

SUBJECT: Generics Onshoring
MEETING DATE: 15.07.20
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For Information	Members are asked to note the contents of the paper
For Discussion	Members are asked to decide on recommendations
For Approval	Members are asked to agree the proposed recommended action areas

Summary

There is an opportunity for Scottish pharma, chemicals and fine chemicals companies to support the supply chain to take advantage of a new business model for medicines manufacture and procurement. Support for business case development is sought.

The Problem

The COVID-19 pandemic has revealed just how heavily dependent the UK is on overseas manufacturers and complex global supply chains for access to the generic medicines essential to meet the medical needs of our citizens. Even in normal times, this reliance leads to regular shortages and price uncertainties in the NHS which can be triggered by problems at any point along the supply chain from raw material availability, manufacturing failures, quality or contamination issues, or distribution disruption.

Now, as a direct result of the COVID-19 pandemic, the NHS is suffering from acute shortages because lower cost economies such as India and China, which dominate global production, have restricted exports of such medicines during the pandemic to protect their own populations.

The long list of medicines in severe shortage include anaesthetics, muscle relaxants, antibiotics and neuroleptics. In hospital geriatric and palliative care departments, midazolam and morphine, diazepam, and clonazepam are in severe short supply. The shortages are forcing some patients on to second line therapies which have inferior outcomes and are often more expensive. The DHSC has a robust mechanism for managing medicine shortages including the extreme measure of banning the export of medicines. Currently, there are 201 medicines on the list of medicines which cannot be exported from the UK – representing an unprecedented problem in the generic medicine supply chain

This supply fragility has been compounded by the fragmented procurement processes which has led to a commoditised market for generic medicines and a race to the bottom in both cost and quality. This has eroded the business case for many UK based manufacturers for both generic and IP protected medicines with the consequence that much of the UK medicine manufacturing capacity has been transferred offshore. Further unintended consequences of a race to the bottom are uncontrolled price fluctuations and shortages as manufacturers enter and leave the market based on price alone. Hence, the UK capability needs to be reinvigorated and strengthened in a major way to assure security of supply of these vital products as well as the short-term reconfiguring of existing infrastructure.

The Solution

We have a unique opportunity for the UK to revolutionise our infrastructure for the procurement, development and manufacture of high-quality medicines. We can create a nationwide ecosystem which will not only largely eliminate future shortages but will give us a powerful new manufacturing capability with the resilience to respond to any future challenge. This can be achieved by harnessing the world-class capabilities across the UK in research, innovation and manufacturing and motivating them with a coordinated long-term procurement process that ensures stability of essential generic medicines supply for every patient in the UK.

Time is short. Already in the USA over 1,000 hospitals have come together to secure supplies of essential generic medicines. Their “re-shoring” programme has been kickstarted with a 0.5 billion-dollar US-centric government funded initiative. A coordinated EU strategy is being developed and implemented for resilience

in Europe. We must act now to unlock the UK's potential strength in this area. Our vision is to establish a secure, agile, cost-effective and environmentally sustainable supply network.

Now is the time to launch a nationwide initiative that establishes a robust procurement and supply chain for essential generic medicines that re-shores medicine manufacturing to deliver the health and economic benefits from this advanced manufacturing revolution.

Medicines developed in the UK, made in the UK, for the UK.

Procurement

In order to stabilise the market for essential generic medicines we propose a move away from a commodity-based trading system to a structured tender process that maintains competitive pricing and builds supply chain robustness.

For a selected set of essential generic medicines, it is proposed that a new Arms-Length-Body (ALB) is established under the auspices of Department for Health and Social Care to procure and distribute products across the nations of the United Kingdom. The products will be defined based on clinical need, supply chain fragility and vulnerability to future pandemics.

Tenders will be multiple year agreements guaranteeing volume and price enabling manufacturers to invest in process optimisation and improvement. The ALB would provide process improvement expertise to successful bidders in order to further guarantee continued supply to the NHS.

In order to provide certainty to the NHS preventing hoarding and ensuring every patient in the UK has access to the right medicine at the right time the ALB will build, maintain and distribute from a strategic six month stock pile.

Reshoring

The UK has invested in the development of advanced manufacturing technologies for medicines. We now have the opportunity to apply our academic and industrial expertise to enable Project Defend and bring medicine manufacture back to the UK.

Target Molecule Selection Logic

A number of data-sets were examined to consider the rationale for identifying potential medicine candidates for holding strategic supply stocks, and/or creating production capability in API, Secondary processing, and/or particular pack formats. The initial analysis included the NHS single-sourcing procurement list, product shortage lists, export restricted products as additional potential filters to the current approach being used to identify candidates for advanced manufacturing.

However, the team has identified the importance of engaging with NHS procurement and those leading Project Defend on the rationale for products being potential candidates as the current data do not discriminate between policy choices and market constraints. This is essential if we are to understand the underlying causes of specific shortages. These proposed follow-up discussions would therefore provide the basis for a more informed multi-decision criteria analysis to identify potential candidates and appropriate solutions.

Furthermore, for manufacturing investments the concept of identifying a single candidate versus defining the minimum viable asset that would support a level of supply security, a usable, reconfigurable and/or repurposable manufacturing base requires a more strategic approach, again requiring engagement with NHS procurement professionals. This makes engagement with the NHS at a strategic sourcing decision making level a pre-requisite to the selection of potential supply-security strategies. Detailed follow up on whether potential suppliers are manufacturers and/or distributors with appropriate regulatory licences.

Once target medicines are identified the team is highly confident that effective technical assessment can be made rapidly, building on a wealth of current knowledge and/or examples, to inform technology selection and develop robust, intensified, cost effective and sustainable processes.

Recommendations:

Continue with a UK wide taskforce involving academic, innovation, manufacturing businesses, technology providers, MHRA and crucially key NHS stakeholders to define the business case.

Business proposals

- Establish a detailed proposal for the long-term procurement of essential generic medicines in collaboration with the NHS across the UK and the Department of Health and Social Care,
- Identify a set of essential generic medicines to be procured through the new mechanism,
- Procure a six-month strategic stockpile of essential generic medicines,
- Identify essential generic medicines to be re-shored through Project Defend,
- Identify organisations and facilities available for re-shoring medicine manufacture using advanced manufacturing technologies across the UK. This information will be sought from the OLS survey.
- A business case should be produced. Short term bandwidth problems at CPI mean we will explore the use of consultants to undertake this work
- The programme should be exploit existing infrastructure and strengths and be run under the banner of the Medicines Manufacturing Innovation Centre (MMIC) with University of Strathclyde's centre for Continuous Manufacturing and Advanced Crystallisation (CMAC) leading a hub of academic input from interested institutions.
- We will seek to publicise the Generics opportunity and challenges across the wide academic, SME, industrial, NHS and regulatory base.

Technical proposal development

- The transformation of UK essential medicines manufacturing requires a co-ordinated suite of activities in order to fully realise the healthcare and economic benefits. These must include: skills development and training, research and development, innovation, business collaboration and growth.
- Short, medium and long term objectives are being identified with current partners to realise impacts quickly whilst establishing the following:
 - o (i) sourcing strategies for stockpiling and manufacturing in the near and long term;
 - o (ii) minimum viable manufacturing assets and technologies for a reconfigurable, sustainable UK generics medicine manufacturing and supply system;
 - o (iii) target medicines based on NHS needs and manufacturing requirements (e.g. high-volume/low-cost; low-volume/high-cost; manufacturing complexity; environmental sustainability);
 - o (iv) longer term structural capability changes required to inform necessary investment, location and deployment of assets.

	Timescale	Capabilities Delivered
Phase 0	Acute, now	Stockpile from existing suppliers of key APIs and products
Phase 1	Short term; 1-2 years	3-5 simple products; API and oral exploiting ready now advanced manufacturing technologies in GMP; build on stockpile; proof of concept; regulatory; high priority NHS needs met
Phase 2	Medium term; 3-5 years	Up to 20; moderate complexity products; API with conversion to oral & sterile as required; innovate processes and technology, QA and regulatory systems; reconfigurability and agility of manufacturing assets for multiproduct supply. Increased UK manufacturing activity. Increased proportion of essential NHS needs secured.
Phase 3	Long term; 5-10 years+	complex products; API, oral & sterile; increased integration and intensity through innovation; highly autonomous production. Sustained increase in UK medicines manufacturing achieved. Increased innovation and competitive advantage. Sustainable supply of medicines to meet priority NHS needs.

Cost

We estimate that to deliver the required capacity, capability, development and supply at a scale to secure the UK's generic medicines supplies, an initial investment of £2-300M is required in the short term rising to a total spend of £1Bn over the next 10 years.

Noting that in 2014 generics accounted for 35% of the UK's total spend on medicines, which by 2018/19 had reached over £18 billion and is growing at ca. 4% p.a.

Recommendations:

LSS is asked to recommend the support for seed funding to develop a business case for Scotland's supply chain to take advantage of this opportunity.

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ATMP Strategy background story v1

Background:

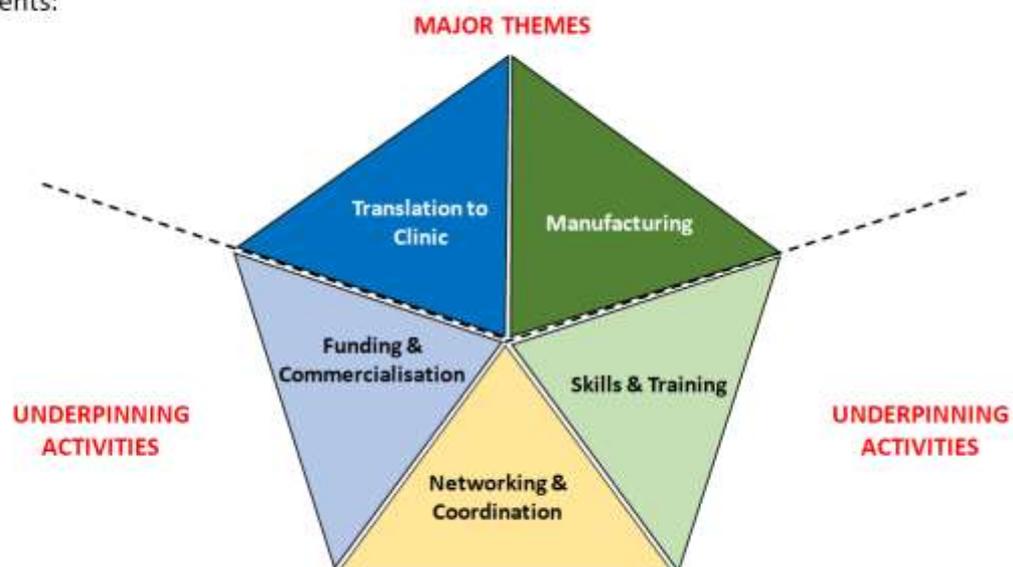
Advanced Therapy Medicinal Products (ATMP) are innovative therapies that encompass gene therapy, somatic cell therapy and tissue-engineered product. ATMPs offer ground-breaking new opportunities for the treatment of diseases which cannot be addressed adequately by existing pharmaceuticals, but they have cost implications.

The Medicines Manufacturing Industry Partnership produced a UK-level Advanced Therapies Manufacturing Action Plan strategy [Advanced Therapies], which outlines the main opportunities and recommended actions to maximise the benefits of translating the pipeline of research into manufactured products, establishing the UK as a global hub for researching, developing, manufacturing and adopting advanced therapies.

In 2018, Mike Leek was tasked by Life Sciences Scotland (LSS) with exploring the potential for an advanced therapies manufacturing strategy for Scotland, building on the existing Scottish strengths and linking to the UK ambition. A paper from Mike Leek, Ian McCubbin, [REDACTED] and [REDACTED] was submitted to LSS on 10 December, which identified a key themes and activities (see figure 1 below by [REDACTED]) and a series of inter-related actions to be delivered.

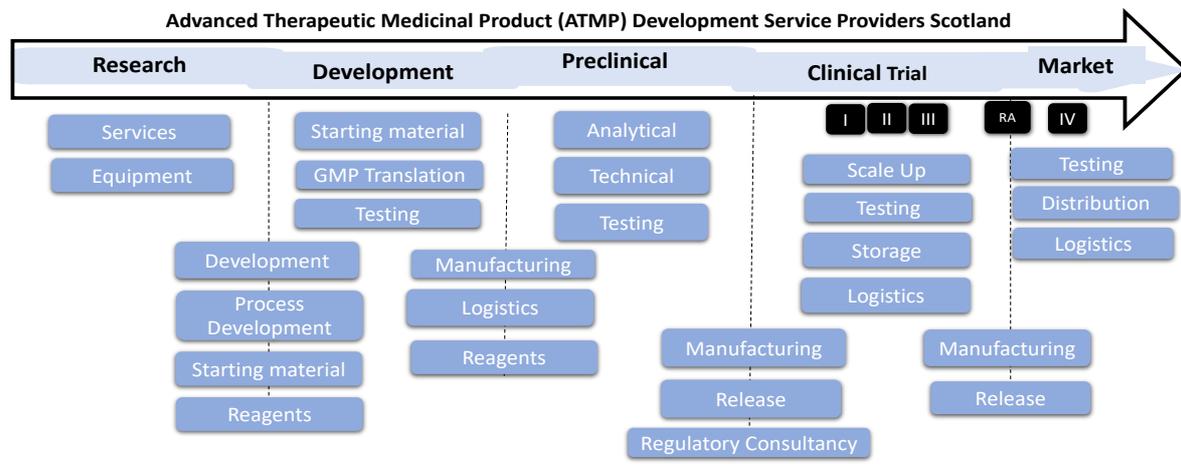
Figure 1: key inter-relating areas of the ATMP strategy

Key Components:



A small group has been formed to progress the recommendations in the LSS paper. The members of this group are Colin Mackay, Symbiosis, Janet Downie, Roslin CT, Ian McCubbin, MMIP and [REDACTED] supported by inputs from [REDACTED] and [REDACTED]. The group is starting with populating the ATMP pipeline (figure 2). Companies and organisations who have been involved in the workshops held as part of the strategy development paper are being invited to complete a table (figure 3) which outlines at which points on the pipeline they are active. This process will identify Scotland's key strengths, where there are gaps to fill, and creates a "picture" with which organisations can identify, building the community. It will be used to promote Scotland as a location for Advanced Therapies from research through the supply chain to manufacturing and into the patient.

Figure 2: the ATMP pipeline



General headings of stages in pipeline

Figure 3: Companies being asked to complete the table to show which services they offer and at which points on the pipeline.

	RESEARCH	DEVELOPMENT	PRECLINICAL	CLINICAL TRIALS					MARKET
				PHASE I	PHASE II	PHASE III	RA	PHASE IV	
STARTING MATERIALS									
REAGENTS									
EQUIPMENT									
TESTING									
GMP TRANSLATION									
SCALE UP									
REGULATORY CONSULTANCY									
- IMPD PREP									
- NDA PREP									
- IND PREP									
MANUFACTURING									
FUNDING									
LOGISTICS									
STORAGE									
DISTRIBUTION									
RELEASE									
Other areas									

Next steps:

Companies and organisations will be invited to complete the table either by email or through a survey monkey format. Once the pipeline is populated, it can be promoted through electronic marketing means, meaning it can easily be updated and shared.

Immediate Opportunities:

There is currently a £16m call from MRC and Life Arc for the creation of a network of Gene Therapy Innovation Hubs across the UK. Further funding may be available from other funders, eg BBSRC. It is envisaged that the Innovation Hubs will provide access to clinical grade viral vector and translational support for early phase academic-led gene therapy clinical trials.

Scottish Enterprise is working with potential partners on a Scottish-led bid, led by the University of Edinburgh to establish a major Gene Therapy Innovation Hub at Edinburgh BioQuarter, building on the extensive ATMP translational infrastructure that already exists. Universities across Scotland have key skills in this area both to support such a hub and provide a pipeline for innovation – particularly in developing new gene therapies and manufacturing process innovation.

Synpromics/ASKBio has developed one of the world's most effective viral vector platforms, and within the Scotland's emerging ATMP strategy, there is evidence of a strong supply chain emerging to support the development of new gene therapies.

In developing Scotland's draft ATMP strategy, the need to establish an effective commercialisation "engine" at scale has been identified – this is needed to sustain a competitive commercial supply chain. The ATMP skills group, led by Skills Development Scotland, has also developed an ATMP Skills strategy, which would fit well with this Innovation Hub proposal.

Deadline for expression of interest is 1 June 2020.

Support is needed to orchestrate the activities of and drive progress within this strategic theme.