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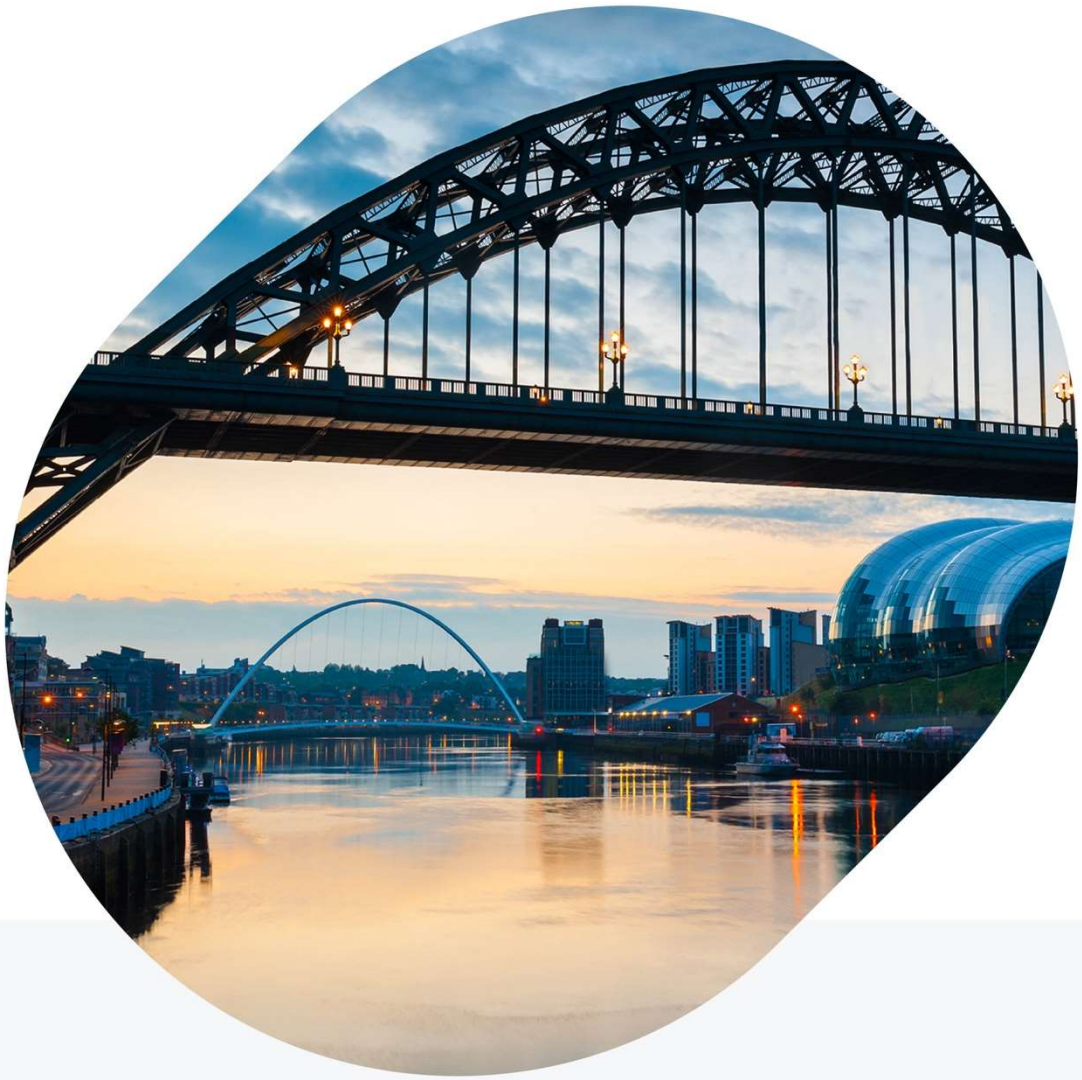
NorthEastPharma
North East of England Pharmaceutical Community

Profile and Importance of the North East

Pharmaceutical Manufacturing Cluster

Growing Its Contribution 2017-2023



NorthEastPharma
North East of England Pharmaceutical Community

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1. Foreword

Foreword

Life sciences is an important strand of the North East's economy. Two of my companies offer examples of its breadth: LightOx is a drug discovery company developing new light-activated compounds as treatments for early-stage cancers; High Force Research is a well-established and growing independent CRO / CDMO with the ability to address a wide range of chemistries across multiple industries, including pharmaceuticals, and so figures in this report.

This and a previous report in 2017 both highlight the economic importance of pharmaceutical manufacturing to the North East of England and to the UK as a whole. North East Pharma's in depth conversations with the region's manufacturers have provided a rich insight into the pharmaceutical manufacturing Cluster's successes and challenges.

" The extraordinary growth of the Cluster's activities and workforce over the last five years are strong proof that these global challenges are being successfully addressed, from Alnwick in the north of the region to Teesside in the south."

The Cluster is unique in the UK and includes CROs / CDMOs, key supply chain companies and large multinational developers and manufacturers of drugs and their delivery devices. It includes both UK and internationally owned businesses of differing scales, spanning 10 to 1500 employees. Taken together, the region's pharmaceutical manufacturers have full capability to develop drug manufacturing processes for clinical development and commercial supply of tableted medicines, biologics and drug-delivery devices. They generate wealth and exports at a scale comparable to another of the region's advanced manufacturing successes – the automotive sector.

In this report we celebrate the Cluster's growth through innovation. We must also pay attention to successes in other areas of life sciences innovation in the North East, Lightox as an example: diagnostics, drug discovery and development, medical devices more broadly. We should be thinking about a further report that gathers together all the region's successes in life sciences.

Sam Whitehouse

Board member, North East Local Economic Partnership

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2. Executive Summary

This report has been researched and produced six years on from our previous assessment in March 2017 of the contribution that pharmaceutical manufacturing makes to the economy of the North East region of the UK. Those six years saw two potentially disruptive events: a pandemic and withdrawal of the UK from the European Union.

The key aims of the report are to:

- Evaluate the economic profile, growth and impact of the North East's Pharmaceutical Manufacturing Cluster.
- Identify the Cluster's opportunities to maintain and grow its international competitiveness and to continue to contribute significantly to the UK's productivity growth.
- Draw out views and insights of senior business leaders about the challenges facing the sector and identify the support needs of businesses.

The report's findings are compared with those reported in 2017. Its conclusions about and proposals for the North East pharmaceutical sector will be of interest to the sector itself, the North East and Tees Valley Mayoral Combined Authorities and the UK Government and its agencies.

Profile of the North East Pharmaceutical Manufacturing Cluster

In updating the 2017 report we researched and interviewed the majority of key companies in the North East Cluster which ranges across Northumberland, Tyne and Wear, County Durham and Teesside. It includes both UK and internationally owned businesses of differing scales, spanning 10 to 1,500 employees.

Despite this diversity, the Cluster continues to grow, is well established and benefits from a global reputation for value, business resilience and regulatory reliability. The Cluster comprises companies with a range of business models, technology scope and scales of production.

The Cluster is unique in the UK and includes contract development and manufacturing organisations (CDMOs), key supply chain companies and large multinational developers and manufacturers of drugs and devices. Taken together, the region's pharmaceutical manufacturers have full capability to develop drug manufacturing processes for clinical development and commercial supply of tableted medicines, biologics and medical devices.

2.1 The Cluster's enduring success factors

Companies gave reasons why the North East Pharmaceutical Cluster has been globally successful and continues to grow.

- A continuing ability to attract business from international clients is a core element of success
- Meeting high quality manufacturing standards alongside a reputation for delivery on time and on budget
- Efficiency and flexibility are key drivers for business performance
- Despite significant competition internationally, a large proportion of the Cluster's assets are committed in the near term, some for several years into the future
- The ability of the Cluster companies and their workforce to flex and be creative in response to changes in markets
- The potential to attract business from international clients is core to the continuing success of the Cluster
- Pharmaceutical manufacture is a global growth business area
- Sustainability is a growing theme, driven by customers' increasing insistence on low-carbon products
- There is insufficient manufacturing capacity in the US to accommodate the numbers of molecules in the drug discovery pipeline

2.2 Summary of Key Facts

There are 13 pharmaceutical manufacturers in the North East of England Cluster with a diverse range of business models, ownership arrangements and relationship structures with the regional and UK economy.

Seven pharmaceutical manufacturing sites in the North East are internationally owned. Owners include individual investors, private equity, US, Japanese, Chinese and Indian companies.

The North East pharmaceutical manufacturing Cluster employs more than **5,600** people within the region. The Cluster companies included in this report contribute at a minimum £1.52 billion to the UK's Gross Value Added (GVA). This is coupled with a total salaries bill in excess of £250 million.

GVA per worker is over £200,000, well above the average of £48,000 for the region

The growth in GVA of the regional pharmaceutical sector companies from 2016 to 2021 is the highest in the UK outside London at 89% in real terms.

The pharmaceutical sector GVA for the North East is 17.9% of the total manufacturing GVA for the region and 2.7% of the region's total GVA; this is a higher proportion than for any other UK region.

The Cluster's value chain contribution is typically 30-fold, rising to 50-fold for products aimed at less-prevalent diseases in high value markets.

Pharmaceutical manufacturing sites in the sector export an average of 80% of their products with 39% of exports going to the United States.

Cluster companies have invested over £850m in capital assets since 2017

The sector workforce has grown by 51% over the last six years and continues to grow. It is expecting to recruit a significant number of additional jobs to its current manufacturing and research workforce this financial year (2023-2024).

Trade, imports and exports

The sector is strongly connected to international markets for the import of raw materials and processing equipment and three-quarters of manufactured products are exported.

Manufacturers reported that they imported lower cost raw materials, chemicals and reagents from Asian markets such as China and India and higher value processing equipment and specialised raw materials from North America, other parts of the UK & Ireland, and mainland Europe.

Between 5 and 80% of the outputs from the different companies is exported to international markets. The United States is the largest recipient of finished products with around 39% of all products exported going to the US market.

Skills

Of the 5,600 people directly employed in the companies surveyed, about 66% are male and 34% female. Over 3,500 of the employees are in research or manufacturing roles with the largest cohort aged between 31 and 50 (47%). 27% are aged under 30 years old and 26% are over 50.

The quality and stability of the employees in the local labour force is one of the North East's competitive advantages in hosting these businesses: the regular circulation of staff is seen as positive, leading to the sharing of ideas and best practice and collectively providing a rich career structure. There has been a significant growth in numbers since 2017 and there is now a growing skills shortage in the North East that needs to be addressed.

Funding and Reinvestment

Different approaches to funding and capital investment are evident, depending on the structure of the business, its relationship to owners and its position in the supply chain. The North East pharmaceutical manufacturing Cluster has been successful in attracting inward investment globally from the United States, Japan, India and mainland Europe, as well as the UK.

Regulatory issues

A uniting feature in all the interviews with companies was the ability to operate successfully globally in an increasingly competitive global market. Businesses in the sector rely heavily on the ability to import materials and export their products and looking forward, interviewees identified that their continued ability to attract business from international clients as core to the continued success of this industrial sector.

An underpinning core common theme identified in all interviews was the importance of the UK's regulatory environment. This was regarded as central to the sector's success, accruing to the sector's advantage due to the sector's ability to meet high quality manufacturing standards alongside a reputation for delivery on time and on budget.

In this context, a key theme identified during the interviews was a concern about the impacts of having left the European Union. Interviewees reported that the devaluation of the GB Pound has eased exchange rate pressure on export-directed industries and feedback suggested that this remains positive for the sector over the longer term. However, the regulatory disruption created as a result of exclusion from European Union single market was viewed as a significant threat to the sector, particularly in view of the strengths that the UK's regulatory framework has historically provided to the industry through the Medicines and Healthcare products Regulatory Agency (MHRA). The MHRA made a strong and valuable contribution to European Medicines Agency (EMA) guidelines; this is no longer possible.

2.3 Key opportunities and challenges

Interviewees identified key opportunities and challenges for the North East sector:

Maintaining and Raising the Profile of the Cluster

- Ensuring that the profile and the sector needs were fully understood at national and regional level, especially with the formation of a new North East Mayoral Combined Authority in the region.
- Ensuring that the North East pharmaceutical Cluster, its capabilities and needs are fully reflected in the UK Government's strategic priorities for manufacturing and life sciences.
- Recognising the need for active engagement across the North East to support skills, business growth and innovation.

Industrial Development

- Strengthening the sector's pharmaceutical supply chain integration through coordinated utilisation of the North East's manufacturing sites.
- Strengthening collaboration with science and research assets in the region and with other advanced manufacturers to develop new products and explore improved processes
- Strengthening the knowledge base using global best practice and continuing benchmarking.
- Exploring the opportunities for improved linkages across Advanced Manufacturing sectors in the North East including the automotive and energy sectors in order to cooperate on innovative process development, for example in industrial digitisation and low carbon manufacturing.

Skills

The rapid growth in the Cluster has led to skills shortages. Businesses identified a number of challenges in the availability of expertise and education within the region with recruitment from outside the region often required for senior-level leadership and strategic-level employees and in key research and analytical roles although graduate level staff are usually recruited locally. Businesses intend to remain proactive looking forward and will increase~~s~~ the use of the apprenticeship levy to aid recruitment planning and to provide appropriately skilled staff. The ability in and necessity of recruiting internationally was also mentioned in most interviews.

Key opportunities:

- Promoting the North East as an attractive and affordable place for talented people to live.
- Developing a skills training programme for the Cluster through cooperation and participation within the industry to meet the skills challenge , taking note that the region's universities are home to over 20,000 STEM students.

Having left the European Union Single Market for Goods

- Ensuring that the UK regulatory framework remains conducive to continuing competitiveness and avoids additional impediments to the smooth integrated global import and export supply chains for raw materials, intermediates or finished products to prevent any further increase in operational complexity, lead times and costs.
- Ensuring that the pharmaceutical sector remains an attractive proposition for UK and global inward investment.

2.4 Key recommendations from the report:

Profile:

The North East pharmaceutical manufacturing Cluster should maintain an active dialogue with local and national governments and their agencies to promote sector growth, recruitment and inward investment.

Industrial development:

Strategies should be developed to foster innovation opportunities both in the North East and across the UK to enhance the performance of manufacturers based in the region, taking advantage of existing regional capability.

Skills:

The Cluster should work with others to develop a responsive understanding of the current and likely future skills gaps starting with the findings within this report. These should be met through cooperation across the Cluster and with training and education providers to develop: a graduate scheme; internships; outreach to schools; and apprenticeship programmes. Consideration should be given to patterns of work that will be attractive to a broad and inclusive workforce.

Regulatory Environment:

The continuing importance of a fit-for-purpose regulatory environment that supports continuing growth in pharmaceutical manufacturing, especially in export markets, should be clearly recognised and reflected in any modification to regulation.

3. Introduction

Background and purpose

This report was put together to provide a much-needed update following Brexit and Covid, and to compare the more recent information we obtained with that collated in a similar study undertaken in 2017 (Profile and Importance of the North East Pharmaceutical Manufacturing Sector).

Since 2017 we have seen changes in the UK Government's industrial strategy, left the European Union, suffered the Covid-19 pandemic and witnessed a war in Ukraine.

For a nine-month period from October 2022 North East Pharma conducted an industry engagement programme with senior managers and executives in North East pharmaceutical businesses.

There was a general belief among the businesses interviewed that the North East pharmaceutical Cluster, all with sites located within a 32-mile radius of Newcastle, is not fully recognised and visible at a level commensurate with its economic impact and that opportunities for growth are consequently missed.

We were offered a variety of reasons for this perception, perhaps the most salient being that the Cluster had been and is successful and so had not required external scrutiny or support.

The engagement and reporting process

The businesses interviewed agreed to respond on an anonymous basis and to provide detailed information about their activities, key operational and financial data and to provide their thoughts and insights on the key issues and opportunities facing the sector based on economic, industrial and policy trends.

Methodology

A survey questionnaire was prepared seeking access to key industry data and setting out a series of lines of discussion. This was circulated to North East pharmaceutical manufacturing Cluster companies.

A programme of face-to-face interviews was scheduled with senior managers or executives who answered the survey questions and discussed key topics areas more broadly.

Leaders from the following organisations took part in these interviews;

Sterling Pharma Solutions, Piramal Healthcare, Accord Healthcare, Quotient Sciences, Organon, Fujifilm Diosynth Biotechnologies, GlaxoSmithKline, High Force Research, Pharmaron, Iksuda, Newchem Technologies, Turbinia, KD Pharma and Thermofisher. Data from two businesses were obtained from material in the public domain.

The interviewees have been open both with information about their businesses as well as their views and concerns on issues and opportunities for them in the current environment. As we agreed at the outset, the information provided to us has been treated on a confidential basis. We should like to record our thanks to all those individuals who took part for their time and for their information and advice. With the benefit of the data secured from the engagement activities in 2017 and 2022/23, the drawing in of national data in consultation with staff from local authorities, the local enterprise partnership and the Office for National Statistics, an economic analysis of the North East pharmaceutical Cluster was developed.

This report:

- Sets out findings from the latest engagement process, draws together a number of conclusions about the profile and structure of the Cluster in the region and identifies opportunities and challenges.
- Compares the 2023 data with that obtained in 2017.
- Provides a summary of data used to evaluate the economic value and impact of North East pharmaceutical manufacturing.
- Provides a set of recommendations for a number of audiences on key next steps to further enhance the growth of the North East pharmaceutical Cluster.

4. Findings from the research

Manufacturing Metrics:

Capacity and Investment

Over 10 billion tablets are produced from four of the Cluster's sites per year, with one site having capacity for up to 6 billion tablets; one site produces 0.5 million packs per day of finished products.

Pharmaceutical devices, such as prefilled syringes for self-administration, are a product growth area, with one site having capacity for up to 7 million devices per year.

The Cluster exports its products to over 140 global markets, with the USA being the largest customer for the regions CDMOs.

Several of the companies reported that over 90% of their product manufactured is exported out of the UK.

Depending on the product and scale of manufacture a single batch of final product can be worth over £2m.

The Clusters CDMO's provide a full range of services from pre-clinical supply to commercial manufacture to over 300 customers worldwide. One CDMO has 53 marketed products on its books.

Since 2017 the Cluster companies have privately invested over £850m in both new and improving assets with companies flagging their intention to significantly invest in new assets in the next 2 years.

A regional SME noted that a drug development company can progress an antibody drug conjugate to complete a Phase I trial and beyond through services available from companies based North of York.

Capability

Efficiency and flexibility were cited as key drivers for performance for the sector's pharmaceutical manufacturing sites.

Sites successfully manage the complexity of having a significant number of products and their intermediates being manufactured at the same time across the site. There may be as many as six intermediate products or more to be made and released to cGMP before the API is isolated and released to the customer.

GSK at Barnard Castle have built a new cutting-edge facility where both the manufacture and release of products is paperless.

4.1 Profile of the North East pharmaceutical manufacturing Cluster

Pharmaceutical companies are often pictured as engaged solely in drug discovery; there is frequently less awareness of the enormous economic value linked to the manufacture of pharmaceuticals which is dominant in the North East pharmaceutical manufacturing Cluster and the innovation and development associated with globally-competitive pharmaceutical manufacture is less visible.

The North East has a long and strong heritage of pharmaceutical manufacturing capability and expertise; it has been home to a diverse range of companies for many years. A significant number of the companies have been based in the North East for more than 50 years and while many manufacturing sites have changed ownership or closed and then reopened, they continue to cover all aspects of pharmaceutical innovation, research and manufacture from biopharmaceuticals and small molecule drugs to tablets and devices, supplying the gamut from pre-clinical doses to commercialised product.

The Cluster is unique in the UK in its end to end offering and is home to the majority of the large CDMO's in the UK producing API and tablets to be used in anything from early phase clinical trials through to commercial sales.

Investment in pharmaceutical manufacturing sites in the 1960s and 1970s generated a skilled workforce and this regional asset has been maintained, developed and built on by different owners and investors.

North East Pharmaceutical Cluster companies are all located within a 32-mile radius of Newcastle and in an area that stretches from Alnwick in the north to Billingham and Middlesbrough in the south. A high proportion of manufacturing sites are rural or semi-rural, on the fringe of urban areas.

In carrying out the survey we aimed to be as inclusive as possible. Listed below are the 16 companies we have contacted and report on. The list is not exhaustive but it covers the major CDMOs and manufacturers both in the bioprocessing of biopharmaceuticals and in the chemical manufacture of small molecule therapeutics.

The North East Cluster has historically been dominated by small molecule manufacture and formulation. Small molecules still account for four fifths of the pharmaceutical drugs market. The biopharmaceutical component is growing in the region, principally represented by Fujifilm Diosynth Biotechnologies and supported by CPI. Both Fujifilm and CPI are seeing major growth in viral vector, RNA and other advanced modalities beyond traditional biologics.

The following table lists the pharmaceutical manufacturers and supply chain companies participated in the study.

Company Name	Location	Company Type	Employees on site	Ownership
Accord Healthcare	Newcastle	Drug & device manufacturer	100 - 500	Indian
FujiFilm Diosynth Biotechnologies	Billingham	CDMO /CMO	500 - 1,500	Japanese
GlaxoSmithKline	Barnard Castle	Multinational drug developer and manufacturer	500 - 1,500	UK headquartered
High Force Research	Durham	CRO / CDMO	20 - 100	UK, independently owned
Iksuda	Newcastle	Clinical stage R&D organisation	20 - 100	UK
KD Pharma UK Ltd	Seal Sands	CDMO / CMO / manufacturer	100 - 500	German investors
Onyx Scientific	Sunderland	CDMO / CMO	100 - 500	Indian
Organon Pharma (UK) Ltd	Cramlington	Multinational drug developer and manufacturer	500 - 1,500	USA
Pharmaron	Cramlington	CDMO / CMO	100 - 500	Chinese
Piramal Healthcare	Morpeth	CDMO / CMO / manufacturer	100 - 500	Indian
Sterling Pharma Solutions	Cramlington	CDMO / CMO	500 – 1,500	UK Investors
Quotient Sciences	Alnwick	CDMO / CMO	100 - 500	UK Investors
NewChem Technologies	Newcastle	CRO / CDMO	20 - 100	UK, now part of Sterling Pharma Solutions
Thermofisher	Cramlington	Supply chain Single use bags	100 - 500	USA
Wasdell Manufacturing Ltd	Newcastle	CDMO /drug and device manufacturer	100 - 500	UK, independently owned
Turbinia	Newcastle	CRO	<20	UK, independently owned

Table 1: General company information: company name, location, company type for the purposes of this study, an employee range for the site and ownership information.

This table captures all the main CRO / CDMO's and pharmaceutical manufacturing sites in the North East pharmaceutical Cluster all but two of which have been visited and have helped with this report.

Location of North East Pharmaceutical Manufacturing Sites with Employment Figures

Map 1: Map showing the distribution of pharmaceutical manufacturing sites within the North East region with approximate employment figures per site.

Linkages to wider North East Life Sciences and Manufacturing assets

The pharmaceutical Cluster forms part of a wider regional life sciences economy. A regional strategy for life sciences and medicines manufacture developed and published in 2021 https://www.northeastlep.co.uk/key-sectors/health-and-life-sciences/ set out four priorities:

- To modernise and grow pharmaceutical manufacturing
- To increase the number of health and life science businesses that are born, grow and scaled up in our region
- To provide access and routes to NHS market whilst nuturing innovation and collaboration
- To develop the ecosystem so that it has the right environment for health and life science businesses and manufacturers to grow

The Cluster benefits from a skilled life sciences workforce supported by life sciences education delivered by the regional universities and colleges. It has and will further develop supply chain links with the regional fine chemicals manufacturing Cluster. There is increasing collaboration with other manufacturing sectors on carbon footprint reduction and reducing environmental impact more broadly. The pharmaceutical Cluster collaborates closely with CPI, which is part of the High Value Manufacturing Catapult, and has the majority of its facilities within the North East region. Catapult centres are research and technology organisations focussed on translation of ideas towards commercialisation and driving research to market.

4.2 Stories of the Cluster

While companies may operate relatively similar equipment and have comparable plant scales, the way in which these are utilised depends on the nature of their business. The sites have varying developmental histories going back in one case as far as 1945. Some are part of a global drug manufacturing network; they may be operating as part of a company's multinational supply chain. Other businesses provide a contract development manufacturing and development (CDMO) service to clients who are often internationally-based. This diversity means that the core focus and nature of the company operations is often unique to each specific site. The varying business models and priorities can sometimes obstruct the Cluster's ability to co-ordinate or present itself as a united, integrated sector.

Confronting these issues formed an important part of our face-to-face interviews; they helped to frame the conversations about the profile, needs and perspectives on future opportunities and the pressures facing individual businesses and the sector as a whole. It became very apparent that each site has its own unique past with some sites changing owners and business models multiple times throughout their history and where the ability to attract inward investment has been vital to the sites continued existence; other sites

have maintained their purpose for which they were built decades ago. Our conversations revealed some notable recent histories of innovation and adaptation and offered stories of success.

Resurrection and Mutation

Accord

The 22-acre factory, closed by Sanofi in 2015, and brought by Accord Healthcare in 2016 has received €50M investment in production facilities and people development to create a world class manufacturing facility to support the UK and EU market. Accord Healthcare, one of Europe's fastest growing pharmaceutical companies, is a leading supplier to the NHS in the UK.

Accords owners had a long-term vision to gradually bring the massive site back to life and in doing so add to the already significant presence by pharmaceutical manufacturing and CDMO companies in the area north of Newcastle.

The site received its licence to operate in August 2017 with approximately 30 employees in place for the start of volume manufacture in early 2018. Accord now employs over 300 people at the site. The growth of the site has come from previous employees keen for the site to be successful and over time these have been supplemented by individuals with no prior experience of the Fawdon site.

Key for the sites future is to bring in higher value manufacturing to supplement its growth in device assembly and to fulfil a key aim for Accord to place Operational Excellence at the core of its manufacturing activities. By delivering late-stage customisation, sterile manufacturing and OSD capacity Accord will meet its commitment to deliver even more critical medicines to patients that need them across the UK and Europe and to provide resilience for UK healthcare.

15 months after reopening the site had its first MHRA regulatory audit and obtained its licence to operate. To date Accord have continued to make strategic investments to in order to grow and the current operations only occupy a fraction of the site footprint leaving lots of space to increase the sites activities for long term sustainable growth.

High Force Research

High Force Research was founded in Durham in 1988 with just 4 people and moved to its present custom-built facility at Bowburn in 1996, which is still its headquarters and main manufacturing site employing over 60 people.

High Force is proud to be the only independent CDMO in the UK, with all of its owners based in the area. The company is one small part of the rapidly growing pharmaceutical Cluster

in the North East and in the last two years has seen both its workforce double and a second facility coming on line at NetPark near Sedgefield, driven by the Life Sciences sector worldwide becoming more buoyant.

High Force Research collaborates with industry, discovery groups, start-up and academic spin-off companies in synthesising and analysing new materials for proof-of-concept, route evaluation and process development/scale-up, stability trials and toxicological studies.

The site is licensed by the MHRA for the development and manufacture of API's for clinical studies. In the early days the company worked mainly with UK companies but now over 70% of its business is from outside of the UK, predominately the US, where UK CDMO's are competitive vs their US competition.

High Force Research has developed a reputation for chemical process development and synthesis coupled with a flexible business approach that is particularly attractive to discovery groups, start-up and academic spin-off companies.

Pharmaron

The Cramlington site was originally built by The Boots Company in the 1980s and has had several owners before it was recently bought from Recipharm by the Chinese pharma giant Pharmaron in January 2022.

Pharmaron made the strategic decision to invest in the site at Cramlington for its large scale, commercial API manufacturing capability which vertically integrates with the business growth and development plans for Pharmaron worldwide. The long-term strategic business plan for the site is to move from semi-continuous and long-term production projects across a few products for a limited number of clients to multiple, niche contracts for development and manufacturing for a wider group of clients to support registration and commercial supply. This will involve the reconfiguration of current operations and a significant investment (>£100m) in new infrastructure over the next few years along with attracting additional talent to the workforce.

Pharmaron already have a large worldwide development group with more than 8,000 chemists, with a significantly sized group based on the UK PR&D (Process Research and Development) site at Hoddesdon acquired from MSD in 2013. The site employs over 100 scientists engaged in work for a large portfolio of clients. Their focus is to develop process for clients New Chemical Entities which can be easily transferred to one of the commercial manufacturing assets such as that at Cramlington.

The Cramlington site then provides the ability to employ those processes for commercial registrations, manufacture and world-wide supply of API for medicinal products.

Quotient Sciences

Quotient Sciences, based at Alnwick in Northumberland, are the current owners of a site with a long history in the pharmaceutical business sector that has persisted and grown thanks to the vision of two North East based entrepreneurs.

The site was originally built by the Sterling Research Group in 1980 and latterly since 2010 was owned by Covance, until the site was put up for sale in April 2015.

In June 2015 Ian Shott and Paul Ryan were asked by Dr Sally Old, the site director, if they could help find a solution to the threat of closure and create a scientific legacy in some shape or form. Following a site visit, it became clear that the excellent facility and high quality, experienced and dedicated team were a real asset. Eight months after that first visit, the site became a stand-alone business for the first time in its history and Arcinova was created. An agile, customer focused, scientifically excellent entity with great potential for sustainable growth started trading in February 2016, with 50 colleagues.

With the help of a win/win land deal with Northumberland Estates, a £60,000 grant from Northumberland's Rural Growth fund to invest in creating API capabilities and the continuation of the site's offerings in ^{14}C radiochemistry, bioanalysis and stability work, the site was up and running. From day one it was decided that the site needed to be focussed on drug substance research and development. Under the leadership of Dr Paul Quigley, a team was hired to set up this capability.

With careful financial management, including a £750k loan from FW Capital and access to an invoice finance facility via Siemens Finance Services as a means to access extra funding coupled with a dedicated work force, the site broke even in Q2 2017 ahead of its plan. This was extremely good news for the pharmaceutical Cluster in the North East and for those who had saved the site from possible closure.

2018 was a significant year for the site when significant external financing was acquired via the Business Growth Fund and the site invested in additional reactor capabilities to meet the growing business demand. 2019 saw Arcinova continuing to grow with a major milestone of a successful MHRA inspection coming in October of that year.

Arcinova's reputation and success as an SME attracted a number of approaches from organisations wanting to buy the company. This eventually led to the acquisition of the Alnwick site by Quotient Sciences in February 2021 who saw the capabilities as very complimentary to their unique Translational Pharmaceutics offering and will enable the integration of drug substance, drug product and clinical testing capabilities all under one organisation, making drug development faster for their customers.

In October 2022, the company announced the completion of a major £6M expansion of its drug substance manufacturing facility which will lead to the creation of an additional 80-100 scientific and technical jobs at the facility.

The Alnwick site continues to thrive, with best ever revenues in 2023 and a workforce of over 200 colleagues, most of whom are graduates; many have PhDs. Alnwick based colleagues in Science, Commercial, Regulatory, Medical Writing, Project Management, Finance and Systems support the Quotient Sciences network across three other UK sites and three in the US. A new Aseptic facility is about to open. The potential for further growth is huge.

And it all started from a meeting on a sunny north eastern day in June 2015.....

Sterling Pharma Solutions

There has been a pharmaceutical manufacturing site at Dudley near Cramlington, a few miles north of Newcastle, since 1969.

The site and its growth are an excellent example of what the North East Pharamceutical Cluster does well, with a dedicated research and development centre and pilot plant, linked to full scale commercial manufacturing facilities. Sterling's Cramlington site specialises in complex and hazardous chemistry, providing innovative API development and scale-up services from small scale to commercial production for companies worldwide.

The 42 acre site is the headquarters of Sterling Pharma Solutions, the largest CDMO of its kind in the UK. The UK company also has two sites in the USA, one in Ireland, a chemistry services facility in Newcastle upon Tyne and an antibody-drug conjugate site on Deeside. The facilities at Cramlington offer small molecule API services for the full product lifecycle from pre-clinical to commercial manufacture. Sterling's vision is to be the preferred partner and provider of services to the pharmaceutical industry.

Thanks to the entrepreneurial business model adopted by its CEO, Kevin Cook, and his executive team, and backed by equity funding from GHO Capital, the site at Cramlington has grown from 380 employees in 2018 to over 650 by the end of 2023., The company also has an award-winning apprenticeship programme with over 40 apprentices on site.

Over £60m has been invested in the site in the last five years in adding reactor capacity, making the business more environmentally sustainable and significantly increasing its R&D and pilot plant capabilities. Plans are in place to grow the site even further and build on its skilled workforce.

4.3 Key capabilities and position in the value chain

Together, the Cluster's pharmaceutical manufacturers have the full range of capabilities to develop drug manufacturing processes for the clinical development and commercial supply of tableted medicines or devices across the pharmaceutical product value chain.

There are three main manufacturing steps in the processing of initial raw materials through to a product that is suitable for clinical and commercial supply; these are:

1. **API Manufacture/Bulk Drug Substance** – This step is the process of taking the initial raw materials needed to make the active pharmaceutical ingredient (API); the API is not in a tableted or formulated form at this stage. For biopharmaceuticals, the equivalent of manufacturing API is manufacturing the *bulk drug substance*.
2. **Formulation & Tabletting** – This step takes the API manufactured in step 1 and formulates the API drug substance with other excipients to form the drug product which the patient will eventually use. The output of this step is the finalised tablet, cream, ointment or liquid in their correct dosages. This step can also involve the incorporation of a fixed formulated drug dose into a device for inhalation or injection. There is movement in the industry to provide devices, that can be used by the patient at home, removing the need for a hospital visit by the patient.
3. **Packaging for commercial/clinical supply** – The formulated or tabletted products or devices from step 2 are packaged into their correct format along with the correct literature in the correct languages needed for varying global geographical regions and distributed; some sites provide one of these steps, others two or more.

Figure 1 shows how the sites pharmaceutical manufacturers (comprising large multinational drug developers and CDMOs/CMOs) cover the three main manufacturing steps from the incoming initial raw materials through to the final packaged product being introduced into the global supply chain. Depending on the size of the organisation, our research identified that manufacturing output can range from 1kg or less batches for preclinical supply to mid-sized supply capability of approximately 150 tonnes per annum of API through to large scale secondary production of 0.5 million packs per day.

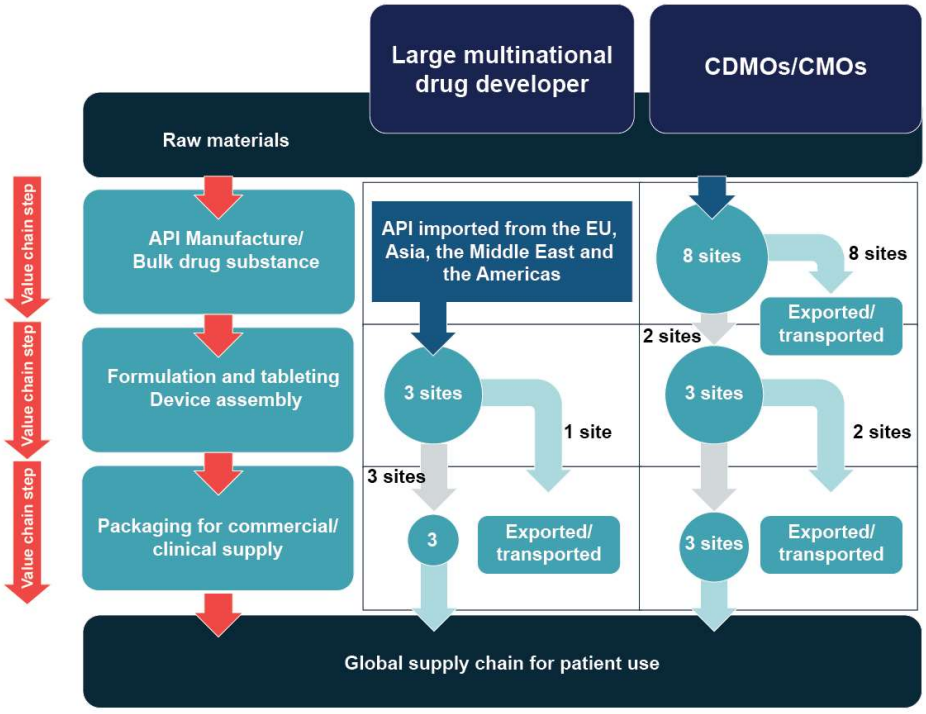


Figure 1: Value chain contribution by number of sites operating within the Cluster.

Regional capabilities range from niche small scale research and process development, preclinical clinical research organisation analytics, to full primary and secondary manufacturing, tabletting, assembly and packaging for global commercial supply. The large multinational drug developers who have sites in the region form part of a global manufacturing network that exports its finished products to other locations in mainland Europe, Asia or the Americas for further processing closer to the destination markets.

These sites have extremely high levels of production: one individual site in the Cluster has formulation capacity for approximately 6 billion tablets per annum ranging across multiple products lines and product families. For these individual sites, the logistical challenge is substantial. As an example, one company can service over 140 countries worldwide from a single site for which labelling and packaging needs to be bespoke for the destination market, meaning that a product range comprising 30 products can demand over 1,500 Stock Keeping Units (SKUs) when varying destinations and drug doses are considered.

Sites enter and leave the overall manufacturing process at defined value chain steps, meaning the number of sites within the Cluster able to fulfil a particular value chain step varies. When a company does not have capability within a value chain step, the product at that point is either exported or transported off site as shown in the diagram. Key points to consider in the context of the figure are:

- Ten sites in the Cluster are part of extensive multinational operations: one site is part of a 37 site global manufacturing capability; ten sites are part of global operations that range from 5-21 facilities; three are based solely in the North East
- The Cluster's large multinational drug developer/manufacturers do not manufacture API in the UK and this is imported largely from the EU, India and the Americas.
- Some of the secondary sites (steps two and three) take bulk tablets from outside of the UK and package them for use in other countries often requiring different pack sizes and configurations together with safety data and outer packaging in the appropriate language.
- Two of the sites interviewed formulate and make tablets for packaging both on site and for export to other facilities for packaging.
- For CDMOs/CMOs, there are eight sites with API manufacturing capability, with three in the next value chain step (formulating & tabletting).
- For CDMOs it is desirable to maintain a large portfolio (in one case >150) of customers, and a rich range of projects from preclinical to launch.
- There are two sites in the Cluster that have integrated capability across all three key value chain steps which spans the ability to process initial raw materials through to a packaged product for commercial/clinical supply.
- As the sector is a key part of the pharmaceutical supply and value chain, the value it creates through the processing of delivered or imported raw materials is a good indicator of its value contribution to the global pharmaceutical industry.

- The Cluster's value chain contribution on the drug product ranges from 20 times as a typical measure, up to 50-fold for drugs that are targeted at higher value markets often aimed at disease of lower prevalence.

Understanding the North East value chain position: an example of one site's value chain contribution

- A product that is made by one of the companies in the North East is sold for an average price of £10 per unit.
- The North East site can manufacture around 3 million units per year.
- Assuming all of these units are sold in the year it will generate £30 m in sales
- The cost of the API (made in Europe) contributes only £0.13 per unit but when put together with all the other items that contribute to the finished product the full cost for manufacture is £15 million per year, giving a manufacturing cost of £5 per unit produced
- This means that the profit generated for the parent company by the North East site for this product could be up to £15 million before taking into account development and start-up costs, sales and marketing etc.

4.4 Trade: Imports & Exports

The worldwide medicines manufacturing supply chain is integrated and complex. Businesses in the North East are strongly connected to other parts of the world, in particular to Asia Pacific, Europe and the United States, importing raw materials and exporting products to key markets and partners.

Figure 2 provides a visual representation on how the sector operates in its micro-environment and sets out some of the factors influencing its macro-environment discussed in this report.

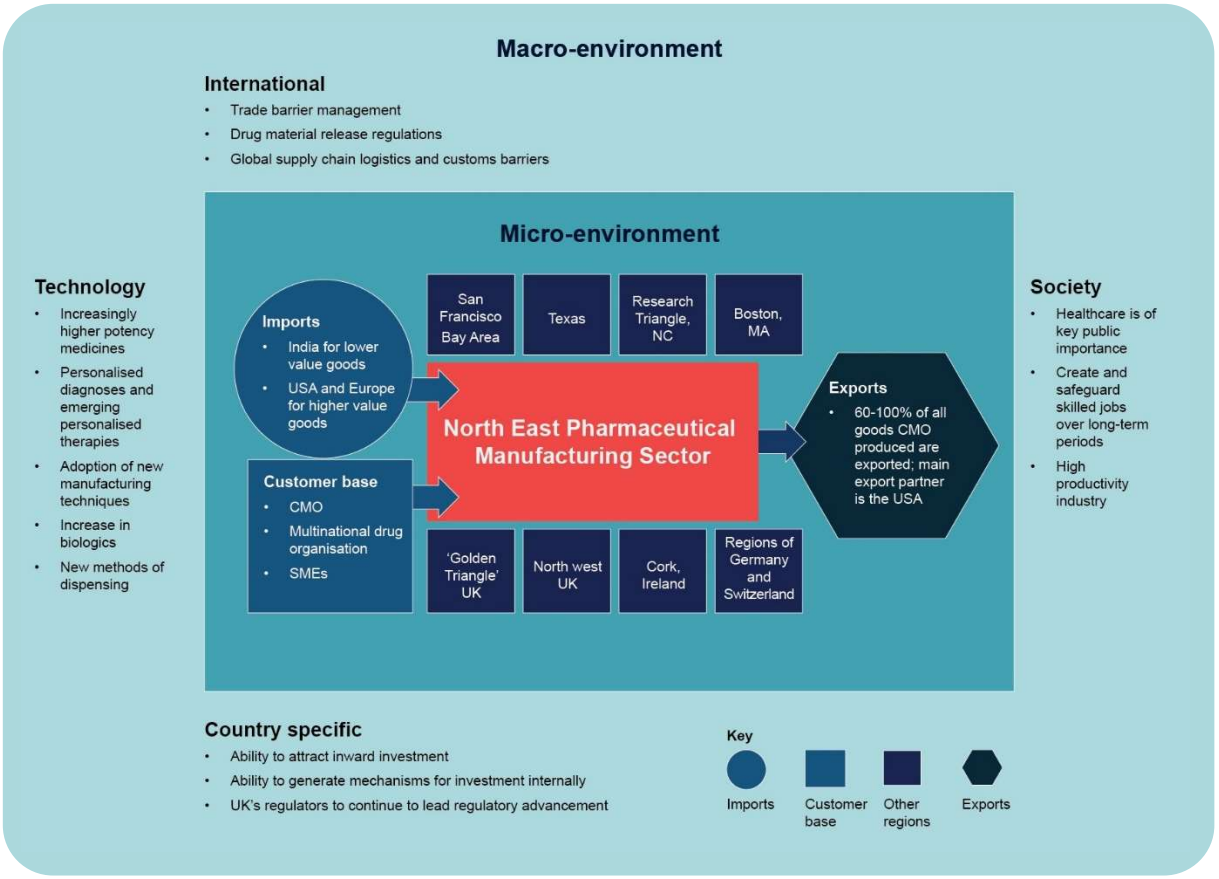


Figure 2: Visual representation of key drivers and dependencies in the micro and macroenvironment for the North East pharmaceutical manufacturing sector.

Imports

Observations identified in the research include:

- The ability to procure raw materials and processing equipment from foreign suppliers is key to the success of businesses in the sector. A common import theme highlighted was the sourcing of lower cost intermediate raw materials, chemicals and reagents from Asian markets such as China and India and higher value processing equipment and specialised raw materials from North America, the UK, Ireland, and mainland Europe.
- Import strategies and models varied substantially depending on the business model and company type. Some generalised patterns can be identified:
    - Large multinational drug manufacturers operate centralised procurement services where cost and on time supply are the key drivers.
    - CDMOs/CMOs operate processes where individual sites are responsible for procurement practices. Some sites have developed a close relationship with key Asian suppliers and agents to minimise any supply chain risks due to quality and delivery.

    - Cost and on time supply are of high importance. Some sites have deliberately chosen higher cost UK and European suppliers due to quality and culture alignment and the ability to overcome any potential supply chain disruption or quality issues.
    - For the CDMO companies especially, the early selection of the source for the key raw materials and solvents can be an important decision taken in conjunction with the client as once these choices are made and become part of a registered process it requires significant effort to change a supplier and leads to delay.
    - Sites operating as part of a multinational drug developer's global manufacturing network import materials, APIs and tablets from other sites within the manufacturing network. This can be from the UK, Ireland, India and China.
- Import transportation by sea or road is favoured by most companies where there is a significant amount of 'low value' material from say China as a starting material, although the costs of container transport across the world have increased significantly in the last few years.
- When timelines or product stability are in danger of being compromised, a route via air can be considered and Newcastle Airport is used by several companies as a point of entry and exit due to its ease of access and turnaround time. Newcastle Airport is actively developing the airport for handling pharmaceuticals, for both import and export.

Exports

Observations identified in the research include;

- 62% of all material produced by pharmaceutical manufacturers in the Cluster is exported out of the UK/EU per annum; of this 39% goes to the United States and 23% to the Rest of the World.
- The percentage distribution varies markedly from company to company with the percentage going to the US swinging from only 4% for one company to 76% for another.
- The annualised value of pharmaceutical exports directly from the North East, is projected to be £850m in 2023, more than double that in 2017.

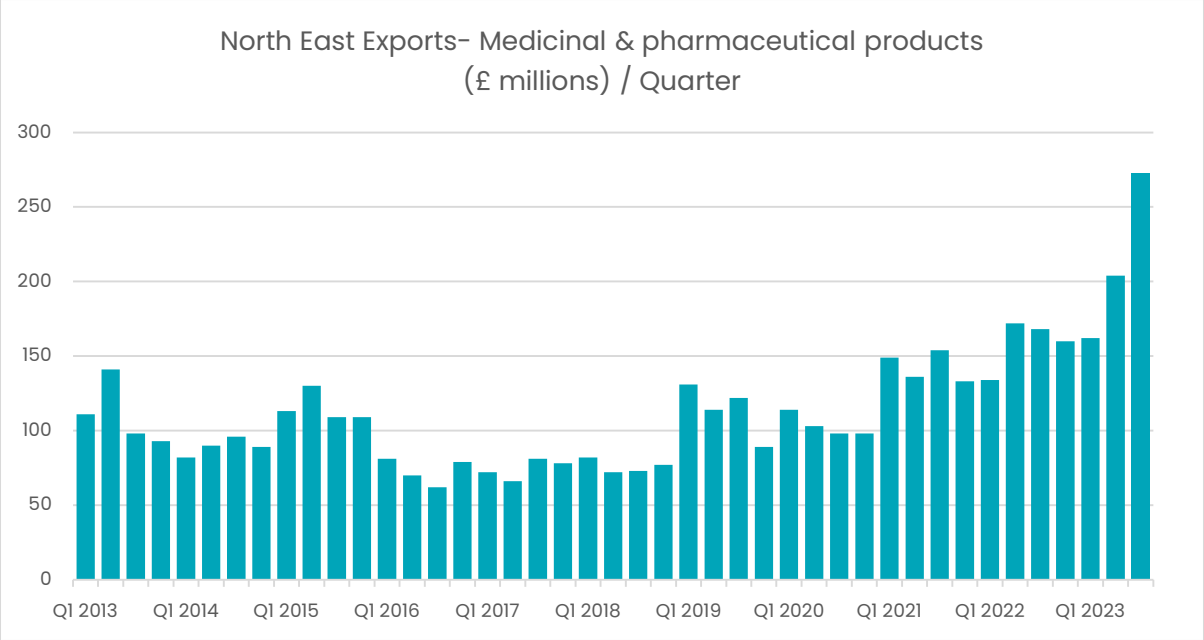


Figure 3: Medicinal and pharmaceutical product exports from the region
Source NE LEP analysis of UK trade data.

- The CDMO companies all have a significant export market in the US. Several factors contribute:
  - The US is the leader in R&D, and biotech private equity funding. 43% of the worlds Pharma R&D companies are headquartered in the US, compared to 5% in the UK.
  - 70% of all molecules in clinical development are with companies headquartered in the US and 7% of these are with small, sometimes virtual biotech companies who have scale up infrastructure.
  - As there is insufficient development and manufacturing capacity in the US to accommodate the numbers of molecules in the discovery pipeline, manufacturing is outsourced to the UK, the EU and Asia.
  - The US like working with people in the UK on account of shared culture, language, values, etc.
  - UK CDMO sites can be competitive on price with US companies.

- Export transportation used all three typical modes across the Cluster's sites: road, shipping by sea and air freight. Air freight, although a higher cost when compared directly with shipping by sea per quantity transported, can offer substantial inventory savings throughout the supply chain due to handling efficiencies and reduced stock volumes at the receiving destination.
- For one company where the shelf-life of certain products is critical to their use then air freight is the only option.

- The transportation method is often dependent on the final destination; for a UK destination, road is universally used, but for foreign destinations, a combination of ship and air freight as appropriate against required delivery date and shipment size is chosen.
- A significant number of manufacturers interviewed use an ex works logistics model: at the site's gate product responsibility is relinquished and is passed either to an external courier or to a customer's internal logistics division. Some manufacturers offer logistical supply chain handling services to their customers which can aid customer retention for CDMOs/CMOs.

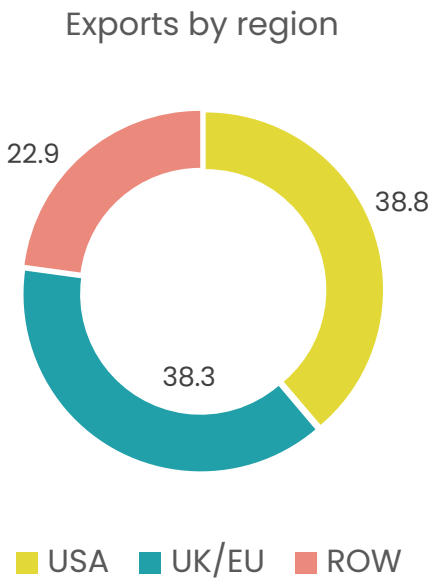


Figure 4: Exports from the Cluster: destinations (ROW: rest of world)

4.5 Contribution to the UK economy

Following on from our 2017 report there are now further good quality data available against which the 2017 data can be compared.

In calculating the overall contribution to the regional and national economy there is a need to consider where the consumer/patient product sits in relation to the factory gate product manufactured by a North East company.

Several of the manufacturers' sites operate as cost centres within the larger parent company, so very little if any data is published for that site and its contribution to the North East data is missing.

Gross Value Added (GVA)

GVA measures the contribution to the economy of each individual producer, industry or sector in the United Kingdom. The Office for National Statistics (ONS) provides annual regional GVA contribution for the pharmaceutical manufacturing industry (SIC07 21). The North East pharmaceutical manufacturing Cluster contributed £1.52bn GVA to the UK economy in 2021. This is the latest year for which these data are currently available.

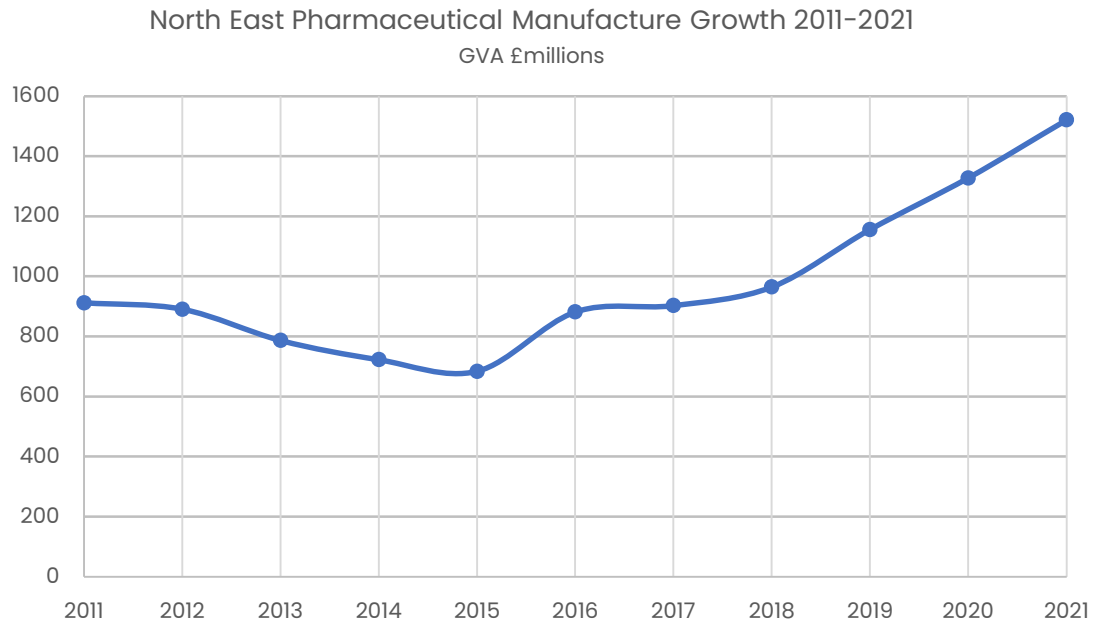


Figure 5: GVA for SIC07 (21) for the North East in current prices by year

The £1.52bn is 10% of UK GVA for Pharmaceuticals and is the fourth highest total and percentage among the UK's 12 ITL regions and nations, with only the North West (24%), the South East (almost 19%) and the East of England (13%) being higher.

The GVA per head of population (2021 census) is significantly higher than any other UK region at £930 per person in the working population (16-64 years old) with the North West at £819 and the South East and East at £522 and £526 respectively. The ONS location quotient measures the relative concentration of commercial sectors' GVA: the quotient for Pharmaceuticals in the North East is 3.53, meaning that the sector contributes three and a half times more to regional GVA than would be expected from the region's total GVA. The quotient for the North West is 2.54 and for the East of England and the South East, 1.54 and 1.31 respectively; all other regions have quotients of 1 or less (mean: 0.52; range: 0.13-1.00)

The North East's growth in GVA in this sector between 2011 and 2021 was remarkable and is the highest of the eight English regions outside London, up 67% using current prices or up

59% in real terms (using a chained volume measure to take account of inflation). The equivalent increases for the sector in the UK as a whole were 14% and 9% respectively. Following a dip in the regional GVA in 2012-2015 to £700M in current prices, the growth in the GVA from 2016 to 2021 was an astonishing 89% allowing for inflation.

The Cluster's growth is exceptional not only because it has the UK's highest rate of growth in pharmaceutical manufacturing but also because it is sustained growth in a Cluster that already in 2017 represented a significant slice of the UK's pharmaceutical manufacturing capability.

These GVA data are selected from tables set out in Appendix 2

Competition

Over the years the pharma sites in the NE Cluster have been very successful in changing what they make and in redefining their business model in response market forces in order to continue to flourish. One company used to make >3,000 tonnes of paracetamol for the UK and European market but as Chinese and Indian companies began to build facilities to manufacture this generic drug it became impossible for the company to compete and it withdrew from the market. The business part was bought by a large French manufacturer of paracetamol and the previous customers were primarily serviced by them. Ultimately under mounting cost pressures a few years later the French company started up its own paracetamol plant in China and some of the customers that were originally supplied from the North East were ultimately supplied by China. The original manufacturing site and its assets has nonetheless gone from strength to strength and is now the base of a pharmaceutical manufacturing company that operates globally through growth and acquisition

In the small molecule API market the North East is home to several large and smaller scale CDMO companies offering their services in an extensive number of specialisms from hazardous chemistry to radiolabelling and formulation.

A significant amount of business in the CDMO area comes from repeat business over a number of years, from building a partnership with clients and gaining a reputation by word of mouth.

As the batch quantities of material required by customers becomes larger, the number of sites and facilities able to manufacture at these scales in the UK decreases, with most of the larger scale facilities being in the North East.

Large pharmaceutical companies especially outsources a significant part of their drug substance manufacture to CDMO's worldwide either from the early stages of scale up or once a product is launched and they require space for new products or are driving for a reduction in costs and risk.

For the large multi nationals making 'own brand products' the future of each site and what it makes will be decided by corporate decisions looking at the parent company's options worldwide. In the case of GSK the site at Barnard Castle is seen as a global supply site, and a key site for new product introduction.

One secondary manufacturer comments that their site in the North East could be competitive with a Chinese site owned by the parent company because whereas the Chinese site could use cheaper and more labour per line the UK site is all about operator competence and skills.

Outside of the UK there are significant CDMO sites owned by companies including Lonza, Dotticon, Omnichem, Hovione, Almac and Fis in Europe and Cambrex, Curia in the USA for small molecules and Lonza, Boehringer Ingelhein, Samsung (Korea), Catalent and Wuxi (Ireland) for biopharmaceuticals.

Historically Ireland, especially around Cork, has also been an attractive place for pharmaceutical companies in invest and the Irish government has encouraged and incentivised this investment for many years. A significant number of companies are located in Ringaskiddy including Pfizer, Hovione, Janssen and a Novartis facility that was recently acquired by the North East's Sterling Pharma Solutions as a part of its growth strategy.

Whilst there is significant competition internationally, a large proportion of the Cluster's assets are heavily committed in the near term, some for several years into the future. Pharmaceuticals is a growth business area.

There are many CDMO- and large pharmaceutical company-owned sites in India and the Asia-Pacific region. The quality of the assets, regulatory compliance and lines of communication coupled with geopolitical issues do have an effect on how competitive they can be especially in the more complex areas of manufacturing. However, some of these companies are learning, and investing heavily in new state of the art facilities.

4.6 Skills & Workforce

One of the major contributions that the pharmaceutical manufacturing industry makes to the North East economy is creating high quality employment opportunities. Across all the companies interviewed approximately 60% of the workforce are directly involved in research and development (R&D) and manufacture, the remaining 40% being support staff.

However, this ratio can vary widely for individual companies; some of the smaller companies are R&D dominated where others involved in more routine manufacture have very few R&D staff on site with the R&D support coming where elsewhere in a company's network of sites.

Using the data from 2017 as a baseline, the North East Cluster has since grown significantly.

Employment

In 2017 on a like for like basis the number of people directly employed by the companies in the Cluster was 3,730 and it is now 5,640, an overall increase of 51% in the number of these high value jobs in the region.

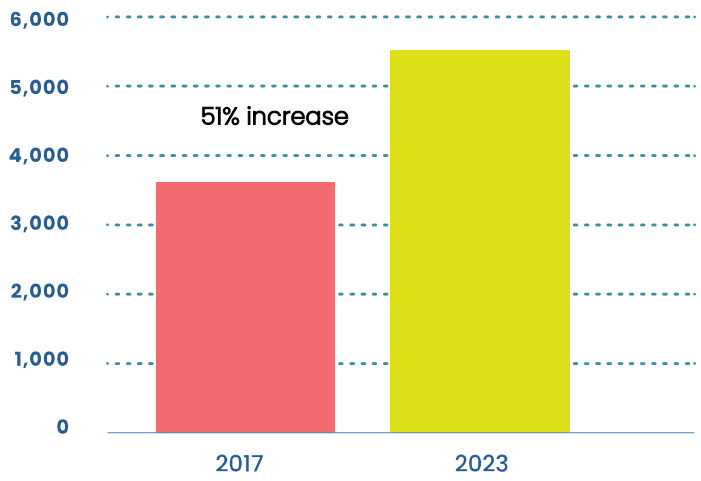


Figure 6: Growth in employment in the Cluster over six years

For some companies the growth has been very significant whereas for others the growth in their workforce has been much less marked yet the way in which these companies operate, deploy their workforce and address their markets have changed. Historically, the ability of these companies and their workforce to flex and be creative in response to the change has led to the retention of their skilled staff in the North East.

Remuneration

On the same like for like basis the aggregate of salaries paid to Cluster employees, of which a significant amount goes into the local economy, was estimated at £130M in 2017; the latest figures provide a total in excess of £250M, an increase of 82% in nominal terms. Comparison with the growth in jobs suggests an average increase in individuals' salaries of around 21%, compared to an average of 23% UK all-sector wage growth over the same period.

The availability of skills and access to a high-quality workforce is important to all the companies. The Cluster is sustaining and generating high quality jobs. Pharmaceutical

manufacturing generates some of the highest value jobs of any sector: a pharmaceutical worker adds over £200,000 of GVA to the North East Economy, against an average of £48,000 across all sectors in the region.

It is felt that having a healthy circulation of employees through companies regionally is positive for the sector as it allows for new ideation and good practices to percolate throughout the sector. A churn rate of around 10% was reported, low by most standards.

A large majority of the companies interviewed are recruiting heavily in many disciplines in order to support their continued success.

With a number of high-performing universities in the North East there has previously been a ready source of graduates of all disciplines to feed the graduate needs of all the companies. These North East educated graduates also understand and appreciate the benefits of living in the North East and in many cases have a desire to remain in the region. However, as the rate of growth has accelerated in the last 2-3 years, companies are having to look further afield, including outside of the UK, to attract candidates.

Recruitment and retention

There has been an initiative in the North East to attract and grow companies linked to sustainable energy and the many technologies associated with it. This means that there are now more opportunities for people looking to progress their careers and salaries and new opportunities have led to some loss of people with transferable skills to these areas, predominately Engineers, Project Managers and Quality Assurance staff. History shows that pharma cannot compete on salaries with the oil and gas industries; we suspect this may also prove to be the case with the renewables / hydrogen sector.

A knowledge of the principles of cGMP (Good Manufacturing Practice, essential for regulatory compliance) is important for many companies.

There is a shortage in the region of experienced managers in all disciplines who are key to managing growth and change within the companies. This has led some companies to focus on more internal training and upskilling of their current workforce.

Those interviewed identified several factors influencing recruitment:

- For those with no connection with or experience of the North East of England it can be considered relatively remote and is not seen as an attractive place to live, the latter a view seldom shared by those who work in the region.
- There is a perception that finding employment opportunities for a partner may be difficult.
- The opportunities for career progression within individual companies and within the Cluster are not widely evident to those outside the region.

- For some staff, the availability of housing is limited by competition for accommodation with students and holiday lettings.
- Manufacturing sites are sometimes not easily accessible from desirable centres of population and housing such as Newcastle and Durham, leading to higher private and public transport costs; public transport links are not always convenient or available.

Initiatives that were suggested to address these adverse factors include:

- Raising awareness of the pharmaceutical Cluster, its successes, strengths and opportunities.
- Improving awareness of the benefits of living in the region - these include a high quality of life and significantly increased disposable income at current salary levels compared to the rest of the UK, especially the South East.
- Maintaining and enhancing relevant employment practices, for example flexible working and working from home.
- Growing the skills pipeline for the existing North East population.

Gender balance

Overall, for the Cluster there has been very little change since 2017 in the male / female proportions despite the growth in overall numbers it remains at:

- Male 67%
- Female 33%

This can in many cases be linked to an historic dominance of males in the manufacturing side of the workforce despite in many cases a desire to address this was reported to us.

For the smaller R&D dominated companies the proportion approaches 50/50.

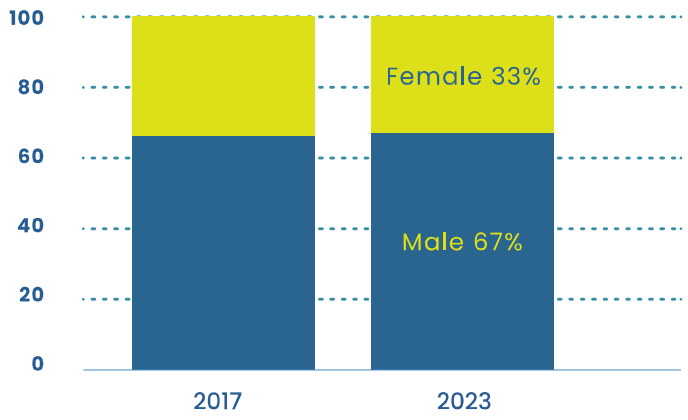


Figure 7: Gender profile of the Cluster workforce

Age profile

The age distribution has changed slightly compared to that reported in 2017.

	2017	2023
Up to 30	22%	27%
30 - 50	49%	47%
> 51	29%	26%

Table 2: Changes in age profile of the workforce 2017-2023

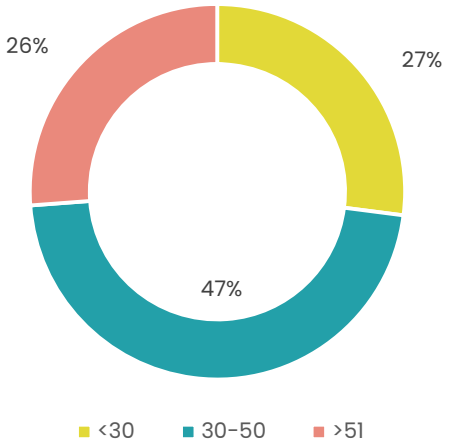


Figure 8: Age profile of the Cluster workforce in 2023

While it is encouraging to see that the number of younger people (<31 years old) is increasing, some companies have concerns about their ageing workforce and are alive to a potential problem on the horizon. Some companies felt that they are seeing a generation gap which reflects a lack in investment in people over a decade ago. Some of the older established companies reported seeing multigenerational family members working at the same site.

Apprentices

Cluster companies recruit apprentices in widely varying numbers (from 0-60 at any one time) and at varying ages and seniority with a plan to upskill staff across all disciplines.

Apprenticeships are available for school leavers. Apprentice programmes are also used to provide career development (level 3-7 degrees) for existing staff with a view both to investing in youth and to promoting from within.

The majority of companies interviewed were very positive about the value that the current increased trend in apprenticeships at all levels is bringing to their business and where they can they are looking to increase their apprentice numbers.

Some companies also offer one-year internships alongside local universities or work experience placements as part of their recruitment strategy.

Overall

The sector identified some key trends in expertise and education within the region:

- Senior-level leadership and strategic-level employees are often sought from outside the North East region, both from other regions within the UK and abroad. Companies have generally been able to recruit successfully into these roles although it is now taking considerably longer and requires more effort than it did in 2017.
- Within research areas, high quality scientific analysts and formulation scientists are more difficult to recruit, whereas technicians and manufacturing operator positions have typically shorter recruitment cycles, largely sourced within the region.
    - One company had recently seen 400 applications for 10 manufacturing operator jobs.
- Many sector companies have either used or are planning to make better use of the Apprenticeship Levy funds. Most cited recruitment planning and the ability to shape employee skills as the key reasons for choosing to regard the Levy as an opportunity.

4.7 Funding and Investment

The ability to reinvest in manufacturing facilities and research development infrastructure was reported as paramount when competing in a global market and in continuing to attract trade to the sector.

The ability to acquire capital and reinvest varies across the sector and is dependent on whether the site acts as an independent legal entity, is part of a larger company but expected to run as a profit centre or is part of wider manufacturing supply chain network. The key behaviours and trends associated with the sector's reinvestment capability are, in summary:

- The sector has attracted inward investment globally throughout its history and continues to draw significant investment from countries such as the United States, Japan, China, India and the EU as well as the UK.
- Capital investment or reinvestment for the global companies is largely done through budget allocation from a larger umbrella company.

- In recent years significant capital has been invested by many of the Cluster companies, resulting in both an increase in long term jobs and a significant increase in contribution to the region's economy both directly and indirectly.

Since 2017 the Cluster companies have privately invested over £850M in both new and improving assets. A large percentage (90%) of this investment has been spent or committed in the last 3 years.

There is also significant evidence of companies headquartered outside of the UK being willing to make long term significant investments in the North East as part of their strategic planning.

The majority of the larger sites are not constrained from expansion by the space on their existing sites. However, while facilities are available for laboratory work by smaller research and development companies there are currently no funded regional initiatives to provide space for the next step, expansion into small scale pilot facilities.

Various investments across the North East span the whole spectrum of activities from API small molecule development and state of the art filling plants to advanced biologics. Those listed below are a small selection of the many and varied investments that are being made.

Quotient Sciences at Alnwick completed a £6-million state-of-the-art building expansion in October 2022. The newly expanded space features multi-purpose capacity of up to 15 cGMP reactor streams with reactor volumes ranging from 5 litres up to 150 litres and deployment of both batch or continuous flow chemistry technologies.

Following this investment Quotient announced in Oct 2023 that it had made a major investment in the sterile fill/finish capabilities at the Alnwick site. This investment will increase the current capacity of the Annex 1 compliant facility to meet increasing industry demand for fully integrated drug development programs. It increases the number of Grade C cleanrooms from one to three.

As part of this expansion, the company has also invested in a new isolator technology, enabling larger batch sizes and reduced cycle times per manufacturing campaign .

Just down the road, in Morpeth, Piramal Pharma Solutions has invested £10M in new equipment, infrastructure and utility systems to meet increased customer demand and improve the site's carbon footprint by replacing obsolete equipment with new, energy efficient alternatives.

The site at Barnard Castle is one of **GSK**'s largest secondary manufacturing sites and manufactures a diverse range of products, including some of GSK's most innovative medicines for HIV, respiratory disease and auto-immune diseases. It is also a New Product Introduction site within GSK and the investment means GSK will be able to launch innovative products at speed whilst reducing waste.

In June 2022, after an investment of £90M GSK opened a 11,500m^2 world-leading, state-of-the-art aseptic smart manufacturing facility at the Barnard Castle site in County Durham.

The facility was constructed in line with GSK's sustainability targets and also demonstrates GSK's commitment to manufacture in the North East.

The cutting-edge new facility, which is known as 'Q Block' is a fully automated, paperless, digital facility that uses the latest technology to make manufacturing operations as efficient as possible. The move to a paperless facility was a first at Barnard Castle and there was significant engagement with the regulators (MHRA) during its design, with data integrity being a big consideration.

In Dec 2021 **FUJIFILM Diosynth Biotechnologies** announced the largest investment in British biopharmaceutical manufacturing for decades with a £400 million planned investment package at its Billingham site, to expand cell culture capabilities, viral vector and gene therapy services, and microbial production as part of its contract manufacturing and development operations. The Billingham site is the largest biologics CDMO facility of its kind in the UK.

This investment has added a new cell culture facility in the expanded Billingham campus and tripled existing cell culture capacity capabilities at the site with the addition of 4×2,000 L and 2x500 L single use bioreactor production capabilities for the manufacture of both monoclonal and novel antibody treatments. The expansion also includes the addition of the company's MaruX™ GMP continuous manufacturing platform to provide customers with a differentiated connected and integrated production platform offering.

In addition to the cell culture facility, the new investment package has expanded the viral vector and gene therapy services offered by FUJIFILM Diosynth Biotechnologies from the UK with dedicated process development capabilities and a commercial-scale viral gene therapy GMP facility, both located on the Billingham campus. The expansion, when fully operational, will deliver a ten-fold increase in gene therapy production capabilities by FUJIFILM Diosynth Biotechnologies in the UK, cementing its leadership in the viral vector market. The investment has also included the expansion of existing capabilities in vaccine manufacturing, along with new capabilities including mRNA production.

Once the expansion is complete in early 2024, the manufacturing capacity of the large-scale microbial production facility will increase by 70%. The finished expansion is anticipated to create up to 350 highly skilled jobs.

The Organon manufacturing facility in Cramlington is a solid dose formulation and packaging plant that commenced manufacture in 1975. It is part of a global healthcare company with a mission to deliver impactful medicines and solutions for a healthier every day for every woman.

Organon are continuing to invest in the site and are currently working on a £20M investment in high shear granulation and another £20M in the installation of new packaging lines and a warehouse extension with more capital expenditure to follow in the future.

The Newcastle Helix is a city-centre site newly-developed by Newcastle University, Newcastle City council and Legal and General that co-locates business and the university. It includes office and laboratory facilities for companies that include the pharmaceutical companies Iksuda Therapeutics and NewChem.

4.8 Regulatory issues

Those interviewed identified multiple factors that define the structure, character and future direction of the individual sites in the sector. However, a uniting feature across all interviews was the importance of the ability to operate globally in an increasingly competitive industry.

The sector's pharmaceutical manufacturers rely heavily on the ability to export their products and on the ability to import raw materials as well as other components required for products. Looking forward, interviewees identified the potential to attract business from international clients as core to the continued success of this industrial sector.

There are many planes of competition and performance within the industry such as supply reliability, expertise, regulatory adherence and cost; interestingly there has been some reversal of an earlier trend for drug development companies to use countries with lower cost bases, such as India or China for outsourced manufacture. The global marketplace has taken account of a number of challenges with these lower cost regions, including degree of expertise, regulatory shortfalls and poor quality standards. However, the sector is aware of increasing investment and upskilling in India, China and the Asia Pacific region as these countries adapt to the regulatory and market feedback they have received, so even though the offshoring trend has reversed in the short-term, there remains a possibility that the trend will resume. One of the companies said that they currently remain competitive with China by employing fewer staff with greater competence and skills.

5. Economic impact

The North East Pharmaceutical Manufacturing Cluster make a major contribution to the regional and national economy. In summary:

Key Messages

1. Pharmaceutical manufacturers in North East employ around 5,600 people:

    - Between 0.4% and 0.5% of North East employment and between 3.8% and 4.7% of North East manufacturing employment.
    - Between 12.0% and 15.0% of Great Britain's pharmaceutical manufacturing employment. The proportion of manufacturing process employment will be higher as the employment figure includes all activities undertaken by pharmaceutical manufacturers.

2. Using the appropriate multipliers for high value jobs*, North East's pharmaceutical manufacturing sector is estimated to support:

    - 17,600 jobs across the UK in their supply chain (indirect effects).

    - 24,600 jobs across the UK through spending by their employees and their supply chain's employees (induced effects).

3. Gross Value Added (GVA) measures the contribution to the economy of each individual producer, industry or sector in the United Kingdom. The GVA contribution of the North East pharmaceutical manufacturers is estimated at £1.52bn::

    - This is 2.7% of North East GVA and 17.9% of North East manufacturing GVA.
    - It is also 9.8% of UK pharmaceutical manufacturing GVA.
    - It is three and a half times more than would be predicted from the region's total GVA
    - It is comparable to that of the North East's automotive manufacturers

4. Exports

    - Amongst interviewed pharmaceutical manufacturers, between 5% and 80% of production is shipped to countries outside the UK.

*see Appendix 2

6. Technology Innovation

The capacity to reinvest should be and is aligned with the future technology innovation needs for the Cluster's companies, and the survey responses offered insights into future industry manufacturing technology demands to address changing drug manufacturing business models and customer needs.

Iksuda Therapeutics Ltd (formerly Glythera Ltd) was founded in 2007 through a co-investment agreement between the University of Bath and the Life Science Investment team at IP Group Plc. This investment supported the development of its PermaLink® (Stable bioconjugation) and PermaCarb® (Fluorinated Sialic Acid half-life extension) technologies.

In 2012 Iksuda completed a transformational £2m investment which allowed the Company to refocus its research activities on the development of Antibody Drug Conjugates.

Iksuda focused on validating its bioconjugation chemistry platform in ADC formats and then began to build a toolbox of enabling technologies including known & novel payloads and novel linker formats, as well as laying the foundations of prodrug approaches via tumor-selective triggers to improve ADC therapeutic index.

In 2018, Iksuda formerly transitioned to an ADC development company through the initiation of its Folate Receptor program (IKS012) and expanded its development capabilities and access to experts through its US (Boston, MA) operations. Iksuda's mission was to design and develop class-leading, next generation ADCs, with the potential for clinically meaningful differentiation over in-clinic and on-market comparators.

In 2020, through its partnership with LegoChem BioSciences, (LCB), the Company in-licensed an anti-CD19 ADC program (now IKS03) and gained access to LCBs ConjuAll platform for multiple targets. Subsequently, Iksuda added LCBs HER2-directed ADC (now IKS014) to its later-stage ADC portfolio and commenced a CA242-directed ADC program for GI tumors.

Iksuda's lead clinical programs are actively recruiting in US, Canada and Australia, with our first IKS014 patient showing a significant reduction in their target Oesophageal lesion after only 2 cycles at the lowest dose with no significant side effects.

The Company completed a $47m Series A financing in 2021 to support (i) development of its lead programs through IND and into early clinical development, (ii) expansion of its ADC asset portfolio and (iii) building an early-stage ADC pipeline.

"Today, through the differentiation that is underpinned by its multi-platform approach to ADC design and tumor-selective payload activation & release, Iksuda's experts have created an 'ADC engine' to build a broad portfolio of class-leading opportunities and generate clinical proof of concept through our in-house programs and with our Biotech and Pharma partners."

David Simpson

The activity of the Cluster companies spans everything from drug discovery to large scale manufacture and packaging. Innovation is possible at all stages whether it be discovery of a new entity or how to better control a new process.

It should be remembered that not all innovation comes from university research and that innovation matches what is needed to what is possible and transforms science into medicine. In fact, pharmaceutical manufacturing contributes three-fold more to UK GVA than life sciences research, according to the ABPI's 1922 report: *Life Sciences Superpower – Growing the leading global hub in the UK*

Quotient Sciences: Innovative Trends in Continuous Drug Substance Manufacturing -the FlowInova Platform

Given that there is a growing trend towards more targeted drugs, small-molecule active pharmaceutical ingredient (API) candidates are becoming more potent. Consequently, the amount of drug substance required has reduced significantly, while the molecular complexity and demands on chemical manufacture have increased. Continuous manufacturing facilities that can meet development and small-scale manufacturing requirements will be a critical solution to this problem.

FlowInova (a collaborative project between Quotient Sciences (Alnwick) and the University of Nottingham) set out to develop a data-driven methodology for process development and continuous manufacturing that enables efficient and intensive scale-up for early-phase development of API candidates.

The FlowInova project was the first to demonstrate that using automated reaction equipment and building models early in the process enables better decision-making for the next round of experiments. As more data is acquired and knowledge of the process increases, the process models become more predictive and allow for 'virtual design of experiments' to be carried out. This permits a greater focus on confirming and optimizing the predicted process parameters, leading to more robust and reliable scale-up.

Continuous-flow chemistry is now embedded as a key tool in Quotient Sciences' process research and development offering for drug substance manufacturing. To be able to develop a continuous-flow chemistry process, there is a need to generate more information about the chemistry we take on as a drug development and manufacturing accelerator. This collaboration helped Quotient to evaluate chemistry automation platforms, such as the EasyMax systems from Mettler Toledo and process modelling using Dynochem. With online process analytical technologies (PAT) giving time-course data on each experiment they run, they can more rapidly develop a greater understanding of the process and operating windows. This accelerates process optimization and de-risks scale-up, whether the process is better suited to continuous or batch reactors. This success has prompted the construction of a flexible, modular, kilo-scale drug substance manufacturing facility at the Quotient Sciences Alnwick site, a £6 million investment which was opened in December 2022. This data-rich approach to process research and development allows Quotient to be much more material sparing during the process development phase. They can get more information out of fewer experiments, while improving process robustness and the ability to deliver the 10s of kilograms that clients need on time and in full.

As well as optimizing for yield, the approach has allowed Quotient to consider wider sustainability metrics, and they have successfully developed a conjugate reduction that scored 77 out of 100 using the Green Motion™ assessment tool, which considers all 12 Principles of Green Chemistry. Demonstrating that continuous, process-intensive unit operations work at the kilo-scale allows Quotient to supply API material to support critical Phase I and Phase II clinical studies without the need to re-develop the process.

Gareth Jenkins / Paul Quigley.

Innovation is often thought of as a highly disruptive process in which newly commercialised technologies transform a well-established industry or create new industries, often dramatically changing or replacing more mature practices and industries in the process. While this form of innovation is powerful and highly visible in the business to consumer markets, this form of disruptive innovation is not common in highly regulated business to business markets such as pharmaceutical manufacturing. Innovation in pharmaceutical manufacturing is often aligned with incremental innovation that brings changes to the industry less sharply and less visibly than disruptive innovation. Nonetheless, the cumulative effect of multiple incremental innovation cycles aggregate and transform the industry over a period of years, maintaining its competitiveness.

Sterling Pharma Solutions believe the best way to innovate and introduce new technologies to the pharmaceutical industry is via collaboration between industry and the IP experts, SME or academia. Over the past 30 years they have collaborated with many academic partners in both the UK and USA to introduce new ways of working. Recently they initiated a Knowledge Transfer Partnership (KTP) with a local university, Northumbria, to increase their understanding of biocatalysis and enzyme development. The focus of the KTP project, which won the top grade of 'outstanding' by Innovate UK, was on the immobilisation of enzymes. If an enzyme can be immobilised it can potentially be re-used again increasing cost efficiency, one process at Sterling has re-used a bound candida lipase over 20 times reducing the cost of goods from approximately £30,000 per batch to £1,200. Immobilisation of enzymes can, in some cases, increase their stability and make it viable to use them in a continuous, or flow, reactor. This collaborative KTP helped Sterling win several new projects, including helping Manchester University in scaling up their Molnupiravir process from 2ml to 5L scale (https://pubs.acs.org/doi/10.1021/jacs.1c11048).

Due to the success of this first KTP, Sterling and Northumbria applied for a 2nd project to introduce molecular biology to Sterling. This KTP, which is currently still running, will allow Sterling to in-silico design novel enzymes and manufacture gram scale quantities for route scouting and development projects, the KTP is also building a network of industrial contacts to take these processes from laboratory kilo scale to industrial levels. The focus is not just on biocatalysis on biocatalysis but also on continuous manufacturing. Many processes use hazardous chemicals, such as azides, diazomethane nitroso compounds or conditions, such as high pressures or extreme temperatures. The philosophy of continuous chemistry is in controlling these hazards by limiting the inventory of materials and using equipment which can both optimise reaction kinetics but also contain these processes in an efficient manner. At Sterling they are collaborating with academics from all over the UK: Imperial College London, Leeds, Newcastle and Northumbria Universities to most efficiently introduce continuous chemistries and work with their internal flow team to scale these processes to the plant. But it isn't only hazardous chemistries that can be improved by continuous processing, the freeing up valuable assets from slow moving batch processes is also of real interest. (Speciality chem jan-feb 2024 p54).

Mark Muldowney

FUJIFILM Diosynth Biotechnologies: The biopharmaceutical industry represents a highly-advanced sector of healthcare, aspiring to improve the quality of patient lives globally, through innovative therapies, medicines and manufacturing advancements. Currently, the cost of development and production of such complex therapies remains a significant barrier to broader distribution and accessibility of such life-changing drugs. By evolving innovative approaches to how such medicines are manufactured, opportunities arise for driving down the cost of goods of such therapies. One such disruptive advancement made by FUJIFILM Diosynth Biotechnologies, UK is the award-winning SymphonX™, a flexible yet disruptive piece of bioprocess equipment designed to simplify biomanufacturing operations and supply chains, whilst advancing levels of automation in the industry.

Biopharmaceutical processes require a diverse range of complex equipment to successfully execute a manufacturing batch. Typically, a production facility requires multiple pieces of different bioprocess equipment, each piece representing varying levels of 1) capital investment; 2) qualification, training and operational requirements; 3) complex supply chains for the associated consumables necessary to operate; and 4) challenges in the automation of such equipment due to their unique design and incompatibility. SymphonX™ was developed as a piece of equipment for downstream processing that can fulfil a number of these functions and hence address such challenges, thus providing a more flexible and cost-effective approach to biomanufacturing, driving complexity and risk out of the industry.

SymphonX™ was invented, designed, assembled and initially deployed in the North East of England. The technology, due to it's multi-functional design, is intended to replace the majority of the existing bioprocess equipment required to manufacture a batch. The use of minimal different types of process equipment reduces capital costs, manufacturing cleanroom footprint, eases training and operations, and simplifies supply chain complexity.

Environmental sustainability is also at the heart of the SymphonX™ design philosophy. Reducing the amount of equipment required in production results in smaller pharmaceutical-grade cleanroom footprint requirements, and thus a reduced level of energy to clean and maintain such environments essential to make medicines safe for the patient. The innovative fluid management design also reduces the quantity of high quality-grade water required in the process, a major cost in today's production operations. Furthermore, the advanced level of automation in the SymphonX™ software reduces the number of manual operators involved in manufacturing, thus further cleanroom reduction and energy benefits. SymphonX™ benefits both patients and the planet.

As an example, a 500L bioreactor was operated continuously for about a month and used multiple SymphonX™ rigs to run all of the downstream unit operations requiring virtually zero operator intervention when running.

SymphonX™ exemplifies world-leading innovation happening right here in the North East of England. Developed and being used to huge benefit in multiple cGMP manufacturing units at Billingham the technology is now being deployed globally across the company's manufacturing network, enabling FUJIFILM Diosynth Biotechnologies to Advance Tomorrow's Medicines™.

Dr Jonathan Haigh

In this context, businesses also identified that process innovation that offers constant and continual improvements to reduce lead times and improve efficiency in the manufacturing, quality and supply processes is the innovation pathway of choice for the pharmaceutical manufacturing industry. This is inevitable, as the highly regulated nature of pharmaceutical manufacturing, with patient safety at its core, means it is hard radically to disrupt manufacturing processes without substantial experimental data at varying production scales to ensure any process changes do not adversely affect drug quality and manufacturing output.

Those interviewed were therefore keen to engage with key sector initiatives that advance, demonstrate or create new manufacturing processes within the parameters of current regulation aligned to the needs of customers, global compliance bodies and investors. This approach is key for the sector: innovations of this sort include lean manufacturing, incremental cost reductions, new chemistry and investment in new equipment, technologies, skills and culture.

Cluster companies take advantage of close collaboration with universities through, for example, Government-funded Knowledge Transfer Partnerships and company-funded consultancy contracts.

Many of the Cluster companies have considerable skills in process development using innovative ideas and approaches to a problem to enable a product idea to become sustainable in a commercial environment. The North East pharmaceutical Cluster companies create the added value and employment by making through innovation something that works, is cost effective and can be marketed.

CPI

CPI is an independent deep technology organisation with a strong focus on the pharmaceutical industry, health tech and sustainable manufacture. It is part of the government-funded Catapult network. CPI has a national remit and has several world leading facilities based in the North East. These include Darlington's National Biologics

Manufacturing Centre, a state-of-the-art facility dedicated to boosting the UK's innovation and manufacturing capability in biologics and the recently opened RNA Centre of Excellence, which is the only current UK based facility that offers R&D, development, scale up and GMP manufacture of lipid nanoparticle encapsulated RNA vaccines and therapeutics. The National Formulation centre in Sedgefield provides significant capabilities in drug formulation, nanomedicine and complex medicines, and hosts the Intracellular Drug Delivery Centre, a distributed Centre of Excellence run in partnership with other UK Catapult and academic groups providing capability for advanced drug delivery technologies. CPI's Medicines Manufacturing Innovation Centre, based in Scotland runs programmes that focus on the future of pharmaceutical production, using cutting-edge digital technology, collaborative expertise, and more sustainable manufacturing practices for drug modalities including small molecules and oligonucleotides. Across the organisation, CPI have undertaken over 1200 projects, the majority including SMEs, but also encompassing collaborations in partnership with universities and larger manufacturers, including Cluster companies.

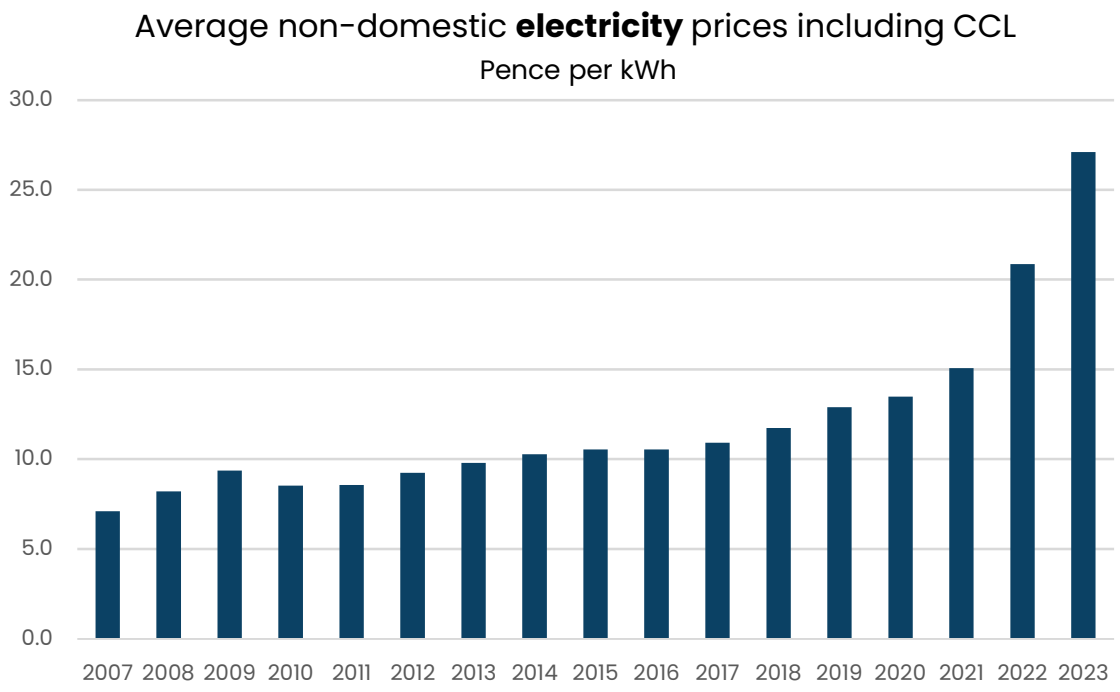
Biopharmaceutical innovation is exemplified by CPI's RNA Centre of Excellence, which opened in 2023, and has gained GMP certification from the Medicines and Healthcare products Regulatory Agency (MHRA). This is a key milestone for the NE cluster in supporting its Pharma base and for meeting the increasing demand for clinical evaluation of this emerging technology.

North East Process Industry Cluster

NEPIC is a not-for-profit cluster organisation serving companies across the process sector. The pharmaceutical manufacturing cluster in the North East is important to the region as a whole, and NEPIC exists to encourage collaboration, best practice sharing and cross-sector learning. Through technical conferences, networking events and special interest groups, NEPIC provides companies with the opportunity to learn about advances in manufacturing processes and technologies, decarbonisation and sustainability improvements. With a critical mass of over 350 members, NEPIC also works to understand key sectoral challenges in order to feed these back to local and national government.

7. Challenges since 2017

7.1 Energy costs



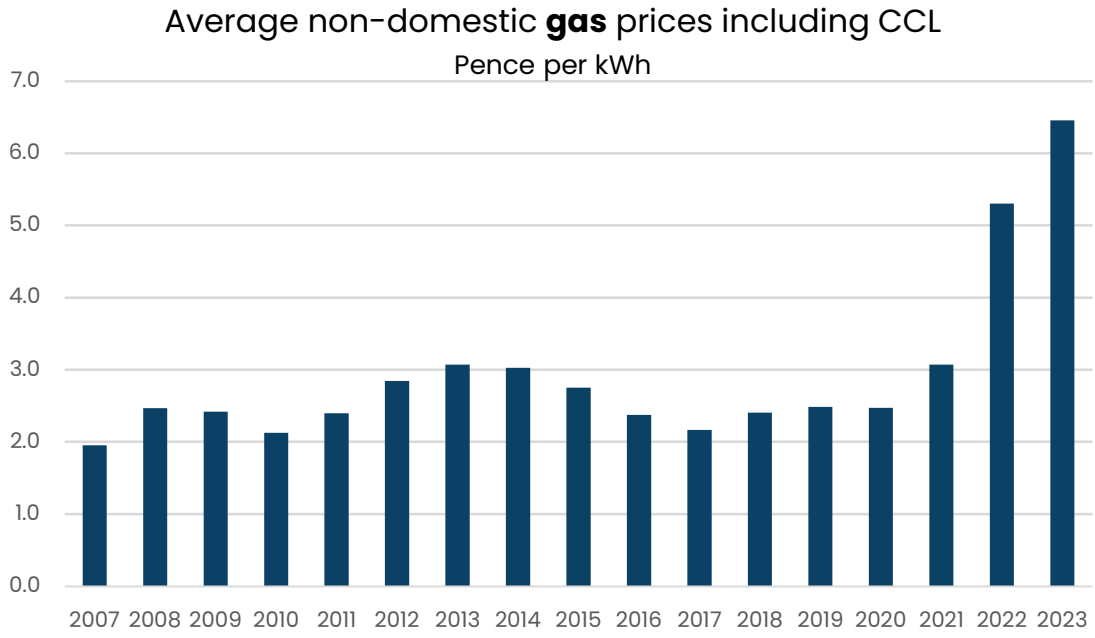


Figure 9: Gas and electricity prices in the industrial sector
(Source: Gov.uk Dept for Energy Security and Net Zero)

The industry has seen continuing to see significant and unprecedented increases (amounting to several million pounds per annum for the larger companies) in cost burden due to the universal and sustained increases in the price of gas, electricity and oil all of which are needed to heat and cool chemical synthesis reactors, operate product lines and run large HVAC ventilation and clean air systems, for example.

Both gas and electricity prices for large non-domestic users in the UK have risen by nearly 200% since 2017, with the majority of the increase occurring from mid-2021. *Source DESNZ*

Many manufacturers operate large equipment for chemical synthesis that requires heating and cooling cycles, while compressors on an HVAC air handling system for clean rooms need to provide at least 20 air changes per hour to meet regulatory standards.

7.2 Mitigating high energy costs

Low-carbon energy

GSK and Farm Energy have formed a partnership and are in the planning stages to build, whilst minimising any potential environmental impacts, a solar farm to the north east of the Barnard Castle Site. This initiative is part of GSK's target of achieving a carbon neutral value chain by 2045.

The GSK site as Barnard Castle manufactures, fills and packs sterile products as well as inhaled and dermatological products treating patients with HIV, asthma, lupus, psoriasis and nasal allergies to name a few. The site is also an important new product introduction site and the investment in solar energy will help to secure its future in County Durham.

The site when operational will be able to provide up to 16MWp and would meet about 52% of the sites current electricity consumption.

High Force Research are committed to doing everything they can to limit the impact of their ground-breaking work chemistry work on the environment, and to show their customers the best means to a more energy efficient way of manufacturing their products. They have reduced the carbon footprint at their Bowburn site by the installation of 300 solar panels onto the roof, the 125kW capacity dramatically reducing the energy consumption of the building, and feeding excess power back into the grid.

Construction commenced in 2015 of a 27.7MW biomass CHP plant in Cramlington. The plant became operational in 2017. It is adjacent to both the Pharmaron and Organon pharmaceutical plants and under a commercial deal will supply electricity and steam to the sites.

As might be expected, this has led most of these larger companies to undertake energy audits, employee education and optimisation of current equipment.

On sites where there are both heating and cooling operations, sites are also considering ways to recycle this energy.

GSK and Organon have operated wind turbines as part of their electricity management for a number of years and at least one other company is considering this as an option. For some companies this not an option for planning reasons.

The installation of both modest and large solar generating capability has been considered by many companies and some are actively moving towards installation of capacity either on site or nearby.

7.3 Moving towards sustainability

Sustainability is a growing theme, driven by customers' increasing insistence on low-carbon products and by owners' and investors' ESG policies. Besides energy, a major focus in on reducing waste.

We have found that for many CDMOs, environmental sustainability now forms part of clients' audit of potential manufacturers. The Cluster's thinking is exemplified by a statement from Sterling Pharma Solutions Ltd:

> The entire world has heightened its focus on **environmental sustainability**. Driven to address the global threat of climate change and safeguard our planet, organisations across a variety of sectors are seeking new ways to operate more sustainably and reduce environmental impact. The pharmaceutical industry is no exception. For drug developers and manufacturers, embracing greener practices and processes has become a key strategic priority.
>
> The pharmaceutical industry often involves significant processing and cleaning for a relatively small amount of active ingredient. Industry-wide, efforts are focused on reducing the waste generated by processing and making sure waste product is used rather than disposed of. As biotechnology and pharmaceutical organisations turn to outsourced service providers, they are increasingly focused on identifying partners that take environmental sustainability seriously.
>
> Companies are always looking for new ways to enhance environmental sustainability and better manage waste throughout the lifecycle of a product this can take many forms such as energy efficient lighting, recycling on or off-site of waste materials, on-site investments such as anaerobic digestion plant,

combined heat and power plant, solar and wind power that drive progress toward energy self-sufficiency.

FUJIFILM Diosynth Biotechnologies SymphonX™ manufacturing techology (described above in section *6 Technology Innovation*) reduces the cleanroom space required for manufacture of biologics and reduced the amounts of purified water needed, so improving the environmental footprint of production.

Sterling Pharma Solutions Ltd has received a gold medal from EcoVadis, placing it in the top 1% of pharmaceutical companies for sustainability

Environmental sustainability is a core part of Sterling Pharma Solutions' ESG (environmental, social, governance) strategy, which sets out our commitment to minimise our impact on the planet and maximise positive impact for our stakeholders.

Its Cramlington facility has become the pioneer site for its environmental sustainability initiatives.

Sterling has achieved a 40% reduction in carbon emissions intensity on site, and now only 10% of electricity is drawn from the national grid. A combined heat and power (CHP) plant powers its manufacturing, lab and office facilities.

The site treats the majority of its process waste through onsite aerobic and anaerobic waste treatment facilities. The AD plant recovers waste solvents, converting them to biomethane, which is injected into the national gas grid, providing enough energy to power the equivalent of 6,000 homes per annum.

Sterling believes that innovation is key in helping the company to achieve its ultimate goal of carbon neutrality, it is working on a number of projects to help deliver this goal, including ammonia-based cooling, upgrading our infrastructure through low grade heat capture, and investigating solar PV to match renewable supply with cooling demands. Additionally, it is training staff on sustainability in labs, with the goal of becoming My Green Labs certified.

The investment and projects at our Cramlington site have established a benchmark for similar initiatives across our network, which are an integral element of the company's ESG Roadmap.

Sterling has recently begun engaging on a larger scale in global risk and sustainability initiatives. For example, the Science Based Targets Initiative; The company has signed the commitment, and believes that its targets are aligned with limiting global warming to 1.5°C. Within the pharmaceutical industry, Sterling is engaging in Manufacture 2030s Activate programme, which facilitates best practice sharing to achieve net zero, as

well as in the Pharmaceutical Supply Chain Initiative. In this, Sterling wants to former deeper relationships with our customers and suppliers to improve sustainability across our value chain.

Sustainability is part of Sterling's business strategy and culture, guiding decisions and investment, and is part of everyday conversations. The company measures its impact not just on the environment, but on employees, the communities it works within and the industry it supports. Sterling aims to be a sustainable business now, and in the future, for the good of all our stakeholders, not least, those it makes lifesaving drugs for.

7.4 Leaving the European Union.

The Brexit Withdrawal Agreement was officially ratified by the Council of the European Union on 30th January 2020.

Prior to Brexit sites who form a part of a global manufacturing network reported concerns regarding potential supply chain disruption due to changes in customs procedures that may reduce the ability of a global manufacturing supply chain to efficiently include UK sites within the process.

Interviewees at that time emphasised the importance of the UK's regulatory strengths being maintained during and beyond the transition to leaving the European Union:

"The MHRA's reputation as regulatory body at the forefront of regulatory innovation both in Europe and worldwide must be maintained into the future".

Cluster companies have had to change and reshape many procedures within their business in order to continue operating and selling their pharmaceutical offerings into the European Union. For some it has been easier than others, depending on their pre-Brexit markets and operations, but there has been general agreement in our conversations that there haven't been many upsides and nothing has become easier.

There has been an increase in the paperwork and the complexity of actions required for importing and exporting to the UK. Companies that were already exporting goods outside of the EU before Brexit have found it slightly easier to navigate the new regulatory regime as they have had experience of customs, regulatory and tariff barriers. The increase in paperwork required for transfers of raw materials and products to and from the European Union has resulted in significant additional costs, in some cases due a significant increase in staffing requirements.

In one company interviewed, a five-person team was now in place where before Brexit, a single employee sufficed. Another company said that it was now easier in some cases to import from China than Europe due to the large amount of paperwork needed for European imports, though using shared loads in order to keep transport costs from China under control was itself challenging.

CDMO's and companies that are only making API drug substance seem to have encountered fewer problems than secondary suppliers where final packaged product that has been QP released in the UK is having to be reanalysed and QP released again in the EU. It has also resulted in some of the larger players having their own testing house in Europe and not having to rely on a third-party testing house which can take months.

This has been influential in one global company's decision on where to do its packaging and final release for the EU market - in the EU, not the UK.

Despite there being an original commitment to ensure harmonisation post Brexit between the MHRA and the EMA this has not as yet happened in reality. The UK no longer exists on the EMA website and material will be treated as coming from a third country.

A drug substance company in the UK now has to prove for every shipment to the EU that it has an MHRA GMP certificate and a Written Confirmation. However, there is no requirement for the API to be reanalysed or rereleased – just extra paperwork to fulfil and an additional payment to be made.

UK registration, evaluation, authorisation and restriction of chemicals (UK REACH)

EU REACH became UK REACH in January 2021 and now lies under the Health and Safety Executive for regulation and enforcement. It applies to all companies and all components of their supply chains and creates a responsibility for the safe use of chemicals used by the company or placed on the market.

As a consequence of Brexit the obligation now falls on anyone importing a substance into the UK to register all materials. Previously only materials imported into the EU had to be registered by UK companies.

The obligation to register chemical compounds above 1 tonne in size such as materials made as intermediates in API synthesis does not change. API's themselves continue to be exempt from registration, as they were under EU regulation.

Following Brexit, the HSE is working with UK companies to review REACH and how it can be made more workable for the UK.

The advice given to UK manufacturers by HSE is:

> Your business must identify and manage the risks presented by substances you manufacture and place on the market in GB. You must be able to demonstrate how the substance can be used safely and you must communicate the risk management measures to the users.
> You will need to consider your role in the supply chain in GB and how you use chemicals to determine what your obligations may be. Your previous role under EU REACH may have changed significantly under UK REACH so you should review your role(s).

7.5 SARS CoV2

No companies were lost from the Cluster due to the pandemic.

Several of the companies interviewed played a role in developing processes and facilities for both biologics and small molecule drug manufacture to meet patient need during the pandemic. The need arose in large part because of severe international supply chain fragility that resulted from the global effects of the pandemic. The value of robust UK pharmaceutical manufacturing capacity and expertise was very evident in this context. At the time, the Department of Health and Social Care and other Government ministries recognised this national weakness; one of those interviewed remarked that though an initiative to support onshore pharmaceutical manufacturing capacity to tackle future international supply chain failure was begun, it has since lapsed in marked contrast to initiatives in other jurisdictions, including in Europe and the US.

The majority of companies responded to the pandemic by changing their working practices and being flexible whilst keeping the business open. This has led to long term benefits in some instances.

The pandemic led to supply-chain and stock challenges for everyone, including shortages of supply of commodity items as well and specialty chemical feedstocks. Post Covid many companies in the bigger pharmaceutical supply chain have encountered either understocking or overstocking issues. Some supply chains are still fragile. For one secondary manufacturer an item that was available in 6 weeks can now be on 40 weeks delivery.

7.6 Dialogue with national government and local authorities

The Cluster maintains a dialogue with both national and local government and with local members of parliament. Its significance and value to the UK economy was highlighted in the 2017 national report *Life Sciences: Industrial Strategy* and forms a key part of the 2021 *Health, life sciences and medicines manufacturing: a growth strategy for the North East,* a blueprint for the region developed by the North East Local Enterprise Partnership.

Companies in the south of the region have productive relationships with the Tees Valley Mayoral Authority. Those from County Durham northwards are integral to growth strategies that are being developed by the incipient North East Combined Mayoral Authority.

Some companies have benefited from Government matched investment in innovative manufacturing. The success of the Cluster has been very largely independent of direct government support.

8. Future Development and Needs

Pharmaceutical manufacturing and life sciences start-ups and SMEs comprise the engines of growth in the North East Local Enterprise Partnership's 2021 *Health, life sciences and medicines manufacturing: a growth strategy for the North East.*

The strategy identifies opportunities in:

- Onshoring of pharmaceuticals manufacture to mitigate extended supply chains and shortage of supply
- Increased manufacture of advanced pharmaceuticals including complex biologics such as antibody-drug conjugates
- Continuous manufacturing and automation
- Sustainable manufacturing

This report has provided examples of how North East pharmaceutical Cluster companies are innovating manufacture to generate growth and maintain their global competitive advantage.

Reputation and visibility

As reported by the companies we have consulted, the Cluster's reputation in the global market is strong, transmitted largely by word-of-mouth and based on quality, innovation, adaptability and timely delivery.

There is a continuing need to communicate widely the Cluster's strengths, its global reach and its major contribution to the regional and national economy. It is crucial to the Cluster that its capabilities and needs are properly understood and are fully reflected in the UK Government's and the Region's strategic priorities.

Manufacturing integration and development

There are opportunities for supply chain integration within the region, drawing on the assets in chemicals manufacture. While there are strong links in research and development with regional universities, more can be made of the CPI's links with other UK universities and its Medicines Manufacturing Innovation Centre. There is also considerable scope for enhanced collaboration with other advanced manufacturing sectors in the region, not least in digital enhancements to manufacture.

The Cluster will continue to strengthen its knowledge base through its awareness and benchmarking of global best practice.

Skills, workforce planning and development

Rapid growth in the Cluster has highlighted the need for proactive recruitment and training initiatives. It is essential that Cluster companies work together to promote the region as an attractive and affordable place for people to live. Cluster companies should also work together and with others to understand current future skills gaps and with education providers to ensure appropriate training is available locally.

The Cluster's workforce would benefit from improved regional transport links.

UK regulatory environment

The Cluster's continuing international competitiveness and success requires a regulatory framework that facilitates the smooth management of global import and export supply chains, avoiding any further impediments to the movement of raw materials, intermediates and finished product. The Cluster would welcome regulatory changes that developed a fit-for-purpose regulatory regime that supports the continued growth of pharmaceutical manufacturing.

Investment into the Cluster

The Cluster has seen significant capital investment made into existing manufacturing sites in the last half-decade, often from international investors. An as-yet unrealised opportunity is inward investment into wholly new sites. There is also an unmet need for follow-on facilities at scale as new companies such as Iksuda and High Force Research grow and expand their businesses.

"It has surprised me that there is a lot of talk of "strategic autonomy" around chips and all sorts of digital technologies but not so much around drugs."

Diederik Stadig of ING, a Dutch Banking Group

"During Covid, we had a lot of political talk about bringing manufacturing back to Europe to avoid these kinds of [drug] shortages. When this problem was finally solved, pricing rules again."

Jürgen Bank, general manager at Excella, a manufacturer of generic APIs

Quoted in the Financial Times March 28 2024

Key Messages

Discussion with Cluster companies produced a number of pertinent observations. Skills, reinvestment capability and future technology innovation are three key areas in which will be vital to ensure the sector's competitive position is maintained and strengthened. The following recommendations aim to ensure that this performance can be sustained by providing a stable environment and support to current and future leaders to enable them to sustain and grow North East pharmaceutical manufacturing in future decades.

In summary:

1. The Cluster must increase the visibility of its capabilities, competence, economic impact and capacity to grow high productivity employment.
2. The Cluster must collectively foster initiatives to enhance recruitment and training.
3. Incremental innovation cycles are the preferred method of the pharmaceutical manufacturing industry. The Cluster must continue to grow its collaborations with research and research technology organisations and take further advantage of the advanced manufacturing expertise within the region.
4. The Cluster must pay close attention to any proposed changes that may reduce its global competitiveness and promote those changes that enhance its global reach.
5. The Cluster must be seen as a magnet to attract new inward investment.
6. The Cluster must maintain and enhance its global competitive advantage by maintaining and enhancing its global reputation for value, business resiience, regulatory reliabiity and sustainable manufacture.
7. The Cluster would benefit from direct, non-stop flights to the US from the region for both freight and business travel.

9. Conclusions

The North East pharmaceutical manufacturing Cluster contributes some of the highest value employment in the region and generates substantial wealth for the North East.

The Cluster is globally competitive and continues to grow at pace.

The Cluster can act as an attractor to new inward investment.

10. Appendices

Appendix 1: Glossary of Terms

Active Pharmaceutical Ingredient (API): Any substance or mixture of substances intended to be used in the manufacture of a drug product and that, when used in the production of a drug, becomes an active ingredient in the drug product.

Contract Manufacturing Organisation or Contract Development Manufacturing Organisation (CMO or CDMO): is a company that serves other companies in the pharmaceutical industry on a contract basis to provide comprehensive services from drug development through to drug manufacturing. This allows small or virtual drug discovery companies and large multinational drug developers to outsource those aspects of the business, which can help with manufacturing scalability or can allow the major company to free internal manufacturing capacity and/or focus on other aspects of drug development. This definition includes companies with the ability to manufacture active pharmaceutical ingredients through to finalised packaging for commercial distribution.

Good Manufacturing Practice (GMP): A manufacturing and quality system for ensuring that products are consistently produced and controlled according to regulated quality standards. It is designed to minimize the risks of noncompliance involved in any pharmaceutical production. Compliance with GMP is a legal necessity, sites are routinely inspected and licenced. Product processes are approved and licenced and product that does not comply with GMP protocols is rejected by internal quality controls, independent of any inspection. GMP regulations are set by the Federal Drug Administration (FDA) in the US, the Medicines and Health products Regulatory Agency (MHRA) in the UK and the European Medicines Agency (EMA) in the European Union. Similar agencies regulate drugs for release in other countries. Specific requirements vary by agency, and deep knowledge of these requirements and capability to meet them is required by sites supplying product to global markets. All regulatory agencies exist to set standards and maintain compliance, ultimately to protect the patient from risk of harm and ensure efficacy of the products they receive.

Large Multinational Drug Developer: discovers, develops, produces, and markets drugs or pharmaceutical drugs. Pharmaceutical companies may deal in branded medications or off-patent generic drugs. These companies have internal manufacturing networks and logistical capability to serve global markets.

Pharmaceutical Manufacturer: Within this report, this term relates to those company types defined by CMO, CDMO or large multinational drug developer. A key point of consideration in this definition is the ability to manufacture to a Good Manufacturing Practise (GMP) standard.

Stock Keeping Units (SKUs): A product and service identification code for a store or product, often portrayed as a machine-readable bar code that helps track the item for inventory. A stock keeping unit (SKU) does not need to be assigned to physical products in inventory,

but in this study the term is used for identification of specific product family type and variations within that product family, such as size.

Supply chain company or small to medium enterprises (SMEs): These are companies based in the North East who are either progressing drug candidates or medical diagnostics through preclinical or clinical trials. They are dependent on venture capital funding raising at their current stage in the company's development.

Appendix 2: Technical Note – Economic Impact

Definitions

The Office for National Statistics (ONS) publishes employment and Gross Value Added (GVA) data by industry. ONS use the 2007 Standard Industrial Classifications (SIC) to define sectors. In this report we have defined pharmaceutical manufacturing as:

- 21 - Manufacture of basic pharmaceutical products and pharmaceutical preparations which includes:
    - 21.1 – Manufacture of basic pharmaceutical products.
    - 21.2 – Manufacture of pharmaceutical preparations.

The International Territorial Level (ITL) is used so as to provide a geocode standard for UK subdivisions for statistical purposes.

The North East ITL region consists of Northumberland, Newcastle, North Tyneside, South Tyneside, Gateshead, Sunderland, County Durham, Darlington, Hartlepool, Stockton on Tees, Redcar and Cleveland and Middlesbrough.

The UK Standard Industrial Classification of economic activities, abbreviated as UK SIC, is a five-digit classification providing the framework for collecting and presenting a large range of statistical data according to economic activity. The SIC code for any given company is visible via Companies House and a major revision of the codes was carried out in 2007.

Gross Value Added

Gross Value Added (GVA) measures the contribution to the economy of each individual producer, industry or sector in the United Kingdom and can be broken down in a variety of ways.

The data in the 2017 report refers to the GVA via the 'income approach' for the ONS figures.

The ONS used to compile regional GVA using the 'income approach', but then they developed a second measure using the 'output (or production) approach'. This led to two versions of the same thing giving different answers, which was awkward. So, they

developed a ‘balanced measure approach’ that takes the two independent measures and combines them using quality metrics to weight the balance towards the stronger of the two, by component. The balanced version is now used for the various by-products and offshoots related to GVA.

In 2021, the manufacture of ‘basic pharmaceutical products and preparations’, (SIC07 21) in the North East generated £1.521bn in GVA for the region. This is equivalent to 9.8% of the total UK GVA for Pharmaceutical products.

The GVA data from the ONS statistics totally relies on the SIC07 code that any individual company has assigned to itself. SIC07 (21) is the manufacture of ‘basic pharmaceutical products and preparations’ consisting of the codes 21100 & 21200 and the data in the tables below uses SIC07 (21)

It’s interesting to note that whilst companies such as Sterling and Pharmaron have a SIC code of 21100 and therefore would be included in the ONS data for SIC07 (21) other companies in our survey use subsets of the code SIC07 (72) ‘Science and Research Development ‘ for example Newchem is 72190. Unfortunately, the (72) code isn’t broken down any further and includes all science and research development across all industries

Looking at SIC07 (72) for the North East gives us an additional figure of £710M, this is 4.3% of the UK GVA for Science and Research and Development and as expected is small compared to the South East at 36.1%. SIC07 (72) obviously captures R&D is a vast number of areas outside of pharmaceuticals.

ITL region	GVA 2021 SIC (21) by region £M (current)	Percentage of total UK GVA for SIC (21) 2021	Percentage change GVA SIC (21) 2011-2021 inflation corrected	Working Age Population per region 2021	Pharma GVA (21) per head of Working Age Population
United Kingdom	15,571	100.0%	8.9%	42,192,673	£369
England	13,339	85.7%	5.1%	35,618,031	£375
North East	1,521	9.8%	59.1%	1,635,449	£930
North West	3,793	24.4%	-13.8%	4,639,384	£818
Yorkshire and The Humber	1,022	6.6%	5.4%	3,416,409	£299
East Midlands	517	3.3%	11.7%	3,042,790	£170
West Midlands	141	0.9%	51.5%	3,684,959	£38
East	2,020	13.0%	-6.7%	3,912,332	£516
London	524	3.4%	14.4%	6,062,210	£86
South East	3,005	19.3%	45.6%	5,758,118	£522
South West	796	5.1%	-28.8%	3,466,380	£230
Wales	660	4.2%	27.7%	1,892,963	£349
Scotland	1,323	8.5%	59.2%	3,494,517	£379
Northern Ireland	249	1.6%	-4.5%	1,187,162	£210

Table A1 : GVA for SIC(07) code 21 by UK ITL region, 2011 to 2021 growth and GVA/ head working population. (16-64 years old) *Source: Nomis Database, official census and labour market statistics, Office for National Statistics*

Inflation corrected GVA data is inflation corrected to 2019 values..

The contribution of the North East to the UK pharmaceutical sector GVA is the 4th highest.

The GVA per head of working population (16-64 years) for pharmaceutical manufacture at £930 is higher in the North East than in any other region.

ITL region	GVA 2021 SIC(21) by region £M	Percentage of total UK GVA for SIC(21) 2021	GVA 2016 SIC(21) by region Inflation corrected £M	GVA 2021 SIC(21) by region Inflation corrected £M	Change in GVA 2021-2016 Inflation corrected £M	Change in GVA 2021-2016 Inflation corrected percent
United Kingdom	15,571	100.0%	13,031	17,186	4,155	32%
England	13,339	85.7%	11,304	14,723	3,419	30%
North East	1,521	9.8%	888	1,679	791	89%
North West	3,793	24.4%	4,217	4,186	-31	-1%
Yorkshire and The Humber	1,022	6.6%	763	1,128	365	48%
East Midlands	517	3.3%	333	571	238	71%
West Midlands	141	0.9%	109	156	47	43%
East	2,020	13.0%	1,645	2,230	585	36%
London	524	3.4%	295	579	284	96%
South East	3,005	19.3%	2,020	3,317	1,297	64%
South West	796	5.1%	1,035	879	-156	-15%
Wales	660	4.2%	571	729	158	28%
Scotland	1,323	8.5%	917	1,460	543	59%
Northern Ireland	249	1.6%	287	274	-13	-5%

Table A2: GVA for SIC(07) code 21 by UK ITL region, 2016 to 2021 growth

GVA data is inflation corrected to 2019 values. *Source: Nomis Database, official census and labour market statistics, Office for National Statistics.*

The growth in the North East pharmaceutical sector (SIC 07) at 89% is the highest in the UK outside London over the period since the last report was written, 2016 to 2021.

ITL region	GVA 2021 SIC (21) by region £Bn (current)	Total Regional GVA all sectors £Bn (current)	GVA 2021 (21) / Total regional GVA Percentage
United Kingdom	15.571	2,041	0.76%
England	13.339	1,761	0.76%
North East	1.521	56.5	2.69%
North West	3.793	196.0	1.94%
Yorkshire and The Humber	1.022	133.4	0.77%
East Midlands	0.517	118.4	0.44%
West Midlands	0.141	146.1	0.10%
East	2.020	171.4	1.18%
London	0.524	487.4	0.11%
South East	3.005	301.5	1.00%
South West	0.796	149.8	0.53%
	0.000		
Wales	0.660	69.5	0.95%
Scotland	1.323	149.9	0.88%
Northern Ireland	0.249	45.7	0.54%

Table A3: GVA for SIC(07) code 21 by UK ITL region and Total regional GVA for all sectors in England. *Source: Nomis Database, official census and labour market statistics, Office for National Statistic*

The percentage of the region's GVA that is attributed to pharmaceuticals (SIC 07) in the North East is higher than it is for any other region in England showing the significant part that pharmaceuticals play in the NE economy. Figures show that GVA for pharmaceuticals was 50% higher than for any other manufacturing sector. However, it should be noted that the UK car industry output, for example, was still recovering from the effects of SARS CoV2 in 2021 which could lead to the percentage of a region's GVA associated with pharmaceuticals being elevated across some of the regions.

Location quotients

An alternative way of looking at this is by using location quotients. Location quotients measure the geographic concentration of industries.

- A value of 1 means that the area has the same share of GVA in the industry as its share of national GVA.
- A value greater than 1 means the region has a higher share of GVA in the industry than its share of national GVA.
- The higher the location quotient for any given industry the more important that industry sector is to a region compared to the national average.

Region	2021 SIC (21) Quotient Value
North East	3.53
North West	2.54
Yorkshire and The Humber	1.00
East Midlands	0.57
West Midlands	0.13
East of England	1.54
London	0.14
South East	1.31
South West	0.70

Table A4: GVA Quotient for SIC(07) code 21 by UK ITL region.

Source: Nomis Database, official census and labour market statistics, Office for National Statistic

The manufacture of 'basic pharmaceutical products and preparations' in the North East had a location quotient of 3.53 – meaning the sector is overrepresented within the North East economy and is the highest regional figure.

There are only 2 industry sectors in the North East with higher location quotients – 'chemicals and chemical products' and 'machinery and equipment not elsewhere classified'.

The quotient for the overall 'production sector' in the North East is also above 1.0 which recognises the level of manufacturing carried out in the region.

SIC07 code	SIC07 description	UK 2021	North East region 2021	% of UK 2021	% of North East region 2021	North East Location Quotient
Total	All industries	2,040,499	56,483	100.0	100.0	1.00
A-E	Production sector	292,521	11,287	14.3	20.0	1.39
A (1-3)	Agriculture, forestry and fishing	15,364	424	0.8	0.8	1.00
1	Agriculture and hunting	13,739	381	0.7	0.7	1.00
2	Forestry and logging	935	32	0.0	0.1	1.24
3	Fishing and aquaculture	690	12	0.0	0.0	0.63
B (5-9)	Mining and quarrying	17,440	137	0.9	0.2	0.28
5-8	Mining and quarrying, excluding support activities	16,308	128	0.8	0.2	0.28
9	Mining support service activities	1,132	10	0.1	0.0	0.32
C (10-33)	Manufacturing	199,850	8,493	9.8	15.0	1.54
CA (10-12)	Manufacture of food, beverages and tobacco	28,671	631	1.4	1.1	0.80
10	Manufacture of food products	22,379	574	1.1	1.0	0.93
11-12	Manufacture of beverages and tobacco products	6,292	57	0.3	0.1	0.33
CB (13-15)	Manufacture of textiles, wearing apparel and leather	6,605	206	0.3	0.4	1.13
13	Manufacture of textiles	4,278	148	0.2	0.3	1.25
14	Manufacture of wearing apparel	1,972	47	0.1	0.1	0.86
15	Manufacture of leather products	355	11	0.0	0.0	1.12
CC (16-18)	Manufacture of wood and paper products and printing	12,990	604	0.6	1.1	1.68
16	Manufacture of wood products, except furniture	4,319	245	0.2	0.4	2.05
17	Manufacture of paper products	4,111	167	0.2	0.3	1.47
18	Printing and reproduction of recorded media	4,560	192	0.2	0.3	1.52
CD-CE (19-20	Manufacture of coke, refined petroleum and chemicals	18,479	924	0.9	1.6	1.81
CF (21)	Manufacture of pharmaceutical products	15,571	1,521	0.8	2.7	3.53
CG (22-23)	Manufacture of rubber, plastic and non-metallic minerals	15,724	550	0.8	1.0	1.26
22	Manufacture of rubber and plastic products	8,642	369	0.4	0.7	1.54
23	Manufacture of other non-metallic mineral products	7,082	182	0.3	0.3	0.93
CH (24-25)	Manufacture of basic and fabricated metal products	21,062	1,091	1.0	1.9	1.87
24	Manufacture of basic metals	5,053	223	0.2	0.4	1.59
25	Manufacture of fabricated metal products	16,009	868	0.8	1.5	1.96
CI (26)	Manufacture of computer, electronic and optical products	12,274	288	0.6	0.5	0.85
CJ (27)	Manufacture of electrical equipment	5,998	325	0.3	0.6	1.96
CK (28)	Manufacture of machinery and equipment	17,145	1,007	0.8	1.8	2.12
CL (29-30)	Manufacture of transport equipment	25,409	866	1.2	1.5	1.23
29	Manufacture of motor vehicles	13,766	761	0.7	1.3	2.00
30	Manufacture of other transport equipment	11,643	105	0.6	0.2	0.33
CM (31-33)	Other manufacturing, repair and installation	19,922	481	1.0	0.9	0.87
31	Manufacture of furniture	4,996	200	0.2	0.4	1.45
32	Other manufacturing	5,571	95	0.3	0.2	0.62
33	Repair and installation of machinery and equipment	9,355	185	0.5	0.3	0.71
D (35)	Electricity, gas, steam and air conditioning supply	33,683	1,318	1.7	2.3	1.41
E (36-39)	Water supply; sewerage and waste management	26,184	913	1.3	1.6	1.26
36-37	Water supply and sewerage	17,261	640	0.8	1.1	1.34
38	Waste collection, treatment and disposal activities	8,358	270	0.4	0.5	1.17
39	Remediation and other waste management services	565	3	0.0	0.0	0.19
F (41-43)	Construction	120,934	3,158	5.9	5.6	0.94
F (41-43)	Construction	120,934	3,158	5.9	5.6	0.94
41	Construction of buildings	40,150	962	2.0	1.7	0.87
42	Civil engineering	25,049	578	1.2	1.0	0.83
43	Specialised construction activities	55,735	1,618	2.7	2.9	1.05

Table A5

SIC07 code	SIC07 description	UK 2021	North East region 2021	% of UK 2021	% of North East region 2021	North East Location Quotient
G-T	Services sector	1,627,044	42,038	79.7	74.4	0.93
G (45-47)	Wholesale and retail trade; repair of motor vehicles	215,527	5,361	10.6	9.5	0.90
45	Motor trades	28,433	774	1.4	1.4	0.98
46	Wholesale trade	85,510	1,451	4.2	2.6	0.61
47	Retail trade	101,584	3,136	5.0	5.6	1.12
H (49-53)	Transportation and storage	63,464	1,727	3.1	3.1	0.98
49	Land transport	21,472	757	1.1	1.3	1.27
50	Water transport	2,894	24	0.1	0.0	0.30
51	Air transport	-2,867	-111	-0.1	-0.2	1.40
52	Warehousing and transport support activities	26,143	631	1.3	1.1	0.87
53	Postal and courier activities	15,822	426	0.8	0.8	0.97
I (55-56)	Accommodation and food service activities	48,682	1,343	2.4	2.4	1.00
55	Accommodation	12,157	271	0.6	0.5	0.81
56	Food and beverage service activities	36,525	1,071	1.8	1.9	1.06
J (58-63)	Information and communication	133,488	2,464	6.5	4.4	0.67
58	Publishing activities	12,610	109	0.6	0.2	0.31
59	Motion picture, video and TV programme production	14,608	68	0.7	0.1	0.17
60	Programming and broadcasting activities	7,178	25	0.4	0.0	0.13
61	Telecommunications	33,268	1,407	1.6	2.5	1.53
62	Computer programming and consultancy	55,030	694	2.7	1.2	0.46
63	Information service activities	10,794	161	0.5	0.3	0.54
K (64-66)	Financial and insurance activities	182,016	2,592	8.9	4.6	0.51
64	Financial service activities	89,061	1,575	4.4	2.8	0.64
65	Insurance and pension funding	34,082	504	1.7	0.9	0.53
66	Activities auxiliary to finance and insurance	58,873	513	2.9	0.9	0.31
L (68)	Real estate activities	256,711	6,779	12.6	12.0	0.95
68IMP	Owner-occupiers' imputed rental	182,346	4,697	8.9	8.3	0.93
68	Real estate activities, excluding imputed rental	74,365	2,082	3.6	3.7	1.01
M (69-75)	Professional, scientific and technical activities	157,273	2,680	7.7	4.7	0.62
69	Legal and accounting activities	57,864	771	2.8	1.4	0.48
70	Head offices and management consultancy	23,428	283	1.1	0.5	0.44
71	Architectural and engineering activities	23,322	515	1.1	0.9	0.80
72	Scientific research and development	16,494	710	0.8	1.3	1.56
73	Advertising and market research	21,817	141	1.1	0.2	0.23
74	Other professional, scientific and technical activities	9,659	145	0.5	0.3	0.54
75	Veterinary activities	4,689	115	0.2	0.2	0.89
N (77-82)	Administrative and support service activities	105,179	2,445	5.2	4.3	0.84
77	Rental and leasing activities	25,451	533	1.2	0.9	0.76
78	Employment activities	31,700	690	1.6	1.2	0.79
79	Travel agency and tour operator activities	6,737	198	0.3	0.4	1.06
80	Security and investigation activities	4,381	100	0.2	0.2	0.82
81	Services to buildings and landscape activities	11,937	349	0.6	0.6	1.06
82	Office administration and business support activities	24,973	575	1.2	1.0	0.83
O (84)	Public administration and defence	106,070	3,822	5.2	6.8	1.30
P (85)	Education	128,791	4,483	6.3	7.9	1.26
Q (86-88)	Human health and social work activities	171,328	6,789	8.4	12.0	1.43
86	Human health activities	127,677	5,017	6.3	8.9	1.42
87	Residential care activities	19,226	756	0.9	1.3	1.42
88	Social work activities	24,425	1,016	1.2	1.8	1.50
R (90-93)	Arts, entertainment and recreation	27,432	630	1.3	1.1	0.83
90	Creative, arts and entertainment activities	8,180	49	0.4	0.1	0.22
91	Libraries, archives, museums and other cultural activities	2,530	45	0.1	0.1	0.64
92	Gambling and betting activities	5,074	189	0.2	0.3	1.35
93	Sports, amusement and recreation activities	11,648	347	0.6	0.6	1.08
S (94-96)	Other service activities	28,071	819	1.4	1.4	1.05
94	Activities of membership organisations	8,289	264	0.4	0.5	1.15
95	Repair of computers, personal and household goods	2,474	43	0.1	0.1	0.63
96	Other personal service activities	17,308	512	0.8	0.9	1.07
T (97-98)	Activities of households	3,012	104	0.1	0.2	1.25

Calculating GVA

The GVA figures used in this report are all sourced from the Office for National Statistics data which is currently available up to 2021.

The ONS use an internal database called IDBR which contains data on companies derived from many sources and includes the whereabouts in the UK of all of a given company's sites together with the types of activity carried out at that, number of employees etc.

The total GVA for any given company is then allocated, by the ONS, to each of its regional sites and that it in turn is then aggregated for a given ITL coded area and also the relevant SIC code. For a company such as GSK this is quite a complex and confidential activity.

This means that although we have a GVA total for SIC07 (21) for the North East and other regions there is no visibility available below the aggregated figure of £1.521Bn.

UK GVA in Life Sciences

The ABPI/PwC 2022 report: Life Sciences Superpower: Growing the leading global hub in the UK provides national data on the three major life science sectors. Pharmaceutical manufacturing contributes £16.4bn to UK GVA and, directly or indirectly, 346,000 jobs, medical technology manufacturing, £15.7bn and 182,000 jobs and life sciences research, £56bn and 56,000 jobs.

Additional jobs

As well as creating employment opportunities within their own organisation, pharmaceutical manufacturers can also support additional employment opportunities:

- in their supply chain (these are known as indirect or Type I multiplier effects);
- through the expenditure of their employees and the employees in their supply chain (these are known as induced or Type II multiplier effects).

Using the multipliers for pharmaceutical development and manufacturing employment provided in the ABPI/PwC 2022 report: Life Sciences Superpower: Growing the leading global hub in the UK (Type I: 3.14; Type II: 4.4), the North East's pharmaceutical manufacturing sector supports:

- 17,600 jobs in their supply chain.
- 24,600 jobs through the spending by their employees and their supply chain's employees.

Combined this means the North East pharmaceutical manufacturing sector supports 42,200 jobs across the UK.

Potential under-reporting of North East manufacturing GVA.

There are a number of potential reasons why the North East pharmaceutical sector GVA may be underreported in the ONS data. These include:

- The company although manufacturing in the North East is not headquartered, according to Companies House, in the region and its numbers will have been dealt with by the ONS using their IDBR database and various algorithms. However, the allocation of the manufacturing sectors GVA values for the North East was examined / crosschecked by the ONS a few years ago and shown to be a realistic figure.
- The company whilst being headquartered in the North East has allocated itself a different SIC07 code other than (21) There is no legal requirement for this code to be correct and in some instances a company whose activity spans several sectors may have chosen another code to categorise what it does

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