Presumably this is not always practical and cold storage would have to be considered. What are your thoughts on the issue?

Richard Harrison I think making assumptions about how DCM would be implemented based on the current logistics and distribution is flawed. Investment in logistics and distribution solutions just isn't as exciting as the headline therapeutic research to most people and thus has been chronically underfunded. A number of changes are finally emerging and we are likely to see great change in how these therapeutics are delivered over the short- to mid-term.

Reg Harris Could you perhaps detail some of these advancements specifically?

Richard Harrison One of the specific advancements is the roll out of a global network in the form of the *ThermoFisher Scientific's CryoHub*. This aims to provide a tailored and scalable solution to Regenerative Medicine products. The scalable aspect in particular highlights the recognition by *ThermoFisher* that even at the development/clinical trial manufacturing stage, global boundaries are detrimental to stakeholder interests. Similar advancements include the *Cryogatt RFID* to manage inventory, the *TrakCel* system to

¹⁰ A 3D-bioprinting exemplar of the consequences of the regulatory requirements on customised processes: Regenerative Medicine. Paul Hourd, Nick Medcalf, Joel Segal and David J Williams, 2015. Loughborough University Institutional Repository.

track inventory through the network and the *Asymptote* thawing unit for managing receipt of good in a replicable manner. All of these tie together to create a network more able to handle the complex logistical needs of CGTs.

Reg Harris This brings attention to the matter of **cryopreservation** and its limitations. Liquid nitrogen is the standard long-term storage medium for biological tissues yet these facilities are often not in suitable proximity to the clinic. A contact of mine at *Loughborough University* who lectures in healthcare engineering and is doing work with cord blood freezing says that cryopreservation technology 'has not changed in the last forty years'. This is confirmed by another contact, a lecturer in biological engineering, at the same university. One of the priorities, according to the first contact, is to find potency assays. I am informed that 'more and more' research into plant-derived anti-freeze proteins (AFPs) is happening. AFPs belong to a class of polypeptides produced by certain plants as well as to some vertebrates, fungi and bacteria, and permit their survival in sub-zero environments.

Is this possibly this is an area of endeavor in the storage and preservation of CBTs that could do with a 'push'?

Richard Harrison This is certainly one aspect. There are a number of media for preservation which might allow us to escape from ultra-low temperature storage in liquid nitrogen at many points in the supply chain. *HypoThermosol* for example is a clinically approved product which allows for refrigerated storage, yet these are only part of the equation. Again, looking back to blood, we can see that it is well characterised, we know how to store it effectively and, more importantly, we know what to look for to carry out those storage trials. We are not quite there yet with CGTs, but we are making progress as development continues on those potency assays you highlighted as crucially important.

Reg Harris Would a **trade-off** between degrees of personalisation (the highest of which would be in DCM) and the need to achieve economies of scale be possible? In other words is the idea of a centralised-decentralised hybrid plausible for specified situations viz some combination of economies of scope and economies of scale?

(Note: A simple definition for economies of scope could be 'a proportionate saving gained by producing two or more distinct CGT products when the cost of doing so is less than that of producing each one separately'. That for economies of scale could be 'a proportionate saving in costs gained by an increased level of production of CGT products.)

Richard Harrison We have discussed this at length, as it is an interesting idea. We termed this '**degrees of decentralisation**' and we are particularly interested with the idea from a quality control (QC) perspective. This is primarily because we see one of the key challenges as maintaining quality throughout the network, yet QC is expensive, technically challenging and requires skilled operators. Thus, until a time this QC can be heavily automated, QC might be better being centralised whilst manufacturing is decentralised. In the decentralised cost of goods work we have carried out, we proposed a hybrid QC method where simple assays are performed at the manufacturing site whilst complex ones are centralised.

Reg Harris I'm sure that in the foreseeable future decentralised manufacturing of some CGTs will become the norm. A shift to this may already have started, at least in the 'general dialogue' led by academia. It could be instructive to the dialogue to think beyond it, to postulate 'what might be'.

Richard Harrison DCM has the potential to affect manufacturing hugely, but it could also have subtle yet effective changes on predominantly centralised models. With products which benefit from **late-stage customisations**, yet can be 'assembled' to a large degree centrally, the principles of DCM as we have discussed them can still benefit that manufacturing value chain.

Reg Harris In your series of papers you raise the promise of DCM 'in countries with small clusters of population in disparate locations, particularly if a microfactory can have **multiple product streams**'. This resonates with the idea of 'economies of scope', as opposed to 'economies of scale', and could have direct relevance to the likes of New Zealand.

Richard Harrison Certainly, I see the end goal of DCM to be a stage where a small franchise-like facility can be transposed easily to any geographic region to produce a diverse array of products (i.e. it's reconfigurable). We aren't at this stage yet but it's certainly the futuristic view. Additionally the concept of resilience comes into play again here. A network of facilities which can operate independently are perfect for avoiding product loss due to large disruptions at one facility thorough flooding or fire etc.

Reg Harris Presumably this reconfigurable, resilient micro-factory concept is also of interest from a **military** perspective?

Richard Harrison We have had conversations around this idea and it is one of the real areas where a reconfigurable micro-factory would be truly revolutionary. This wouldn't even have to be for Regenerative Medicine *per se*. But any system which is able to turn a generic-resource into a specialised component for military use at a battlefield location is of great interest to the defence community (think generic plastic used to form spare widgets for a range of equipment). For defence medicine, a micro-factory able to churn out patient-customised therapeutics is somewhat distant given our current level of technology, but the premise and enticement is definitely there.

Reg Harris So, at the risk of overstating it, one of the key emerging themes to look out for within the DCM space would be **multiple product streams from a stand-alone micro-factory.....yes?**

Richard Harrison Yes. I believe so. It is certainly an excellent concept, one factory able to churn out products to suit a range of conditions. We have examined the cost of goods for provisioning CGTs in a decentralised manner, and it seems clear that sharing product streams over one facility makes financial sense. Yet, this again is something which isn't common. Manufacturers would ideally like to own their infrastructure not share it with their competitor. Having said that, this concept is arguably very similar to the contract manufacturer (CMO) model and a challenge that is not insurmountable.

Go to <https://www.cmdt.org.nz/theme5-science-tech-comment> for other discussions relating to or in support of Regenerative Medicine including: biology and electrospinning, biology and mechatronics, biology and microfluidics, blood products manufacture, kidney manufacture, magnesium-substituted hydroxyapatite, and tissue interface computational modelling.

EXPERT INSIGHT

DECENTRALISED MANUFACTURING OF CELL AND GENE THERAPIES

A discussion between Richard Harrison¹ and Reg Harris²

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