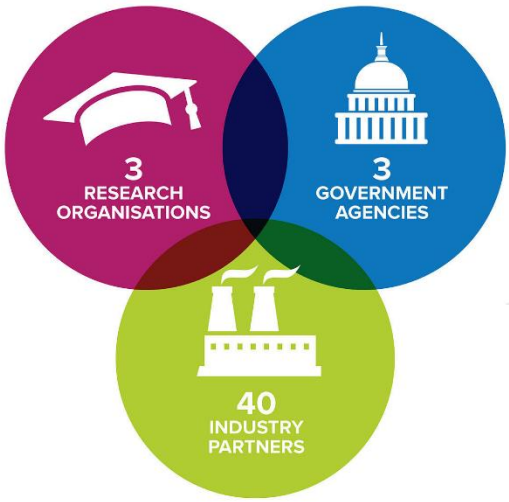
# (BIO) PHARMA IRELAND

Innovating Medicine Manufacture

# (BIO) PHARMA IRELAND WHITE PAPER

## May 2017

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# (BIO)PHARMA IRELAND WHITE PAPER:

## THE CASE FOR A STRONG EU (BIO)PHARMACEUTICAL MANUFACTURING INDUSTRY

### 1. INTRODUCTION

Pharmaceutical manufacturing is crucial for delivering timely and reliable access to safe, innovative, and cost effective medicines. Without a sustained and strategic approach to the (bio)pharmaceutical manufacturing process that supports such medicines supply (highly potent small molecules, large molecules, and cell therapies) it will be impossible to address the challenges posed by the increasing need to deliver healthcare in Europe and globally. Improved manufacturing is essential to enable this.

The EU institutions have in various statements and documents recognized that the (bio)pharmaceutical industry contributes to the well-being of citizens through supporting the availability of medicines, economic growth, and employment.[1] The pharmaceutical industry is the European high technology sector with the highest value-added per person employed[2]. The EU has invested considerably in the discovery of innovative medicines but the investment is significantly lower in how to develop and manufacture these products. There is currently a gap to bridge between investment in discovery and manufacture, especially in support of scientific and engineering programmes. Moreover, growth in the pharmaceutical sector is declining due to reduced pipelines, launch delays, non-approvals and negative effects of scale in ever increasing organisations. But in parallel, thanks to advances in science and technology, the industry is entering an exciting era in medicines development. Research methods are evolving and there are many promising prospects, from the possibilities offered by personalised medicines, to the potential offered by novel biopharmaceuticals. For Europe to compete in the global market, it must help industry address the challenges and embrace the opportunities.

Future innovation can only be enabled through supporting policies and regulations. The need in future would be for regulation to enable a step change in the manufacturing process, including supply and distribution. One area for this would be the potential revision of Regulation (EC) No 726/2004, which established the European Medicines Agency (EMA).

[1] See, for example: http://ec.europa.eu/health/files/pharmacos/pharmpack_12_2008/communication/citizens_summary_communication_en.pdf

[2] Source: http://www.efpia.eu/uploads/Modules/Documents/the-pharmaceutical-industry-in-figures-2016.pdf

The aim of this White Paper is to outline the (bio)pharmaceutical manufacturing landscape and to explore how the (bio)pharmaceutical manufacturing industry in Europe can be successfully sustained long term with appropriate policy and funding mechanisms. The White Paper showcases how a strong EU (bio)pharmaceutical manufacturing, industry under the leadership of (bio)Pharma Ireland, could better deliver the benefits for the EU economy and society. This will not happen without an optimized policy and regulatory environment in Europe.

### 1.1. About (bio)Pharma Ireland

(bio)Pharma Ireland was formed in 2015 to highlight the collective research priorities and industrial capabilities of the Irish (bio)pharmaceutical sector within the European community; encourage research collaborations and opportunities; and ultimately contribute to the development of European policy. The working group, coordinated and chaired by the SSPC, has representation from the pharmaceutical industry: BiopharmaChemical Ireland (BPCI); government agencies: Science Foundation Ireland, Enterprise Ireland and the IDA; and public research organisations: the Synthesis and Solid State Pharmaceutical Centre (SSPC), National Institute for Bioprocessing Research and Training (NIBRT) and the Pharmaceutical Manufacturing and Technology Centre (PMTC). The SSPC leads the way for next generation drug manufacture and spans the entire pharmaceutical production chain from synthesis of the molecule, to the isolation of the material, and the formulation of the medicine. NIBRT is a world-class institute that provides training and research solutions for the bioprocessing industry and the PMTC focusses on advanced technology solutions which focusses on the use of Process Analytical Technology, continuous processing, use of soft sensors in process control and plant cleaning, faster product testing, and packaging innovations.

On 28 February 2017 (bio)Pharma Ireland organized a high-level seminar entitled The Future of (Bio)Pharmaceutical Manufacturing in Brussels. The seminar, which brought together around 80 participants from research and academia, business and industry, policy-making sphere, and other interested stakeholders from across Europe, explored the future of advanced drug manufacturing and addressed the enabling policy environment required for innovative pharmaceutical and biopharmaceutical manufacturing process that would support new methods of drug delivery and quality healthcare in Europe.

The key outcome of this event was the launch of a consultation process on this white paper, which establishes a case for a strong EU (bio)pharmaceutical manufacturing industry, and a commitment to setting up the (bio)Pharma Europe initiative. The list of organizations present at the event is available in the annex 3. This white paper is a consolidated document and includes the comments on the first draft by interested participating parties.

## 2. CURRENT TRENDS AND CHALLENGES

Ageing populations and pandemics present a challenge to our healthcare systems and societies, demanding a new approach to medicines supply. Moreover, the (bio)pharmaceutical industry is facing a paradigm shift in how medicines are manufactured and must respond with the implementation of disruptive technologies to stay competitive and deliver the required benefits to patients. Aside from decreasing rate of growth recently the industry faces key technology challenges, which, if properly addressed, will ensure continued success of the sector. The main trends and challenges, as identified by (bio)Pharma Ireland, are presented below.

### 2.1. Medical innovation and progress

Recent technological developments are influencing medical innovation, as well as the (bio)pharmaceutical market and supply chain: if in the past, advances in medicine belonged mainly to the R&D departments of pharmaceutical companies, it is the small innovative companies that develop and produce new solutions.[3] The role of medical devices is growing. We see ever expanding number of healthcare providing players, as well as a shift to an outcomes-based therapy. With the advent of personalized medicine – *"a medical model using characterization of individuals' phenotypes and genotypes for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention"*, as the Horizon 2020 Advisory Group has defined it[4] – the prominence of safe, innovative, and affordable medicines will also rise. The growth in personalized medicine poses a fundamental challenge to existing medicines supply chains. In order to plan for the advent of personalized medicine, the sector will in future need to manufacture increasingly complex products on demand. One consequence of this development will be that inventories will be much lower. Manufacturing also has to deliver ever increasing numbers of therapies to an increasingly diverse cohort of patients. In addition to this the age of the "blockbuster" therapy is widely accepted to be declining. Currently most manufacturing facilities use batch production which is inflexible, large volume and in most cases uses decades-old technology. There is also a shift within the industry towards the development of lower dosage highly potent active ingredients. As such the need for large scale manufacturing facilities is becoming redundant. These facilities will be replaced by more modular plug and play (in some cases disposable) manufacturing plants of the future. Disruptive innovation must be deployed to design such facilities and meet these growing demands to remain competitive.

In the past it has been recognized that existing pharmaceutical manufacturing operations tended to be inefficient with a low rate of introduction of modern engineering process design principles, new measurement and control technologies, and knowledge management

[3] Source: http://medicalfuturist.com/6-surprising-trends-shaping-the-future-of-pharma/
[4] Source: http://ec.europa.eu/research/health/index.cfm?pg=policy&policyname=personalised

systems. Manufacturing innovation, driven by the need to reduce cost and increase effectiveness, technology developments, changing consumer needs, new market requirements, and global competition, therefore needs to be made a strategic priority.[5] As previously identified, innovation requires both public and private investment, as private investment in R&D and innovation is often below an optimal level due to uncertain returns. Strategic public investment therefore plays a crucial role in fostering investment in R&D and innovation.

The developments outlined have induced a period of transition for the (bio)pharmaceutical manufacturing sector, which is now moving from a predominately small-molecule batch-manufacturing-based business model. Often easy to replicate with a fraction of the R&D investment – to more novel therapeutics (highly potent small molecules, large molecules, cell therapies) involving a wide variety of processing techniques to produce same economically. Techniques such as continuous processing, the use of process analytical technology, and the introduction of modular plug-and-play processing equipment are being widely researched internationally as the future of the processing sector of the industry.

### 2.2. Need for sustainable healthcare systems

The fast pace of therapeutic progress has, aside from benefits to patients, also brought both therapeutic complexity and higher costs, putting additional pressure on EU health systems[6], to both patients and the governments. Public spending on health already accounts for more than 7% of GDP in the EU28 (data for 2012)[7]. By 2060 public expenditure on acute health care and long-term care is expected to rise to between 8.5 and 9.1% of GDP, although not equally across all Member States. The urgency of the issue is also underlined in the EU 2012 Ageing Report, which concludes that the sustainability of public health expenditure is largely related to its projected increases. Based on research findings, it is not only demographic change that is driving up healthcare costs, but also non-demographic determinants of care, such as medical innovations. Similarly, in 2015 the OECD reported[8] that healthcare costs are rising so fast in advanced economies that they will become unaffordable by mid-century: maintaining today's healthcare, and funding future medical advances, will be difficult without major reforms, the report entitled "Fiscal Sustainability of Health Systems: Bridging Health and Finance Perspectives" reads. According to the OECD projections, public expenditure on health and long-term care in OECD countries is set to increase from around 6% of GDP today to almost 9% of GDP in 2030 and as much as 14% by 2060. At the same time the economic crisis of recent times has led to a significant reduction in expenditure in the healthcare sector in Europe.

[5] Source: http://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/pharma-manufacturing-for-a-new-era
[6] Source: http://apps.who.int/medicinedocs/documents/s21793en/s21793en.pdf
[7] Source: http://ec.europa.eu/economy_finance/publications/european_economy/2015/pdf/ee3_en.pdf
[8] Source: http://www.oecd.org/health/healthcarecostsunsustainableinadvancedeconomieswithoutreform.Htm

Developing and delivering medicinal products is complex and risky. One also must note that new drugs are costly to develop: the cost to develop new a pharmaceutical drug exceeds $2.5 billion[9], with the combined cost of manufacturing and clinical testing for some drugs adding up to $1 billion[10]. As indicated in the draft report by the European Parliament on EU options for improving access to medicines, a fair price for medicines should cover the cost of drug development and production[11].

Supply chains for medicines are currently up to 2 years long, which is in part due to the global outsourced production networks that are used by the industry (see also the chapter below). With process innovations, such as continuous manufacturing (e.g. telescoped reactions), companies may be able to develop shorter supply chains located entirely within the EU. This would increase responsiveness and security of supply of medicines.

With the increased costs of healthcare and the growing need for patients to receive new and effective medicines, the urgency of improving access to safe, affordable high quality medicines through innovative manufacturing practice proves more significant.

### 2.3. Global competitiveness

Apart from playing a role in guaranteeing effective healthcare, a strong pharmaceutical industry is also a major contributor to EU's competitiveness and growth; in 2012 the sector produced an output of €220 billion[12]. The sector saw a production index increase, which amounts to 2.5% (between 2006-2011) and is also a major contributor to the EU's trading power.[13] Pharma and biotech are continuously among world's top R&D investors with a high R&D intensity, both in the EU and globally. The pharmaceutical industry is also one of Europe's major high-technology industrial employers. A significant proportion of these jobs are valued skilled jobs, aiding Europe in maintaining a high-level knowledge base and preventing the "brain-drain". It is highly regarded as an employer providing much sought after occupation in a hi-tech, high remuneration sector providing excellent career opportunities for those in its employ. It is also one of the industries with the highest labour productivity. EFPIA[14] reported that the research-based pharmaceutical industry employs directly around 725,000 people with 3 to 4 times more indirect employments. This accounts for around 1.8% of the total manufacturing workforce[15].

[9] Source: https://www.scientificamerican.com/article/cost-to-develop-new-pharmaceutical-drug-now-exceeds-2-5b/
[10] Source: http://www.forbes.com/sites/matthewherper/2012/02/10/the-truly-staggering-cost-of-inventing-new-drugs/#7f8b3b414477
[11] Source: http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-%2f%2fEP%2f%2fNONSGML%2bCOMPARL%2bPE-587.690%2b01%2bDOC%2bPDF%2bV0%2f%2fEN
[12] Source: http://ec.europa.eu/growth/tools-databases/newsroom/cf/itemdetail.cfm?item_id=7862&lang=en
[13] Ibid.
[14] Source: http://www.efpia.eu/uploads/Modules/Documents/the-pharmaceutical-industry-in-figures-2016.pdf
[15] Source: http://ec.europa.eu/growth/tools-databases/newsroom/cf/itemdetail.cfm?item_id=7862&lang=en

The research-based (bio)pharmaceutical industry can thus play a critical role in ensuring EU's future competitiveness in an advancing global economy. However, the sector faces real challenges: besides the additional regulatory hurdles and escalating R&D costs, the sector has been severely hit by fiscal austerity measures introduced by governments across much of Europe since 2010, and is also facing increasing competition from emerging economies: emerging markets will represent about 45% of the world's GDP by 2018 and are expected to grow twice as fast as developed markets between 2008 and 2018[16].

In 2013 the Brazilian and Chinese markets grew by 17% and 14% respectively compared to an average market growth of 1% for the five major European markets and 3% for the US market. Such factors can also present great opportunities however. One striking trend in global population growth is the rapid increase in the proportion of the population with real purchasing power. The combination of unprecedented growth in demand for premium products along with the trend towards customisation provides both a challenge and opportunity to all manufacturing jurisdictions to supply emerging markets. Investment in the manufacturability of therapeutics can pave the way for Europe to become the jurisdiction of choice for supply of medicines globally.

Moreover, the industry has for some time been increasing its use of outsourced providers for manufacturing innovation. These are rarely located in Europe and are more likely in China or India, which increases the strength of other regions in this field and creates gaps in the ability of EU based organizations to innovate manufacturing processes wholly inside the EU. Please see the annex 2 for case studies on investments in Asia, which is fast becoming the site of choice for both the pharmaceuticals and biopharmaceuticals industries. Moreover, in this region global pharma companies are increasingly partnering with academic institutions and local biopharmaceutical companies and establishing innovation centres and manufacturing facilities[17].

Europe's status as the default launch site for manufacturing new chemical entities can be maintained and further developed if the ability to innovate manufacturing processes is retained in the region. Launches are a multi-year effort and a high level of innovation is required to accommodate new processes on site. EU R&D supports for this innovation could increase both the speed and number of such launches in Europe.

### 2.4. Regulatory issues and compliance

Manufacturing innovation in the (bio)pharmaceutical sector requires the support of the relevant regulatory bodies, unlike the other parts of the 'process' industries. It is vital that the EMA is involved in future innovation structures and programs to support manufacturing

[16] Source: http://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/pharma-manufacturing-for-a-new-era

[17] http://blog.waters.com/a-view-of-the-biopharmaceutical-industry-in-asia-an-interview-with-ken-fountain

innovation. Here it is worth mentioning the proactive role of the US Food and Drug Administration in encouraging manufacturing innovation, partly to develop a more resilient and responsive supply chain, but also to minimize the need for regulatory oversight and ease the regulatory burden and cost through well designed, efficient manufacturing based on fundamental understanding, since ensuring compliance is often adding significant overhead to the product lifecycle.

### 2.5. Global anti-counterfeiting measures

Unauthorised distribution of counterfeit medicines globally remains a significant threat to patient safety, as counterfeit or stolen medicines are sold more efficiently than ever. The roll out of legislation in the US (Drug Quality and Security Act) and EU (Falsified Medicines Directive) is driving significant investment by the industry into technologies to protect the supply chain from manufacturer to patient. Stronger security measures require the integration of cloud based data management, encoded verification systems, tamper evident technologies and industry research efforts, bringing the digital single market agenda to bear on the distribution and use of pharmaceuticals in Europe and elsewhere.

One arena where this has already been introduced is the serialization of pharmaceutical manufacturing lines, which is now taking place in Europe to meet the legislation compliance. This change in pharmaceutical packaging lines, providing a unique identification for each individual medication package, has already generated new ideas for better track and trace and anti-counterfeit solutions than the existing ones. These ideas might have big impacts also outside pharmaceutical industry, wherever product safety or brand protection is important.

A strong and well-developed (bio)pharmaceutical manufacturing sector already exists in Europe, which performs well and is able to compete with skills and innovation, and the EU should strategically build upon this with a view to supplying both the existing and emerging global market. The (bio)pharmaceutical industry has and will continue to be an innovator, generating intellectual property, knowledge, and know-how, which directly addresses health challenges, but sustains wider innovation through technology transfer, spin-offs, and its ability to support industry hubs. These clusters provide the centres of excellence which sustain innovation capacity. In the case of Ireland as well as elsewhere this is an important factor in foreign direct investment and local investment in infrastructure and capacity building. A strong and innovative (bio)pharmaceutical sector requires the support of the relevant regulators. The EU with its current focus on the future of industry and the skills to sustain that industry should recognize the strategic importance of (bio)pharmaceutical manufacturing and the contribution of the sector to sustaining healthcare delivery and sector competitiveness.

## 3. (bio)Pharma Ireland Recommendations

A viable European (bio)pharmaceutical industry is vital for public health, economic growth, trade and science. (bio)Pharma Ireland are innovation leaders and are playing a critical role in supporting the pharmaceutical sector, committed to developing and training highly skilled scientists and engineers with an understanding of industrially relevant challenges to support the advancement of (bio)pharmaceutical manufacturing in Europe.

With industrial modernization and digitization, innovation in the (bio)pharmaceutical sector will be a cross-cutting efforts, involving sectors from both upstream processing (chemistry, biologics, pharmaceuticals, engineering etc.) and downstream processing (formulations, sensors and measurements, analytics, manufacturing etc.). Collaborative and transversal innovation will be a key success factor, therefore strategic support through policy, funding, and regulation for networks combining various disciplines and industries is vital. (bio)Pharma Ireland argues that their vision for future (bio)pharmaceutical manufacturing innovation will address the complete manufacturing process from a scientific, process and engineering, supply chain, and regulatory perspective. For this to happen more R&D is needed in the key research priorities of the sector, namely in:

- Continuous manufacturing; flexible scalable processing
- Predictive design and control technologies; track and trace
- Modular manufacturing facilities
- Single use technologies
- Biopharma manufacturing
- Use of 3D printing
- Bioanalytical characterization
- Downstream processing and purification technologies
- Convergence of drug-device technologies
- Anticounterfeiting technologies and data management
- Innovations in packaging and patient information technologies
- Sustainable manufacturing
- Digital agenda in advanced manufacturing: use of the cloud, augmented reality
- New regulatory science approaches for support of safe medicine supply

Moreover, the manufacture of innovative therapies such as cell and gene therapies has significant clinical impact, but manufacturing models for them are yet to be determined. Please see annex 1 for more detailed recommendations.

**(bio)Pharma Ireland's vision is to lead the way in (bio)pharmaceutical manufacturing for the future to deliver timely and reliable access to safe, innovative, and cost effective medicines.**

While the (bio)pharmaceutical sector faces many challenges globally there are also opportunities. Such opportunities can only be grasped by a jurisdiction that is innovation led, and that is the vision of the (bio)Pharma Ireland. Europe is very well placed to lead the way in assuring timely and easy access to safe, high quality and affordable next generation medicines due to existing infrastructure and track record. However, this advantage is only short lived without future investment. Only a strong EU-based (bio)pharmaceutical manufacturing industry will be able to effectively address the security of medicines supply and production and help achieve overall sustainability of healthcare in Europe. Moreover, it will contribute to securing and sustaining the competitiveness of the EU economy through boosting innovation, skills development, advancing coordination of the R&D, and building partnerships.

Recommendations to the EU thus are:

1. **An enabling policy and regulatory environment with a new regulatory approach, which is data and technology driven;**
2. **Stronger support for (bio)pharmaceutical manufacturing in the 9th Framework Programme and in the structural funds;**
3. **A network process or a technology platform to support next generation manufacturing;**
4. **To facilitate the establishment of a structured dialogue between (bio)Pharma Ireland and IMI 2;**
5. **To facilitate the launch of the (bio)Pharma Europe platform;**
6. **Strengthening the link between manufacturing and R&D;**
7. **A stronger consideration of manufacturing with regards to patient related initiatives and the Digital Single Market Strategy.**

The strategic support of the EU for the (bio)pharmaceutical manufacturing would result in:

1. **Enhancement of skills and trained workforce;**
2. **New technologies, especially in the areas of flexible biotechnology manufacturing, which will allow faster and lower cost production; and**
3. **The ability to manufacture and supply sufficient products for the EU population.**

## Annex 1: (BIO)PHARMA IRELAND VISION FOR (BIO) PHARMACEUTICAL MANUFACTURING PROCESS OF THE FUTURE

A vision for the (bio)pharmaceutical manufacturing process of the future includes:

1. **Widening of the manufacturing lifecycle to include supply/distribution/regulation.**
2. **Continuous manufacturing.** Continuous manufacturing will deliver small volume niche products with higher quality profiles. High production rate and in-line quality checks makes it more effective and it will be both cost and time effective process as compared to batch manufacturing. However, it is difficult to implement for small volume size and difficult to get acquainted for operators. It also has the potential to be extended to portable manufacture which could be rapidly deployed to produce drugs needed to handle an unexpected disease outbreak or to prevent a drug shortage.
3. **Flexible scalable processing**.
4. **Modular manufacturing facilities.** Modular manufacturing facilities based on standardized platforms can manufacture a diverse array of innovative medicines.
5. **Single use technologies**.
6. **Precise control.** Recently, there has been a shift to collect Process Analytical Data through appropriate deployment of technology but to date this has had little impact on efficiency as, in general, it is collected rather than acted on. The digitised age will allow precise control of manufacturing offering a paradigm shift in efficiency and effectiveness.
7. **Measurements.** Measurements have importance for the whole manufacturing chain, especially as the pharmaceutical manufacturing develops from batch processing to continuous manufacturing and eventually manufacturing methods for personalized medicine. Recently, there has been great progress in sensor technologies, which have become smaller, cheaper, and more connected than ever. Developing and integrating the sensor technology into the (bio)pharmaceutical manufacturing is not just engineering work, but would require innovations that could be vital for the future success of instrument companies working for the pharmaceutical industry.
8. **Bioanalytical characterization**.
9. **Purification technologies**.
10. **Convergence of drug-device technologies**.
11. **Use of the cloud.** MNC pharmaceutical companies currently generate over 500 terabytes of data daily. This data is often siloed in individual sites. Use of the cloud to create a digital backbone in organisations would increase competitiveness by reducing lead times, controlling inventory, reducing waste, and creating greater flexibility. It would also present opportunities for developing new materials science, process models, tracking medicine/healthcare needs and demands, tracking

products through supply chain to usage, and more responsive digitalized supply chains.

12. **Data Integrity**. Brining to bear the full potential offered by advances in digital technology to enhance the way medicines and prescribed and used, monitored with regards to safe use etc., and innovating how they are made, packaged, and distributed accordingly.
13. **Real time release.** Real time release means the ability to evaluate and ensure the quality of in-process and/or final product based on process data, which typically include a valid combination of measured material attributes and process controls.
14. **3D printing.** 3D printing has recently been demonstrated for production of single tablets, however the throughput is several of orders of magnitude below where it needs to be. 3D printing has the potential to deliver personalised precision, individual and novel combinations, which could address serious unmet medical need.
15. **Augmented reality.** Manufacturing is an administratively heavy process and augmented reality would lead to integrated data analytics, reporting, and trouble shooting. This would link with disruptive technologies previously described.
16. **Sustainable manufacturing**.
17. **Anticounterfeiting technologies**.
18. **Innovation in packaging and patient information technologies.**
19. **Regulatory sciences.** Flexible and risk based approaches to process improvements are needed. EU must be proactive in promoting and supporting the adoption of innovative manufacturing technologies else they become a barrier for a global industry. Cooperation with other regulators is vital.
20. **Building on previous EU investments**.

## Annex 2: CASE STUDIES

**Case study 1: SSPC, Ireland**

Launched in 2013, the Synthesis & Solid State Pharmaceutical Centre (SSPC) is a unique collaboration between 24 industry partners, 9 research performing organisations and 12 international academic collaborators from North America, Europe and Asia. It is the largest research collaboration in Ireland, and one of the largest globally, within the pharmaceutical area. The SSPC research programme comprises new frontiers in pharmaceuticals synthesis, process crystallisation, particle engineering, and active pharmaceutical ingredient formulation. The fundamental research by the SSPC significantly increased the sector's capability to produce pharmaceutical solids with predefined characteristics, including crystalline or amorphous composition particle size, habit and morphology, tensile strength, powder flow and release properties. The research at SSPC has been from the beginning informed by the needs of the pharma end users, creating the most inclusive pharmaceutical/academic partnership in the world and a collaborative environment in which potentially competing industry partners work with each other and the academics in the areas of common interest. The total funding for SSPC amounts to over €90 million, primarily through grants from Science Foundation Ireland and industry. The SSPC has produced over 213 publications in high-impact research journals and is engaged in extensive capacity building through education and training. Its activities also have a broad range of economic gains, such as creating or retaining in Ireland high value jobs, significant savings, and optimization of products and processes. SSPC coordinates and chairs the (bio)Pharma Ireland group.

**Case study 2: Novartis-MIT Centre for Continuous Manufacturing**

Launched in 2007, this 10-year research collaboration initiative aims to transform the traditional drug manufacturing process. The centre develops new technologies, to replace the pharmaceutical industry's conventional batch-based system with a continuous manufacturing process by combining the industrial expertise of Novartis with MIT's scientific and technological leadership. Novartis committed to invest $65 million in research activities at MIT[18]. Expected benefits of continuous manufacturing include accelerating the introduction of new drugs through efficient production processes, using smaller production facilities with lower building and capital costs, minimizing waste, energy consumption, and raw material use, monitoring drug quality on a continuous basis rather than through post-production, batch-based testing, and enhancing process reliability and flexibility to respond to market needs.[19]

[18] http://news.mit.edu/2007/novartis-0928
[19] http://novartis-mit.mit.edu/

**Case study 3: Amgen - Next-Generation Biomanufacturing facility in Tuas Biomedical Park in Singapore, the company's 1st manufacturing site in Asia**

Amgen's Biomanufacturing facility in Tuas Biomedical Park in Singapore was inaugurated in November 2014. There, single-use bioreactors with a maximum size of 2,000 litres each are used instead of a standard 20,000-litre bioreactor. Water and energy usage is cut by 80 percent and carbon dioxide emissions are reduced by 75 percent. The facility uses disposable and single-use technologies, which eliminate the need for costly cleaning, sterilisation and miles of piping. The facility is about 75 percent smaller than traditional plants, yet is still able to produce the same volume of product, about a metric tonne a year. With its modular, reconfigurable design, it can also be replicated anywhere else in the world in the future.[20] The investment in this facility is $160 million.

**Case study 4: Pfizer Inc. - Global Biotechnology Centre in the Hangzhou Economic Development Area (HEDA), China, the company's 3rd global biotechnology centre and 1st in Asia**

Announced in June 2016, the Global Biotechnology Centre will ensure local production of biosimilar medicines. It will include an advanced modular facility by GE Healthcare, based on flexible single-use bio-manufacturing technology that, according to Pfizer, "meets strict international standards for quality, safety and efficiency, as well as accelerated speed of construction and superior environmental standards". The centre is expected to be ready in 2018[21]. Planned investment is approximately $350 million[22].

**Case study 5: Samsung - World's largest biotech "mega factory" in the Incheon Free Economic Zone, Songdo, Korea, the company's 3rd plant in Korea**

World's largest biotech "mega factory" was announced in December 2015. The total investment is $740 million, with the company planning to further invest in the 4th and 5th plant. The capacity is 180,000 liters[23]. The plant is expected to be completed by 2017 and the operation is expected to begin in the fourth quarter of 2018 after validation. Once in full operation, Samsung BioLogics expects this plant will be able to reach 2 trillion won in annual sales and 1 trillion won in operating profit.[24] Samsung Biologics recently revealed[25] its goal to become the largest manufacturer of biologic drugs in the world by 2020.

[20] https://www.futurereadysingapore.com/2014/amgen-unveils-next-generation-biomanufacturing-facility-in-singapore.html
[21] http://www.pfizer.com/news/press-release/press-release-detail/pfizer_advances_biosimilars_leadership_with_investment_in_a_new_world_class_global_biotechnology_center_in_china
[22] http://www.gereports.com/pfizer-will-use-ges-modular-factory-to-make-next-generation-drugs-in-china/
[23] http://www.biopharma-reporter.com/Upstream-Processing/Samsung-Biologics-Inside-Korea-s-budding-biomanufacturing-giant
[24] http://www.prnewswire.com/news-releases/samsung-biologics-to-construct-worlds-largest-biopharmaceutical-manufacturing-plant-300195678.html

## Annex 3: High-level seminar "The Future of (Bio)Pharmaceutical Manufacturing", held in Brussels on 28 February 2017 – list of participating organizations

Centre for Process Innovation
Agilent
bioPharmaChem Ireland
BioWin Health Cluster
Central Denmark EU Office
Centre for Process Innovation Ltd
Copenhagen EU Office
Daiichi Sankyo Europe GmbH
Dublin Institute of Technology
EBE
EFFRA
EIOPA
Eli Lilly
Enterprise Ireland
European Commission
European Parliament
GetReSkilled Limited
Ghent University
Government of Castilla - La Mancha (Spain)
Graz University of Technology
Helsinn
Hitech Health ltd
Ibec
IC PerMed / Innovation Funds Denmark
IDA Ireland
Innopharma
Invent, Dublin City University
INVITE GmbH
Janssen
Luxembourg Institute of Health
Medical University Graz
Medicines for Europe
National Institute for Bioprocessing, Research and Training
Research Center Pharmaceutical Engineering GmbH
Roquette
Scale-up Systems
Science Foundation Ireland
SOST-CDTI
SSPC
Steris
Strathclyde University
SwissCore
Taipei Representative Office in the European Union and Belgium
Tallinn University of Technology
TU Delft / BE-Basic
University College London
University of Eastern Finland
University of Limerick
Valitacell
VTT Technical Research Centre of Finland

[25] http://blog.waters.com/a-view-of-the-biopharmaceutical-industry-in-asia-an-interview-with-ken-fountain