Digital innovation for flexible, high quality medicines manufacturing supply chains

Using standards to drive adoption

May 2018

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About

BSI

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Over 95% of BSI's work is on international and European standards. In its role as the UK National Standards Body, BSI represents UK economic and social interests across the international standards organizations ISO, IEC, CEN, CENELEC and ETSI, providing the infrastructure for over 11,000 experts to work on international, European, national and PAS standards development in their chosen fields.

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Executive Summary

Background

BSI, supported by the Institute for Manufacturing, has undertaken a roadmapping exercise to establish how best a standards programme can encourage adoption of digital technologies within medicines manufacturing supply chains. This is in response to a number of related initiatives designed to promote innovation within the manufacturing and medicines industries more generally.

Major challenges to be addressed by standards

The main way that standards can help the UK medicines manufacturing industry adopt digital technologies is to contribute to the UK becoming a global pioneer in various aspects of medicines manufacture, such as:

- Returning API production, biotech, and packaging production back to the UK.
- Retaining the UK's position as one of the leaders in advanced therapies production.

BSI will help the UK medicines manufacturers achieve this in a number of ways, including:

- better connectivity and feedback directly from patients;
- working at lower defect rates and reducing waste;
- encouraging companies within the medicines manufacturing supply chain to collaborate more effectively to meet patient needs;
- developing more flexible, responsive, and lower cost automated production processes; and
- better control of inventories through higher visibility of supply chain logistics.

Recommendations

Recommendation 1: Identification of smart factory good practice from other sectors

BSI will establish how manufacturing sectors more advanced in their digitalisation journey are using digital technologies in smart factory, product, process, and network design, and codify this as good practice. Aspects of this will be described in a PAS on Design for Digital Manufacturability (DFDM).

Recommendation 2: Interoperability and architectures

BSI will establish the requirements for interoperability and data and business architectures for the UK medicines manufacturing industry, and will work with other groups working in digital manufacturing interoperability to ensure this is reflected in international standards.

Recommendation 3: Working with others to integrate patient and manufacturing data

Standardization of data formats at trial phase would speed up time to market. Additionally there are huge benefits from assessing the effectiveness of medicines directly from patients at the post-launch phase, which helps to understand how effective a medicine is in the real world. One particularly important barrier is that there needs to be a mechanism for deciding if data can be shared or not, due to issues including privacy, confidentiality, and ethics. BSI proposes to establish and develop a decision-making framework for data sharing, with input from NHS stakeholders.

Recommendation 4: Standards strategy for smart medicines packaging

This is a challenging area because of its complex nature, partly due to it being an integration of mature and newer technologies. There are currently some standards for packaging using radio-frequency identification (RFID). For instance, ISO Technical Committee 122 *Packaging*, has already published a number of standards relating to RFID applied to freight containers, returnable packaging, transport units, product packaging, and product packing. There are also standards to enable quality management of medicinal product manufacturing, but there is nothing that links medicinal product packaging with RFID. BSI will establish how best to use the domestic, European, and international standards activities to unlock the potential of smart medicines packaging manufacture in the UK.

Recommendation 5: Adoption and development of existing digital manufacturing activities in the medicines manufacturing supply chains

There is an opportunity for medicines manufacturers to work directly with healthcare providers to use digital technologies to improve patient outcomes via better diagnostics, adherence, education, and training. This would require the digitalisation process to be accompanied by a shift in ethos from a product centric approach to more of a service offering. These services, involving the timely and lower cost delivery of necessary medicines, would be much higher value than are currently delivered and would make the UK a world leader in their provision. Many of these principles of user-centric services are described in PAS 280 *Through-life engineering services – Adding business value through a common framework* and we propose to establish how best to implement this service ethos into the medicines manufacturing sector.

1 Digital innovation for flexible, high quality medicines manufacturing supply chains - The role of standards

Digital manufacturing

In 2017 BSI undertook a roadmapping exercise to establish a standards programme that would encourage the adoption of digital technologies by UK digital manufacturing supply chains, building on the recommendations BSI and the Institute for Manufacturing published in 2016.[1] That report identified a number of key challenges that standards could address:

- **Design for digital manufacturing** - digitalisation will be an enabler of a more collaborative, end-user focussed design process.
- **Simulation, verification and validation (including digital twins and in-process modelling)** - assurance in the results of simulations and models, as well as the wider adoption of good practice in their use, will be needed.
- **Intelligent data gathering and analysis** - the ability to extract knowledge from data in a widely understood and compatible way will be a key development arising from digitalisation.
- **Rights management, data governance and security** - a major challenge emerges from the difficulties in identifying how the ownership of data in a shared environment needs to be recognized, and how revenues would be distributed amongst collaborators. Additionally, issues around data security, reliability, and provenance need to be dealt with.
- **Equipment plug and play, capability and discovery** - a major enabler of higher productivity manufacturing sectors will be the ability to create manufacturing lines that can self-configure, communicate and virtualize their capabilities in the supply chain.

1 Available from: www.ifm.eng.cam.ac.uk/news/the-importance-of-standards-in-a-digital-world/

To meet these challenges BSI proposed to create a series of communities of interest (CoIs) in the following areas:

- Interoperability. A key requirement for global standards is that machines and data are platform and format independent, and that manufacturers are not locked-in to a particular system or vendor, which would negate many of the potential advantages digitisation could bring and reduce competitiveness;
- Supply chain capability. Many UK original equipment manufacturers (OEMs) are pioneers in the use of digital technologies to add value to their manufacturing capabilities. However, there are real challenges and opportunities in enabling existing manufacturing companies to make the shift to digital, and also enabling digital companies to offer innovative services to the manufacturing supply chain;
- Through-life, end-to-end, connected supply chains – design. Many of the opportunities for UK manufacturing and adoption of digital technologies arise from the connection of the manufactured product in use to the design stage. This builds on existing UK strength in design and R&D, particularly in high-value manufacturing sectors such as aerospace, automotive, and pharmaceuticals, where the UK has a comparative advantage;
- Governance, security, and assurance of data. Alongside interoperability, this theme was consistently amongst the first to arise whenever discussing the role of standards in digital manufacturing innovation;
- Through-life end-to-end connected supply chains – service innovation. Digitizing manufacturing technologies opens up the value chain and gives rise to opportunities for new services that can improve performance. Examples include through-life engineering services that have been developed in the aerospace sector, new ownership models offered by toolmakers, and new digital services (such as product lifecycle management) that could be offered by digital companies that are not currently operating in the manufacturing sectors.

Many of these recommendations are generally applicable across a number of manufacturing sectors, and are particularly applicable to the aerospace and automotive sectors which are amongst the most advanced in their adoption of digital technologies and also in their ability to collaborate in innovation. However two sectors that operate in a very different regulatory environment, and where the relationships with supply chains and customers are not comparable with the assembler industries, are the medicines manufacturing and food sectors. BSI's recommendations suggested that both of these sectors are sufficiently different, and significant in economic size, to warrant a separate roadmapping approach to establish how best to promote digitalisation within their end-to-end supply chains.

Medicines manufacturing in the UK

There have been a number of recent reports highlighting the opportunities and risks for the UK medicines manufacturing industry. The Medicines Manufacturing Industry Partnership (MMIP) recommended a number of priorities for investment, and much of this was echoed in the government's Made Smarter Review 2017. In addition other strategies have emerged, such as the Vision for UK Pharma, the Life Sciences Industry Strategy, and the Biomanufacturing Technology Roadmap which all demonstrated that investment in the UK medicines manufacturing industry offered great potential for productivity and exports growth. In addition, in October 2017, Biopharma-Reporter published its latest survey on the challenges and opportunities facing the biopharma industry.

The MMIP Technology and Innovation Roadmap identified four areas where the UK should create centres of excellence and that offered significant opportunities for these sectors. These are:

- process innovation in all small molecules and established medicines – into clinic;
- process innovation in larger molecules (with HCF) – into clinic;
- pack/device/supply chain and material innovation; and
- advanced therapy innovation and production.

The roadmap highlighted a number of recent challenges for the UK medicines manufacturing industry, including:

- The loss of much of the biologics development and manufacture to the US, Japan, Singapore, Switzerland and Ireland.
- The offshoring of much application programming interface (API) production to the Far East, which has led to reliability and quality problems.
- A limited capability to produce packaging components, meaning much of the UK medicines production is effectively exported in a semi-finished state, reducing the total export value of the industry.

The Made Smarter Review estimated that adoption of digital technologies by the medicines industry could be worth £22.4 billion over 10 years. Digitalisation can help remove non-viable drug candidates from the development process much earlier, thus reducing time and costs to the industry. Additionally digitalisation would enable the transformation from large-volume manufacturing plants to more agile, localised, and smaller production facilities. This would lead to significant productivity improvements, estimated at 30-35% by 2030. Digitalisation will also create closer links with patients and clinics, and give rise to better information for manufacturers. It will also speed up the rate at which clinical data are available, increasing its value significantly. Logistics will be improved, and companies will benefit from reduced waste via better inventory management.

More broadly, the global pharmaceutical industry is estimated to be wasting 7-10% of the input materials, and this could be addressed by digitalisation. Digitalisation will enable continuous monitoring and adjustment, which will be particularly useful in cell and gene therapies where there are fewer starting materials to work from. If the UK medicines manufacturing supply chains can be encouraged to use digital technologies to collaborate effectively to better meet patient needs, this would have both a positive economic and environmental impact.

Project overview

This roadmapping project followed the approach outlined below.

1) **Domain research report** - This report is available in Annex 1. The purpose of this initial piece of work was to provide an:
   a) overview of relevant current formal standards published by National Standards Bodies (NSBs) or Standards Development Organisations (SDOs); and
   b) insight of what the medicines digital manufacturing industry encompasses including:
      - trends and drivers within the medicines digital manufacturing market, including key challenges that the market needs to address in order to embrace the new technologies required;
      - digital manufacturing value propositions, new technologies inside factory gate and outside factory gate which will influence the progression of medicines digital manufacturing; and
      - details regarding relevant legislation and regulations.
2) **Use cases** - This piece of desk research created a number of use cases from sources, such as the MMIP technology and innovation roadmap, to identify the opportunities and challenges created by digitalisation and examine how these could be addressed through standards. The use cases are detailed in Annex 2.
3) **Standardization roadmap** - This research was undertaken with the Institute for Manufacturing (IfM) at the University of Cambridge and consisted of three activities:
   - a stakeholder survey;
   - supply chain capability assessment workshop;
   - standards roadmapping workshop.

   The outputs of all three activities are detailed in Annex 3.

4) **Final project report** - The final project report summarizes all of the above project activities, and sets out recommendations for how standards could accelerate the digital innovation of medicines manufacturing supply chains in the UK.

Analysis

Across the stakeholder survey and the workshops, a number of trends and drivers became apparent across the sector and fell into a number of different categories.

Technological. Feedback loop capability – potentially integrating data along the value chain and supply chain. Additionally there will be significant impact from simulation and models on design for manufacture.

Economic. The need to significantly reduce the cost of development, and also smaller lot size, more personalization, links with better diagnostics and stratified medicine with a move towards more high-value personalized medicines.

Opportunities. These would arise from having access to and analysis of, large datasets across multiple organizations. The opportunities would also require good management of data for patient derived materials flowing to the factory and personalized therapies flowing back to the manufacturing process.

Challenges and threats. These were varied and included:

- shortage in experienced bio process engineers and other skills;
- optimization of supply chain (storage, tracking of components, inventory);
- data storage, management and analysis;
- maintaining safety and efficacy in novel and innovative treatments; and
- the lack of UK packaging manufacturing capability.

1) Domain Research

- The keyword searches identified 942 standards, published and in development, that relate to the UK's medical digital manufacturing.
- Within 'Enablers', which detail the standardization, legislation and regulations from formal and private industries, the top areas of representation by standards were assurance and certification, governance and security, and interoperability.
- Within Sectors, the top area of representation by standards was within the packaging, labelling and distribution sector, followed by advanced therapy medicinal products (ATMP) manufacturing innovation and production sector. Active pharmaceutical ingredient (API) and molecular process innovation and biotechnology also featured to a lesser extent.
- There appears to be a clear gap in the standards identified in relation to Internet of Things (IoT) technologies and digital manufacturing within the medical field. This is also reflected in the limited results within the supply chain, an area seen as priority by MMIP.

2) Use cases

BSI created a number of use cases (see Annex 2) that demonstrate different ways that digitalisation could add value to the UK medicines manufacturing supply chains which are, in summary:

- **Smart labels**. The use of smart labels would enable security of supply and tracking, traceability, and monitoring.
- **Wearables and associated apps**. Wearables are useful for monitoring patients in both clinical trials and for commercial use. They are particularly helpful for manufacturers to better understand how their products are used by patients and therefore to enable better disease management.

- **API manufacture.** Many of the APIs that form part of medicines formulated in the UK are manufactured overseas. There are a number of opportunities to make the UK a world leader in the manufacture of APIs by using digital technologies.
- **Digitisation and artificial intelligence to transform pathology and imaging.** Linking pathology and imaging to the supply chain using digital capabilities would create more efficient procedures and a higher quality of decision making.
- **Digital/smart factory.** Digitalising many aspects of the factory will create more flexible and reconfigurable processes, and will also lead to higher productivity and efficiencies.
- **Analytical capability and equipment.** Ongoing improvements and more rapid processes place new demands on analytics that give appropriate levels of assurance on product quality.
- **Automation and robotics.** Many of the developments relevant to the digitalisation of medicines manufacturing require further use of automation and robotics technologies.
- **Additive technologies.** Additive manufacturing/3D printing offers a number of potential new ways to produce drugs.
- **Sensors and integrated electronics.** Greater connectivity across end-to-end supply chains will require sensors that work as expected and to appropriate levels of quality.
- **Advanced Therapy Medicinal Products (ATMPs).** ATMPs offer enormous potential for better patient outcomes, and the potential to deliver highly personalized solutions.
- **Accelerated drug development.** Digital innovation and modelling has the potential to reduce developments times, particularly with respect to stability testing.
- **Smart packaging.** Digitalisation could enable more personalized packs and improve pack formats.

3) Stakeholder survey

The stakeholder survey responses suggested that the biggest benefits are likely to be realized at the production stage of the supply chain. These benefits included:

- reduced costs;
- the ability to treat higher impact diseases by manufacturing lower volume medicines;
- better quantification;
- more personalized medicines;
- more flexibility regarding the dosage forms; and
- improved availability of medicines for patients.

These opportunities will be realized through the development of capabilities related to flexible manufacturing, and would lead to more personalized offerings for the patients.

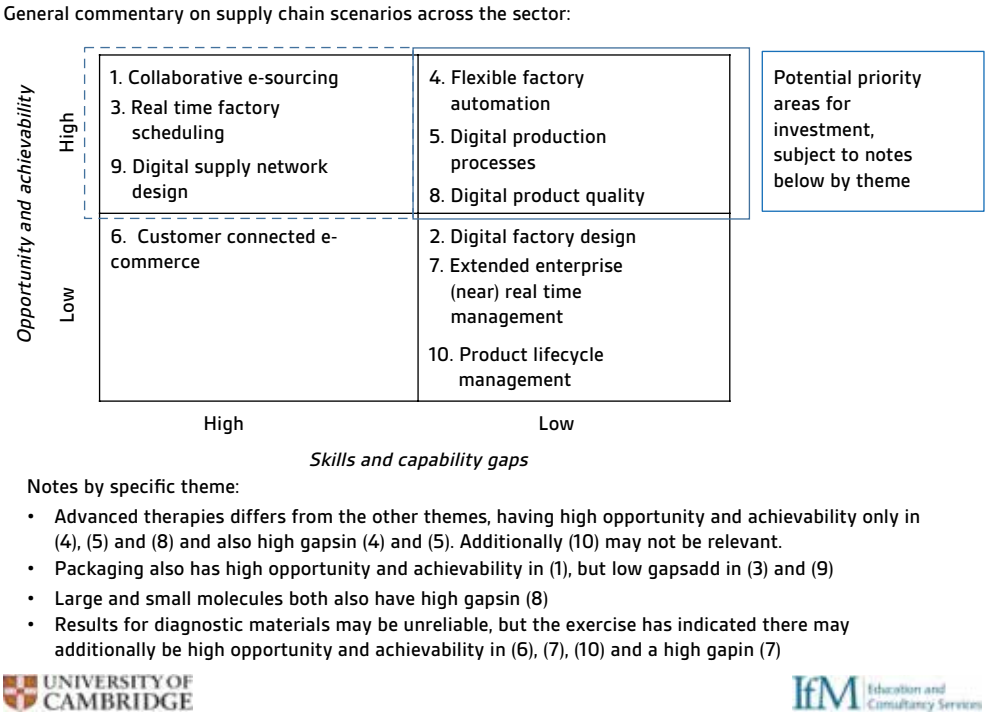
The key competences that need to be developed are:

- supply chain and business models;
- new processes;
- sensor technologies; and
- automation and robotics.

4) Supply chain capability workshop

This workshop and its attendees identified a number of priority areas for investment. Figure 1 identifies the scope of the opportunities and their achievability compared with the skills and capability gaps currently existing within them,

Figure 1 – Supply chain capability assessment



The high priority given to scenarios 3, 4, and 5 means that innovation in the smart factory is likely to be of significance to the UK medicines manufacturing industry. However scenario 2 (digital factory design) was not considered to be a high priority by workshop attendees, although this might be due to a lack of awareness in the use of digital factory design in other sectors where it currently adds significant value. It is likely that digital factory design will be a key enabling technology in the creation of flexible, automated factories.

5) Standards roadmapping workshop

Workshop attendees identified a number of priorities for standards programmes within the four main medicines manufacturing sectors. These were:

- **Advanced therapies.**
    - Data collection. This would be needed to increase the value of the data and the ability to cope with increasing volumes. It would also identify what data are appropriate and enable links with metadata.
    - Data sharing. Many of the advanced in ATMPs will require data to be shared in a safe and manageable way. Development of standards in this area could help define how to share data across the manufacturing supply chain, how best to share data during pre-competitive collaboration, and also how to share data with regulators.
- **Large and small molecules.** A priority in both these areas was to enable the integration and security of patient data. Development of guidance and standards in this area could include:
    - data aggregation and mining;
    - storing data ethically and securely; and
    - integration with smart packaging data.

a) **Small molecules** - Two of the highest priority standards programmes identified by workshop attendees were:

- Modelling verification and validation. The need for reliable and consistent model outputs in support of agile and highly personalized medicines would require programmes in:
  - data handling and pre-processing;
  - verification and validation of models;
  - clarification with regulators on how to use such digital capabilities;
  - consensus on how to use a systems based approach to describe the whole process; and
  - links with smart packaging data.

- Manufacturability underpinned by "quality by design". A digital manufacturing environment requires a different decision framework to enable the transformation of a concept into a viable drug product. The use of digital technologies will enable this process to happen quicker, cheaper, and more easily. However, this will require a common language to be developed, as well as open standards and common data formats.

b) **Large molecules** - Workshop attendees identified the connectivity of plant equipment as being necessary to increase quality and speed of drug development and manufacture. Connectivity of plant equipment would require the creation of standards to achieve connectivity across the development and production processes, as well as across the whole supply chain.

- **Packaging.** Workshop attendees from this sector identified two main priorities:
  - Smart supply chain feedback loop. Development of a standards programme in this area could enable serialisation to all stock tracking, and also recipient resupply requirements to support "just in time" production.
  - Smart packaging and labelling. There is an increased need for packaging to be more sustainable, patient friendly for an ageing population, secure, and also with enhanced safety features. Development of a standards programme in this area could address pack design, digital leaflets, guidance on digital tools for adherence, and smart labels.

2 Main challenges to be addressed by standards

The main way that standards can help the UK medicines manufacturing industry adopt digital technologies is to contribute to the UK becoming a global pioneer in various aspects of medicines manufacture, such as:

- Returning API production, biotech, and packaging production back to the UK.
- Retaining the UK's position as one of the leaders in advanced therapies production.

BSI will help the UK medicines manufacturers achieve this in a number of ways, including:

- better connectivity and feedback directly from patients, including clinical and post-launch;
- working at lower defect rates and reducing waste both in production and through poor patient compliance;
- encouraging companies within the medicines manufacturing supply chain to collaborate more effectively to meet patient needs;
- developing more flexible, responsive, and lower cost automated production processes; and
- better control of inventories through higher visibility of supply chain logistics.

The main challenges that BSI can work with stakeholders to address are:

- **Smart factory.** Standards can help capture and transfer good practice from other sectors in areas such as virtual commissioning, modelling, and automated and flexible production. Standards can

also contribute to the creation of lower cost plug-and-play technologies by enabling higher levels of interoperability. One important role standards will have to play is in achieving necessary levels of quality and improved defect rates or DFDM. DFDM will include design of the product, the process, and also the production environment and supply chain.

- **Integration with patient data.** Finding a way to use patient data in a way that can lead to better targeted medicines delivery would need those data to be integrated with manufacturing and product data. This would need the data architectures to be opened up in a controlled manner so that integration would be secure and effective, and would meet all regulatory requirements with respect to privacy.
- **Smart packaging and devices.** These technologies will become the main way that patient data can be accessed. Some of these benefits can currently be realized at the clinical trial stage but there is additional value to be created from understanding how effective a medicine is in use in the real world. Better monitoring can help manufacturers understand demand more effectively, and also lead to better patient outcomes through increased adherence to their prescription. This is particularly applicable to the ageing population. Many of the benefits of digitalisation of medicines supply chains depend heavily on the development and use of smart packaging. Packaging technology is already heavily standardized, and so any action regarding standards creation and adoption needs to take this into account.

3 Recommendations

Recommendation 1: Identification of smart factory good practice from other sectors

BSI will establish how manufacturing sectors more advanced in their digitalisation journey are using digital technologies in smart factory, product, process, and network design, and codify this as good practice. Aspects of this will be described in a PAS on Design for Digital Manufacturability.

Recommendation 2: Interoperability and architectures

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Recommendation 3: Working with others to integrate patient and manufacturing data

Standardization of data formats at trial phase would speed up time to market. Additionally there are huge benefits from assessing the effectiveness of medicines directly from patients at the post-launch phase, which helps to understand how effective a medicine is in the real world. One particularly important barrier is that there needs to be a mechanism for deciding if data can be shared or not, due to issues including privacy, confidentiality, and ethics. BSI proposes to establish and develop a decision-making framework for data sharing, with input from NHS stakeholders.

Recommendation 4: Standards strategy for smart medicines packaging

This is a challenging area because of its complex nature, partly due to it being an integration of mature and newer technologies. There are currently standards existing for packaging using radio-frequency identification (RFID). For instance, ISO Technical Committee 122 *Packaging* has already published a number of standards

relating to RFID applied to freight containers, returnable packaging, transport units, product packaging, and product packing. There are also standards to enable quality management of medicinal product manufacturing, but there is nothing that links medicinal product packaging with RFID. BSI will establish how best to use the domestic, European, and international standards activities to unlock the potential of smart medicines packaging manufacture in the UK.

Recommendation 5: Service innovation by manufacturers for better patient outcomes

There is an opportunity for medicines manufacturers to work directly with healthcare providers to use digital technologies to improve patient outcomes via better diagnostics, adherence, education, and training. This would require the digitalisation process to be accompanied by a shift in ethos from a product centric approach to more of a service offering. These services, involving the timely and lower cost delivery of necessary medicines, would be much higher value than are currently delivered and would make the UK a world leader in their provision. Many of these principles of user-centric services are described in PAS 280 *Through-life engineering services – Adding business value through a common framework* and we propose to establish how best to implement this service ethos into the medicines manufacturing sector.

Annex 1 – Domain research report

A1.1 Introduction

Background

During 2016 and early 2017, IfM Education and Consultancy Services (IfM ECS) and BSI collaborated in a study which confirmed that the widespread adoption of digital standards and good practice is a critical element in accelerating change. IfM ECS then supported BSI in providing input to the standards strand of the Made Smarter Review. This work focussed on defining the immediate and long term optimal landscape of standards to accelerate the capability and competitiveness of the UK's digital manufacturing supply chains, leading to the development of world-class, end-to-end solutions.

Adoption of digital technologies requires ensuring interoperability between data and machines, developing assurance to promote trust in data-based decision-making, and aligning supply chain behaviour. Standards are a critical 'enabler' to digital manufacturing and a further programme is proposed by BSI to encourage small and medium-sized enterprises (SMEs) in the uptake of digitalisation, and to encourage innovation in products and services along the value chain. BSI proposed three immediate elements of this new programme:

1) Specification for security minded management of digital manufacturing processes.
2) Vocabulary for the design and delivery of through life engineering services.
3) Standards roadmap for the medicines manufacturing sector.

This research report builds on the approaches and outputs of this earlier work, and concerns item 3, development of a standards roadmap for the medicines manufacturing sector.

Purpose

The primary objectives of this research report are:

- To provide an overview of relevant current formal standards published by National Standards Bodies (NSBs) or Standards Development Organisations (SDOs).
- To provide an insight of what the medicines digital manufacturing industry encompasses including:
  - Trends and drivers within the medicines digital manufacturing industry, these include key challenges that the market needs to address to embrace the new technologies required.
  - Digital manufacturing value propositions, new technologies insight factory gate and outside factory gate which will influence the progression how medicines digital manufacturing.
  - Digital manufacturing through life capability development and supporting research and development.
  - Enablers detail the standardization, legislation and regulations from formal and private industries.

A1.2 Research methodology

Overview

Desk-based research has been undertaken for standards identification, collating information on industry standards, key players, initiatives, regulatory bodies and legislation. An initial meeting with Natalie Grant, Amy Rowley, Ben Sheridan and BSI's Knowledge Centre confirmed the format, keywords and delivery of this domain research report.

Policies and legislation

Web searches helped identify the correct sites to gather policy and legislation from the U.S Food and Drug Administration, the EU Commission Directives and Regulation and relevant government bodies. This section is meant to cover legislation that relates to the Good Manufacturing Practice (GMP) in respect of medicinal products.

Formal and private standards

Desk based research was conducted making use of BSI's in-house standards database, to identify formal standards relating to medicines digital manufacturing. All pure European (CEN) and International (ISO) standards, pure British Standards (BSI) as well as national standards from European countries have been included in the results. Draft for public comment documents are also within the results which provide an outline of standards work currently in development.

The keywords selected for the desk research were drawn from key documents provided by IfM and narrowed down using the 'enablers' in standards terms from the sector landscape template (demonstrated as the horizontal in Table 1), and by medical sector derived from the researchers understanding of the medicines digital manufacturing field (demonstrated as the vertical in Table 1). Search queries were created by combining keywords from the 'sector verticals' and the manufacturing horizontals to find the most relevant standards.

Table 1 – Standards landscape keyword search

	API and Molecular Process Innovation	**Biotechnology**	**ATMP Manufacturing Innovation and Production**	**Packaging, Labelling and Distribution**
Enablers	Molecule, Pharmacology, Pharmaceutical Technology, Drug, Medicine, Chemical technology processes, chemical engineering, chemistry	Biotechnology, Bio Processing, biopharmaceutical, Microbiology, Bioassay, Biocompatibility, Cytometry	Genetic Product, Somatic Cell, Tissue Engineer(ing), Medical Technology, Genetic Engineering	Packaging, Packaging Materials, Packages, Dose(Drug), Sterilization(hygiene), Containers, Clean Rooms, Drug administration, Labelling, Machine readable, Codification, RFID, Transport Packing
	AND	AND	AND	
Interoperability	Common language, Authentication, Network, Flexible, Administration, Automation systems, Guidance systems, Interface(s), Process Control, Parallel Bus, EDP, Information exchange, Data processing, Medical Informatics	Common language, Authentication, Network, Flexible, Administration, Automation systems, Guidance systems, Interface(s), Process Control, Parallel Bus, EDP, Information exchange, Data processing, Medical Informatics	Common language, Authentication, Network, Flexible, Administration, Automation systems, Guidance systems, Interface(s), Process Control, Parallel Bus, EDP, Information exchange, Data processing, Medical Informatics	Common language, Authentication, Network, Flexible, Administration, Automation systems, Guidance systems, Interface(s), Process Control, Parallel Bus, EDP, Information exchange, Data processing, Medical Informatics

(*Continued*)

Table 1 – Cont.

Supply Chain	E-sourcing, Enterprise resource planning, Connected automated replenishment, Digital supply network, Electronic data interchange (EDI), Optimisation, End-to-end, Real time supply chain, Resource optimisation	E-sourcing, Enterprise resource planning, Connected automated replenishment, Digital supply network, Electronic data interchange (EDI), Optimisation, End-to-end, Real time supply chain, Resource optimisation	E-sourcing, Enterprise resource planning, Connected automated replenishment, Digital supply network, Electronic data interchange (EDI), Optimisation, End-to-end, Real time supply chain, Resource optimisation	E-sourcing, Enterprise resource planning, Connected automated replenishment, Digital supply network, Electronic data interchange (EDI), Optimisation, End-to-end, Real time supply chain, Resource optimisation
Digital Manufacturing	Identification methods, Digital factory, Process simulation, Computer-aided manufacturing (CAM), Virtual manufacturing, Digital production, Continuous process*, Real time manufacturing, Predictive maintenance, Sensor enabled network, Industrial internet of things (IIoT), Product lifecycle management, Sensor(s), Robot(s), Modular	Identification methods, Digital factory, Process simulation, Computer-aided manufacturing (CAM), Virtual manufacturing, Digital production, Continuous process*, Real time manufacturing, Predictive maintenance, Sensor enabled network, Industrial internet of things (IIoT), Product lifecycle management, Sensor(s), Robot(s), Modular	Identification methods, Digital factory, Process simulation, Computer-aided manufacturing (CAM), Virtual manufacturing, Digital production, Continuous process*, Real time manufacturing, Predictive maintenance, Sensor enabled network, Industrial internet of things (IIoT), Product lifecycle management, Sensor(s), Robot(s), 3D Printing, Modular	Identification methods, Digital factory, Process simulation, Computer-aided manufacturing (CAM), Virtual manufacturing, Digital production, Continuous process*, Real time manufacturing, Predictive maintenance, Sensor enabled network, Industrial internet of things (IIoT), Product lifecycle management, Sensor(s), Robot(s), Modular
Governance and Security	Public Health Protection, Corporate Governance, European Communities, Confidentiality, Administration, Risk assessment/ analysis, Data security, Laboratory accreditation, Management	Public Health Protection, Corporate Governance, European Communities, Confidentiality, Administration, Risk assessment/ analysis, Data security, Laboratory accreditation, Management	Public Health Protection, Corporate Governance, European Communities, Confidentiality, Administration, Risk assessment/ analysis, Data security, Laboratory accreditation, Management	Public Health Protection, Corporate Governance, European Communities, Confidentiality, Administration, Risk assessment/ analysis, Data security, Laboratory accreditation, Management
Assurance and Certification	Quality assurance, Quality assurance system(s), Quality management, Certificate(s), Patent(s), Specification (Approval), Conformity, Marking, Testing, Licence(s)	Quality assurance, Quality assurance system(s), Quality management, Certificate(s), Patent(s), Specification (Approval), Conformity, Marking, Testing, Licence(s)	Quality assurance, Quality assurance system(s), Quality management, Certificate(s), Patent(s), Specification (Approval), Conformity, Marking, Testing, Licence(s)	Quality assurance, Quality assurance system(s), Quality management, Certificate(s), Patent(s), Specification (Approval), Conformity, Marking, Testing, Licence(s)
Other	Autoclave(s), Smart Device(s)		Autoclave(s), Smart device(s)	

Please also be advised that for the purposes of the domain research, searches on medical devices have not been included.

Key players

In addition to the formal standards research, desk-based research was conducted to identify UK stakeholders relevant to the scope of the project. There are many more potential stakeholders in this field; further searches would need to be conducted.

Resources

The method for conducting this research was all desk-based and involved: the use of BSI Standards databases and public sites, internet, and search engine research; as well as documents provided by the IfM, and the European Commission Eur-Lex database and the U.S Food and Drug Administration website.

- **In-House Standards Database**

  A bibliographic standards reference database, which indexes worldwide standards, the formal European and International standards scope of this research is covered by our database, however publications from informal bodies are limited.
- **Eur-Lex**

  Eur-Lex is a service providing free access to legal texts, directives and regulations of the European Union via its website www.eur-lex.europa.eu.
- **U.S Food & Drug Administration Website**

  The fda.gov website provides access to all FDA guidance, regulation and approvals via multiple databases and directories.

Limitations

The author of the domain research report is an Information Professional within BSI's Knowledge Centre. The team has experience of researching the global standards landscape by using databases and web searches with pre-determined search criteria, and has no subject specialism in any one technical area. The team relies on technical experts for the analysis of the data that is produced and are therefore unable to provide interpretation of the standards research. The team can however give findings based on factual information.

A1.3 Trends and drivers

Global trends

Social

- Health systems are coming under pressure due to not only an aging population but also as the burden of chronic disease is soaring, exacerbated by dietary changes and more sedentary lifestyles. A Technology and Innovation (T&I) strategy will help secure access to better and more affordable treatments for all patients.
- The current situation is not-sustainable, a T&I strategy is a part of a disruptive technology driven collaboration that tackles the big challenge head on, and quickly.[2]
- The MHRA Business plan for 2017/18 details the challenging financial context that they are operating in; the regulatory environment has become more competitive and increasingly global. Brexit and the Agency's uncertain future mean that financing for the agency is uncertain.

2 (Association of the British Pharmaceutical Industry, 2013)

- For the National Institute for Biological Standards and Control (NIBSC), the primary objective is to continue to grow and invest to remain the global leader in biological medicines.[3]

Technological

- Big Data is a common theme underpinning many of the proposed solutions to the "Big Challenge" discussed above, the challenges facing the NHS, the life sciences research community and the pharmaceutical industry.
- Big Data technologies make it easier to work with large datasets, link different datasets, detect patterns in real time, predict outcomes, undertake dynamic risk scoring and test hypotheses.
- The above data driven applications span the value chain from drug discovery to healthcare delivery and there is real long-term potential to underpin breakthroughs in clinical development and safety monitoring of medicines.
- Healthcare data can be structured or unstructured data from anonymized electronic health records and biometric data sources, big data technology has been used in prescriptions, compliance and response patterns, pathology results and laboratory tests and probabilistic models of outcomes.[4]
- Technology enabled manufacturing, including process automation, Flexible Manufacturing Systems (FMS) and Computing Integrated Manufacturing (CIM) is now influencing the future of highly flexible process automation. Driven by data captured by intelligent tags and sensors and shared across a wireless mesh, this supports multivariate control algorithms that drives the industrial process to its optimal point, integration with "just in time" supply chain deliveries leading to the co-ordination of the entire process by a modular, networked facility automation system.[5]

Economic

- While the UK has a strong medicines manufacturing industry, with more than 1,300 companies producing £26 billion in exports in 2015, its relative impact has declined in recent years.[6]
- The T&I strategy is a strategic goal which will help lever the UK as the destination of choice for investment in development and manufacturing and will ultimately secure access to better and more affordable treatments for patients.[7]
- The Advanced Therapies Manufacturing Taskforce (ATMT) was set up to identify actions that the UK must consider taking in order to anchor manufacturing of advanced therapies in the UK, and capture investments to secure the UK position as a world class hub. Their recommended actions include strengthening and securing an internationally competitive fiscal landscape to attract investment, target and capture internationally mobile investments through a proactive and simplified process of engagement, maintain science and innovation funding to support industry developing cutting-edge technologies, set out an end-to-end talent management plan to secure the relevant skills for emerging manufacturing technologies, clearly set out a swift, predictable and viable route to market for these innovative products, give industry confidence that the UK is a progressive global hub and develop a long-term regulatory strategy, and plan for the medicines and healthcare products regulatory body (MHRA) to lead in global standards, supporting the scientific activities and international outreach of NIBSC.[8]
- The UK has a strong and well established pharmaceutical industry, composed of a mix of domestic companies and inward investors. Over the last decade the industry has evolved with small biotech's being spun out of universities. The sector is characterised with significant direct investment with high exports – £25.8 billion, but this is essentially neutralized by pharma imports of £28.7 billion.

3 (MHRA Business Plan, 2017)
4 (Association of the British Pharmaceutical Industry, 2013)
5 (Road4FAME, 2015)
6 (.gov.uk, 2017)
7 (Medicines Manufacturing Industry Partnership, 2017)
8 (MMIP Action Plan, 2016)

- The pharma sector has the opportunity to challenge this with recent changes such as: improved fiscal incentives, a skills review, earlier collaboration with regulators and potential funding. The UK has strengths for discovery, development and manufacturing of new medicines which will assist in building up the exports including a strong academic base in chemistry, pharmacy, biochemistry and biomedical sciences amongst others, established non pharma chemical manufacturing industry collaboration, research collaboration and funding by companies like AstraZeneca and GlaxoSmithKline, and by having the MHRA as a progressive regulator and NIBSC developing the majority of global standards for biological medicines.
- The UK now needs to leverage and connect its current capabilities and plug the identified technology and facility gaps that will position the UK as a 'one stop shop'.[9]
- The ATMT identified approximately 250 overseas-based companies who are ready to invest in the next two to three years. This means that by 2025 the global market could be worth (base estimate) £14 billion across cell and gene therapy products within the broader sector of ATMP's. The projected 2025 UK market size sits at £0.4 billion, which is only possible if the UK targets this investment by making available competitive or loan/grant funding.[10]

Environmental

- The environmental impact of pharmaceutical manufacturing is a key trend in the medicine manufacturing field. The concept of green chemistry will help to minimize the environmental burden of medicine manufacturing by reducing waste using tools such as, lifecycle analysis throughout the development process to aid decision making and, help to understand the environmental impact.
- With the non-classical therapeutic agents a new set of challenges face the pharmaceutical industry, the technology and innovation proposal must factor in the environmental impact of these new agents and strategically work to minimize process waste. The advantage of doing this is not only a sustainability one but also potentially a value added cost benefit.
- Environmental considerations must also be applied to the packaging materials. All medicinal products must be protected throughout the supply chain and these have to meet performance expectations, all materials must be stable and offer acceptable shelf life and protect against, environmental influence, biological contamination and physical damage.[11]

Political

- The MHRA early access to medicines scheme (EAMS) aims to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorization when there is a clear unmet medical need. Under the scheme, the MHRA will give a scientific opinion on the benefit/risk balance of the medicine, based on the data available when the EAMS submission was made. The opinion lasts for a year and can be renewed.[12]
- The Information Governance Review of March 2013 outlined the data security challenge of technological advancement and the potential to make use of data to assist in the development of digital manufacturing technology in medicines, where the integrity of the health and social care services with users relies on the trust that the sensitive matters that they discuss with a doctor, nurse or social worker is not being improperly disclosed elsewhere. However, people also expect professionals to share information with other members of the care team who need to co-operate to provide a seamless, integrated service. The term used to describe how organizations and individuals manage the way information is handled within the health and social care system in England is "information governance".[13]

9 (Medicines Manufacturing Industry Partnership, 2017)
10 (MMIP Action Plan, 2016)
11 (Medicines Manufacturing Industry Partnership, 2017)
12 (EAMS, 2017)
13 (Caldicott, 2013)

- The Life Sciences and Industrial strategy report sets out that there must be more fiscal investment in SME UK science companies in order to see sustainable growth and retention of these businesses.
- The UK has relied heavily on angel investment and venture capital (VC) support for its SME sector which allows little time for companies to grow and scale. Most UK VC companies lack the deep pools of risk capital seen in American equivalents which, in turn, appears to condition UK life sciences companies' ambition and approaches to raising private and market finance.
- The UK government should optimize the fiscal environment for manufacturing investment to drive investment in industrial buildings, equipment and infrastructure for manufacturing and late stage R&D. As well as consider nationally available financial incentives to support capital investment in scale-up, which ultimately supports attracting further large and small capital investors in life science manufacturing facilities in the next five years.

Legal

- Biological medicines are set to be of increasing importance in the healthcare landscape over the next five years with a greater number of products and ATMPs available as well as representing an increasing proportion of healthcare expenditure. The MHRA is a part of implementing a value and innovation strategy, where standardization has an important place in the assurance of quality and the enabling of innovation.
- As part of MHRA's 2017/2018 strategy, it is implementing the Innovation Office & Regulatory Advice service for Regenerative medicine (RASRM) which will work through the Innovation Office to provide joined-up regulatory and scientific advice and customer service to industry.
- The MHRA will also seek to evaluate the effectiveness of the changed regulatory process for the reclassification of medicines. The aim of the new process and timetable is to streamline the reclassification process by providing a specific, dated, predictable timetable with key milestones for contact between the assessors and the applicant.
- Further specific deliverables for the MHRA in 2017/2018 include; work with partners to develop a model for regulation in the post-Brexit environment throughout the year ahead, work closely with industry to develop and deliver proportionate regulation, and to embed robust process for regulatory policy development and delivery across the Agency.[14]

Market and customer needs

- There has been a shift from traditional small molecules to more innovative asset designs, cell and more recently, gene-based technologies have treated many thousands of patients globally but their potential is far from being realized. This move to more complex molecules opens up exciting opportunities.
- The challenges with this market shift is that there is more complexity in the synthesis steps, more highly potent products, smaller volumes, more products licensed and growing asks for patient-targeting and advanced packaging solutions and devices.
- The technology challenges with these more complex molecules are ultimately the Good Manufacturing Practice (GMP) of them to get them into the clinic early. Accelerated development tools are needed as many of these new chemical entities will require novel processing.[15]
- The ultimate vision is for improved manufacturability of current and future biopharmaceuticals, an improved understanding of bio manufacturing processes through improved analytics and characterization tools and techniques.

14 (MHRA Business Plan, 2017)
15 (MMIP Action Plan, 2016)

Challenges and threats

- The pharmaceutical supply chain is one of the most complex supply chains in the world, varying challenges include managing active materials, short shelf life, and high levels of regulation, mean that effective tracking of components and finished products (outside factory gate) throughout the supply chain is vital.
- With the potential of small batch pharmaceuticals, this challenge will continue to be more and more complicated. Automated e-Sourcing using technologies such as "process robotics" could be the next evolutionary step. Enterprise process robots are different from traditional automation tools in that they automate an entire business process rather than a limited individual task approach.[16]
- Better knowledge within ATMP manufacture is needed on product viability and the impact of preservation techniques in processing is an area for more ongoing specialist innovation.[17] Big Data innovations will also play a role where real-time data can begin to influence the behaviour of the supply chain and manufacturing.
- The GS1 system for the NHS e-procurement aims to enable a single global source of master data to be created, captured and shared across multiple supply chains, from the brand owner through to the end user.[18]
- The Life Sciences Industrial Strategy states that Government funding, combined with charitable funding should create a program to attract up to 100 world-class scientists to the UK with substantial financial packages to support the growth of talent.[19]
- The appropriate training and professional development courses need to continue to be developed, as well as making use of Centres of Excellence as training grounds not only for graduates but also for apprentices. Industry and SMEs should be encouraged to offer internships and placements for graduates.
- With any new and rapidly evolving industry there is always the need to support its growth with a suitable skilled workforce that cannot only create hardware needed to manufacture the product, but also develop and manage the subsequent quality and consistency of the product from small lab scale to full commercial supply.[20]

Opportunities

- Short term plans should include a shift from ad-hoc collaboration to more streamlined and efficient sharing of assets.
- There is a need to develop the entrepreneurial framework and ecosystem to support increased connectivity between companies. Policy interventions may be required at a European level to support this change.
- A legal framework is required to allow contracts to be rapidly set up between companies specific to manufacturing applications.
- There is a need for standardized data formats for interoperability between client and service providers to facilitate a service based on data transfer.[21]
- The shared objective of industry and Government should be to deliver outstanding patient outcomes. The NHS has made positive initial steps towards being more transparent by focussing on patient care; it should continue to pursue an ambitious agenda using independently-assessed publically available outcome metrics at a national and regional level.[22]

16 (Barratt, 2016)
17 (MMIP Action Plan, 2016)
18 (Dept of Health, 2014)
19 (Bell, 2017)
20 (Medicines Manufacturing Industry Partnership, 2017)
21 (Road4FAME, 2015)
22 (Bell, 2017)

- 2020 should see technology and analysis of Big Data allowing better decision making, and ultimately more personalized therapies.

A1.4 Sectors of activity

Small molecules

- 2020 should see the optimization of medicine dispensing based on more informed trials using big data.
- Industry 4.0 should play a large role in the manufacture of small molecules by 2020.

Biotechnology

- In the short term, the sector should see a common technology platform, new tools, technologies and assays and materials for viral vectors.
- The Factory of the Future (FoF) should be a part of the vision for 2020, it will have integrated equipment to research, make and measure, which will support the deployment of advanced technologies. The flexible manufacturing environment will need an appropriate digital and data infrastructure and supporting service.

Packaging

- All medicinal products need to be protected throughout the supply chain and these have to meet a range of standards and specifications. Materials must be stable, offer acceptable shelf life and protect against environmental influence, biological contamination and physical damage.
- More pack standardization will be needed as pharmacies and supply chain becomes more automated. Quality standards have improved organically as process development has increased, but realistically the pharma industry is not known as a pack or pack material innovator.
- Effective tracking of components and finished products throughout the supply chain is vital. Close collaboration is needed with the pharma community, along with logistics providers and customers to standardize where feasible.
- Digital solutions to enable patient centric design such as digital leaflets and guides will become more common, there is already a project underway through REMEDIES to digitize patient instruction leaflets onto mobile devices.[23]

Advanced therapies

- The technology sector around healthcare has exploded recently. Digital lifestyle devices, mobile health and telecare apps are now regularly seen.
- The UK can be a hub for innovative products, but it must provide a viable market for these products. The ATMT recommends that the UK establish a network for Cell and Gene Therapy Treatment Centres with Government funding delivered through a competitive process managed by Innovate UK, with widespread industry involvement to develop and implement the new systems needed to allow these Centres to operate.
- ATMPs are a new paradigm in healthcare and the UK currently has a leading position in ATMP discovery and development, supported by academia, innovation hubs (Cell and Gene Therapy Catapults), SMEs and now big Pharma focussing research in the UK. To position the importance of the opportunities that ATMPs offer, 939 clinical trials were underway in Q1 2016, and nearly 10% of these were carried out in the UK.

23 (Medicines Manufacturing Industry Partnership, 2017)

- The challenge is to translate this early research and development into manufactured products more consistently and on a commercial scale.[24]

A1.5 Manufacturing and supply chain competencies

Product technology

- There is opportunity to embrace the FoF concept in pharmaceutical manufacturing. Bringing in new technologies around electronics, sensor technologies, robotic technologies and through life engineering.
- The FoF will have connected and integrated equipment to research, make and measure, underpinning this there will have to be a total digital platform that will support deployment of advanced technologies. The flexible manufacturing environment will need an appropriate digital and data infrastructure and supporting service. The FoF principle will align with the wider Industry 4.0 initiative and act as a conduit of expertise across pharma and tiered suppliers.[25]
- Life science manufacturing makes a significant contribution to the UK economy. In 2016, UK life science exports were £30.7 billion, accounting for 11.4% of all manufactured goods.
- Many of today's medicines are manufactured through established platforms; the final drug product involves a complex supply chain and often takes 18-24 months. These established platforms are generally inflexible, and new processes and approaches are urgently needed to allow for more agility, to incorporate an increasing role for automation and digitisation, to adapt to new therapeutic and product modalities, and to adapt to the requirements for more personalized or "near patient" manufacturing.[26]
- Looking to the future, the highly flexible process automation world is likely to be driven by data capture by intelligent tags and sensors and shared across a wireless mesh to support multivariate control algorithms that drive the industrial process to their optimal point, supply chains supporting just in time deliveries, dynamic and complex order, delivery and return systems, power, cooling, heating and other infrastructure, and the co-ordination of the entire process by a modular, networked facility automation system.[27]

Materials competency

- Future processes looks to include nanomaterials and nanotechnology, Graphene, biologically manufactured materials and other lightweight material.

Management and operational

- Advances in technology will allow the medicines manufacturing industry to move to a more patient centric service, with better data capture and management of therapeutic effect, patient centric packaging design and dispensing devices.
- Beyond the core technical and analytical requirements, it is relatively easy to apply big data approaches to one organization, but where opportunities for further analysis of data sit across organizations there are potential commercial, legal and ethical barriers which need to be overcome.
- The pharmaceutical and healthcare sectors also face greater risks than many other sectors, since wrong treatment decisions can result in serious or irreversible harm to patients. As big data analytics and algorithms will increasingly lie behind commissioning and clinical decisions, they will have a significant impact on individuals and may shift public expectations and perceptions of accountability.[28]

24 (Medicines Manufacturing Industry Partnership, 2017)
25 (Medicines Manufacturing Industry Partnership, 2017)
26 (Bell, 2017)
27 (Road4Fame, 2015)
28 (Association of the British Pharmaceutical Industry, 2013)

Enabling technology

- The Technology and Innovation road map set out by the MMIP is not only driven by the goal of pharma being a key industry in leading UK economic production, but it could also enable an improved healthcare service.
- A key lever in delivering forward growth is the ability to get medicines into the clinic early; this will primarily benefit patient access but also crucially accelerate investment making this an important industry.[29]

Production technology

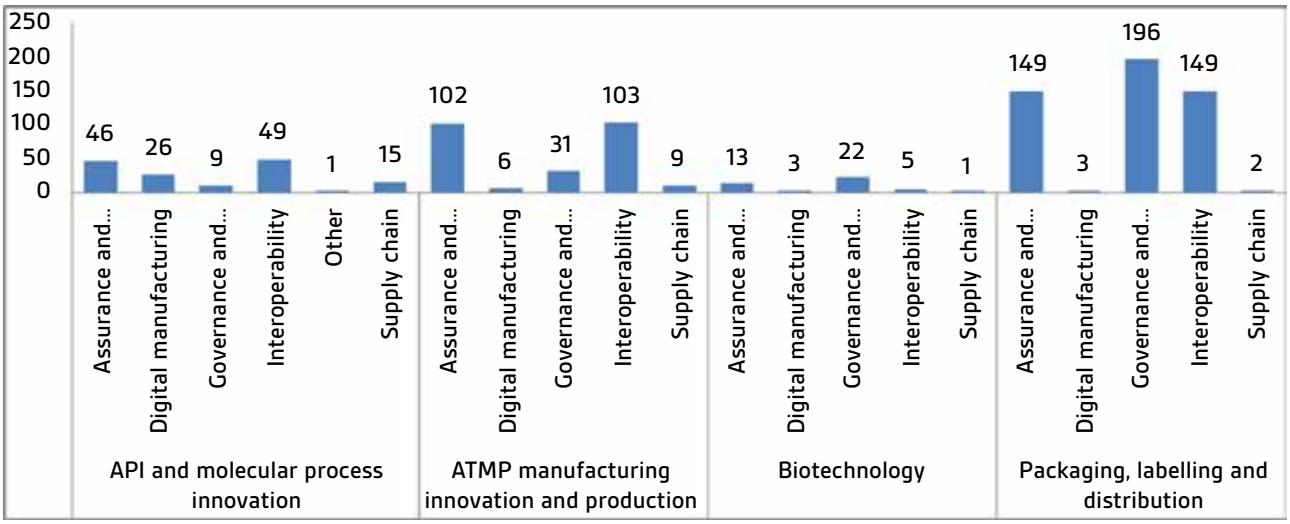
- A study has been done to evaluate the potential supply chain benefits of adopting continuous processing technologies for a diverse set of pharmaceutical products. The approach integrates upstream "continuous" processing considerations for the production of active ingredients and the final product formulation, with the downstream implications for packing and distribution. Currently, these upstream and downstream operations largely operate as decoupled operations with independent coordination and governance mechanisms, the new approach attempts to identify opportunities for an integrated end-to-end supply chain enabled by continuous flow technologies.
- Advances in continuous formulation to increase the bioavailability of APIs would significantly help reduce overall cost of goods and improve treatment adherence.[30]
- Analytic tools, process technologies and the MMIP Centres of Excellence can all contribute to quality by design being an initial and integral first step of pharma development.[31]

Supply chain

- Pharmaceutical supply chain is one of the most complex supply chains in the world, varying challenges include managing active materials, short shelf life and high levels of regulation, mean that effective tracking of components and finished products (outside factory gate) throughout the supply chain is vital.
- With the future potential of small batch pharmaceuticals, this challenge will continue to be more and more complicated. Automated e-Sourcing using technologies such as "process robotics" could be the next evolutionary step. Enterprise process robots are different from traditional automation tools in that they automate an entire business process rather than a limited individual task approach.[32]
- Better knowledge within ATMP manufacture is needed on product viability and the impact of preservation techniques in processing is an area for more on going specialist innovation.[33] Big Data innovations will also play a role where real-time data can begin to influence the behaviour of the supply chain and manufacturing.
- The FoF concept is set out to accelerate adoption of emerging and novel manufacturing technologies and transform the chemical/pharmaceutical manufacturing. The FoF will have connected/integrated equipment to research, make and measure, underpinning this there will have to be a total digital platform that will support deployment of advanced technologies. This will include analytical design, using data driven modelling to help develop suitable real time equipment including sensors.
- The supportive use of effective and high capability analytical measurement equipment that could in parallel offer real-time decision making that will maximize efficiencies, ultimately fully automating this 'make/monitor/correct' principle.

29 (Medicines Manufacturing Industry Partnership, 2017)
30 (Srai)
31 (Medicines Manufacturing Industry Partnership, 2017)
32 (Barratt, 2016)
33 (MMIP Action Plan, 2016)

Figure 2 – Spread of standards results across the 'sector verticals' and 'enablers'



Funding sources

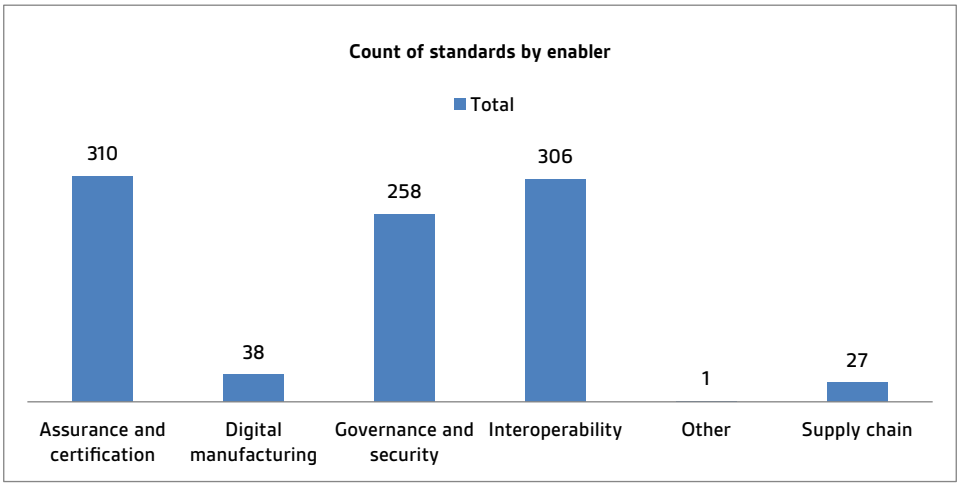
- Patient capital funds look to optimize their returns over the full development life of companies. These vehicles are essential for the scaling of life sciences companies. More of these are emerging and include Woodford Patient Capital fund, OSI, and Syncona.[34]
- The UK Government is a key source of funding for both basic biomedical science and translational science research, with £2 billion of life sciences research funded by Government through a number of mechanisms, including the Medical Research Council (£928 million in 2015/16) and the National Institute for Health Research (~£1 billion p.a).
- The Biotechnology and Biological Sciences Research Council, Economic and Social Research Council and the Engineering and Physical Sciences Research Council also provide substantial funding in lie sciences. This is bolstered by significant industry (~£5.7 billion p.a), European and medical research charities' investment (£1.6 billion p.a) from bodies such as Cancer Research UK, British Heart Foundation and the Wellcome Trust.[35]

A1.6 Findings

- The keyword searches identified 942 standards, published and in development, that relate to medical digital manufacturing.
- Within the 'enablers', the top areas of representation by standards were assurance and certification, governance and security and interoperability, in that order (see Figure 3).

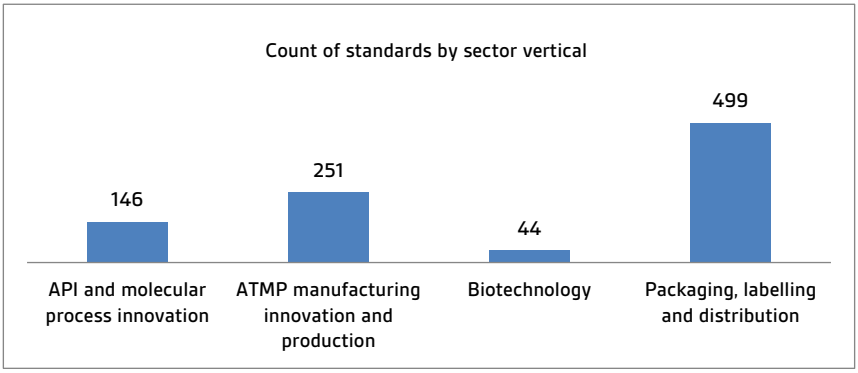
34 (Bell, 2017)
35 (Bell, 2017)

Figure 3 – Count of standards by enabler



- Within the 'Sector Verticals', the top area of representation by standards was within the packaging, labelling and distribution with 499 standards, followed by ATMP manufacturing innovation and production with 251. API and molecular process innovation found 146 standards and biotechnology found 44 (see Figure 4).

Figure 4 – Count of standards by sector vertical



- As part of the results some directives relating to packaging, labelling and distribution has been retrieved and kept within the results.
- Table 2 is an example of the cross section of standards found in the research, some are included multiple times in the research as results for the cross-section between the 'enablers' and the 'sector verticals'.

Table 2 – Example of cross section standards

Identifier	Standard title
ISO 13408	Aseptic Processing for Healthcare Products
VDI 6305	Technical Good Manufacturing Practice Application Guideline for Projects
ISO 11418	Containers and accessories for pharmaceutical preparations
EN ISO 8871	Elastomeric parts for parenterals and for devices for pharmaceutical use
EN 12128	Biotechnology Laboratories for research, development and analysis – Containment levels of microbiology laboratories, areas of risk, localities and physical safety requirements.

- There appears to be a clear gap in the standards in relation to IoT technologies, digital manufacturing within the medical field, as demonstrated by the standard searches only finding 38 results. This is also reflected in the limited results within the supply chain, an area seen as priority by the MMIP.[36]

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36 (Medicines Manufacturing Industry Partnership, 2017)

Annex 2 – Use cases

Smart labels. The use of smart labels could ensure the security of supply and enhance tracking and traceability & monitoring. Specific temperature/humidity and shock monitoring is driven more by the complex supply chains in the pharmaceutical industry but also is pertinent with advanced therapies and personalized medicines. Tracking and proof of provenance will become more critical post-Brexit as component and finished product location is important. Tracking will also assist in improving inventory management efficiencies and encourage waste avoidance (through stock outs/right offs, etc. which can be seen with pharma products which have shorter shelf lives). Security standards will need further review to incorporate issues such as digital piracy. An enabler for the use of smart labels will be serialization and the scope of this platform needs further investigation (beyond track and trace). One of the examples that smart labels and serialization can enable is the potential for electronic leaflets. This would simplify the supply chain considerably, enhance patient experience (and safety), reduce costs and improve sustainability.

Wearables and associated apps. The use of wearables has extended within pharma and although typically used in clinical trials to monitor patient progress, there is real potential to transfer these technologies over to commercial use. However, there are a number of risks associated with this, including data security and data accuracy. Existing standards will also need to be reviewed to ensure that there is a robust closed loop of diagnostics/data analysis/dispensing. Studies where wearables have been used to monitor the effectiveness of medicines include the Salford Study where patients' mobility was measured to show 'real life' improvements with a launched (Phase IV) drug. These Phase IV studies will become more important in justifying medicines value in the future. Wearables will also help manage disease and as a platform are fundamental to any digital revolution within healthcare management. Connected devices can come under this banner and companies like Propeller Healthcare are good examples to consider (and how standards can be enhanced to incorporate these 'add on' tools).

Active Pharmaceutical Ingredient Manufacture. The ADDoPT progam has been running for 2 years in the UK to review the opportunities for API manufacture using digital tools. It considers the impact of digital technologies on the API manufacturing process and would make an excellent case study. The aim of the ADDoPT project is to secure the UK's position at the forefront of pharmaceutical development and manufacture through more sophisticated definition, design and control of optimized pharmaceutical manufacturing processes using data analysis and first principle models in order to deliver new, higher quality medicines to patients, faster and more cost effectively.

The ADDoPT partners are working across the pharma value chain to define a system for top-down, knowledge-driven digital design and control for drug products and their manufacturing processes. This program will bring together a wide range of predictive models and insight from industrial case studies at four major pharmaceutical companies, allowing better targeted future experimentation, a better understanding of risk, and hence better design and scale-up for robust products and processes.

Digital design combines research insight and qualitative and quantitative mechanistic modelling to provide links between raw materials, manufacturing processes and the needs of the patient. It spans all unit operations, processes and procedures during the manufacture of medicines and their impacts, both upstream on the efficiency of product and process design, and downstream on product performance.

Digitisation and artificial intelligence to transform pathology and imaging. Data in the healthcare system provides crucial opportunities to fundamentally change the way health services are provided and developing digital tools, such as artificial intelligence (AI), are going to form an increasingly important segment of the life sciences sector. An area repeatedly highlighted as being ripe for innovation is pathology where modern tools should allow digital images to replace the manual approach based on microscopy. Systematic digitisation of pathology images could be readily established providing substantial efficiencies in the pathology service within the NHS, allowing the system to become increasingly virtual and reducing the need for every hospital

to have the full on-site set of pathologists. Importantly however, this also creates the opportunity to create AI-based algorithms that could provide grading of tumours and prognostic insights that are not currently available through conventional methodology. Again, this opportunity requires a partnership with the NHS to provide a steady flow of well-characterized samples in combination with good longitudinal data, as these two characteristics will inevitably allow the creation of the most competitive algorithms both in the immediate future and over time. No other system has the scale to provide such important data that, when captured, could produce a globally dominant commercial offering in this diagnostic space.

AI is likely to be used widely in healthcare and it should be the ambition to develop and test integrated AI systems that provide real-time data better than human monitoring and prediction of a wide range of patient outcomes in conditions such as mental health, cancer and inflammatory disease.

Therefore, there is a significant commercial opportunity; this is primarily an opportunity for digital and engineering medtech companies and could be embedded in the NHS to provide commercial evaluation capabilities.

Standards will be needed for any of these systems and there is the opportunity to use AI and as libraries are built confidence in this tool will grow.

The digital (smart) factory. Enhanced process design and truly connected processes will require data sharing and analysis across the manufacturing process. This will encompass not only small and large molecule manufacture but also the advanced therapies and more complex medicines. Digital management systems will analyse and adjust automatically and at the same time will have to comply to existing requirements expected in the medicines manufacturing industry but with more 'machine' intervention. The use of electronic notebooks and digital collaboration will be required, and standards will have to be updated to encompass the full potential of the digital factory. Industry 4.0 is driving this and having integrated standards to ensure seamless data transition/transfer has to be a core consideration.

Analytical capability and equipment. There is an ongoing need for more rapid and scalable analytical capability within pharma. With every new molecule there is a required analytical method and with increased availability of data and measurement, standards will have to evolve to meet these needs. With additional drivers such as quality by design (QbD) and process analytical technologies (PAT) the analytical technologies that meet required quality standards (and data management of these) need to be robust. With digital tools such as predictive technologies CQAs can be defined, and in the production process quality can be measured (and corrected using real and predictive data based on knowledge libraries) and effective controls implemented using novel detection/imaging systems (including cytrometry). This capability is even more important with small batch production. New methods and tools to measure more at scale up (e.g. biomarkers, purities) are needed and, as such, improved instrumentation will be developed. Standards in this area are imperative and examples of this include the use of technologies as developed by Anatune.

Automation and the use of robotics. The use of automation in pharma is by default extensive. Pharma has used automation for many years (throughout the development and manufacturing process). Automation ensures the ability to make quality, high-volume products safely and at competitive cost. Batch production has been a typical format and each batch is tested for quality. New platforms for some medicines manufacture include continuous processing and this will further improve manufacturing efficiencies, but this production method does not lend itself to batch production. With automation machine learning and connected part of the process can ensure a 'make/monitor/correct' capability but continuous manufacturing will challenge this even further. Having full closed loop manufacturing systems that are driven by automation will require standards for quality (including imaging), in all parts of the end to end process. Scale up and scale out (clinical to commercial) will have to meet regulatory standards and have transferability from both highly manual (early development) to fully automated (commercial) supply. Automation will continue to be an invaluable tool in the development process for high-speed evaluation of markers (including cell and gene therapy).

Additive technologies. The use of additive technologies in the life sciences (with a focus on medical devices and some surgical use) however with relation to pharma the implementation of this technology has been limited. Only one drug has been made using a 3D printed format and the limitations of additive technologies (primarily 3D printing) have been speed to manufacture, material properties, consistency and limited material choice. The potential growth of additive technologies is considerable and as materials and processes improve standards will have to be positioned.

Sensors and integrated electronics. The use of electronics and sensors will inevitably grow exponentially within pharma. They will be incorporated into wearables, packaging and even the medicines themselves. There are technical challenges with size, accuracy, batteries and this extends not only to the manufacture and assembly of these but also to any extractables and leachables, misuse, reliability and ultimate disposal. Standards for electronics already exist but, as they are enhanced, these standards will have to be consistently challenged. Standards will also be needed for the various components. The use of sensors and electronics will not only encompass pharma devices (including combination devices) but also diagnostic tools (these will continue to be a potentially valuable area for patient self-monitoring with diseases such as respiratory). Sensors and electronics are the route to getting and giving data and information and without them any digital revolution in medicine will not accelerate.

Advanced therapy medicinal products (ATMP). These are medicinal products for human use, i.e. gene and cell therapy or tissue engineered. The manufacture of these products has a range of challenges including characterization, contamination, comparability, potency, speed of production and product stability. Improved reproducible production will remain a core target and this will leverage more robust analytics to ensure the quality of products. Products are made in small volumes and their manufacture and dispensing requires a different standards approach. The ATMP industry will need to work closely with researchers/industry/healthcare providers to develop effective and relevant standards.

Accelerated drug development. Digital tools will have to enable faster development times. One of the rate limiting steps with current drug development is stability testing. This is currently done in accelerated and real-time scenarios and requires a new approach to reduce the risk of stability issues but without real-time testing. One step forward is the use of mathematical modelling to evaluate the stability of new molecules with a range of packaging materials. A wider knowledge is needed based on real-time versus mathematical model comparators and an appropriate library of data build. This approach will require new standards as the use of modelling for stability work is still an early development (compared to the traditional methods). Modelling could extend to cold chain packaging, etc.

Packaging standards (and standardization). With the advent of more personalized packs and pack formats (plus better printing and coding technology) there is the opportunity to review formats such as late pack customization. These formats need more standard pack formats which will flow through the supply chain.

Annex 3 – Supply chain capability and standards roadmapping

Contents

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Trends and drivers identified across the sector

Technological:

- Feedback loop capability - potentially integrating data along the value chain and supply chain
- Impact of simulation and models on design for manufacture

Economic:

- Cost of development

Market and customer need:

- Smaller lot size, Personalisation, Diagnostics and Stratified Medicine
- Individually tailored treatment, patient-centric design, move towards more high-value personalised medicines

Opportunities:

- Access to, and analysis of, large datasets across multiple organisations
- Management of data for patient derived materials flowing to the factory and personalised therapies flowing back

Challenges and threats:

- Skills shortage in experienced bio process engineers and other skills
- Optimisation of supply chain (storage, tracking of components, inventory, ...)
- Data storage, management and analysis
- Maintaining safety and efficacy in novel and innovative treatments
- No UK Packaging Manufacturing Capability

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General observations

- Customer benefits come from cost reduction, personalisation and availability
- Security of patient data is of very high importance
- Suppliers have major opportunities, but also significant gaps to close in production and optimising supply chain performance, underpinned by digital product quality
- Advanced therapies has unique challenges in combining value chain and supply chain integration around individual patients
- Large and Small molecules at the highest level have similar characteristics as regards digital manufacturing
- Whilst Packaging has fewer gaps, evidence exists that key areas such as e-commerce remain relatively immature
- The consultation has not generated a full set of input on Diagnostic materials and linkage should be made to other more focussed initiatives

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Recommendations relevant to standards development

- All three consultations (Web Survey, Supply Chain Capability assessment and standards Roadmapping) placed a significant emphasis on production and manufacturability
- Preliminary mapping of use cases onto the MMIP supply chain suggests that close supply chain integration is essential if the benefits of the use case are to be realised
- Across the value chain integration of R&D, design and production including scale up emerge as important areas for standards to support rapid exploitation of new drug discoveries
- Workshop delegates identified some specific opportunities within each theme for standards around data collection, sharing and security, modelling and verification, manufacturability, plant connectivity, smart packaging and supply chain feedback

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Programmes recommended by the workshop participants

Advanced Therapies

- Data collection
- Data sharing

Large and Small Molecules

- Integrate and secure patient data

Small Molecules

- Modelling verification and validation
- Manufacturability underpinned by 'Quality by design'

Large Molecules

- Connectivity of plant equipment

Packaging

- Supply chain feedback loop
- Smart packaging and labelling

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Next steps

Longer term next steps might include establishment of communities of interest to :

- Investigate further the 'through supply chain' requirements from Standards within particularly as regards Flexible factory automation, Digital production processes and Digital product quality
- Investigate further the value chain requirements from Standards particularly as regards the digital facilitation of scale up and manufacture of new pharmaceuticals
- Develop some or all of the programmes recommended by the teams in the context of the above

Immediately this report will input to a first draft 'final report' drafter by BSI for wider consultation including with the regulator

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Objectives and deliverables of the programmes

Objectives	Deliverables
• Establish what standards framework will enable uptake of digital technologies across all TRL levels • Develop an initial roadmap, as appropriate associated sub element roadmaps and business cases for the development of those standards • Understand the role of regulators and standards bodies in delivering the transformation • Input learnings to the wider standards development programme	• Desk research report and proposed frameworks for standards development • Interim report of scenarios, draft architectures and proposed use cases • Key standards areas for development, associated roadmaps and cases for action • Standards architecture for digital manufacturing of medicines • Integrated roadmap, executive summary of key findings (including the role of the regulator) and recommended next steps • Input to co-branded report developed by BSI

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Scope

The scope will include the full supply chain and value chain and align with the sub areas identified in the recently developed MMIP technology roadmap:

- Process innovation in all small molecules
- Process innovation in medium/large molecules
- Packaging
- Advanced therapy innovation & production

Consideration has also been given to inclusion of diagnostic materials, as these play an important part in patient-centric 'bedside' treatments. This was reviewed during the process with the conclusion that input should be made in parallel to other national activities already in hand

Results for each of the four MMIP sub areas have been collated through desk work for common themes facilitated by the common data structures and taxonomies

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High level approach

- Desk work to review outputs to date from BSI, IfM, MHRA, MMIP, CMAC, REMEDIES, AMSCII programmes and IS Challenge
- Framework and methodology development linking IfM research frameworks in the areas listed above
- Use case development and framework pre-population
- Web survey
- Industry workshop(s) applying the agreed frameworks, building on use cases and developing the architecture
    - Supply chain capability assessment
    - Strategic roadmapping
- Draft interim report preparation and circulation/review
- Final report review and completion

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Participant groups

Innovate UK lead technologists M&M and Life Sciences*

HVM Catapult

BSI*

KTN*

Relevant contributors to last workshop series

Regulators

Participants in:

- MMIP*
- MHRA*
- CMAC
- AMSCII REMEDIES, ADOPT
- RIHN
- **IS Grand Challenge participants??***

Note(*) Early discussion with lead confirmed scope, expectations and identified use cases

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Definition: Four sector themes

Advanced Therapy Medicine Products - innovation & production

Ensuring appropriate production (volume/quality/cost) of viral vectors with a focus to leverage academic research into industrialisation (and treatment)

Process innovation in all small molecules (85% of UK Pharma market)

Taking existing small molecule platforms (ie solid dose-tablets-) and making them faster and leaner using new manufacturing capabilities (including continuous)

Process innovation in medium/large molecules

Developing enhanced manufacturing methods for more complex medicines (typically sterile) including vaccines and high potency products

Packaging

This includes the primary, secondary and tertiary packaging of medicines plus disposable and refillable dispensing devices (including the use of digital tools)

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Definition: BSI Work Streams

Interoperability

A key requirement for global standards is that machines and data are platform – and format – independent, and that manufacturers are not locked-in to a particular system or vendor, which would negate many of the potential advantages digitization could bring and reduce competitiveness.

Supply chain capability

Many UK OEMs are pioneers in the use of digital technologies to add value to their manufacturing capabilities. However, there are real challenges and opportunities in enabling existing manufacturing companies to make the shift to digital, and also enabling digital companies to offer innovative services to the manufacturing supply chain.

Through-life end-to-end connected supply chains – design

Many of the opportunities for UK manufacturing and adoption of digital technologies arise from the connection of the manufactured product in use to the design stage. This builds on existing UK strength in design and R&D, particularly in high value manufacturing sectors such as aerospace, automotive, and pharmaceuticals, where the UK has a particular degree of comparative advantage.

Governance, security, and assurance of data

Alongside interoperability, this theme was consistently amongst the first to arise whenever discussing the role of standards in digital manufacturing innovation.

Through-life end-to-end connected supply chains – service innovation

Digitizing manufacturing technologies opens up the value chain and gives rise to opportunities for novel services that can improve performance. Examples include through-life engineering services that have been developed in the aerospace sector, new ownership models offered by toolmakers, and novel digital services (such as product lifecycle management) that could be offered by digital companies that are not currently operating in the manufacturing sectors.

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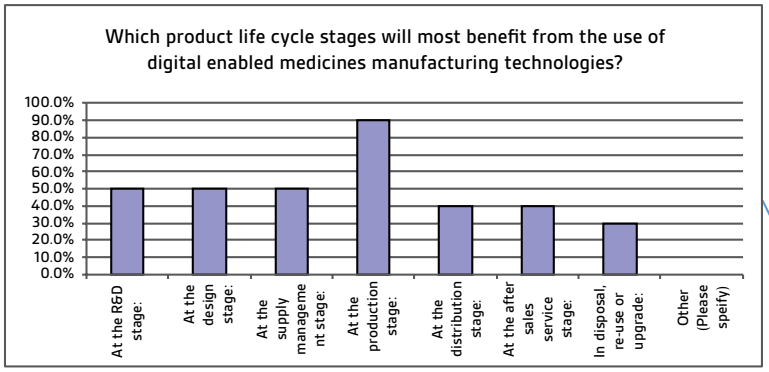
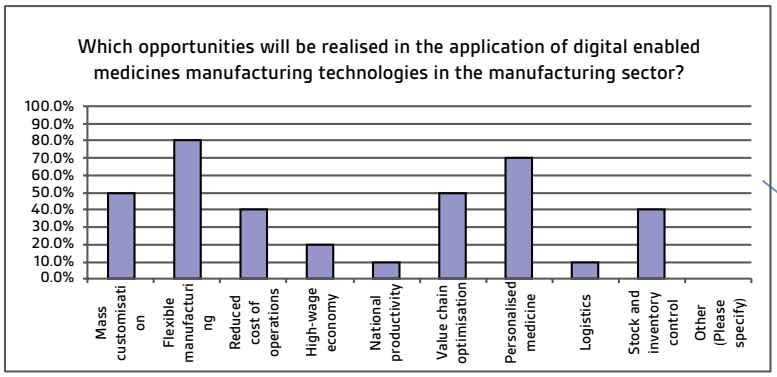
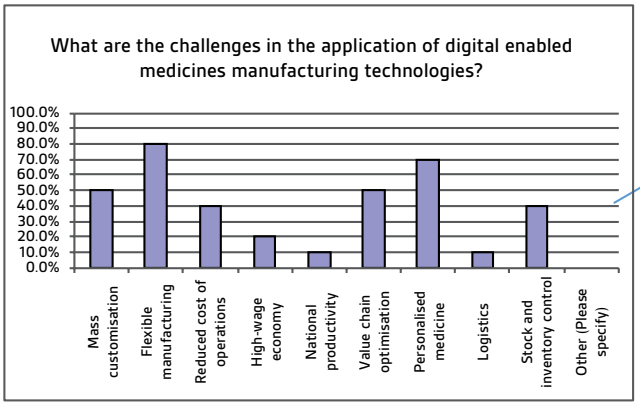
Web survey key findings



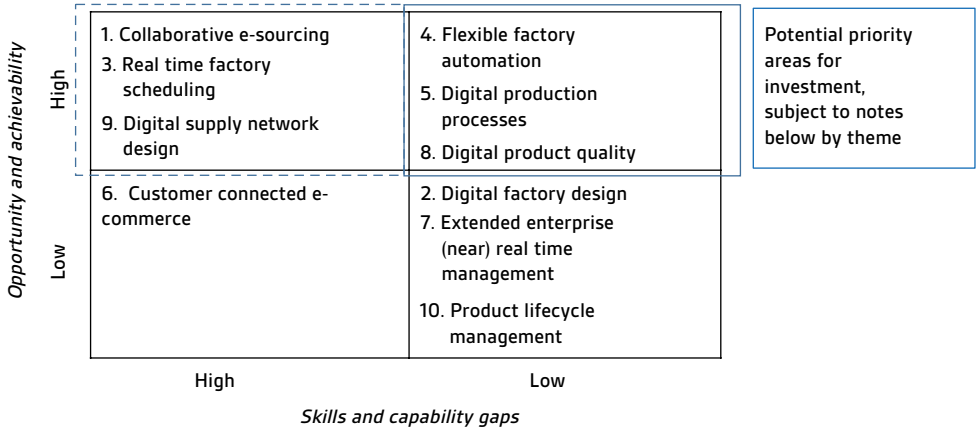




- Limited responses, primarily outside industry
- Customer benefits from cost, personalisation and availability
- Impact is seen as across the value chain, with emphasis on production
- Biggest opportunities lie in flexible manufacturing, value chain optimisation and personalisation
- The biggest challenges also lie in these areas

Supply chain capability assessment

General commentary on supply chain scenarios across the sector:



Notes by specific theme:

- Advanced therapies differs from the other themes, having high opportunity and achievability only in (4), (5) and (8) and also high gapsin (4) and (5). Additionally (10) may not be relevant.
- Packaging also has high opportunity and achievability in (1), but low gapsadd in (3) and (9)
- Large and small molecules both also have high gapsin (8)
- Results for diagnostic materials may be unreliable, but the exercise has indicated there may additionally be high opportunity and achievability in (6), (7), (10) and a high gapin (7)

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Advanced Therapies

Title	Description	Needed because	Proposed programmes
Data collection	Standardise data capture and augment data value: • Increased value of data and ability to cope with increasing volume • Standardise data capture generation of data and links to meta data	Current, bespoke, fragmented, inconsistent data sets limit there usefulness, e.g. difficult to share, high costs of developing data management systems etc. • Presently no unified way • Standards required for good practice and meta data architecture	• Good practice identification and sharing • Structured data standards
Data sharing	Share data in a safe, manageable and standardised way: • Increased value of data and ability to cope with increasing volume • Standardise data capture generation of data and links to meta data • Common data structure and protocol for sharing • Across partners and devices	Current approaches impair collaborative efforts, face regulatory challenges and data transfer lacks guidelines: • Presently no unified way • Standards required for good practice and meta data architecture • Protocols exist but the landscape is very messy • Standardised processes will improve efficiency • Need to restrict personal data in line with regulatory requirements	• Internal sharing of data within the manufacture process • External sharing pre-competitive collaboration etc. • Guidelines on data filtering and data sharing from a regulatory point of view to avoid conflicts of interest

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Large and Small Molecules

Title	Description	Needed because	Proposed programmes
Integrate and secure patient data	Fully realise the benefits of modern, effective, safe and efficient medicines through the potential of ethically sourced and processed patient data and establish who will keep this data – global store vs 'blockchain', in line with data protocols	We need better plan for modern medicines and manage the spiralling costs of life saving medicines that can't be sustained: • Global and aggregate data is essential to produce low cost effective medicines • All will need to be regulated • A better approach is required for low cost modern medicine • Existing standards protect integrity, good practice and UDPR but lack overarching perspective	• Data aggregation and mining • Storing data ethically and securely • Integrate with data from smart packaging Suggest urgently required and should involve patient representatives

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Small Molecules

Title	Description	Needed because	Proposed programmes
Modelling verification and validation	Delivering reliable and consistent model outputs to support agile manufacturing of personalised medicine	Regulatory interactions require a programme for robust model development, interconnected across the sector's operations • Reliable & consistent outputs from models are needed to satisfy regulatory requirements • Only way to deliver agile manufacturing platform for personalised medicine	• Data handing and pre-processing • Verify and validate individual models including involvement of SMEs and model specialists • Engaging external regulators to develop regulatory guidelines • Systems based approach to describe the whole process - integration and validation approach needs agreement if the individual elements are already validated Requires link with smart packaging data
Manufacturability underpinned by 'Quality by design'	Make a good manufacturing decision framework to enable molecule to medicine transformation to make drug product available to patient quicker, easier and more cost effectively • Set up common language • Open standards and common data formats • Cross body standards comparison	• Pharma is behind other sectors such a food and UK risks being left behind	• Review and collate current standards • Examine KPIs of product performance including innovation • Agree standards and definitions

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Large Molecules

Title	Description	Needed because	Proposed programmes
Connectivity of plant equipment	Increase the quality and speed of drug development and manufacture through standardisation of plant equipment communication Establish standard for connectivity of development and production processes and analysis across the supply chain	Disconnected plant equipment challenges quality and speed of drug development/ manufacturing • None exists today • Advantages include elimination of errors through reduced manual intervention, support for innovation	• Common standards • Pilot projects • Enterprise level and cloud level application This problem is not restricted to Large Molecules and we should look at an industry wide approach before finalising the programmes, which might involve innovative equipment suppliers, supply chain and producers as well as IT

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Packaging

Title	Description	Needed because	Proposed programmes
Supply chain feedback loop	Apply 'smart' to pharma logistics to the patient: • Item serialisation allows stock tracking • Recipients data gathering and resupply requirements fed to factory and support JIT production	50% waste, no clinical feedback, clinical alerts 'no stockouts' • Circular economy - 50% on unused drugs feedback reduces waste • Patient outcomes monitored by combining with Medtech allows automatic re-prescription • Few standards presently	• New 'message standard' rediscovery chain • Regional supply chain trial • User test including usability
Smart packaging and labelling	Deliver digitally enabled and enabling, sustainable 21st century packaging • Sustainable • Patient friendly (Esp. with aging population) • Secure • Offering enhanced safety	• There is waste in the supply chain • Personalised medicine is an expectation • Patients/user expect digital solutions/options	• Pack design (Materials, Format) • Digital leaflets • Standard adherence tool (app/ phone service/ fully integrated) • Smart serialisation exploitation • Smart labels

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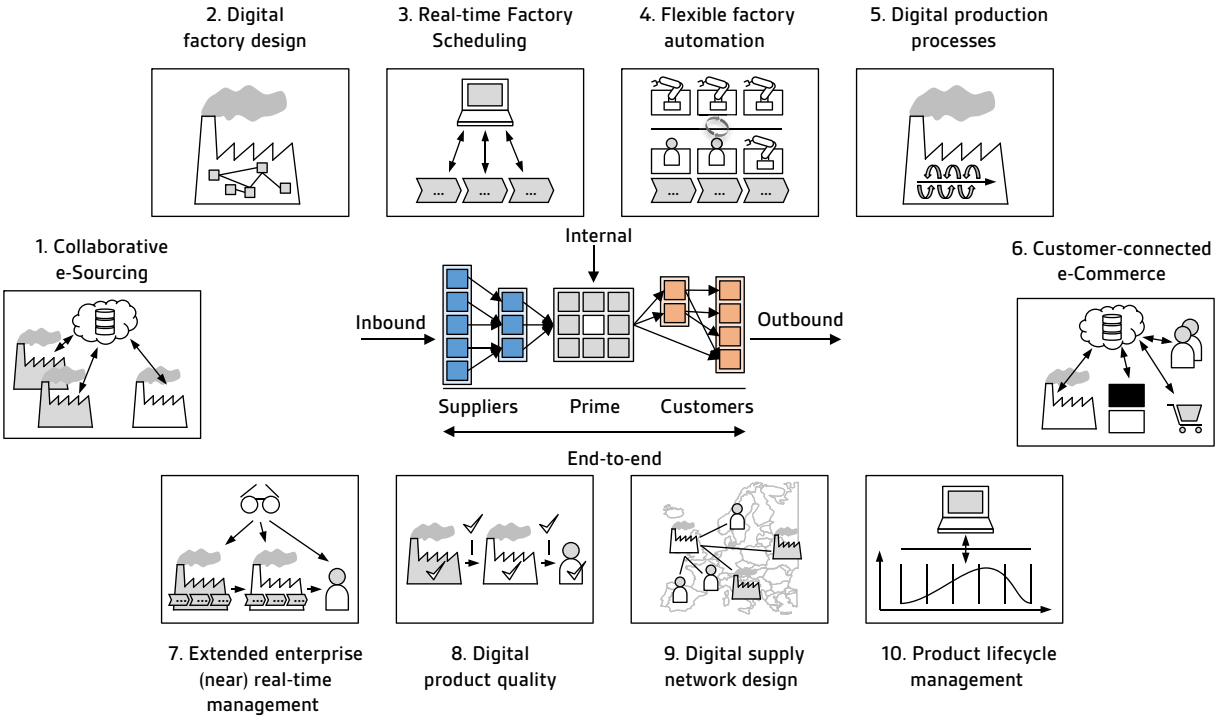
The scope covers ten future digital supply chain scenarios



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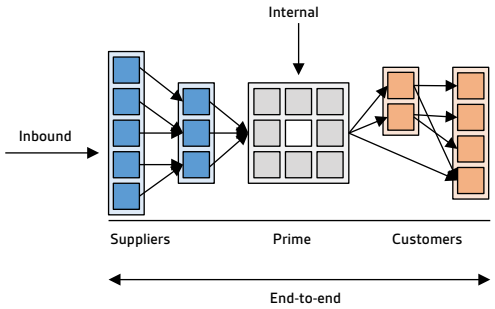
The ten scenarios link with a capability maturity model which helps to define opportunities, barriers, technology/skills maturity levels and achievability

2 Digital factory design digital 3D modelling systems for factory layout design, process and material flow simulation

3 Real-time Factory Scheduling Advanced factory execution systems with sensor-enabled, smart devices, real-time data KPI monitoring, predictive maintenance

4 Flexible Factory Automation Advanced manufacturingplant/machine reconfiguration, scale flexibility, varied levels of human-robot-collaboration

5 Digital Production Processes Application of digital production processes (e.g. additive manufacturing, continuous processing) with advanced process analytics



1 Collaborative e-Sourcing Seamlessly connected, automated and collaborative procurement in line with real-time KPI monitoring, with predictive disruption analytics (all upstream tiers)

6 Customer-Connected e-Commerce Web-based, personalised configuration, transparent order management, omni-channel access and last-mile delivery (all tiers through to end users)

7 Extended Enterprise (near) Real-Time Management End-to-end supply chain planning, scheduling and 'watch towers' for near real-time monitoring and decision making.

8 Digital Product Quality Digital product quality management systems for connecting 'traceability islands' back from customers to suppliers (root cause analytics)

9 Digital Supply Network Design Design tools to architect supply network configuration –optimisation and visualisation of site location, capacity, inventory etc.

10 Product Lifecycle Management Nextgen PLM systems that provide accurate, up-to-date product information accessible throughout the value chain and product lifecycle

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DRAFT BSI LANDSCAPE TEMPLATE - DIGITAL MEDICINE MANUFACTURE

		Past	Short term 2017 - 2019	Medium term 2020 - 2025	Long term 2026- 2030	Vision
TRENDS & DRIVERS						
Global Trends	Social					
	Technological					
	Economic					
	Environmental					
	Political					
	Legal					
Market and Customer Needs						
Challenges and Threats						
Opportunities						
Other						
VALUE PROPOSITIONS IN SECTORS OF ACTIVITY						
Sectors	Small molecules					
	Biotechnology					
	Packaging					
	Advanced Therapies					
	Diagnostic Materials					
	Other					
MANUFACTURING AND SUPPLY CHAIN COMPETENCES						
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RESOURCES						
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Theme: LM/SM/P/AT/DM (Please circle)

Digital standards programme title:

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Team:				

What challenge could be addressed by standards being in place for digital medicines manufacturing?				
Why is this needed, i.e., ***how wouldthis support*** knowledge diffusion between ***which activities*** in particular?				
Are there any ***existent standards*** applicable?				
List programmes suggested (e.g.: development of new standards, or revision of existent standards)	***When*** (short-term, medium-term, or long-term) might this be undertaken?	***What would be the prime outcome on the programme?***	***What might be the key actions?***	***Who (stakeholder groups)*** should be involved? (e.g., academia, researcher, industry, manufacturers, customers...)?
Programme 1				
Programme 2				
Programme 3				
Programme 4				

We need a programme to...

This is needed because...

Immediate actions to set this up would be..

The implications for the proposed communities of interest are...(add list)

- Interoperability
- Supply chain capability
- Through-life end-to-end connected supply chains –design
- Governance, security, and assurance of data
- Through-life end-to-end connected supply chains –service innovation

Exhibition feedback

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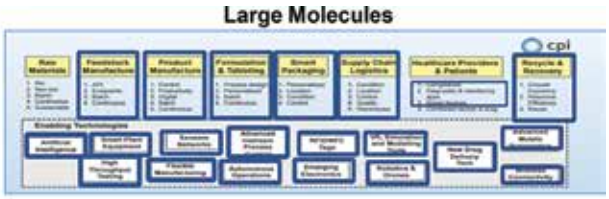
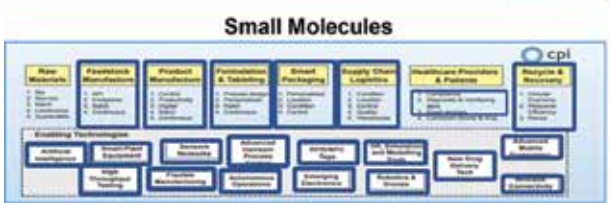
Use case analysis – implications for standards architecture

Use case analysis and implications for standards architecture:

- The eleven use cases have been mapped onto the MMIP supply chain model for each of the four themes
- With the exception of packaging, where use cases appear focussed primarily on manufacture and the post factory supply chain, other themes appear to require integration along the full supply chain, with the exception of raw materials for effective development of the associated use cases





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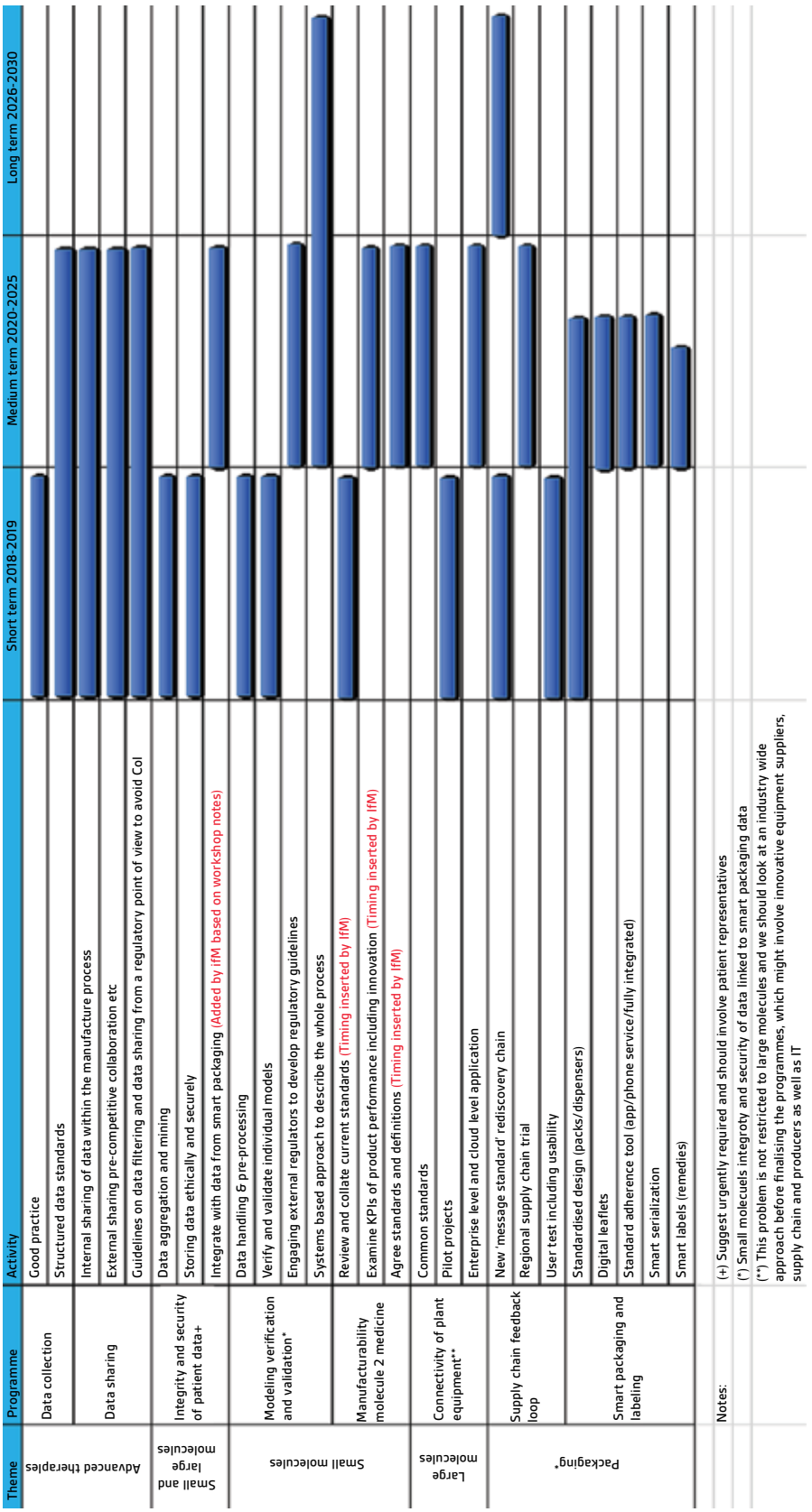
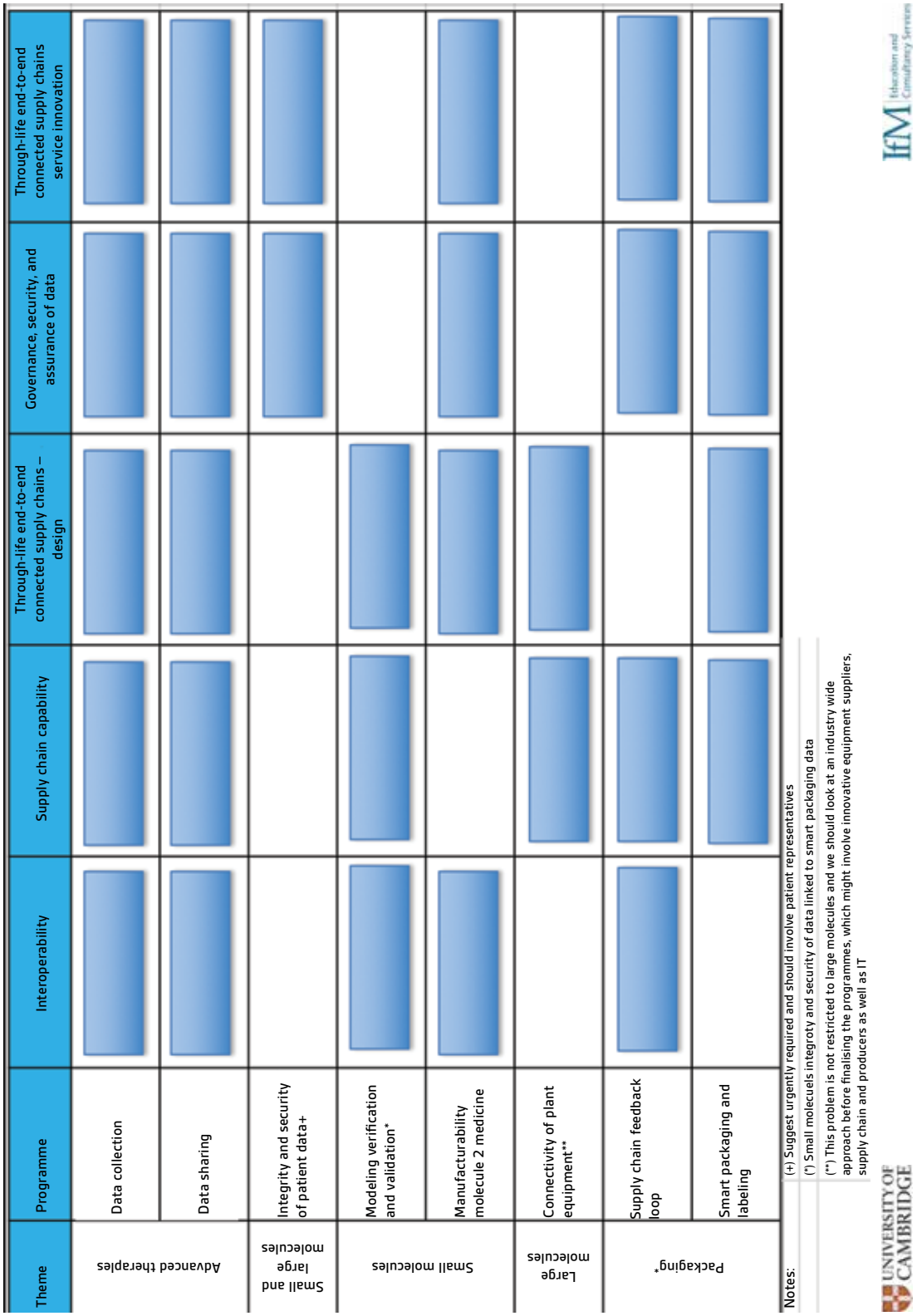
Standards programmes roadmap



Impact on existing BSI digital manufacturing themes



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