

# Digitalisation of Development and Supply Networks: Sequential and Platform-Driven Innovations

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## Abstract

We draw from an eight-year dataset of 98 organisational entities involved in pre-competitive innovation networks across the UK pharmaceutical sector. These data map into three networks that are representative of: (i) a product development-led sequential pathway that begins with digitalised product development, followed by digitalisation of supply networks, (ii) a supply network-led sequential pathway that starts with digitalised supply networks, followed by digitalisation of product development, and (iii) a parallel — platform-driven — pathway that enables simultaneous digitalisation of development, production, and supply networks. We draw upon extant literature to assess these network structures along three dimensions — strategic intent, the integrative roles of nodes with high centrality, and innovation performance. We conduct within-case and cross-case analyses to postulate 10 research propositions that compare and contrast modalities for sequential and platform-based digitalisation involving collaborative innovation networks. With sequential development, our propositions are congruent with conventional pathways for mitigating innovation risks through modular moves. On the other hand, we posit that platform-based design rules, rather than modular moves, mitigate the risks for parallel development pathways, and lead to novel development and delivery mechanisms.

**Keywords:** Central nodes; Design rules; Digitalisation; Platforms; Pre-competitive consortia; Network effects

## 1. Introduction

A key theme of the Industry 4.0 phenomenon is the claim that digitalisation makes the supply chain more efficient, agile and customer-focused (Xu et al., 2018). Think tanks such as the World Economic Forum and consulting firms including PWC and McKinsey have defined digitalisation descriptively as an all-encompassing term (Pearce, 2018; Schrauf and Berttram, 2016; Leclerc and Smith, 2018). For instance, it has been used to describe not only data analytics but also as a mechanism for altering the structure of supply chain configurations. According to Schrauf and Berttram (2016):

“The supply chain today is a series of largely discrete, siloed steps taken through marketing, product development, manufacturing, and distribution, and finally into the hands of the customer. Digitization ...[Digitalisation]... brings down those walls, and the chain becomes a completely integrated ecosystem that is fully transparent to all the players involved — from the suppliers of raw materials, components, and parts, to the transporters of those supplies and finished goods, and finally to the customers demanding fulfilment. This network will depend on a number of key technologies: integrated planning and execution systems, logistics visibility, autonomous logistics, smart procurement and warehousing, spare parts management and advanced analytics.” (p. 1)

Such descriptions raise questions about the theoretical foundations of evolving digitalisation phenomena based on network-centric developments. Are conventional theories of supply chain innovation sufficient to address network-wide and platform-centric digitalisation? For instance, digitalisation has enabled path dependent (i.e., sequential, and typically cumulative) innovations (Murray and O' Mahony, 2007). In some service-based sectors, digital platform-driven innovations (Parker and Van Alstyne, 2005; Parker et al., 2016) have been the dominant transformation challenge. In this research, we examine manufacturing and supply network-related digital transformations that feature complex product and production technology challenges, coupled with the complexities of a multi-tier supply network. Pre-competitive innovation in the pharmaceutical sector, the focus of our research, provides a relevant industrial context where the multi-actor network context is deployed to address the combined challenges of regulated product development and security of supply across multiple entities, both requiring robust governance mechanisms. In this context, should

the risk associated with design of digital supply chain configurations centred on sequential innovations be managed in the same manner as the risks for platform-driven innovations?

We observed a variety of pharmaceutical digitalisation initiatives using the industry study approach (Joglekar et al., 2016). Based on our eight-year study of network-based, pre-competitive, pharmaceutical consortia in the UK, we report on innovations that ranged from informatics and digital factory designs focused on small molecule chemistry and the production of traditional solid oral dose forms (i.e., pills) to the more recent development of bioanalytical 'lab-on-a-chip' devices and protein-based biologics (i.e., large molecules). This industry faces many business challenges that have driven the requirements for digitalisation and subsequent industry-wide efforts that affect all types of entities such as focal firms and their suppliers (e.g., Shah, 2004; Pedroso and Nakano, 2009; Munos, 2009). The nature of problem solving, including the need for regulatory oversight, render networked collaboration an essential element of innovation in the pharmaceutical industry (Powell et al., 1996; Hora and Dutta, 2013). Thus, our choice of this industry offers an ideal window to observe network-based digital innovations. The innovation networks in our study draw on pre-competitive collaborations involving 98 individual entities that range from the largest multinational corporations (MNCs) in this industry (e.g., GSK and Astra Zeneca) and academic institutions (e.g., University of Cambridge) to material and logistics suppliers (e.g., DHL), and UK regulatory bodies (e.g., the Medicines & Healthcare products Regulatory Agency - MHRA) needed for approval of clinical tasks and trials.

At the outset of our study, in 2011, the size of these networks was small, involving 24 organisations in the case of the EPSRC Centre for Innovative Manufacturing in Continuous Manufacturing and Crystallisation (CIM CMAC) (UK Research and Innovation, 2018a). Initially, the focus of innovation was on individual digital technologies such as predictive analytics and modelling in drug development, and process analytical technologies to improve drug quality and lower production cost. Due to rapid technological developments and rising customer expectations (e.g., wider and greater data access to suppliers, care providers and patients), digitalisation has become a much broader phenomenon (Venkatraman, 2017). Such escalations expanded network size and scope because participating entities recognised that their collaborative networks had to be transformed to capitalise on a wider variety of digital innovation opportunities relevant to their segments of the pharmaceutical industry. Owing to the growth in the scale and scope of such innovations, these

consortia contributed to a UK technology road map in 2012 which is summarised in Appendix A. The roadmap illustrates various pathways with anticipated digitalisation milestones, such as individual diagnostics tools for outcome monitoring, incorporation of continuous unit (i.e., modular) operations, the development of high-volume, non-volatile compounds, and greater use of platforms. As with all roadmaps (Phaal et al., 2004) this UK technology roadmap omits operational details such as choice and type of performance outcome and allied trade-offs and does not account for the variegated nature of technology ‘jumps’ along these digitalisation pathways. The potential for such variation underscores the need to build operations management theory based on the network-centric digitalisation phenomena. Note that this roadmap in Appendix A features both sequential and parallel (and thus platform-based) pathways. That is, it was possible to pursue development parallelisation without platform-based practices (Joglekar et al., 2001), for example while setting up two-sided design rules and application programming interfaces for managing demand and supply. However, based on our evidence and for the purpose of this study (e.g., to explore the rapidly expanding role digital technologies play in drug development and manufacturing, and how organisations could best appropriate the value of digital innovations in their supply networks), we ignore that possibility and use the terms *parallel development* and *platform-based digitalisation* interchangeably. Also, we use the terms *digitalisation* and *digitisation* interchangeably.

Published research on pre-competitive networks has focused on R&D issues (e.g., how absorptive capacity negatively affects the relationship between collaboration with research organisations and the performance of technologically new or improved products) without exploring the impact of digitalisation (Tsai, 2009). And, prior research on the use of digital technologies in supply networks has largely focused on electronic procurement and procurement process performance (Mishra et al., 2013; Srai and Lorentz, in press). Commensurate with new technology developments and rising end-customer expectations, multi-organisational networks and industry consortia have been employed to institute new types of collaborative knowledge exchange (Srai and Alinaghian, 2013) and associated risk management practices for, e.g., ‘coopetition’ arrangements between organisations which could impact all entities in the wider network and the industry as a whole (Gnyawali and Park, 2011; Pathak et al., 2014). The growth in digitalisation capabilities, ranging from data collection and sharing tools, analytics and machine learning — along with heightened consumer expectations — brings new demands on innovations (Nambisan et al., 2017). Such growth also raises

a host of theory questions, in addition to the basic question of sequential innovation pathways in network settings (raised previously): How do organisations identify and set up their outcome performance goals and metrics for digital competition and collaboration? Conventional operations management theory, such as the sand cone model, call for sequential pathways that enable organisations to establish quality and dependability cumulatively before pursuing delivery speed and cost-reduction challenges (Ferdows and De Meyer, 1990; Schroeder et al., 2011). Such models, and the nature of the underlying knowledge network exchanges and knowledge accumulation, have not been tested in network-centric digital innovation settings, thus creating a gap in the literature.

At a strategic level, the issue of intent is relevant particularly where the motivation behind digitalisation is for a truly transformational impact across organisations, networks, and industries. Recent analysis of the role of integrative supply management practices (ISMP) for outsourcing have identified key integration dimensions such as failure-prevention and performance-enhancing practices (Narasimhan et al., 2010) as constructs that accompany the intent for innovation. However, digitalisation may prompt organisations to set additional strategic goals (i.e., business models enabled by digitalisation, for example, ‘microfactories’ with 3D drug printing capability) that may require a complete disruption of existing ISMPs. And, if we are to study the broader digital integration challenges identified by practitioners (e.g., Schrauf and Berttram, 2016), the framing for ISMP may have to be broadened to include rising customer expectations and evolving strategic intents involving such novel business models. Thus, the underlying theory has gaps. For instance, do organisations that wish to achieve such digital ambitions need to commit to alternate ISMP mechanisms? Given these gaps, and as a point of departure, we set up an initial research model linking strategic intent and innovation performance outcomes (see Figure 1). Consistent with Narasimhan et al. (2010), this model posits a positive, mediating role for network integration.



Figure 1. Initial model for exploring network centric digital innovations

Our research fills these gaps in the digital supply network literature through a grounded theory-building exercise (Eisenhardt, 1989; Barratt et al., 2011). We describe our methodology, which requires the examination of three separate collaboration networks, with each network drawing out unique innovation pathways, as part of our research design. We divide our analysis of these networks into two stages: a within-case analysis that captures the nature of innovation pathways in each network, and a cross-case analysis to compare and contrast the essence of the observed network-centric innovation structures. These analyses lead to 10 research propositions, and to a refined framework on the relations between key constructs associated with network-centric innovations along alternative digitalisation pathways. We find that, with sequential development, our propositions are congruent with conventional pathways (e.g., the sand cone model) for mitigating innovation risks through modular moves. On the other hand, we posit that platform-based design rules, rather than modular moves, mitigate the risks for parallel pathways during product development and delivery. We conclude with a discussion of the managerial relevance of these propositions and the implications for future research.

## **2. Literature review**

### ***2.1. Strategic Intent: Aligning Business Models with Environmental Needs***

Organisation studies, information systems and operations management literatures reflect a long tradition of research that assesses strategic intent in terms of its fit between a firm's inter-organisational choices (e.g., location decision) and its environment (e.g., changes in customers' needs) (e.g., Venkatraman 1989; Bensaou and Venkatraman, 1995; DiRomualdo and Gurbaxani, 1998; Salvador and Villena, 2013; Ketokivi et al., 2017). Many early studies in the operations strategy literature attributed these concepts to specific variables. For instance, in the sand cone model, quality and dependability take precedence over speed and cost (Ferdows and De Meyer, 1990) in terms of development pathways, and as such, organisations' intent was to manage underlying trade-offs sequentially (Boyer and Lewis, 2002; Flynn and Flynn, 2004; Schroeder et al., 2011). And, why might digitalisation prompt novel theory constructs around strategic intent along such pathways? On the organisational theory side, Venkatraman et al. (2014) argue that digitalisation has resulted in two novel outcomes: (1) digital business innovation (DBI) platforms and (2) digital business innovation capability at the network level of analysis. For instance, early IT and innovation literature has

analysed innovations at individual and organisation levels, but rarely at the inter-organisational level. However, since digitalisation occurs both intra- and inter-organisationally (Snow et al., 2017), it must be understood in the context of innovation ecosystems (and their underlying networks).

A second view of emergent theory is based around data and analytics logic. Here, unique sets of competitive measures and outcomes could emerge through optimisation and allied data analytics. Guha and Kumar (2017) reviewed emerging analytics capabilities drawing upon the organisational goals (Romano and Formentini, 2012) and supplier performance (Chai and Ngai, 2015) literature. They point out that supply network design using digitalisation can generate a massive amount of data and visibility for customers. This raises customer expectations in terms of cost, quality and time-to-market parameters (Bloch 2011; Srinivasan et al., 2012). In the analysis of the combined organisational strategy and data analytics literature, Venkatraman (2017) marshalled evidence to show the potential for multiple digital transformation options (e.g., 'experimentation at the edge', 'collision at the core', 'reinvention at the root') in network-centric innovations.

In the supply network domain literature, Narasimhan and Narayanan (2013) synthesised a variety of constructs and called for a joint study of strategy integration (i.e., organisational factors), absorptive capacity (i.e., organisational learning), supply network integration (i.e., external knowledge and supplier integration) and contextual variables (e.g., innovation culture), while focusing on supplier-enabled innovation. We extend their framing logic to posit that strategic intent around digitalisation can drive network performance. Our case analysis, therefore, seeks evidence on the fit between inter-organisational choices (i.e., strategic intent) and their digital environments as its point of departure.

## ***2.2. Network Integration: Role of Nodes with High Centralisation***

Many organisation studies scholars have analysed innovations by mapping information and material exchanges on to network structures (e.g., White, 1981; Gulati et al., 2000). This literature posits that markets are more than sites for transactions between buyers and sellers. Firms that act as buyers, sellers, and suppliers continuously and jointly construct networks of information and material flows as a means for addressing internal and market uncertainties and to exploit opportunities. Powell et al. offered a seminal finding, informed by the innovations in the biopharmaceutical industry (1996):

“[When the] knowledge base of an industry is both complex and expanding, and the sources of expertise are widely dispersed, the locus of innovation will be found in networks of learning, rather than in individual firms.” (p. 116)

Following Powell et al. (1996), networks and underlying relational structures have been studied in terms of constructs such as centrality and structural holes (Ahuja, 2000). Choi and Hong's 2002 study examined evidence from supply networks for Honda Accord, Acura CL/TL and DaimlerChrysler's Grand Cherokee product lines to capture the system structure in three dimensions: formalisation, centralisation and complexity. While formalisation refers to the degree to which increasingly complex supply networks are controlled by explicit rules, procedures, and norms, our focus here relates to roles and responsibilities and what influence central nodes play in integrating multi-organisational networks. In a more recent review Kim et al. (2011) further analysed these network data using social network analysis to contrast material flows and contractual relationships. Their work emphasised the importance of taking a network-centric view for supply chains, such as examining centrality (i.e., measure of influence within a network). They found that firms with high centrality play a vital role in networks and, thus, require a unique set of capabilities for enhancing network-centric performance outcomes. In particular, they posited that the role of nodes is that of integrator (in transforming systems and promoting architectural innovation), allocator (distributing resources to meet demand loads), pivot (to facilitate operationally critical flows across networks), coordinator (influencing and aligning goals), navigator (in acquiring information) and broker (to process information). Nuanced roles have also been analysed with a variety of centrality measures to better understand networked knowledge integration in the design of products (Parraguez et al., 2016), processes (Roth et al., 2016) and supply chains (Jayaram and Pathak, 2013).

Kim et al. (2011) have explicitly argued that organisations with high betweenness centrality can better engage in supply chain risk management, because of dependencies nodes have on a central node to interact with the rest of the network. In addition, network structure can significantly determine the likelihood of disruption, with different levels of resilience linked to specific structural relationships among network entities (Kim et al., 2015). We extend their logic to digital innovation pathways and posit that centrality can moderate the relationship between strategic intent and



innovation performance. Our case analysis, therefore, unpacks evidence on the role of nodes with high centrality while exploring network integration practices.

### **2.3. Innovation Performance: Modalities for Mitigating Risk**

While the examination of material flow and contractual relations remains a mainstay of the network-centric supply chain literature (Bai et al., 2016), theories for network-based assessment of innovations have also been informed by product architecture and allied modular moves for risk management (Baldwin and Clark, 2000). Following Baldwin and Clark, various studies have looked at complexity management issues such as the duality between design and organisational networks (Sosa et al., 2004), risk sharing (Camuffo et al., 2007) and network-based problem-solving capabilities (Gomes and Joglekar, 2008). A key question involves the concurrent design of product, process and supply chain (Three-Dimensional Concurrent Engineering (3D-CE), see Fine, 1998). Simultaneous design of product, process and supply chains highlights the importance of information sharing (Blackhurst et al., 2005) across these often-siloed tasks. Fine et al. (2005) examine the underlying task conflicts via a goal programming approach to address multiple and interdependent challenges in designing and planning a product market launch. Petersen et al. (2005) argue that an integrative view (involving technical and business performance goals) directly impacts supply chain configuration decisions. Forza et al. (2005), while framing these three aforementioned articles from 2005, found that coordinated decisions across these three domains outperform uncoordinated decisions. They also raise questions about the limits of such arguments; for instance, is it possible, cost-effective and efficient to evolve one 3D-CE system from another? Longitudinal studies of such evolution, and allied risks, using network-centric innovation are sparse. And the impact of digitalisation, in particular, platform-based digitalisation, is yet to be analysed carefully in such evolving settings. For instance, we are beginning to understand the impact of platform creation on demand and supply management (Parker and Van Alstyne, 2005; Parker et al. 2016). With companies shifting innovation initiatives centred on internal resources to those dependent on external networks (Nambisan and Sawhney, 2011), when would a modular design move, with or without digitalised platforms, affect both the technical and business performance of network-centric innovation?

In summary, there is a large stream of literature on network-centric innovation performance. This literature lacks robust theory for risk-adjusted network performance in the digitalisation context.

We therefore focus on modalities of mitigating risk adjustments as measures of interest while engaging in grounded theory building based on network analysis.

### **3. Research Method**

This study explores network-centric innovation via the case study method involving network mapping. We discuss our case selection criteria and then lay out our process of identifying pertinent cases. In addition, we outline the specific network mapping approaches used, which support within-case and cross-case analyses as the underpinning evidence base for grounded theory development.

#### **3.1. Background**

In 2004, the US Food and Drug Administration (FDA) Critical Path Initiative<sup>1</sup> helped foster the formation of numerous consortia focused on specific drug development challenges (Woodcock et al., 2014). This was followed in 2008 by the European Commission's launch of the Innovative Medicines Initiative (IMI) linked to the European Technology Platform on Innovative Medicines. The most recent IMI programme (2014-2020) aims at accelerating the development of, and patient access to, innovative medicines, particularly where there is an unmet medical or social need (IMI, 2018). Multiple Global initiatives continue to emerge across the pharmaceutical sector and are predominantly based on the principles of pre-competitive collaboration (Srai et al., 2015a). Pre-competitive collaborations that build enabling platforms often focus on developing standards and tools and aggregate data to achieve a necessary scale for research by accessing resources and capabilities across organisations (Institute of Medicine, 2010).

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<sup>1</sup> The Critical Path Initiative (CPI) is FDA's national strategy for transforming the way FDA-regulated medical products are developed, evaluated, and manufactured. ... [it aimed to address] the reasons for the widening gap between scientific discoveries that have unlocked the potential to prevent and cure ...[diseases] ... and their translation into innovative medical treatments. ... [given the] increasing difficulty and unpredictability of medical product development, the report concluded that collective action was needed to modernize scientific and technical tools as well as harness information technology to evaluate and predict the safety, effectiveness, and manufacturability of medical products (FDA, 2018).

This study focuses on the UK pharmaceutical ecosystem and explores how public-private partnerships (consortia) have been structured to deliver strategic goals and objectives relating to specialised research programmes. For example, the establishment of a national multidisciplinary research Centre for Innovative Manufacturing in Continuous Manufacturing and Crystallisation — CIM CMAC (UK Research and Innovation, 2018a). 16 cases spanning development and production were short-listed for this study based on specific criteria: The organisations and consortia had to engage in innovation and technology development activities with a distinct supply chain focus or supply network reconfiguration element. For example, network partners can collectively assess the consequences of adopting digital process technologies — on supply network designs and business models in different development–launch–supply scenarios — and how they compare to existing ‘batch’ process-based supply models.

Data-gathering efforts began in 2010, in advance of the launch of the CIM CMAC in 2011 and concluded with an interview with the director of the most recently created consortium (FPC@DCU) in June 2018. The consortium approach enabled ongoing access to expert informants over this eight-year period and allowed for refinement and the gathering of additional data, where applicable. In terms of validation, checks and balances were established and are evidenced in the authors’ contributions to key scientific publications linked to specific technologies and individual research programme outcomes during this eight-year period (e.g., inkjet printing capability review (Daly et al., 2015); precision manufacturing workflow development (Brown et al., 2018)). Table B1 in Appendix B outlines details of the 16 consortia cases which span activities in digital development, digital production, and/or digital supply networks across the pharmaceutical sector.

### *3.1.1. Selection criteria*

With hundreds of networked tasks, and sub-projects to choose from, all involving new materials and emerging technologies, it was deemed of little benefit to map a representative ‘product’ or set of ‘generic’ product families given the complexities and specificities of the pharmaceutical sector. Therefore, we first employed industrial systems and value network mapping approaches to construct a ‘one-off’ current state sector view capturing key consortia actors, activities and measures (Srai et al., 2016a; Srai and Alinaghian, 2013).

This process facilitated a decoupling of individual network innovation ‘stories’, outlined in Table B1 in Appendix B, to explore how emerging activities could affect existing supply network configurations, measures and interactions. This was enabled by engaging with key consortium partners in the case selection process. We identified six cases out of the short-list of 16 based on the following key criteria:

1. Cases had to contain a digital element in terms of drug development or medicine production.
2. The technology intervention demonstrates new functionality or a certain ‘proof of concept’ linked to digitally enabled testing, validation or production.
3. These interventions had to have high potential for supply network reconfiguration in supporting new supply models (e.g. ‘make-to-order’) and/or disrupting existing conventional development and production approaches based on ‘batch’ processing.

The mapping techniques were then used to capture alternative supply network configurations, transitions and evolutionary phases for the cases all of which met the above criteria. Finally, to examine network structure, the formal and informal knowledge exchanges between the different organisational entities (academic-industry-institutional) and the governance mechanisms (partnering arrangements for e.g., hub-spoke models and platform-based programmes) involving the consortia, we explored six representative cases in greater depth (see sections 4.1–4.3). An illustration of the three representative innovation networks relating to these cases are shown in Figures 3-5.

### *3.1.2. Case samples*

As we explore emerging phenomena involving network-centric digital innovations, where research and theory are at an exploratory or formative stage, a mixed methodology was employed (Eisenhardt and Graebner, 2007). This involved key industrial stakeholder and expert group input, followed by assessment of multiple cases across the activities of the six consortia. This research strategy aligns with our study’s empirical inquiry into a contemporary phenomenon, both in-depth and within its real-life context (Yin, 2009).

To increase external validity and develop generalisable propositions, our case study approach aimed to maximise the diverse network innovation contexts that co-exist. With an emphasis on digital development, production and supply networks, our case samples span network-centric

product, process and business model innovations consistent with Williamson and Zeng (2009) and Srai et al. (2016a), namely:

- (1) Digital Design
- (2) Adaptive Clinical Supply
- (3) 3D Printing including 'Lab-on-a-Chip'
- (4) Process Analytics
- (5) 'Intelligent' Packaging
- (6) Continuous Processing End-to-End (E2E)

These categories were also deemed appropriate as they are consistent with both the developmental and commercial goals of the multiple consortia under study and involve technology interventions with a digital element. Secondly, the highly overlapping nature of the six consortia (membership, geography, technologies, activities, stages of evolution) enabled our exploration of specific, complementary innovations, reducing both complexity and variation in terms of fit and context.

### **3.2. Data Collection for Individual Cases**

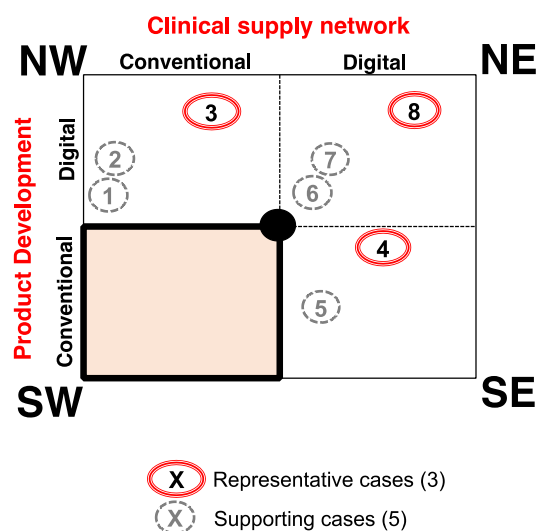
In addition to semi-structured interviews, secondary data and observations from network-centric digital initiatives involving the various consortia (see description before Table B1 in Appendix B), the process also involved a series of workshop-type engagements involving academia and industry between 2014 and 2016. These interactions linked with Royal Society of Chemistry and MIT-CMAC themes and events focused on specific outcomes, for example, emerging equipment and analytics, future structure of pharmaceutical development and manufacturing, future supply chain design, and targeting technology interventions (e.g., Page et al., 2015; Nepveux et al., 2015; Srai et al., 2015a; Srai et al., 2015b; Harrington et al., 2017).

For the Reconfiguring Medicines End-to-End Supply (REMEDIES) consortium, eight workshop-type engagements (aligned with stakeholder meetings and involving all 24 consortium partners) were conducted on a six-monthly basis between 2014 and 2018. Furthermore, given the clinical and commercial platform design of the programme's activities, bi-weekly meetings involving six applications ('Apps') and specific digital flagship projects over the same period enabled the

authors to interview multiple respondents and observe the evolution of eight network innovation cases. When conducting interviews, we sought a minimum of three individuals aligned to each network innovation case. Given the interplay within and between activities involving the five UK consortia, individuals who were involved in multiple consortia were targeted so that data could be collected on, for example, information flows between nodes of multiple networks.

To ensure reliability of the data collection, a semi-structured interview protocol was built around a base framework and a generic example, exploring the operations management challenges of digitalisation (see Appendix C). The protocol outlined the aims and outcomes of the study, and guided our information gathering on the respondent and primary data involving specific digital experiments and the consortia. Interviewees were also asked to discuss any other distinguishing features from a network innovation perspective for each of their programme activities (e.g., ... [the] 3D printing of drug combinations with specific drug release profiles involved [X] key network partners and focused on specific generic drug product [Y] for the following reasons...). From the shortlist of 16 cases, Figure 2 summarises the positioning of the six representative cases across different contexts and environments, represented by four quadrants: Southwest (SW), Northwest (NW), Southeast (SE) and Northeast (NE).

### (i) Product Development



### (ii) Production

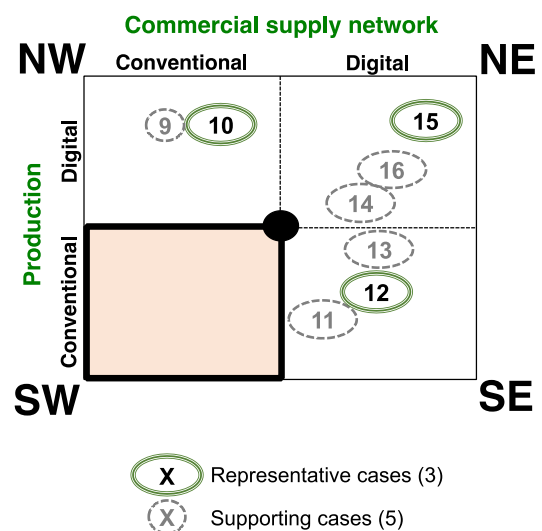


Figure 2. Positioning of 16 cases using a base framework

(See Table B1 in Appendix B for further details on individual cases.)

In terms of (i) product development, the SW quadrant represents conventional development and conventional supply networks. This base framework enables us to chart 'pathways' and 'transitions' away from conventional settings using the digital cases. Respondents 'self-identify' the position of their specific activity on the grid, outline what best describes this positioning, and then provide evidence to support this positioning (e.g., secondary data sources to validate, and to support context). For example, the NW quadrant represents contexts where there is digital product/production development but the supply network remains conventional, and the SE quadrant represents contexts where the supply network is digitalised, yet development remains conventional. Finally, the NE quadrant represents those cases where there are activities involving both digital development and digital supply network design. Similarly, for (ii) production, the SW quadrant represents conventional production activities and conventional supply networks in commercial settings.

The shaded SW quadrant denotes our point of departure and the conventional/current state in terms of extant theory and evidence from the literature and industrial practice. The pathways from the SW to NW quadrants represent 'sequential' transitions in digital product development (case 3) and production (case 10) respectively, where product development/production is first digitalised followed by supply network digitalisation (i.e., in the NW to NE pathways). The SW to SE pathways capture sequential transitions for digital supply in development (case 4) and production (case 12) settings. Here, the reverse is true — the supply network is digitalised first, followed by product development/production digitalisation (i.e., the SE to NE pathways). Finally, direct transitions to the NE quadrant from the SW quadrant, represented by cases 8 and 15, explore 'parallel' pathways. While Figure 2 depicts a separation of product development and production cases, we do not consider these in isolation because behind this pairing arrangement are increasing linkages between specialist actors and the integration of development and commercial activities in the pharmaceutical sector. For example, with the transfer of many elements of clinical supply to commercial supply inherently built-in, we specifically focus on alternative clinical supply chain designs and technology solutions — i.e., (i) product development; SE quadrant, that are readily transferable to commercial settings, i.e., (ii) production; SE quadrant — in terms of improved product quality, inventory savings, increased flexibility and quicker response to customer demands. And vice versa — technical performance goals, for example, from 'smart label' interventions (case 12), around near-field communication tags and cloud-based software systems for effective tracking informs clinical supply.

As Eisenhardt (1989) suggests, this strategic arrangement of case pairs enabled us to tease out theoretical insights, which led to more generalisable propositions. These cases are explored in sections 4.1–4.3.

### **3.3. Data Analysis**

As outlined in section 2, our research method and investigative process revolves around three dimensions of analysis — strategic intent, network integration (and the role of the central nodes) and innovation performance (and the modalities of risk mitigation). We analysed the interviews using thematic and process coding techniques to gain clarity on different contexts and to identify any patterns within selected network innovation cases (Gioia et al., 2012). After completing the within-case analyses, we conducted cross-case analyses looking for additional patterns and linkages to our three analysis dimensions. These formed the basis of our proposed theoretical framework and 10 propositions that frame the key insights of this research paper. Section 4 now presents individual case descriptions and the within-case analyses. Detailed network analyses are also covered in this section.

## **4. Within-case Analyses**

In this section, three matched pairs of cases (six case studies in total) are briefly outlined in order to demonstrate the digital intervention and explore how strategic intent around digitalisation could drive network performance. Structured around the conceptual model outlined in section 1, within-case analyses of the three matched pairs involving interpretation of qualitative data, are presented in sections 4.1–4.3. In some instances, technical papers have been published in domain journals based on this work (e.g., Brown et al., 2018). We report on their results and then cite such papers for brevity.

### **4.1. Sequential Innovation: Northwest Pathway**

The ‘Dial-a-Molecule’ and ‘Golden Batch’ cases (see Table B1 in Appendix B) are representative of sequential SW→NW and NW→NE pathways (see Figure 2) involving digital and conventional contexts. Specifically, product development and production were digitalised first where outcomes of the case pairs represent the iterative two-way information flows between a ‘targeted’ experimental design, prediction and advanced modelling of new molecules and formulated materials (e.g.,



synthesis design), and the control and the optimisation of industrial processes needed to manufacture them (e.g., crystallisation unit operation).

#### *4.1.1. Strategic intent: Aligning business models with environmental needs*

We explore the fit between emerging business models and UK ecosystem needs by charting coordinated academic-industry initiatives since 2011 on transforming 3-4 $\sigma$  sector performance in terms of manufacturing 'right-first-time' (i.e., comparable to yields of 93.3-99.4%). Typically, the cost of poor quality at these levels of sigma ( $\sigma$ ) result in 15-20% spend of revenues on rework, inspection, and testing for organisations (e.g., Jacobs et al., 2015) and equates to global losses of £15 billion annually for the pharmaceutical sector (Srai et al., 2015a). In particular, we explored industry practices that have traditionally been based around conventional 'batch' development, production, and testing, to benchmark performance outcomes against other sectors (e.g., the design and manufacture of microprocessor chips), where operating at >5 $\sigma$  results in reducing defects, errors, and failures to near zero within the manufacturing process (Panat et al., 2014).

The 'Dial-a-Molecule' case embodies the digital design innovation category that incorporates activities of both the Dial-a-Molecule Grand Challenge Network, established in 2007, and the Advanced Digital Design Transforming Pharmaceutical Development and Manufacture (ADDoPT) consortium, launched in 2015. These UK initiatives are part of a long-term coordinated effort from researchers and industrialists to contest conventional bench-scale and 'make and test' R&D approaches. The 'Golden Batch' production case represents current 'digital factory' initiatives in the pharmaceutical sector and links to outputs from development activities across three of the consortia under study. In both cases, we examine the interplay and evolution involving modular (unit) operations of active pharmaceutical ingredient (API) synthesis and crystallisation. Our representative cases focus on digital inputs involving two sequential transitions: (1) from conventional batch processing and off-line quality-control testing to modular batch processing that incorporates 'real-time' process analytics and (2) from modular batch processing to fully modular continuous systems.

Synthesis and crystallisation steps have been specifically targeted for several reasons in this study. First, crystallisation processes have historically been operated in batch mode to enable flexibility in response to varying customised design requirements and changing market demands. However, the approach can also lead to massive batch-to-batch variations in product quality which

directly impact (i.e., increase) manufacturing costs due to waste and necessary re-working (Su et al., 2015). Second, API synthesis and crystallisation operations are sequential steps at the beginning of the drug manufacturing process, so they enable exploration of concurrent design thinking in terms of the molecule-process-platform technology. Third, API synthesis and process intensification at this step is critical in determining the overall yield. Finally, API crystallisation performance determines the purity of most APIs at this early stage of the process, which directly impacts pharmacological properties and therapeutic efficacy of drug performance (Variankaval et al., 2008; Yu et al., 2014).

#### 4.1.2. Network integration: Role of nodes with high centralisation

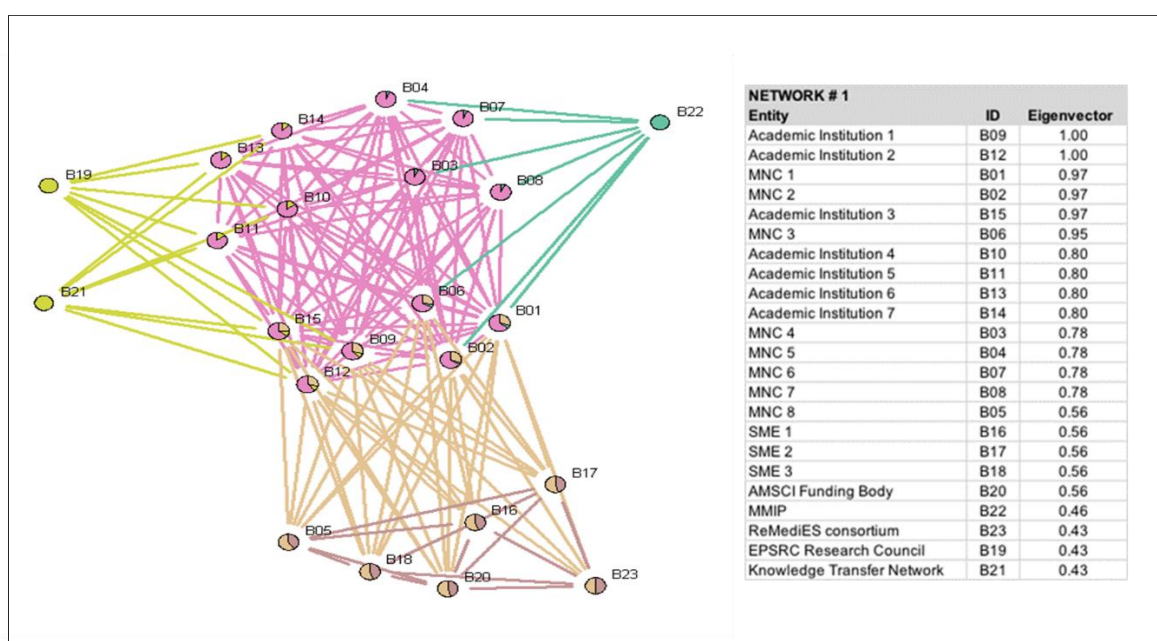


Figure 3. Network structure for Northwest (NW) pathways involving sequential transitions (SW→NW and NW→NE)

Information exchanges between individual organisational entities (including eight MNCs, seven academic institutions, and three SMEs) across three consortia are summarised in Figure 3. The patterns and insights derived from the sequential transitions (SW→NW and NW→NE) relate to the dynamics of information transfer between associated activities involving specific communities of individual network players. Based on a social network analysis (SNA) approach (Parraguez et al., 2016), five such communities across the three consortia are active, with 23 critical nodes and 163

edges (maximum partition density of 0.7412158). Each of these five communities represent a subnetwork. The connections for these subnetworks are summarised as follows:

- A dense COORDINATION subnetwork comprised of seven industrial and seven academic partners (all with eigencentrality measures  $> 0.74$ ) is focused on relationship coordination and reducing the amount of load on the network as a whole.
- The ACADEMIC subnetwork centres around three core academic institutions (nodes B09, B12, B15, with eigencentrality measures  $> 0.97$ ) with links to four 'supporting' academic institutions (nodes B10, B11, B13 and B14). All seven entities have close links with the main UK government agency that funds research and training in engineering and the physical sciences, EPSRC (node B19), and a Knowledge Transfer Network (KTN) specialising in cross-sector collaboration and innovation networking (node B21).
- A COMMERCIAL subnetwork involving the seven core industrial stakeholders is further coordinated by an industry alliance, the Medicines Manufacturing Industry Partnership (MMIP) (node B22) established jointly by the UK Government and the biopharmaceutical industry in 2014. In a similar configuration to the ACADEMIC subnetwork, the COMMERCIAL subnetwork centres around three core industrial stakeholders (nodes B01, B02, B06, with eigencentrality measures  $> 0.95$ ) with interests in two or more consortia. Four industrial stakeholders (nodes B03, B04, B07 and B08) are actively engaged in only one consortium but have multiple interactions with other consortia members.
- The three core academic institutions (nodes B09, B12, B15) and three core industrial stakeholders play an important role (eigencentrality measures  $> 0.97$ ) in a DESIGN RULES subnetwork involving a series of specialist SMEs (nodes B16-18, with eigencentrality measures of 0.56).
- Three sector specialists form an outlier subnetwork designated here as ANALYTICS and have close links with the REMEDIES consortium (node B23).

In terms of relationships, governance and coordination, these cases are characterised by multiple and complementary knowledge exchanges involving leading Global MNCs, technology SMEs and specialist partners from UK universities (e.g., University of Cambridge and the University of Strathclyde), and research centres (e.g., CIM CMAC). Our analysis first focused on six key (i.e., with

high eigencentrality) nodes of the Dial-a-Molecule Grand Challenge Network (nodes B01, B02, B09, B15, B11, B14), which comprises of a cross-disciplinary, cross-sector community of over 650 academics, early career researchers and industrial stakeholders. Phase 3 of this network (2016–2020) is underway and involves a more decentralised structure involving three specialist themes supported by a central resource (based at node B14). Using these nodes as a baseline, we can track the formation, expansion and transitions of major networks and subnetworks that have been facilitated by funding from two UK government agencies (nodes B19 and B20) and the KTN (node B21).

The second consortium (ADDoPT) is a four-year collaboration structured around a specialist SME (node B16) that acts as the ‘consortium coordinator’. Consisting of 12 members, the goals of the programme are organised around eight research strands and a series of case studies set within the development and manufacturing supply chain of one of the four manufacturing partners (nodes B01, B02, B05, B06). Here, we focused on information exchanges concerning development of the advanced control and monitoring strategies critical to integrating a greater degree of digital design into practice.

These interactions between partners in development align with the activities and aims of the third consortium — the Future Continuous Manufacturing and Advanced Crystallisation Research Hub (CMAC Hub) — for example, the rapid screening of drug compounds and model-based predictive capabilities linked with the scale up, design and modelling of new manufacturing and supply network processes. Relationships, governance, and coordination in the ‘Golden Batch’ case, sees a Hub (node B12) and Spoke model involving 12 core academic partners engaging with a growing network of ~ 50 industrial partners and new actors to the sector (UK Research and Innovation, 2018b).

As for roles, four organisational entities (nodes B01, B02, B09, B15) are actively involved across all three consortia. Indeed, participation in these consortia has contributed to valuable ‘internal networking’ within their organisations or academic institutions and access to, hitherto, unrealised capabilities on their very doorstep. These entities serve as a ‘backbone’ to the COORDINATION subnetwork in that they can align network members and their activities with the strategic goals of the various consortia. This is a significant advantage as it links the DESIGN RULES subnetwork in supporting increased information flows between digital design activities and full-scale manufacturing processes. The two principle nodes within the academic network (B09 and B12) act as both ‘pivots’

and ‘navigators’ in an integrated fashion. Together, they explore and facilitate flows of information across their network of partners by specialism (i.e., the configuration of commercial supply networks and modular operations in batch and continuous modes, respectively). In a design context, the central node (B09) serves as the ‘integrator’ tasked with organising and incorporating a range of ‘outcomes’ from various work streams, demonstrating an increasing influence exerted by the DESIGN RULES subnetwork.

#### *4.1.3. Innovation performance: Modalities for mitigating risks*

One key question we explore is how networks are setting up performance goals based on digital inputs, which relate to the acquisition, sharing and scaling of data and information across the subnetworks (outlined in section 4.1.2).

A good starting point here has been the development of ‘digital workflows’, which have recently provided development activities with standardised data acquisition, analysis and reporting protocols. A seven-stage systematic approach for crystallisation process design (Brown et al., 2018) looks to reduce complexity and mitigate the risk of decision choices — where one or multiple aspects of a crystallisation process could result in performance issues at a later development step or operation. Design and process criteria inform progression to the next step, and if not met, the stage is re-visited. Decisions are made on feasibility — based on experimental data (actual and modelled) to ensure optimisation of reaction conditions, and to ensure that specific processes are directed towards the most suitable platforms, such as, modular batch or modular continuous configurations (e.g., Baldea et al., 2017).

In terms of information sharing, laboratory-based virtual networks have emerged through the consortia’s adoption of Electronic Laboratory Notebooks (ELNs), which have facilitated the rapid exchange of reaction and processing data. This has the potential to transform the very nature of synthesis to become a ‘data-driven discipline’ and enable better prediction of properties and the performance of ‘target’ molecules. By extension, through acquisition and sharing across consortia, prediction of experimental outcomes (e.g., Bryant et al., 2018) can create opportunities to accelerate the design and modelling of new molecules, manufacturing processes, and combinations of different unit operations in single-process equipment.

Specific to the 'Dial-a-Molecule' case, innovation performance in a network context can be summarised using lower levels of a sequential progression involving quality and dependability (Ferdows and De Meyer, 1990; Flynn and Flynn, 2004). Measures linked to strategic intent of the cases focus on improved process control through the development of Quality-by-Design (QbD) principles where advanced control and monitoring strategies can eliminate the need for physical experimentation and testing (Yu et al., 2014). At higher levels of a sequential progression involving responsiveness/speed and cost, differentiation in a digital development context focuses on prediction ability to meet predefined quality ('right first time') and 'scale-up' characteristics. In product development, such predictive capabilities, which enable the transition from physical testing and experimentation to better informed and targeted molecule selection, can facilitate increased success rates, shortened product development time, and decreased waste due to fewer clinical trial (Phase I, II and III) failures.

In terms of lower levels of a sequential progression in a digital production context ('Golden Batch' case), targeting ideal process parameters has enabled more 'robust' processes. For example, targeted process parameters enabled the development of a scalable and transferable crystallisation process route to a hitherto elusive demonstrator API using specialist equipment developed by a consortium SME (Agnew et al., 2016). Indeed, the overall goal is to demonstrate 'dial-an-attribute' performance for final products — exploiting predictive control models and automated optimisation tools — across the whole process design space. With increasing confidence and evidence-based adoption in advanced process analytics linked to QbD principles (e.g., Yu et al., 2004), the 'real-time' release of products can become a reality. Defined as "... the ability to evaluate and ensure the quality of in-process and/or final product based on process data" (ICH, 2009: p 17), this is possible because of consistent and predictable performance when actual processes can be compared to 'Golden Batch parameters' (typically, valid combinations of measured material attributes and process controls, in-line). At higher levels of sequential progression, critical parameters and data — linked to predictive product quality controls and process feasibility — can vastly reduce the number of experiments required and eliminate non-viable drug candidates earlier in the R&D pipeline because of increased speed in decision-making and allied responsiveness. In commercial contexts, experimentation in using data from small-scale experiments to virtually design full-scale manufacturing processes is evidenced by a specialist CMAC Hub work package on 'integrated predictive development pathways'.

With particle engineering at its core, a fully integrated modelling approach guides the design of processes and materials at molecule, particle and formulation levels — with a specific goal of reducing cost through enabling rapid development timescales (UK Research and Innovation, 2018b).

#### **4.2. Sequential Innovation: Southeast Pathway**

The ‘On-Demand Clinical Supply’ and ‘Smart Label’ cases (see Table B1 in Appendix B) represent the sequential SW→SE and SE→NE pathways (see Figure 2) and also explore digital and conventional contexts. Beyond transforming how products are designed and manufactured, digitalisation can enable new approaches to managing future supply demands which are in line with recent US and EU regulations around serialisation. In short, pharmaceutical serialisation refers to the track and trace of prescription drugs movement throughout the supply chain from point of manufacture to dispense.

Specifically, desired outcomes of the case pair are analogous in developing more ‘localised’ capabilities in a series of clinical and commercial contexts. For example, using information and data to enable more demand-driven and customised product design (‘personalisation’ in terms of country-clinic-individual) coupled with ‘on-demand’ logistics supply.

##### *4.2.1. Strategic Intent: Aligning business models with environmental needs*

Clinical trials account for an estimated 50% or more of drug development costs (Huber and Howard, 2016). Over the eight-year period of this study, the average estimated cost of advancing a drug from concept to market (incorporating post-approval Phase IV expenses) has risen from ~ £600 million to £2.2 billion (DiMasi et al., 2016). While R&D spending growth has also overtaken both revenues and sales, general and administrative (SG&A) expenses during this time (Dixit and David, 2017), firms are increasingly ‘hedging their bets’ and strategically redirecting efforts to alternative therapies. The discontinuation of promising molecules in late Phase II and Phase III trials can have serious repercussions for patients, as recently evidenced by Pfizer’s cessation of all neuroscience and dementia-related drug development activities because of the high failure rate of clinical trials and poor return on investments (Le Couteur, 2018).

In exploring strategic intent around how digital experiments drive network performance and choices, we use the ‘On-Demand Clinical Supply’ case to represent the Adaptive Clinical Supply

innovation category. Here, organisations are moving towards more collaborative models involving specialised networks to improve the non-competitive aspects of demand and supply chains, for example, in designing clinical trials with built-in flexibility and agility. This is a key industry goal as consortium partners estimate that between 50–75% of clinical trial material is not dispensed, which is resulting in massive annual inventory write-offs (write-offs are in the £10's of millions per year for each of the major MNCs).

While the 'Smart Label' case has more of a commercial focus in developing systems for the effective track and trace of 'high-value' drug products across the E2E supply chain, outcomes will have direct implications for clinical supply. Serialisation is a critical requirement for the pharmaceutical industry, particularly since the US Drug Supply Chain Security Act (DSCSA) took effect in 2013. DSCSA "outlines steps to build an electronic, interoperable system to identify and trace certain prescription drugs ... distributed in the United States" (FDA, 2018). It aims to protect consumers from "counterfeit, stolen, or contaminated ... or potentially dangerous drugs and establishes national licensure standards for wholesale distributors and third-party logistics providers" overseen by the FDA (ibid). As a result, supply chains are expected to be electronically integrated with nodes of traceability to be established by November 2023 (EY, 2018). As for the UK, the EU's Falsified Medicines Directive (FMD) mandates serialisation at a unit (pack) level and dispenser authentication by February 2019 (European Commission, 2018). In response, consortia are leading experimentation around more 'intelligent packs' that offer clear signals about the condition of a product, its observance of storage and transit environmental conditions, and the use of printed-electronics for smart labels. Whilst far from realisation, the technology lends itself to potential opportunities for flexible 'best before' labels that could disrupt multiple elements of hitherto conventional delivery models.

Adding to the complexity around pharmaceutical supply chain models are current uncertainties over BREXIT which could impact £450 billion in overall annual trade between the UK and the EU (Goasduff, 2016). How will future EU legislation affect both UK pharmaceutical operations (in terms of influence and scale) and, critically, funding streams for future academic-industry consortia?



#### 4.2.2. Network integration: Role of nodes with high centralisation

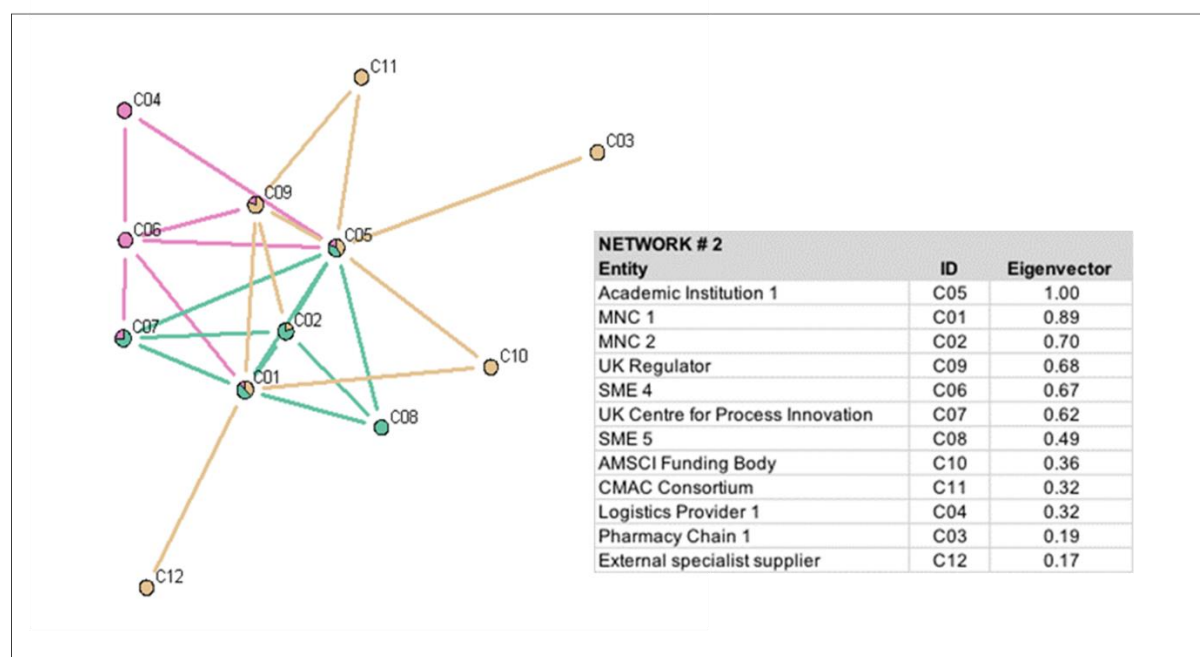


Figure 4. Network structure for  
Southeast (SE) pathways involving sequential transitions (SW→SE and SE→NE)

Based on the approach from Parraguez et al. (2016), patterns and insights from information exchanges between individual organisational entities and the REMEDIES consortium are derived using two sequential transitions (SW→SE and SE→NE). As illustrated in Figure 4, three loosely interconnected communities are in operation, with 12 critical nodes but only 24 edges (maximum partition density of 0.4444'). Some specific characteristics include:

- An INTEGRATION—COORDINATION subnetwork centres on the academic research lead of platform activities (central node C05, with an eigencentrality of 1.00) along with the industrial stakeholder (node C01) leading the clinical platform (eigencentrality measure, 0.89).
- With a community membership of eight, the CLINICAL subnetwork is sparse and based largely on the central academic partner and two core industrial stakeholders (all with eigencentrality measures > 0.70).
- Critically, the UK regulator MHRA, is a key contributor to both CLINICAL and INTEGRATION—COORDINATION subnetworks (node C09) with an eigencentrality of 0.68.
- A RISK subnetwork, comprised of four key partners, assesses a range of clinical and commercial technologies and is led by a pharmaceutical risk specialist (node C08) with an

eigencentality of 0.49. One area of focus, led by sector specialists, relates to 'informed logistics' initiatives, including the development and integration of 'intelligent' pharmaceutical packaging, e.g., led by the process manufacturing partner of the UK government's network of 'Catapult' centres (node C07).

- Given the specialist nature of the activities across the supply network, nodes C03 and C04 are most recent additions to the consortium, in addition to node C12 (in an informal partnering arrangement)

#### *4.2.3. Innovation Performance: Modalities for mitigating risk*

In terms of clinical trials, many new medicinal products are introduced early and/or exclusively into locations with limited pharmacovigilance capabilities and capacities (WHO, 2017). High-level strategic goals of the overall REMEDIES research programme help to inform new models of care based on improved 'compliance', 'adherence' and 'personalisation'. In terms of innovation performance, we can again view digital inputs linked to business outcomes in terms of sequential progression (Ferdows and De Meyer, 1990; Flynn and Flynn, 2004).

Lower-level measures linked to strategic intent in a clinical setting relate to the development of new operating regimes that drive Quality Assurance (QA) dominant product releases. Specifically, the 'On-Demand Clinical Supply' case initially targets 'low hanging fruit' with reconfiguration potential for replacing the current manual Quality Control (QC) testing regime (e.g., high-volume stock keeping units (SKUs) for which traditional demand forecasting could provide stable volume projections for lead-time critical products). At higher levels of sequential progression, QA dominant product releases, coupled with improved compliance, lends itself to a radical shift to 'adaptive' clinical trials where production planning could be driven by clinical trials and performance outcomes (e.g., responsiveness and flexibility involving supply). Digital interventions enabling late postponement and product customisation initiatives could potentially collapse standard transaction and processing times and eliminate costly write-offs of unused clinical stock, typically in excess of £50 million per MNC per year.

As for lower level sequential progressions in a commercial digital supply context, experimentation with printed electronics for packaging is providing information and validation around anti-counterfeiting, product tampering and product consumption safety. In essence, quality and dependability measures relate to the 'integrity' of the product, specifically, 'transparency' and

‘security’. As packaging capabilities are upgraded in line with serialisation requirements, significant changes will impact operational routines, standard operating procedures and workflows, as well as risk evaluation and mitigation strategies. At higher levels, efforts have extended to product ‘personalisation’ and experimentation in handling SKU volume and variety in line with both policy requirements and future therapy areas. Likewise, serialisation is enabling data and information exchanges for advanced analytics which could lead to deeper insights into consumption patterns, geographical penetration, and sales and marketing cost-benefit effectiveness (EY, 2018). Experimentation around ‘speed’ involving ‘tracer pack’ trials have demonstrated improved supply responsiveness, which could significantly reduce patient kit waste and costs when transferred to clinical trial contexts.

#### **4.3. Platform-based Innovation: Parallel Pathway**

The ‘Lab-on-a-Chip System’ and ‘Digitalisation Lab’ cases (see Table B1 in Appendix B) are positioned in the NE quadrant (see Figure 2) and enable us to explore parallel pathways (SW→NE) involving the simultaneous digitalisation of supply networks and development/production. In contrast to the previous cases outlined in sections 4.1 and 4.2 which were of a ‘sequential’ nature, the parallel pathway is different, with multiple dimensions of changes in each digitalisation effort. Here, firms need to consider ‘unconventional’ requirements in a rapidly changing industrial landscape. For example, digitalisation concepts coupled with increasing ‘personalisation’ will greatly impact institutional contexts in many sectors (Cesuroglu et al., 2017). Hence, we go beyond sequential transition pathways to investigate how next-generation pharmaceutical products and services are being developed. Using platform-based design principles — which require radically new supply network configurations — we explore potential sea-change requirements in supply collaboration, site location, capacity, inventory, and customer engagement using the two case studies.

Specifically, characteristics of the case pair centre on ‘miniaturisation’ and the delivery of lower volume, high variety niche products and complementary services (e.g., data analytics) to new markets. In essence, desired outcomes of the NE quadrant appear as polar opposites to those of traditional high volume, low variety blockbuster business models.

#### *4.3.1. Strategic Intent: Aligning business models with environmental needs*

Experimentation around 'point-of-care' and 'digital microfactory' concepts are forcing organisations to rethink how best to (re-)configure supply chains to manage (increasingly) 'two-way' interactions and new relationships involving both customers and suppliers.

The 'Lab-on-a-Chip System' case charts the emergence of microfluidics-enabled 'sample-to-answer' solutions that are both reliable and fast and could support operations in more decentralised settings. Microfluidics ... [is defined as] "...the engineering or use of devices that apply fluid flow to channels smaller than 1mm in at least one dimension. Microfluidic devices can reduce reagent consumption, allow well controlled mixing and particle manipulation, integrate and automate multiple assays (known as 'lab-on-a-chip'), and facilitate imaging and tracking" (Nature, 2018). With current diagnosis procedures often being time-consuming and costly, 'miniaturisation' has enabled improved biomedical applications in terms of cost reduction, high-throughput, ease-of-operation and analysis (Wu et al., 2018). In terms of future business models, we also use the case to explore the rise in strategic importance of biologics in the pharmaceutical sector (Waltz, 2014; see also Appendix B), specifically, 'smart' materials and emerging capabilities that support a broad spectrum of bioanalytical assay formats targeting proteins, nucleic acids and cells (e.g., Burger et al., 2015; Nwankire et al., Saez et al., 2018). While production processes of synthesised chemical drugs (small molecules) may be relatively well defined, biologics, however, have more complex production processes that tend to yield much smaller quantities with less uniform batch-to-batch equivalence. It is also difficult to scale biologics from laboratory quantities used for early analysis and pre-clinical testing to larger-scale batches while maintaining product purity (Morrow and Felcone, 2004).

In terms of digital inputs, a QbD platform approach integrates virtual prototyping enabled by modelling and simulation, novel 'scale-down' paradigms and rapid design-for-manufacture practices. Specifically, a scaffold module forms the basis of the QbD platform (e.g., Smith et al., 2016), with flexible functionality achievable through 3D-printed components or reactionware-type modifications as per Kitson et al. (2012) and Dragone et al. (2013). In addition, some 'Lab-on-a-Chip' studies have begun to incorporate digital and mobile technologies (Wu et al., 2018) in developing smarter digital supply chain concepts to interact with customers throughout the entire product lifecycle (Harrington and Burge, 2018).

The 'Digitalisation Lab' case is a Proof-of-Concept reference facility conceived by a Global MNC to facilitate the E2E integration of modular and continuous manufacturing equipment streams. Contract manufacturing organisations (CMOs) and primes leverage an open-access network of assets for rapid assessments of flagship project innovations involving information exchanges between upstream with downstream processes to drive business model-changing shifts. Various consortia are leveraging facility expertise in many technical areas — for business processes aligned with development and production, process automation, manufacturing execution systems, IT, and data science — to transform new technologies into solutions that address specific business challenges. With new systems comes the need for new regulations, where regulatory confidence and internal buy-in is paramount. According to one central node respondent:

*“we needed to make the required transition real to people — including having a working production unit — so they could experience physically what can be achieved, and also embrace the changes and challenges associated with it.”*

The goal for developing this reference facility is an entirely digitalised and virtual approach to the design and launch of new products. Here, the conventional new product introduction (NPI) process, where products are taken through design, manufacturing and supply stages sequentially and separately, is replaced by a digital approach that enables NPI in a rapid, connected and continuous E2E manner — 'from microfactory-to-activated patient'. Rather than identifying and solving problems in isolation, manufacturing challenges are viewed holistically and managed as a team effort. Greater integration of R&D and manufacturing functions is enabling better understanding of the complete system of product design, manufacture and supply, through effective use of data, to enable rapid assessment of manufacturability, robustness, consistency and performance.

#### *4.3.2. Network integration: Role of nodes with high centralization*

Using the SNA approach (Parraguez et al., 2016), information exchanges between individual organisational entities are presented for the 'Digitalisation Lab' case in Figure 5. Four communities are interacting with 24 critical nodes and 143 edges (with a maximum partition density of 0.6057472), and are summarised as follows:

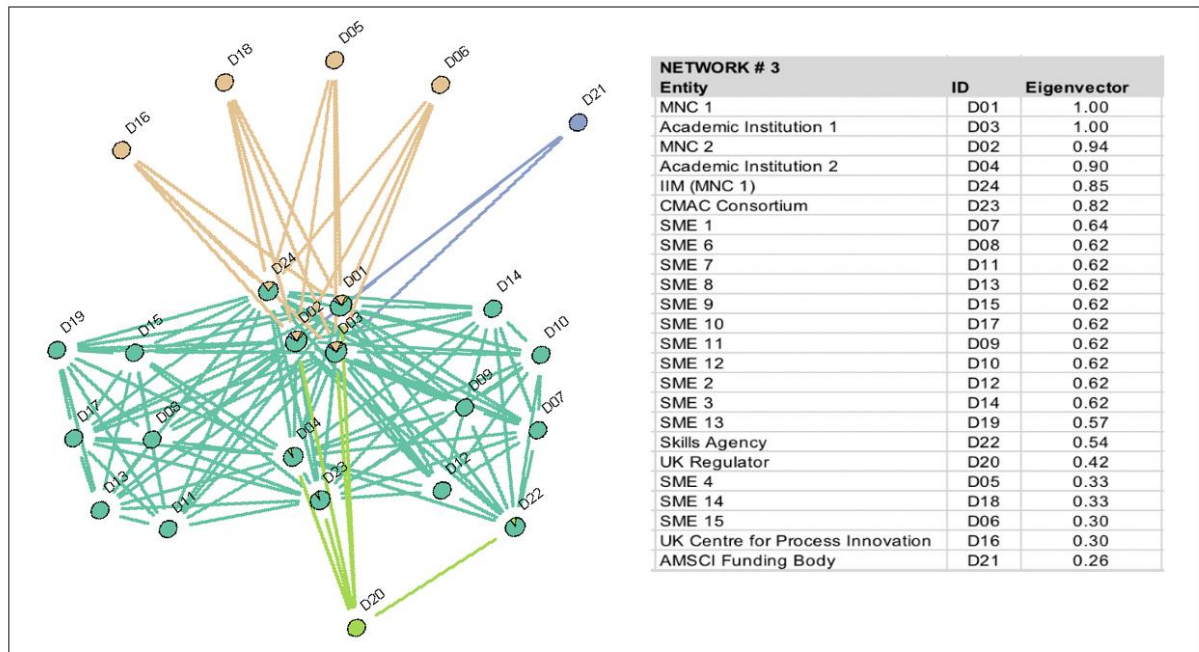


Figure 5. Network structure – Parallel pathway (SW→NE)

- A platform-based COORDINATION subnetwork of 18 consortium partners revolves around six central nodes (all with eigencentality measures > 0.82). The 12 remaining nodes form two distinct outlier networks each with a community of six members. They are designated here as LEFT- BRANCH and RIGHT- BRANCH respectively (eigencentality measures in the range of 0.54-0.64).
- The LEFT-BRANCH outlier network (nodes D08, D11, D13, D15, D17, and D19) represents an individual workstream led by a central academic partner (node D04) focused on platform technologies and 'plug-and-play' equipment development.
- The RIGHT-BRANCH outlier network (nodes D07, D09, D10, D12, D14, and D22) represents an individual consortium work stream led by a lead industrial partner (node D02). Technical outcomes focus on both data organisation and analytics.
- A community of eight members make up the APPLICATIONS subnetwork, which is based around four central nodes (academic institution D03; industry partners D01 and D02, and D24). The four remaining nodes represent stand-alone work streams and digital experiments led by specialist partners (D16, D18, D05 and D06).

- A REGULATORY subnetwork consisting of four core members (academic institutions D03 and D04; MNCs D01 and D02) and the UK regulator (node D20) began collective engagements in 2016.
- The PLATFORM DESIGN subnetwork is a three-way research-industry-government engagement (nodes D01, D03 and D21) to support collaborative industrial projects in the UK. The rationale for platform-level interventions is underpinned by: traditional market failures, spill-over effects associated with R&D activity, and difficulties in internalising the full benefits of training (BIS, 2015).
- As part of platform design, all research strands and subnetwork communities develop new tools and training packages to support consortium activities. Accordingly, a not-for-profit organisation (node D22) with a focus on specialist skills acts as a strategic partner to industry in providing support to the UK's Science Industry Partnership and membership forums. Node D22 is now also linked to the UK regulator (node D20) through consortium activities.

The 'Lab-on-a-Chip system' case explores a dyadic partnership newly established to target techno-economic requirements for a range of increasingly decentralised applications. Organised in two segments — 'core platform' and 'pilot applications' — the project-focused initiative operates as a virtual institute headquartered at an academic institute in Ireland (node E01) and partners with a complementary mirror group at a German-based institute specialising in production technology (node E02). The core platform provides a basis for a series of pilot applications demonstrating bioanalytical assay formats, general chemistry and immunoassays, nucleic acid testing and cell analysis techniques. Specific assay targets are discussed with existing and potential industry partners who have an opportunity to set the direction for the pilots. Within a joint development environment aligning manufacturing and characterisation equipment, node E01 leads microfluidic design, simulation, prototyping, fluidic testing, project acquisition and management while node E02 is mainly responsible for 'scale-up' initiatives.

#### *4.3.3. Innovation Performance: Modalities for mitigating risk*

High level strategic goals of the cases involve using a range of diverse digital technologies to 'connect' previously disparate upstream and downstream operations. Key to this is the integration of data generated along the product lifecycle in a variety of digital contexts. In terms of data timescales — days, hours and minutes are no longer considered digital. Data integration is defined as the automatic generation, recording, and assembly of data streams and its subsequent presentation — in 'real-time' — to provide meaningful information for optimising existing processes.

In terms of parallel transitions from the SW to the NE quadrant, data and information is central to determining the viability (technical, operational, societal) of 'continuous' processing platforms and a suite of data tools to support more 'localised' production ('microfactory' concepts) and 'personalisation' in terms of diagnosis ('Lab-on-a-Chip' systems). For example, novel design thinking and ethnographic approaches are being utilised to better understand the needs of the individual. The aim to 'join up data' and engage with the patient has resulted in new measures relating to 'levels of parallelisation' in the case of microfluidic platforms. Here, 'scaling effects' have led to new phenomena that enable entirely new applications that are not accessible with classical liquid handling platforms. For example, early diagnosis and prognosis of prostate cancer is increasingly moving towards evaluations based on a strategic combination of biomarkers (Mishra et al., 2018). This has greatly improved patient safety by minimising the risk of errors for individual patients by enabling integrated devices to address point-of-care challenges in a more simple and consistent manner (e.g., Mark et al., 2010). These advances reflect a changing ecosystem where multiple partners and 'platform strategies' are favoured in delivering tailored solutions according to critical requirements of different applications for increasingly niche market segments, i.e., the capability to 'parallelise' multi-parameter detection on the same device when compared to conventional single-marker methods. In terms of actors, new-to-sector 'designers' are increasingly talking directly to end-users, which has helped them to refine formal and informal connections and underscored the need to do so. This is evidenced by central nodes leveraging their extensive networks, particularly in scouting for new and new-to-the-sector partners.

However, questions remain about data ownership (use and protection) and compensation in developed countries (Harrington and Burge, 2018). Who exactly will capture value, for example, platform sponsors, consumer users, developer users, or other platform participants? (Parker et al.,



2018). And for remote locations and developing countries where digital literacy will be required to enable access and influence solutions? Hence, there is a concerted institutional focus on 'digital standards', where consortia are looking to engage with UK regulators in this space and gain expertise in the area of data and legal frameworks.

## 5. Cross-case Analyses

Using the cases outlined in section 4, we explore network effects relating to transition pathways and transformations impacting 'current state' 3-4 $\sigma$  sector performance. Specifically, we focus on innovations that challenge both conventional 'batch-based' philosophies in development and production and industry practices built around traditional 'make-to-stock' models.

As per Edmondson and McManus (2007), we first use the base framework (see Figure 2) to link cross-case observations on transitions to intermediate and nascent theory development. As depicted in Figure 6, sequential transitions (SW→NW and SW→SE) positioned beyond conventional settings (e.g., the SW quadrant) enable us to explore provisional explanations of phenomena, the potential of new constructs and the relationships between these and well-established constructs. Subsequent sequential transitions (NW→NE and SE→NE) go beyond intermediate theory settings (e.g., the NW and SE quadrants). Based on these we propose tentative answers to novel questions of how and why these transitions take place (over other options and pathways) and tease out new connections among phenomena. Finally, parallel transitions (SW→NE) with potentially no intermediate framing enable us to explore platform-based phenomena based on 'direct routes' to synchronised digitalisation involving development, production, and supply network activities.

In summary, as shown in Figure 6 — in terms of time scales — if  $T1 + T2 < T3$ , then sequential transitions are characterised by organisations and their networks largely leveraged legacy systems with 'one side' digitalised first to ensure a 'rapid' test to determine success or failure. As a rule, product development and production activities tend to be digitalised first before supply networks (SW→NW before SW→SE), hence, supply network reconfigurations remain largely reactive.

In the case of  $T1 + T2 > T3$ , the parallel pathway forces organisations to radically reconfigure and to rethink production/supply/regulatory networks, customer acceptance and business models in tandem. For example, pre-competitive consortia are 'proactive' in efforts to deliver new systems and

new regulations in a ‘non-conventional’ manner, as evidenced by E2E digital demonstrators (linked to our cases) that do not operate under current regulations.

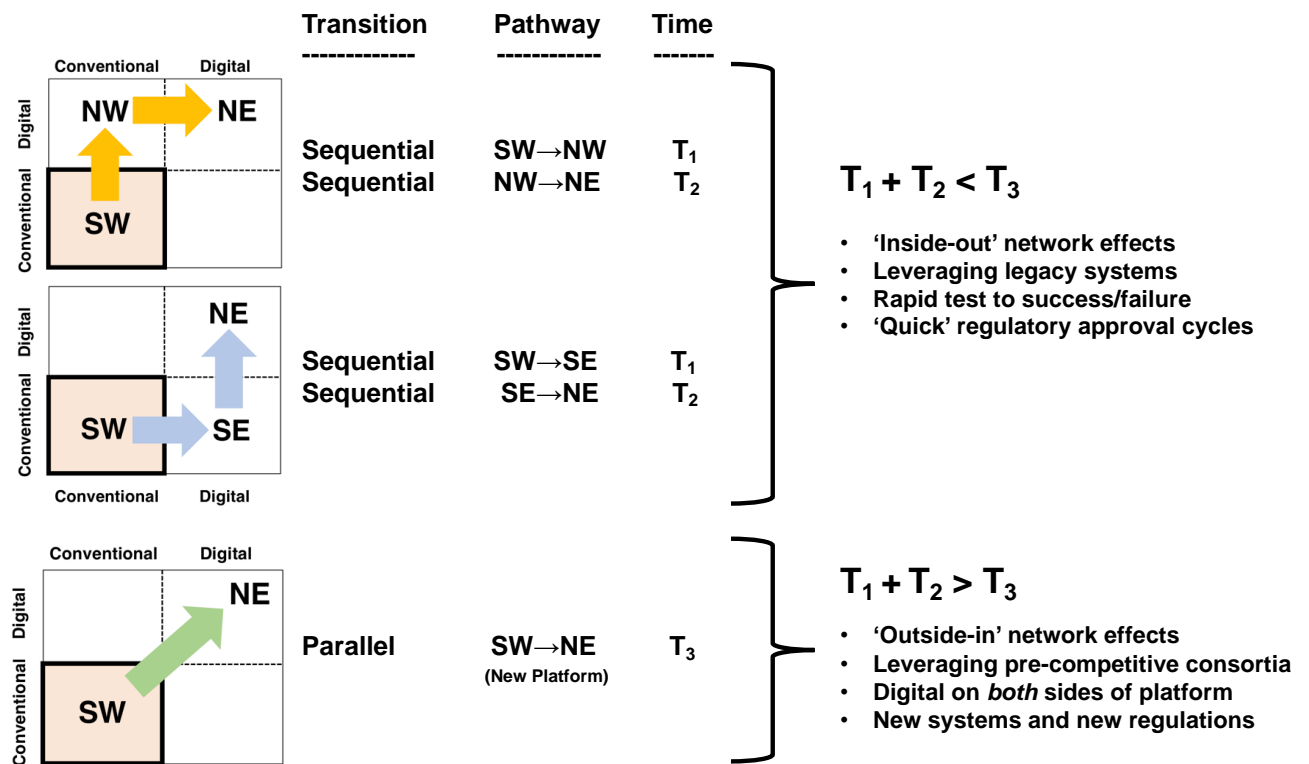


Figure 6. Base framework charting sequential (vertical and horizontal) and parallel (diagonal) transitions

Findings to support these initial observations are outlined in our cross-case analyses in sections 5.1–5.3 and are again structured around the three analysis dimensions: strategic intent, role of central nodes, and innovation performance. Key summary points are outlined in Table 1.

Table 1. Cross-case analyses

	<b>‘Dial-a-Molecule’ and ‘Golden Batch’</b>	<b>‘On-Demand Clinical Supply’ and ‘Smart Label’</b>	<b>‘Lab-on-a-Chip System’ and ‘Digitalisation Lab’</b>
<b>Type of Network Innovation</b> (Framing of cases)	Digital Development & Digital Production	Digital Supply Network	Digital Development, Digital Production, & Digital Supply Network
<b>Transition</b>	Sequential	Sequential	Parallel
<b>Strategic intent:</b> Aligning Business Models with Environmental Needs	<ul style="list-style-type: none"> <li>• Moving from ‘one-experiment-at-a-time’ traditional empirical approaches towards modelling-based design of drug products &amp; manufacturing processes</li> <li>• Experimentation goes beyond traditional DoE by leveraging modelling tools &amp; process analytical techniques to support delivery of targeted molecules &amp; ‘robust’ processes</li> </ul>	<ul style="list-style-type: none"> <li>• Traditional ‘make-to-stock’ supply chains enhanced through ‘adaptive’ approaches enabled through digital information</li> <li>• Data systems reconfigured for improved traceability &amp; compliance monitoring, requiring new regulatory constructs</li> </ul>	<ul style="list-style-type: none"> <li>• Parallel reconfiguration paths to meet future techno-social sector requirements implying a ‘de facto’ platform approach with emergence of new design rules</li> <li>• Cases focusing on ‘data organisation’, the E2E integration of ‘modular’ equipment &amp; continuous process innovations that operate at much lower and unconventional scales</li> </ul>

	<ul style="list-style-type: none"> <li>Sequential changes in predictive capabilities enabling 'real-time' comparison of batches against 'ideal' process states for selected processes</li> </ul>	<ul style="list-style-type: none"> <li>Sequential changes in process &amp; packaging redesign supporting potential for more Quality Assurance (QA) dominant product releases in certain cases</li> </ul>	<ul style="list-style-type: none"> <li>Evidence that organisations have now scrapped 'batch' development, which could trigger future domination of 'make-to-order' models</li> </ul>
<b>Network integration:</b> Role of Nodes with High Centralisation	<ul style="list-style-type: none"> <li>Multidisciplinary communities take active roles facilitating the development of collaborative research proposals, interdisciplinary mobility funding &amp; proof-of-concept awards</li> <li>Principle nodes within the academic subnetwork co-developing initiatives as pairs of 'pivots' &amp; 'navigators' related to their specialisms; brokering access to potential end-user groups</li> <li>Virtual integrated networks of 'asset libraries' and advanced reaction</li> </ul>	<ul style="list-style-type: none"> <li>New 'outcome-based' product delivery models coordinated by clinical &amp; commercial central nodes focused on quality &amp; dependability measures relating to the 'integrity' of products</li> <li>Specialised subnetworks commissioned to design clinical trials &amp; protocols with built-in flexibility &amp; agility</li> <li>Consortium approach &amp; subnetwork activities now</li> </ul>	<ul style="list-style-type: none"> <li>'Unique pairings' &amp; 'platform-based strategies' required to deliver an increasingly diverse scope of applications</li> <li>Hybrid role of nodes with high centrality often interchangeable with multiple combinations in play, based around evolving modes of innovation</li> <li>Central nodes increasingly using language around 'new measures', such as 'levels of 'modularisation', 'scale juxtapositioning,' capabilities for 'convergence' &amp; 'precision'.</li> </ul>

	platforms made accessible by network members and their wider communities	enabling active engagement with regulators	
<b>Innovation performance:</b> Modalities for mitigating risk	<ul style="list-style-type: none"> <li>• 'Quality-by-Design' (QbD) principles have emerged over time based on advanced control &amp; monitoring strategies which are mitigating but linear</li> <li>• Initiatives have made multiple albeit small changes to existing batch-based processing routines</li> <li>• Pre-competitive focus on small molecules; high-volume low-variety solid oral dose forms dominant</li> </ul>	<ul style="list-style-type: none"> <li>• Supply network design rules emerging linked to archetypes &amp; segmentation around 'personalised' solutions</li> <li>• While hitherto sequential in nature, network-centric experimentation around increasing SKUs sees partners leveraging consortium links</li> <li>• Moving towards more 'coopetition' at platform level with potential for rapid two-way transfer of design &amp; manufacturing data</li> </ul>	<ul style="list-style-type: none"> <li>• Relevance of network innovation dimensions (supply network &amp; operations) becoming fundamentally different in parallel pathways</li> <li>• Consortium effect enabling shifts from 'passive' interactions (single-firm) towards unique conversations &amp; transactions beyond the 'norm' (platform-centric)</li> <li>• While coopetition on quality, dependability, service &amp; cost required as "qualifiers", competition now shifting to other measures, depending on new business models</li> </ul>

### **5.1. Strategic Intent: Aligning Business Models with Environmental Needs**

Digital experimentation results in better targeted product designs, more optimised processes and enhanced customisation, as evidenced by our case studies. Increasing use of 'digital workflow' methodologies underpin the digital development and production cases (SW→NW and NW→NE pathways). As a result, it is theoretically feasible to avoid extensive experimental stages of development through data-driven model predictive control approaches for a series of process platforms. In practice, a hybrid approach is often adopted where parameter estimation, based on experimental results from traditional design of experiment (DOE) approaches, are used to assess specific process conditions (e.g., cooling rate, concentration, seed loading) using specialist software developed by SMEs. A common thread of enabling 'crystal quality' is evident for the case pair, which define both basic attributes of a 'targeted molecule', i.e., specific crystal-size distribution, shape, polymorphic form and purity (Laird, 2013), and 'robustness' in terms of 'control' and 'right-first-time' synthesis and crystallisation. In practice, predictive capabilities and 'ideal' process states are well developed for select processes in large-volume and low-variety contexts, for example, the crystallisation of model compounds such as paracetamol (acetaminophen) (Brown et al., 2018).

For sequential pathways focused on supply (i.e., SW→SE followed by SE→NE), the use of 'just-in-time' technology has demonstrated a step change in traditional 'dependability' measures such as 'provide fast deliveries', 'meet delivery promises' and 'reduce production lead times' (Boyer and Lewis, 2002) — from 4-6 months to <1 week. What is also clear is the impact of 'quality' in terms of supply chain information and its role in reducing waste within clinical supply. With improved information quality, zero-stock-out (patient-level) clinical supply chains with low waste and high velocity (and by association, lower cost) is a targeted business output, as is the strategic intent to extend the application to 'make-to-order' delivery models.

In meeting basic future requirements of the pharmaceutical sector that support lower-volume, high-variety niche products, parallel pathways (SW to NE) enabled by platform-oriented approaches have highlighted the need for new design rules around 'scale'. Enabled by 'converging' technologies, data and information, these parallel pathways operate with the new paradigms of 'process intensification', 'modularisation', and 'combinations' in continuous modes, which challenge the traditional location-decision logic (and that of the 'large batch' pharmaceutical plant). Data organisation is seen as a critical step in building predictive models (Mukherjee and Sinha (2017)).

These models are essential building blocks for design rules that enable parallel development. For example, the design rules are required for integrating smaller footprints — in setting up E2E configurations that offer both flexibility in terms of production capacity, and speed in terms of ‘scale-out’ — with digital twins providing additional options for distributed manufacturing-type blueprints (Brennan et al., 2015; Srai et al., 2016b).

## **5.2. Network Integration: Role of Nodes with High Centralisation**

The combination of fundamental and applied research in drug discovery being pursued in academia is creating more opportunities for novel interactions and partnering models with industry (Tralau-Stewart et al., 2009).

For digital development and production pathways (SW→NW; NW→NE), multidisciplinary communities of practice leverage knowledge gained from previous collaborations. This has lowered risk while bringing together multiple funded groups to tackle specific ‘grand challenges’. Firm practices pre-2011 (before this study commenced) can be best described as ‘single-firm led’ and as having a sequential nature, avoiding operational tasks that were loaded with risk in transitioning. Post-2011, consortia (e.g., CIM CMAC) have enabled a more network-centric collaborative and multi-disciplinary approach to evaluate business cases and risky investment decisions. Specific partners have been identified based on their specialisms and this has resulted in consortia growing well-coordinated networks of assets and resources.

We examine digital supply pathways (SW→SE; SE→NE), in the context of growing patient involvement through information and communication technology and ‘intelligent’ technologies looking to transform wider healthcare provision. Again, innovations in this space are a marked departure from traditional ‘one-size-fits-all’ supply network configurations where initiatives have made multiple — albeit small — changes to conventional routines. What is now clear is the need for more E2E collaboration at a system-level, as evidenced by the development of business models based around new ‘outcome-based’ product delivery models being coordinated by clinical and commercial central nodes. A common approach here has been to first build temporary partnerships to tease out explicit links between the ecosystem, the innovation and capabilities needed. We have seen the establishment of specialised subnetworks engaging with non-consortium partners on equipment to facilitate more ‘adaptive’ clinical trials.

Where traditional engagements involving conventional rules (e.g., around compliance) may typically result in a once-off interaction between a single firm and the UK regulator, the consortium approach is now enabling active engagement and two-way information exchanges with regulators. Collective conversations have centred on promoting 'regulatory innovation' and up-front agreement on, and validation of, a consortium programme of digital initiatives. An example is the case of adaptive clinical trials, with directed feedback on validation requirements involving pre-production and real-time production data to support 'near-real time' product release. This is particularly evident in the case of the parallel pathways (SW→NE), where 'unique pairings' are aiming to deliver an increasingly diverse scope of applications at 'non-standard' scales. Our cases highlight the interchangeable roles of key actors with multiple combination options (e.g., 'integrator-allocator', 'pivot-coordinator', 'navigator-broker') based on the product's or service's stage of emergence and mode of innovation (e.g., a modular 'plug-and-play' technology, coupled with hot melt extrusion or 3D printing). Furthermore, our studies provide evidence of shifts away from industry standard 'scale-up' regimes and thinking with emerging design rules (idea of 'scale juxtapositioning') driven by novel SME-MNC combinations, i.e., tech entrepreneurs and industry incumbents.

### ***5.3. Innovation Performance: Modalities for Mitigating Risk***

Moderating practices in the pharmaceutical sector are often seen as 'ultra-conservative' and 'old school' compared to other industries that routinely implement sophisticated technologies to increase both process and product understanding and implementation (Rantanen and Khinast, 2015). As shown in sections 5.1 and 5.2, this 'slow' route of 'incrementalism' associated with sequential pathways is driven by entities avoiding operational tasks burdened with risk in 'transitioning'. However, recent preliminary studies have shown that benefits of digitalisation most significantly outweigh the considerable risks, for example, in the area of digital production processes (BSI, 2016).

To link innovation performance with specific risk-based regulatory approaches, we examine pathways in the context of (1) how manufacturing process factors affect product quality and performance and (2) the capability of process control strategies to prevent or mitigate the risk of producing poor quality products (FDA, 2004). Initiatives in primary manufacturing and formulation processing have acted, somewhat, as 'show pieces' resulting in only minor modifications to existing routines (e.g., less physical testing). Traditional control strategies for batch processing, have been



based around fixed recipes and profiles. For sequential pathways SW→NW and NW→NE, digital inputs relating to the quality control of unit operations have largely centred on 'near-continuous' monitoring conditions within mixing vessels, tablet presses and other critical equipment. Here, QbD principles are mitigating yet linear, evidenced by a sequential approach to API crystallisation, which is a key focus of three consortia outlined in section 4.1. Upstream and downstream operations (to crystallisation) continue to be 'batch' or 'semi-continuous' and operate as decoupled operations often with independent coordination and governance mechanisms (Srai et al., 2015b). This sequential approach to crystallisation has had a knock-on effect as it is essentially the 'rate-limiting step' that most influences subsequent 'modular moves' right up to when the crystal dissolves upon administration to a patient, enabling the molecular form of the drug to be absorbed (Brown et al., 2018).

For digital supply pathways (SW→SE; SE→NE), it is now possible to map emerging supply network design rules to segmentations based on product types in some cases (e.g., small molecule, formulation type, chemistry, stability), study design (complexity, shelf-life, phase and speed), customer demand profiles, technologies and risk profiles. Archetypes can also be developed through data analytics involving public domain data sources to identify opportunities to increase product personalisation capability and tailor supply chains accordingly. While hitherto sequential in nature, network-centric experimentation around increasing SKUs sees partners leveraging consortium links. This enables a reduction in investments at risk via delayed decision requirements (spanning both development and production contexts). As outlined in Table 1, the goals of participating organisations with a focus on traditional solid oral dose forms are changing and will require a move towards greater 'coopetition' at a platform level. Here, 'scale-out' concepts are now radically different with potential for rapid two-way transfers of design (clinical) and manufacturing (commercial) information and data.

For parallel pathways (SW→NE), the nature of the supply network and operations are fundamentally different in these transitions, with a shift from 'standard' dialogues and 'passive' interactions, towards 'unique' conversations beyond the 'norm'. Multiple partners are now required to deliver a wide-ranging set of applications and future large-scale integration of, for example, 'point-of-care' solutions that could move beyond the multiple risk approaches identified for disruptive innovation. Reflecting on collaborations, designed around platforms, a consortium co-founder and steering group member stated (REMEDIES, 2018):

*“Before... [the launch of the consortium] collaborations were on [a] scale of each of our individual workstreams. We were advised that a programme with 24 partners, and the breadth of work we wanted to undertake, would be unmanageable. We managed to achieve this super-sizing by finding coherent themes, creating technical work packages, or Apps, that sat within our two overriding workstreams for the clinical and commercial supply chains.”*

It is argued that this platform effect could prompt the need to re-define the role of regulators beyond that of traditional regulatory control and governance tasks, to facilitate performance ‘outcomes’ (e.g., Huber, 2013). In addition, while ‘coopetition’ on quality, dependability, service, and cost are qualifiers in platform moves, we argue that competition is shifting to other measures based on new business models (e.g., a batch-to-continuous-conversion tipping point, a small molecule to biologics strategic shift). More ‘continuous’ digital production processes, in conjunction with digital design, could enable future production of novel medicines without the intermediate role of batching, or the scheduling issues associated with traditional pharmaceutical manufacturing and supply. Real game-changing opportunities emerge when such technologies (digital tools for design, 3D printing, continuous manufacturing, smart packaging for compliance and counterfeit detection, mobile phone apps) converge and interact, for example, in supporting patient stratification and the target-driven design of nanomedicines and cell and gene therapies (Hare et al., 2017; Harrison et al., 2018b).

## **6. Results: Research Propositions**

Drawing on the emerging technologies (e.g., advanced process analytics) and contexts (e.g., design, production, supply network) outlined in this study, we now explore theoretical implications that a series of digital interventions could bring to theory and practice. For example, how relevant are ‘conventional’ theories of supply chain innovation today in addressing network-centric digitalisation and complementary digital innovations. Hence, we articulate the following propositions in this section on how digitalisation could affect development, production and supply networks. See Appendix D for a summary of the propositions and evidence base from our cases that support their development.

Our initial discussions, based on the cross-case analyses, began with an overarching observation regarding the nature of cumulative capabilities. Here, we first explore what digitalisation means for conventional core constructs — quality, dependability, speed and cost. Organisations

continue to view measures such as 'quality' and 'dependability' as critical, for example, in digital supply contexts as relating to 'integrity' 'transparency' and 'security', as well as improved 'quality' for the end-consumer (e.g., availability and quality of information ensuring specification compliance). In summary, the sand cone model and conventional supply network dimensions (e.g., Srai and Gregory, 2008) work well in sequential pathways; however, the nature of the constructs are continually evolving and are driven by central actors and their networks. The following two propositions serve as overarching principles, in terms of sequential pathways:

***Proposition 1A:*** *When transitioning from Conventional–Conventional to Digital–Conventional or Conventional–Digital configurations, quality and dependability processes are established by central network actors before cost and responsiveness.*

***Proposition 1B:*** *When transitioning from Digital–Conventional (or Conventional–Digital) to Digital–Digital configurations, the presence of quality and dependability processes mediate the risk of achieving desired cost reduction and responsiveness outcomes.*

Second, we examined how organisations and networks aim to manage the changing nature of quality, dependability, speed and cost definitions and any underlying trade-offs (as per Boyer and Lewis, 2002) in a digitalisation setting. Our study finds that to avoid resistance and mitigate organisational risk, sequential pathway initiatives continue to make numerous yet minor changes at the individual unit operations level. While 'modular' batch arrangements (enabled by process intensification initiatives) have replaced more conventional batch-based processing routines, maintaining inventories and performing off-line quality control testing remain the norm. In summary, conventional reconfigurations also carry risk (and are in line with propositions 1A and 1B). Focus continues to centre on lower-level measures that are easier to handle in conventional settings. As a result, sequential transitions (e.g., SW→NW; NW→NE and SW→SE; SE→NE) may never quite arrive at the end-goal (NE) because of variations in the modular nature of the innovations, cycle time considerations and desired delivery targets. Thus, we offer three additional propositions as overarching principles to address these issues.

**Proposition 1C:** *Modular moves by central actors serve as risk abatement mechanisms in delivering outcomes (for example, quality and dependability, responsiveness and cost reduction).*

**Proposition 1D:** *In order to cut the cycle time ( $T_1+T_2$ ) it is desirable to stay conventional either on the demand or supply side in the intermediate stage.*

**Proposition 1E:** *The basis for competition after the collaborative stage is associated with the precision with which you can deliver operational measures.*

In contrast, the parallel pathway is different, with numerous dimensions of changes in each digitalisation effort. Here, firms need to consider the changing industrial landscape in incorporating emerging business model measures, and risk abatement mechanisms (e.g., institutional engagement and the confluence of multiple partners; degrees of freedom in 'stress-testing' the existing regulatory regime, product architectures and standards). The following two propositions serve as overarching principles in terms of parallel pathways:

**Proposition 2A:** *Goals for transitioning from Conventional–Conventional to Digital–Digital configurations are aligned with the strategic intent of new business models.*

**Proposition 2B:** *When transitioning in parallel form from Conventional–Conventional to Digital–Digital configurations, organisations attempt to leverage all four measures (e.g., quality, dependability, responsiveness, cost reduction) simultaneously.*

In terms of regulation, traditional batch processing with new digital factory elements (process analytics) has seen firms following the same conventional rules (e.g., for compliance), which has resulted in transitory exchanges with the regulator. In continuous E2E and micro-factory cases, new rules, multiple engagements, multiple partners, eco-system and platform thinking, and other 'unconventional' practicalities are in evidence. The mode of innovation is also changing here – linked to evolution/maturity (evidenced by firms abandoning 'batch' development in favour of 'continuous flow' approaches). A rapidly growing number of consortium-driven cases based around continuous processing have been identified, as opposed to fleeting early successes (one-off case studies)

observed in the traditional firm-firm competition phase pre-2011. In summary, three additional propositions are offered as overarching principles in terms of parallel pathways.

**Proposition 2C:** *New 'platform-driven' risk abatement mechanisms are brought into play by central nodes where the risks in this transition are moderated by network centric platform constructs (e.g., regulatory support to such platforms).*

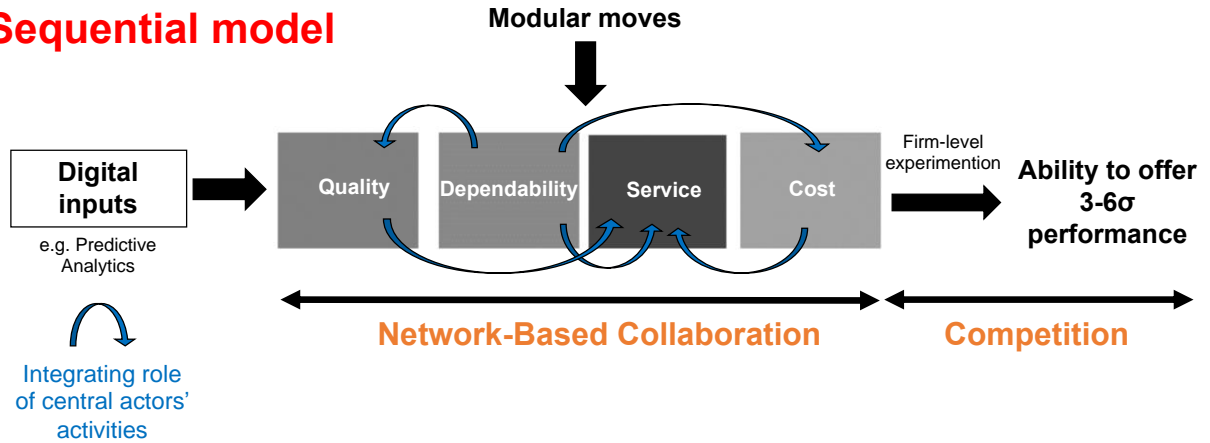
**Proposition 2D:** *There is no intermediate stage in defining platform-based design rules. Both the demand and supply side of the platform much be digitalised simultaneously to reduce cycle time.*

**Proposition 2E:** *Following the collaborative stage the basis for competition is associated with the ability to redesign the business model. Such redesigns often lead to alternative measures beyond quality, dependability, responsiveness and cost as the critical success factors.*

## 7. Discussion

Figure 7 provides an integrated view of the ten propositions discussed thus far into sequential and platform-based models for digitalisation pathways. The sequential model at the top of Figure 7 is centred on network-based collaboration; the outcomes are moderated by modular moves. Firm-level 'experimentation' to enhance collaborative work can take many forms yet are based on traditional performance measures such as cost, quality, service, and dependability (and an ability to offer improvements  $>4\sigma$ ). On the other hand, the parallel pathway model at the bottom of Figure 7 leverages the creation of platforms where central actors play an integrating role involving a series of digital inputs in order to generate outcomes relating to new business models. Firm-level 'experimentation' involves 'customisation' in this platform setting. As digital transformation implies new technologies, standards, and radically different interpretations of performance measures (e.g., 'quality', 'dependability' 'service' and 'cost', as examples from our cases) the risks in transitions are being moderated by the presence of new network-centric constructs. Quality, dependability, service and cost now act as qualifiers, as partner organisations attempt to leverage all four measures simultaneously to compete on different platform/system measures.

## Sequential model



## Platform model

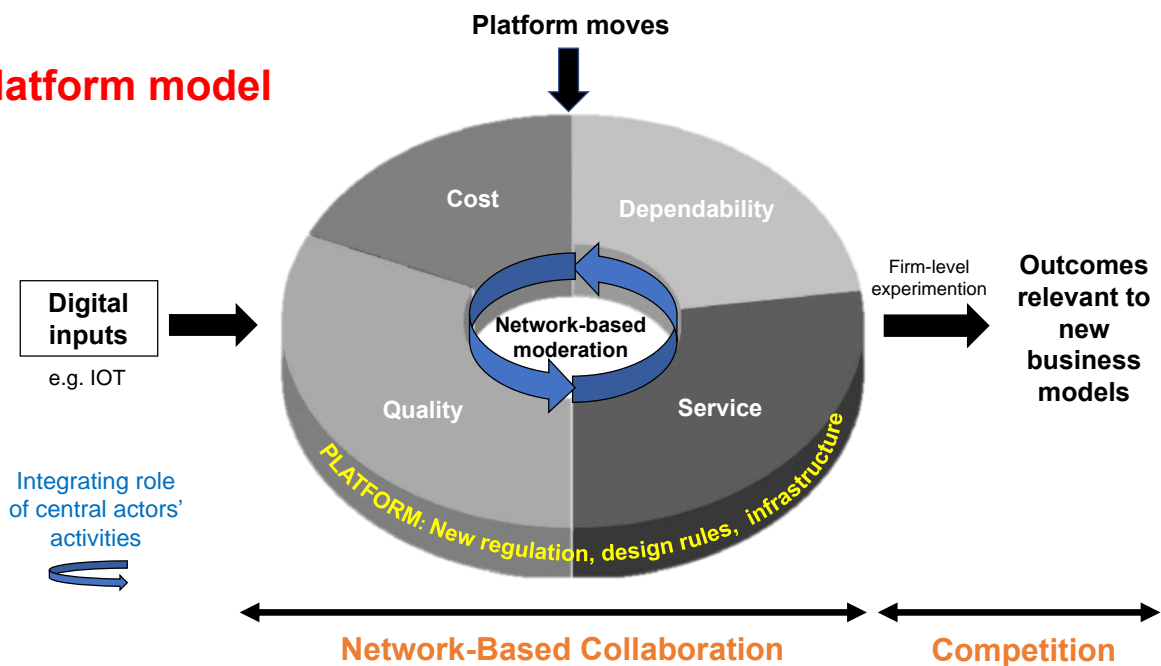


Figure 7. Integrative View of Sequential and Parallel Digitalisation Pathways

### 7.1. Comparison between Sequential and Parallel Digitalisation Pathways

#### 7.1.1. Overlapping and divergent results

Overlapping features involving sequential and parallel digitalisation pathways include a collective moderating effect of the consortium approach that is evident in de-risking projects and enhancing resources (with communications between subnetworks formed). Vulnerabilities associated with moderating practices and transition are demonstrated by the case studies, where sequential and

parallel pathways in each case require configuration changes. A key question here is about the drivers of pathways and how firms 'handle' configuration change i.e., sequential (and never arrive at the end-goal) versus parallel transitions (loaded with risk).

This research suggests that sequential models (e.g., the sand cone) begin to break down as they encounter a 'perfect storm' (a dust storm?) in a digital context. We present evidence of emergent business model measures arising from the experiments/cases in diagonal pathways only. Here, the risks in the parallel transitions are moderated by the new network constructs, and platform-based design rules, which also amplify value creation.

#### *7.1.2. What sequential pathways offer that parallel pathways do not*

Quinn (1978) proposed that most effective strategies tend to emerge step-by-step from an iterative process in which organisations probe the future, then experiment, and learn from a series of partial or incremental commitments. While moderating firm practices are often sequential, avoiding those actions that are loaded with risk in transitioning to a future (desired) state, modifications can be immediate in instances where no regulatory changes are needed. As outlined in our case studies, they can be easier to define (compared to uncertain, and hypothesis-driven, platform-based developments), hence, organisational buy-in is easier. Finally, our sequential cases offer a myriad of 'exceptions' to existing rules that serve to promote sequential moves when improving operational routines. This finding supports a recent study on pharmaceutical regulation which reports resistance to the implementation of Global pharmaceutical norms for quality standards where, most notably, variation among developed countries is marked (Pezzola and Sweet, 2016).

#### *7.1.3. What parallel pathways offers that sequential pathways do not*

In transition paths to 'on-boarding', internal initiatives by incumbent firms tend to self-serve and are often characterised by linear growth. A 'design-first' then 'figure-out-how-to-attach-to-a-system' mentality has resulted in 'inside-out' network effects that are sequential in nature. With increasing requirements for platform shifts, our cases offer a series of new design rules to which the 'exceptions' (see sec. 7.1.2) will ultimately need to adhere to. In summary:

- *Platforms are digital on all sides and accelerate via network effects*: 'True' platforms are 100% digital on all sides (supply and demand, or design-production-supply network in this study).
- *Platforms promote 'outside-in' network effects*: In coupling internal and external ecosystems, platform approaches promote 'outside-in' network effects that are 'parallel'. 'Outside-in' network effects are truly collaborative and can influence and leverage the needs of incumbents. This means that work from one subnetwork gets impacted by another subnetwork. That is, parallel moves trigger 'flywheel effects', enabling 'discoverability' and 'visibility' at each network node, enriching the larger network or ecosystem
- *'Outside-in' network effects enable 'parallel' moves in terms of risks*: Leadership is critical to navigating risk. In minimising risk of failure, legacy firms sacrifice the benefits of success, whereas, platform companies foster an innovation and risk-taking culture. In pre-competitive consortia, network integration sees central nodes (actors) reducing friction between the different stakeholders.

## 7.2. Academic Contributions

The rapidly expanding role of digital technologies across industry sectors motivates this paper, along with the challenges and opportunities these interventions create in driving structural shifts in supply networks linked to development and production. This study presents specific information and details regarding pathways to delivering future scenarios across design, production and supply networks and assessment of the barriers to implementation. It examines digital pathways to new product development and supply network development and explores the contexts in which 'traditional' project approaches can benefit organisations.

The operations and supply network digitalisation concepts outlined in this paper contribute to a growing digital supply network literature domain, specifically around: (1) product variety, consistency and functionality, (2) inventory and customisation options and, (3) evolving industry structure.

Grounded in the extant literature, our sequential and platform-based models address network-centric innovation in three main areas: (1) strategic intent and the fit between business models and environmental needs, (2) network integration and the role of the central nodes, and (3) innovation performance in terms of risk-adjusted outcomes. Using a base framework (2x2 matrices), we explore



theoretical implications in a series of conventional and digital contexts. Our casework focuses on a UK perspective with a 'flashlight view' on a complete digitalisation element. We decouple the digital stories using an industrial systems' mapping approach to capture emerging platforms, activities and actors. Observations related to our digital cases suggest a need to re-examine or modify existing theories and well-developed constructs that have been studied over time, for example, cumulative capabilities and trade-offs.

First, our study reports on how organisations revise traditional practices using digitalisation capabilities (e.g., inventory management, production scheduling, and batch sizing). Digitalisation is driving the need for change, but also forcing organisations to radically reconfigure, to adopt platform strategies and parallel transitions, and decouple functional solo or single-firm optimisations.

Second, business models and consortia engagements result from emergent risk management mechanisms arising from digital differentiation. A key question for organisations is whether digital capabilities are moderating parallel pathways, that is, whether risks in this transition are moderated or whether opportunities are intensified. Here, for both demand and supply sides, firms need to consider the business ecosystem — incorporating their business model, their institutional stakeholders and emerging digital standards, which offer empirical opportunities for follow-on theory development.

Our observations on sequential and parallel digitalisation in networks, and allied data-driven decision-making, which is consistent with Guha and Kumar (2017), offer opportunities for follow-up optimisation research. For instance, how would network-centric measures with either sequential or platform-based modalities affect goal programming associated with three-dimensional concurrent engineering (3D-CE) (Fine et al., 2005)?

### **7.3. Managerial Contribution**

From a practice perspective, this research applies and advances operations and supply chain digitalisation concepts to provide insights and inform both strategic and operational decision-making. For example, technological advances change the nature of trade-offs by advancing the overall 'performance frontier' (Boyer and Lewis, 2002), however, their study is a static case study looking at 'performance frontiers' in various combinations. Our study explicitly examines transitions up and across this 'frontier', based on business model needs, how and when sequential and parallel platform-

based innovations are similar and different, and when an organisation or network of partners could benefit by choosing one or the other.

We demonstrate how transitions and networks organise and behave (often very differently), and where and how return-on-investment (ROI) and risk drive the pathway choice. In sequential pathways, 'use cases' have typically been the *modus operandi* but have often been characterised by 'narrow tactical items' (e.g., new technology adoption at one process step that is implemented for just one product type) as a means of getting internal buy-in within an organisation. Hence, 'attractive' cases often determine the pathway choice which can result in short-term incremental gains (but possibly never the 'strategic intent' end-point in the long-term).

In contrast, parallel pathways require the development of hypotheses and a future vision at a strategic level. As immediate ROI is not apparent — investing in a platform requires many players and pooled resources (intellectual and financial). The consortium effect serves to 'de-risk the risk conversation', which helps consortium partners sell the hypotheses to internal stakeholders in their respective organisations and defer collective decisions on, for example, the regulatory pathway until necessary. This is a departure from when organisations had to attempt strategic breakthrough agendas with large ROI pressures on their own, which were often doomed to fail from the outset (akin to activities pre-2011 where single-firm investments in continuous processing development are estimated to have been in excess of £800 million in aggregate yet resulted in low adoption rates of 5% and often only at pilot scales (e.g., RSC, 2011; Badman and Trout, 2015). We observed the flywheel effect of multiple pre-competitive collaborations, which suggests that platform approaches need both radical and incremental projects to support transition from their outmoded established practice.

#### **7.4. Limitations and Future Directions**

We adopted a consortia mapping framework with temporal and completeness elements in order to capture case studies involving tens of prominent sector stakeholders over eight years. These consortia maps illustrate a cumulative effect over a finite timeframe and are consistent and legitimate, ensuring generalisability based on the industrial systems mapping approach outlined in section 3.2. The approach enabled us to build evidence one-step-at-a-time; that is, to develop micro-maps charting evolutions and patterns pre-2011, from 2011-2014 (sequential cases), and from 2014-2018

(sequential and parallel cases) with supporting evidence from published papers, industry white papers, and consortium annual reports. However, this provided us with a 'once-off' sector view — we captured only 16 cases and associated organisations, and it should be clarified that parallel moves need not map onto platforms every time, i.e., in a structural sense, it is possible to have parallel development without platform-based design rules. We have elected to ignore that aspect of development because in our observed data, the network entities did not wish to take the risk of parallel development without the benefit of platform-based design rules.

While we examine other cases to inform our narrative on how the pharmaceutical industry is evolving, and UK consortia links to other Global programmes and geographies (e.g., the US-based Centre for Structured Organic Particulate System - CSOPS), it is possible that other scholars and practitioners could have different views on digitalisation. Another limitation of this study is a focus on developmental target drugs that are based on small molecules and on solid oral dose forms. With the trend towards large molecules (i.e., biologics) and drug device combinations, future research will include testing and refining the models and frameworks using case studies involving other industry segments (e.g., stratified medicines).

Replication and extension of our work (e.g., testing and optimisation of the 10 propositions) in other ecosystems such as Google's Alphabet firms or the many network-centric partnerships assembled by Amazon could help to extend our collective understanding of sequential and platform-based digitalisation.

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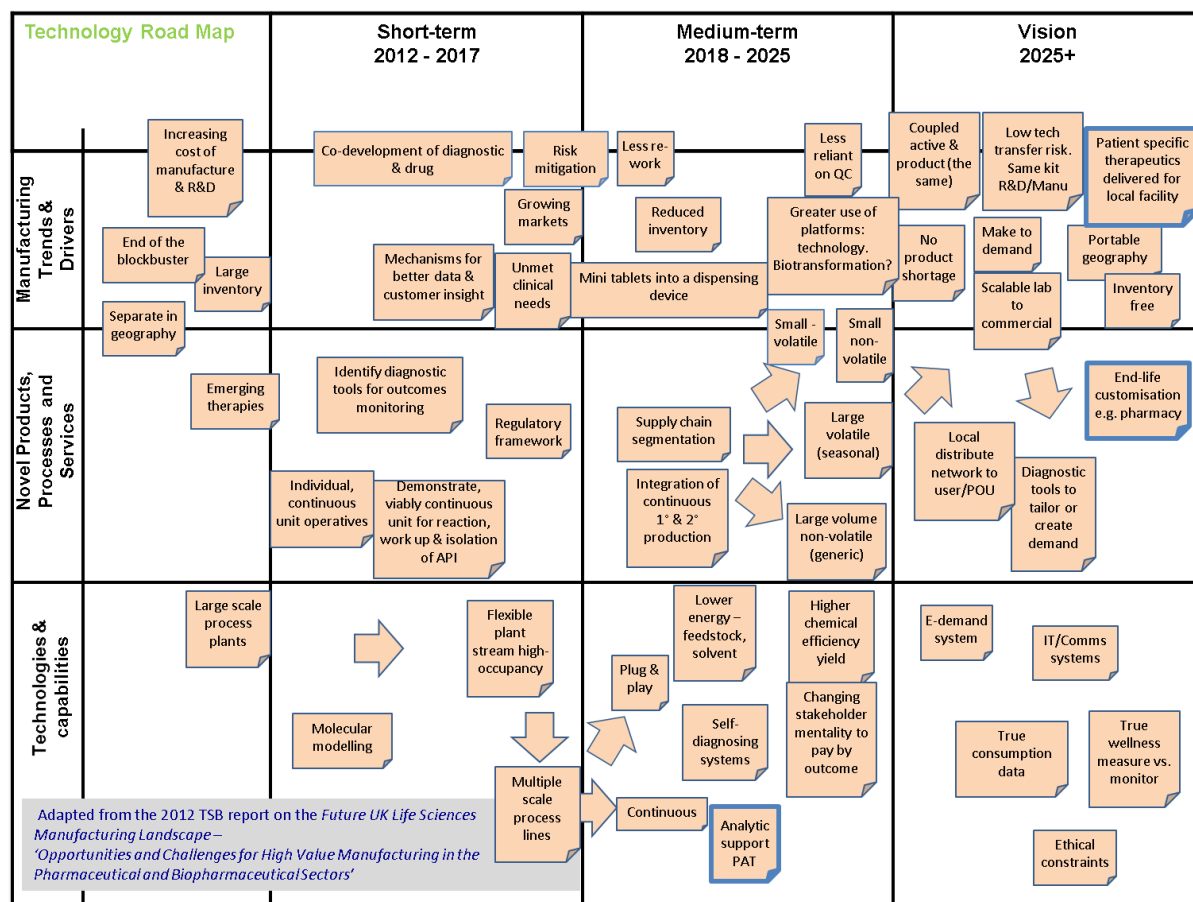
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## Appendix A: UK pharmaceutical and biopharmaceutical technology road map 2012-2025+

Source: UK Technology Strategy Board/Innovate UK (TSB, 2012), adapted by the authors



## Appendix B: Consortia

As shown in Table B1 below, six consortia were sampled over an eight-year period (2010–2018), with the technologies or innovations under study determining the specific type of network. The six consortia can be further classified based on their funding sources and specialties as follows:

- The Centre for Innovative Manufacturing in Continuous Manufacturing and Crystallisation (CIM CMAC), the Future Continuous Manufacturing and Advanced Crystallisation Research Hub (CMAC Hub) and Dial-a-Molecule Grand Challenge Network are funded by the UK's Engineering and Physical Sciences Research Council (EPSRC). They largely focus on R&D involving the chemical synthesis of small molecule compounds (with the final product being the traditional pill) and their subsequent exploitation in industry. Research funding of approximately £60 million was allocated by EPSRC and other institutional actors across these three consortia and matched by industrial partners (total investment estimated at ~ £120 million). Supporting initiatives include the £2.6 million Intelligent Decision Support and Control

Technologies programme (ICT CMAC, 2018) in collaboration with a number of industrial stakeholders (2013-2018), as well as a £4.3 million Doctoral Training Centre (2012-2018) as part of the UK's 'Manufacturing the Future' programme (EPSRC, 2012). A UK Research Partnership Investment Fund (UK RPIF) capital award (£32.6 million in total) specifically supports research and innovation around the development of bespoke, mobile and reconfigurable manufacturing platforms (UK Research and Innovation, 2018b).

- Strategic goals of the Advanced Digital Design Transforming Pharmaceutical Development and Manufacture (ADDDoPT) and Reconfiguring Medicines End-to-End Supply (REMEDIES) consortia centre on design, clinical and commercial activities focused on developing E2E pharmaceutical supply chains. This involved connecting key players, including major CMOs, equipment manufacturers along with knowledge transfer networks and healthcare providers. Sponsored by the UK Department for Business, Innovation and Skills (BIS) Advanced Manufacturing Supply Chain Initiative (AMSCI), matched funding from industrial partners brought research funds to ~ £42million.
- It has been argued that organisations should strategically shift their R&D investment to large molecule compounds, also known as biopharmaceuticals or biologics (Waltz, 2014). The average biologic offers a greater return on investment owing to higher average peak sales and less drop-off in sales following a loss of exclusivity (David et al., 2010). The sixth consortium, while not UK but Ireland-based, was selected as it represents a platform-based initiative between two European research institutes that demonstrates transitions in a biologics context.

Given the complexities in effectively engaging with all entities involved in the network innovation cases, multiple engagements with the central nodes (predominantly, the consortium and work-package leaders especially in terms of research and commercial strands of activities) was conducted and data regarding structure and information flows between these central nodes and key partners was sought (maximum number of nodes was fixed at 24). Where applicable, we targeted engagement with academic institutions, MNCs and SMEs involved in three or more of the consortia for data triangulation efficiency and increased validity of our findings (Eisenhardt and Graebner, 2007).

Table B1. Overview of our 16 case studies across six network innovation categories

<b>Case ID</b>	<b>Network Innovation Category</b>	<b>Product, Process, or Capability</b> (supporting journal articles or industry commentary)	<b>Network Type</b>	<b>Network Name</b> (Timeframe of activities & funding) <u>Weblinks</u>	<b>Digital Element</b>	<b>Technology/ Network Innovation Intervention</b>
<b>1</b>	<b>Digital Design</b>	<b>Drug Discovery Portal</b> (Clark et al., 2010)	Academic Network	Centre for Innovative Manufacturing in Continuous Manufacturing and Crystallisation (CIM CMAC) (2011-2016) <a href="https://www.cmac.ac.uk/CIM_Summary.htm">https://www.cmac.ac.uk/CIM_Summary.htm</a>	Platform linking scientists with appropriate chemical expertise through a target-matching virtual screening approach	Digital workflows & intelligent virtual screening enabling standardised data acquisition, analysis & reporting approaches

2	Digital Design	Machine Learning & Prediction (Chi et al., 2009)	Academic & Industrial Network	Future Continuous Manufacturing and Advanced Crystallisation Research Hub (CMAC Hub) (2017-2027) <a href="https://www.cmac.ac.uk">https://www.cmac.ac.uk</a>	Prediction of experimental outcomes	Initial screening of drug compounds to predict success in compound activity & interaction; accelerating the scale-up, design & modelling of new manufacturing processes
3	Digital Design	'Dial-a-Molecule' (Kilpin et al., 2015; Houben & Lapkin 2015; Sans & Cronin, 2016)	Academic & Industrial Network	Dial-a-Molecule Grand Challenge Network (2010-2020) <a href="http://generic.wordpress.soton.ac.uk/dial-a-molecule/">http://generic.wordpress.soton.ac.uk/dial-a-molecule/</a>  Advanced Digital Design Transforming Pharmaceutical Development and Manufacture (ADDoPT) programme (2015-2019) <a href="https://www.addopt.org">https://www.addopt.org</a>	Transform synthesis to become a data-driven discipline	Better predicting properties & performance of target molecules; automatic discovery & optimisation of chemical processes

4	<b>Adaptive Clinical Supply</b>	<b>‘On-Demand Clinical Supply’</b> (Moore, 2015)	Global MNC-led network of academic & specialist partner	Reconfiguring Medicines End-to-End Supply (REMEDIES) programme (2014-2018) <a href="https://remediesproject.com">https://remediesproject.com</a>	Digitally-enabled ‘on-demand’ supply & new protocols	Assembly-to-order investigational patient packs
5	<b>Adaptive Clinical Supply</b>	<b>Patient Kit ‘Tagging’</b> (Harrington et al., in press)	Global MNC-led network	REMEDIES	Convergence of multiple digital technologies in clinical	Integrating packaging and continuous manufacture developments to identify opportunities to tag patient kits
6	<b>3D Printing including ‘Lab-on-a-Chip’</b>	<b>3D Printing (Clinical)</b> (Alomari et al., 2015)	Joint initiative led by two Global MNCs &	REMEDIES	Additive Manufacturing for personalised medicines	‘On demand’ extemporaneous manufacture of unit doses

			their networks			
7	<b>3D Printing including 'Lab-on-a-Chip'</b>	<b>3D Printing (Drug Product)</b> (Khaled et al., 2015)	Academic & Industrial Network	CMAC Hub	Additive Manufacturing for personalised medicines	3D printing of drug combinations with specific drug release profiles
8	<b>3D Printing including 'Lab-on-a-Chip'</b>	<b>'Lab-on-a-Chip System'</b> (Ihalainen et al., 2015; Smith et al., 2016; Wu et al., 2018)	Joint initiative led by two European Research Institutes	FPC@DCU (2018-2023) <a href="https://www.dcu.ie/fpc/index.shtml">https://www.dcu.ie/fpc/index.shtml</a>	Novel diagnostics, pharmaceutical production & cell line developments incorporating digital connectivity	Portable point-of-care solutions involving biomolecules & cell-based applications
9	<b>Process Analytics</b>	<b>'Digital Twin'</b> (The Economist, 2017)	Specialist SME-led network	CMAC Hub	Virtual replica of experiments, equipment & measurements	Data from small-scale experiments to virtually designed full-scale

						manufacturing process 'digital twins'
10	<b>Process Analytics</b>	<b>'Golden Batch'</b> (Wojewodka et al., 2011)	Academic & Industrial Network	CIM CMAC CMAC Hub	Model-based predictive control	Real-time comparison of current batch with ideal process state
11	<b>'Intelligent' Packaging</b>	<b>'Agile Pack'</b> (Moore, 2015)	Global MNC-led network	REMEDIES	Methods for agile & cost-efficient component supply	Next generation RFID technologies; Compliance & anti-counterfeiting focus
12	<b>'Intelligent' Packaging</b>	<b>'Smart Label'</b> (Moore, 2015)	UK Technology innovation centre & its network partners	REMEDIES	Digitally tracking individual packs within the supply chain — from manufacturer to healthcare	Near-field communication tags, printable electronics components & cloud-based software systems for effective tracking of pharmaceutical products



					professionals & patients	
13	<b>'Intelligent' Packaging</b>	<b>'Mobile Apps'</b> (Bauer & Murphy, 2017)	Specialist SME-led network	REMEDIES	Digital leaflets & mobile phone apps	Links with serialisation for track & trace
14	<b>Continuous Processing End-2-End</b>	<b>'Mobile continuous platforms'</b> (Mulgrew, 2017)	Academic & Industrial Networks	CMAC Hub REMEDIES	Modular large lab/small pilot plant configurations capable of a range of chemistries	Open access asset network for use by contract manufacturing organisations (CMOs) & primes
15	<b>Continuous Processing End-2-End</b>	<b>'Digitalisation Lab'</b> (McLaughlin, 2016)	Global MNC-led initiative	Global MNC & specialist network partners REMEDIES	Proof of Concept reference facility integrating real equipment streams	Network enabled E2E digitalised model acts as a digital factory blueprint for a network of manufacturing sites

16	<b>Continuous Processing End-2-End</b>	<b>'Microfactories'</b> (Harrison et al., 2018a)	Academic & Industrial Networks	CMAC Hub	Integrated predictive development pathways	Rapid assessment of Manufacturability, Robustness, Consistency & Performance
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## **Appendix C: Case study protocol outline**

### **Section 1. Exploring the Digital Evolution of Product Supply Networks**

**Aim:** This research project aims to explore the operations management challenges of digitalisation. Our exploration involves examining conventional constructs in a series of digital development and manufacturing contexts. Consortia-led experiments/projects were specifically identified that could lead to radically new supply network design principles.

**Background:** Beyond transforming how products and services are designed, manufactured and delivered, digitalisation can enable new approaches to both designing and managing future supply networks. This has unprecedented implications for Operations and Supply Chain Management (OSCM) research and practice. Previous studies have focused on 'shoring up' through 'conventional' Supply Network Configurations (Structure, Dynamics, Relationships, Governance, and Coordination). We are keen to revisit these findings, in light of the emergence of digital technologies, to explore the rapidly expanding role that digital technologies play across many industry sectors, and the challenges and opportunities these changes present to drive structural shifts in supply networks.

**Approach:** We wish to interview key stakeholders involved in consortia and obtain key insights from interviews to reveal emerging trends and explore generalised patterns. This study is built on established mapping techniques previously employed by the authors.

**Outputs:** This research project aims to identify and codify key trends in the digitalisation of supply networks. The findings will be used to support organisations in making critical decisions in response to such trends, and to inform programmes and consortia that are looking to manage innovation risk and outcomes.

### **Section 2. Statement of confidentiality**

All your responses will be anonymised and all information that could in any way permit the identification of your organisation will be regarded as strictly confidential. It will be used for the purposes of this research only and will not be released or disclosed without your prior consent. You can withdraw your participation at any point of this project.

### **Section 3. Semi-structured interviews**

#### **Primary data involving digital experiments, programmes, and consortia**

- 1) What is your position in your organisation, and how long have you been in post?
- 2) What is your role/are your roles within the consortia you are involved in?

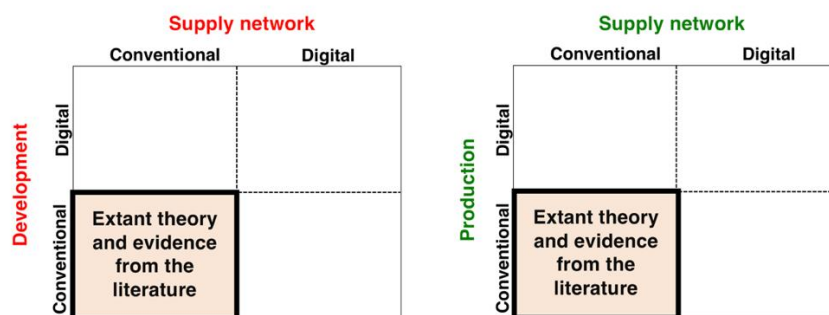
3) Interviewees will then be asked to define a discrete project activity within a consortium programme.

Criteria for selection of activity:

- a. Involves a technology intervention
- b. Has a digital component
- c. Development or Manufacturing (Commercial) context
- d. Involves one or more of the following: Product, Service, Process or Capability, Supply Network

4) Other (e.g., Institutional, Regulatory)

#### **Section 4. Base Framework**



- (1) Interviewer explains base framework (x-axis, y-axis, criteria for 'High' and 'Low' within quadrants)
- (2) Interviewees will then be asked to 'self-identify' the position of their activity on the grid
- (3) Interviewees will then be asked to describe what best describes this positioning
- (4) Interviewees will then be asked to provide evidence to support this positioning (e.g., secondary data sources to validate, and give context)
- (5) Interviewees will then be asked to comment on effects of digitalisation on:
  - *Conventional measures and trade-offs* (based on Ferdows and DeMeyer 1990; Boyer and Lewis, 2002)
- (6) Interviewees will then be asked to comment on:
  - *Role of central nodes*
  - *How the consortia manage innovation risk*
  - *Strategic integration of goals*
  - *Any other discriminating features, from a network innovation perspective*

## Appendix D: Summary of Research Propositions

Table D1. Sequential pathway propositions and evidence base

#	Pathway	Research Proposition	Supporting cases
1A	Sequential	When transitioning from Conventional–Conventional to Digital–Conventional or Conventional–Digital configurations, quality and dependability processes are established by central network actors before cost and responsiveness	<ul style="list-style-type: none"> <li>• ‘Dial-a-Molecule’</li> <li>• ‘Golden Batch’</li> <li>• ‘On-Demand Clinical Supply’</li> <li>• ‘Smart Label’</li> </ul>
1B	Sequential	When transitioning from Digital–Conventional (or Conventional–Digital) to Digital–Digital configurations, the presence of quality and dependability processes mediate the risk of achieving desired cost reduction and responsiveness outcomes	<ul style="list-style-type: none"> <li>• 3D Printing (Clinical)</li> <li>• 3D Printing (Drug Product)</li> <li>• ‘Mobile continuous platforms’</li> <li>• ‘Microfactories’</li> </ul>
1C	Sequential	Modular moves by central actors serve as risk abatement mechanisms in delivering outcomes (for example, quality & dependability)	<ul style="list-style-type: none"> <li>• ‘Dial-a-Molecule’; ‘Golden Batch’; ‘Digital Twin’</li> <li>• ‘On-Demand Clinical Supply’; ‘Smart Label’; Patient Kit ‘Tagging’</li> </ul>
1D	Sequential	In order to cut the cycle time (T1+T2) it is desirable to stay conventional either on the demand or supply side in the intermediate stage	<ul style="list-style-type: none"> <li>• Drug Discovery Portal; Machine Learning &amp; Prediction</li> <li>• ‘Mobile Apps’; ‘Agile Pack’</li> </ul>
1E	Sequential	Basis for competition after the collaborative stage is associated with the precision with which you can deliver operational measures	<ul style="list-style-type: none"> <li>• ‘Dial-a-Molecule’; ‘Golden Batch’</li> <li>• ‘On-Demand Clinical Supply’; ‘Smart Label’</li> <li>• 3D Printing (Clinical); 3D Printing (Drug Product); ‘Mobile continuous platforms’; ‘Microfactories’</li> </ul>

Table D2. Parallel pathway propositions and evidence base

#	Pathway	Research Proposition	Supporting cases
<b>2A</b>	Parallel	Goals for transitioning from Conventional–Conventional to Digital–Digital configurations are aligned with the strategic intent of new business models	<ul style="list-style-type: none"> <li>• ‘Lab-on-a-Chip System’</li> <li>• ‘Digitalisation Lab’</li> </ul>
<b>2B</b>	Parallel	When transitioning in parallel form from Conventional–Conventional to Digital–Digital configurations, organisations attempt to leverage all four measures (e.g., quality, dependability, responsiveness, cost reduction) simultaneously	<ul style="list-style-type: none"> <li>• 3D Printing (Clinical); 3D Printing (Drug Product); ‘Lab-on-a-Chip System’</li> <li>• ‘Mobile continuous platforms’; ‘Digitalisation Lab’; ‘Microfactories’</li> </ul>
<b>2C</b>	Parallel	New ‘platform-driven’ risk abatement mechanisms are brought into play by central nodes where the risks in this transition are moderated by network centric platform constructs (e.g., regulatory support to such platforms)	<ul style="list-style-type: none"> <li>• ‘Lab-on-a-Chip System’</li> <li>• ‘Digitalisation Lab’</li> </ul>
<b>2D</b>	Parallel	There is no intermediate stage in defining platform-based design rules. Both the demand and supply side of the platform must be digitalised simultaneously to reduce cycle time	<ul style="list-style-type: none"> <li>• 3D Printing (Clinical); 3D Printing (Drug Product); ‘Lab-on-a-Chip System’</li> <li>• ‘Mobile continuous platforms’; ‘Digitalisation Lab’; ‘Microfactories’</li> </ul>
<b>2E</b>	Parallel	Following the collaborative stage, the basis for competition is associated with the ability to redesign the business model. Such redesigns often lead to alternative measures beyond quality, dependability, responsiveness and cost as the critical success factors	<ul style="list-style-type: none"> <li>• 3D Printing (Clinical); 3D Printing (Drug Product); ‘Lab-on-a-Chip System’</li> <li>• ‘Mobile continuous platforms’; ‘Digitalisation Lab’; ‘Microfactories’</li> </ul>