Annual Report 2018

Promoting world-class biopharma investment in Ireland
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Who we are

- NIBRT is a world-class institute, based in Dublin, Ireland whose mission is to deliver training and research solutions for the global biopharmaceutical manufacturing industry
- NIBRT partners with industry to support international best practice in all aspects of biologics manufacturing
- NIBRT’s research and training building (6,500m²) features state-of-the-art pilot scale manufacturing facilities
- Established with IDA Ireland, NIBRT partners with all higher education institutes to provide training and research infrastructure facilities not previously available in Ireland

What we do

- Train and educate over 4,000 people annually to work in all areas of biopharma manufacturing
- Collaborate with industry on scientific research to drive biopharma innovation
- Support major biopharma investment in Ireland
- Provide a test bed for new technologies and processes

NIBRT’s vision

- Become a global leader in biopharmaceutical manufacturing research education and training
- Build out our research and development scale, capability and critical mass to establish NIBRT as a globally recognised centre for industry applied research and process development
- Be the hub for bioprocessing manufacturing research in Ireland and internationally
- Continue to support the growth and development of the biopharmaceutical industry in Ireland and internationally
Message from NIBRT CEO

2018 was another excellent year of growth for NIBRT which saw a continuation of significant training for biopharma companies, an innovative training collaboration with Jefferson University in Philadelphia, and winning of substantial EU research funding. The Business Plan for 2019 – 2023 was approved after extensive stakeholder engagement.

The biopharma manufacturing sector continues to grow in Ireland. Foreign Direct Investment in biopharma continued with announcements from MSD Biotech, Wuxi, Takeda, Abbvie, and others. With significant career opportunities on offer in the sector, training activity continued at an exceptionally busy pace through the year. We have seen a trend of increased international participation at our courses in addition to an increased requirement for general introduction to bioprocessing from the broader sector. We were delighted to announce our collaboration with Jefferson University in Philadelphia. Discussions are ongoing with a number of other countries regarding assistance in setting up NIBRT like facilities and curricula.

The Springboard Programme for biopharma continues to be a major government success introducing much needed talent to the sector. The expansion of this programme offers a great opportunity to help alleviate the skills needs for industry.

Research activity continues to grow. Dr Colin Clarke had great success in securing European funding as coordinator for a Marie Skłodowska-Curie Innovative Training Network. Prof Jonathan Bones’ characterisation activity expanded into Advanced Therapy Medicinal Products (ATMPs) with securing a number of industry research projects in this area.

Contract Research, our fee for service bioanalytical characterisation activity, had a particularly strong growth year with the addition of many new client companies.

We added a number of major collaborations through 2018. Shire, now Takeda Dunboyne Biologics, have commenced significant training and will also take up a laboratory in NIBRT for their quality team in advance of their facility being available. We announced a major research collaboration with the Siemens-NIBRT Biopharma MindSphere Applications Center. The Emerson Room at NIBRT was completed which demonstrates the latest Delta V applications for bioprocessing.

We are delighted that our 2019-2023 Business Plan has been approved. Extensive engagement with industry, academia, funding agencies and government was concluded and the plan has been approved by the NIBRT Board and also the IDA Ireland Board. The plan supports the continued growth of NIBRT over the next period.

As we move into 2019 we look forward to continuing to work with our many clients in providing them with their customised training needs, in the expansion of our research activities by providing research solutions to industry and expanding on our collaboration agenda.

My appreciation goes to all the NIBRT staff who contribute to our success and deliver great performance in achieving our mission.

Dominic Carolan
CEO, NIBRT
The global biopharma sector continued to show robust growth throughout 2018 with industry worldwide revenue now at ~$275 billion/year and forecasted to exceed $300 billion in 2019.

The importance of biopharmaceuticals as a portion of total pharmaceutical revenue continues to expand, with ≥40% of overall pharmaceutical industry R&D and products in the development pipeline being biopharmaceuticals.

Nonetheless, significant challenges remain in the sector such as the fundamental complexity of bringing new therapeutics to market, reimbursement and pricing models, Brexit uncertainties and global skills shortages.

Notwithstanding these challenges, the Irish biopharma sector continued its strong performance in attracting foreign direct investment. As validation of the capabilities available in Ireland, companies with existing operations here such as MSD, BioMarin and AbbVie all made significant new biopharma investments.

Of particular note – and perhaps indicative of a future emerging trend for the industry - was strong investment coming also from the East, with Chinese company, WuXi Biologics decision to invest in Dundalk to create the world’s largest single use facility, and Takeda’s investment in a cell therapy facility to complement their existing operations here.

While these investments are very welcome, there is no room for complacency. In order to remain competitive Ireland needs to maintain a sharp focus on its core value proposition of compliant, reliable and cost effective advanced manufacturing. But this alone is not enough. In order to sustain and grow operations and ensure Ireland continues to play a leading role in global healthcare delivery, it is key that all stakeholders focus on developing the innovation and research capability of the sector. This will help ensure Irish operations continue to be a location of choice for future investments, particularly as the industry pivots to more personalised medicines, with the rapid advance in more complex therapeutics such as cell and gene therapies.

The role of NIBRT and other partners in the education sector to ensuring the delivery of the skilled workforce required to support these investments is key and we look forward to playing our part also in preparing the advanced skills that will be critical to future growth in this highly competitive sector.

In this context, the Board welcomed the Government’s approval of the NIBRT Business Plan 2019-2023. This plan builds on the success of the Institute to date and sets out ambitious targets for NIBRT to further develop its research capability, alongside continued expansion of its training and education activities. The plan also challenges the NIBRT team to be at the forefront in enabling new developments in the manufacture of next generation therapeutics and manufacturing technologies such as Industry 4.0, continuous manufacturing, etc.

As we reflect on a very successful 2018, I’d like to thank the NIBRT team for their outstanding performance in 2018, as well as my Board colleagues and IDA Ireland for their continued, exemplary support of the Institute and we look forward with confidence to the opportunities ahead in 2019 and beyond.

Brendan O’Callaghan
NIBRT Chairman

2018 NIBRT by the numbers

4,300
Number of trainees in 2018

18,200
Number of training days delivered

541
Number of students trained in 2018

50%
% of NIBRT research that is funded by Industry

37
Number of peer reviewed publications

26
Number of events, conferences held in NIBRT

€10.6 million
Value of equipment donations in 2012-2018

0
Lost time accidents

50:50
Gender balance at NIBRT

16
Number of nationalities working at NIBRT
Over the last decade the Irish biopharma sector has seen $10 billion in capital investment in new facilities which represents close to the largest wave of investment in biopharma manufacturing anywhere in the globe.

There was further good news for the Irish biopharma sector throughout 2018 with the announcement of several major investments. These investments saw the continued diversification of advanced biopharma manufacturing capabilities in Ireland including facilities for Antibody Drug Conjugates (ADCs), cell therapies, immuno-oncology products and the world’s largest single use contract manufacturing capacity, included:

- AbbVie Expands Oncology Capability at the Company’s Site in Ballytivnan, Sligo
- MSD is to develop a new biotechnology facility in Dublin, with the expected creation of up to 350 new jobs
- Takeda to invest €25m and create up to 70 new roles in a new facility at their Grange Castle site in Dublin
- WuXi Biologics to invest €325 million to Build Largest Biomanufacturing Facility Using Single-use Bioreactors in Ireland
- Phibro Animal Health to establish new biotech facility in Sligo, creating up to 150 jobs
- BioMarin Expands its Cork Facility to add Drug Product Filling capability
- MSD to construct a second manufacturing facility at its existing site in Carlow - new investment will create 170 new jobs
In addition, the supply sector has shown strong growth to support the advanced manufacturing base with investments including:

- **Almac Group** announces further expansion in support of Clinical and Commercial drug supplies at its European Campus in Dundalk, Ireland
- **BD** opens new state-of-the-art R&D facility, creating 85 new jobs in Limerick
- **West** opens new global manufacturing facility in Waterford
- **PCI** open new high containment packaging facility in Drogheda and welcomes announcement of 100 new jobs
- **Eurofins BioPharma Product Testing Ireland, Ltd.,** opens state-of-the-art laboratory extension in Dungarvan
- **ILC Dover** opens new production facility in Cork creating 70 Jobs
- Pharmaceutical company, **Central Pharma**, expands contract packaging and supply chain services with a facility at IDA Advanced Technology Building in Tralee, Co. Kerry, creating 100 jobs.

A notable feature in 2018 was the significant expansion of indigenous lifesciences companies including:

- **Genomics Medicine Ireland** - $400 million Investment Programme Positions Ireland for Global Leadership in Genomic Research and Advanced Life Sciences
- **Nuritas** secures €30m investment from EU’s financial arm
- **APC** completes €10 million expansion

**The biopharma industry in Ireland**


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The NIBRT effect – biopharma companies come to Ireland for many different reasons. One of those is because of our world class NIBRT. This purpose built and state of the art facility is a global leader in cutting edge high quality training and research. It is a testament to the high quality of NIBRT that many of the pharmaceutical companies that locate in Ireland cite it as a critical factor in their decision to invest here.

**Minister Heather Humphries, TD Minister for Business, Enterprise and Innovation, Feb 2018**
Notwithstanding these notable success the sector in Ireland must continue to evolve at a rapid pace to address key challenges and maximise new opportunities. While current investment is focused mainly on CHO based production of monoclonal antibodies, it’s clear that there is an exciting diversification in product pipelines. Cell, gene and RNA therapies are making remarkable progress while posing many manufacturing and supply chain challenges. Other jurisdictions have made significant investment to support these emerging therapies and NIBRT is driving a next generation biologics forum with leading stakeholders to ensure Ireland is well positioned to capitalise on this wave of investment.

With the strong growth of the sector, it remains critical that all stakeholders continue the deep collaborative efforts to ensure Ireland is producing the talented workforce of the future. In this regard, the Government’s ongoing support and expansion of the Springboard+ programme is very welcome.

As always a strong focus on manufacturing efficiency and cost competitiveness is key. NIBRT were pleased to form a strategic partnership with Boston Consulting Group to create the Biopharma 4.0 Alliance. This Alliance of biopharma manufacturers aims to provide the platform, capabilities and expertise needed to deliver a step change in performance through smarter adoption of disruptive Industry 4.0 technologies.

At the BioPharma Ambition conference in February 2018 leading international policy leaders, renowned researchers and senior industry personnel, highlighted how all stakeholders in Ireland must continue to support innovation in discovery, development, manufacturing and healthcare solutions to ensure Ireland builds on its success in establishing a thriving biopharma sector.

Killian O’Driscoll
NIBRT Director of Projects
MSD, also known as Merck & Co., Inc. of Kenilworth, NJ, USA, announced a number of significant developments in 2018. In February 2018 the company announced plans to develop a new biotechnology facility in Dublin, with the expected creation of up to 350 new jobs.

Known as MSD Biotech, Dublin, the facility is currently being constructed on an existing MSD-owned property, the site of its former facility in Swords, Co. Dublin. It will play a pivotal role in the manufacture of MSD’s biologics-based medicines, including in the area of immuno-oncology, and will expand MSD’s current internal network of biologics drug substance manufacturing plants. Full manufacturing operations are expected to begin in 2021.

The company announced further expansion in October 2018 with the decision to construct a second manufacturing facility at its existing site in Carlow with the creation of 170 new jobs. The new facility will focus on the production of vaccines and biologics and there will also be an expansion of warehouse and laboratory services at the site with manufacturing operations due to commence in 2023. Currently employing over 400 staff, MSD Carlow opened in 2008 as MSD’s first vaccines facility outside of the US. The expansion is as a result of continuing increased global demand for MSD’s medicines and vaccines.

Ger Brennan, Managing Director, MSD Ireland (Human Health) commented “MSD is one of Ireland’s leading healthcare companies and we currently employ approximately 2,000 employees across our current operations in Carlow, Cork, Dublin and Tipperary. MSD continues to invest significantly in R&D to invent new vaccines and medicines for areas of unmet need. MSD’s continued investment in Ireland is due to continued access to highly-skilled employees as well as our collaborative partnerships with Government, NIBRT and Third Level Institutions. The decision to further invest in Ireland is a real testament to the talent of MSD Ireland’s wider employee base and reinforces MSD’s commitment to Ireland, further strengthening our 50-year strong legacy here. The construction of the two new facilities announced in 2018 only adds to our ability to be able to offer current and future employees a truly unique experience across our sites in Ireland, offering an opportunity to experience all elements of pharmaceutical and biotech manufacturing within Ireland”.

Further information regarding open roles in MSD Ireland can be accessed at www.msdirelandjobs.com
NIBRT Research and Innovation

NIBRT performs world class, industry-aligned research in all areas of biopharmaceutical manufacturing with the overarching aim of delivering practical solutions for the biopharma industry.

NIBRT’s strategy in manufacturing research focuses on enhanced product quality and productivity. To achieve this, there are four central strands of research that are interconnected by NIBRT’s Principal Investigators. These elements include Cell Biology and Engineering, Bioanalytics, Advanced Manufacturing and Bioinformatics/Data Analytics span the disciplines of molecular biology, bioprocess engineering, protein analytics and bioinformatics.

Throughout 2018, NIBRT also enhanced our involvement in downstream processing and are becoming increasingly involved in the global trend of developing advanced therapeutic medicinal products (ATMPs). The year also saw the announcement of significant new industrial collaborations with Siemens, Valitacell, Kerry Group and others. Existing collaborations with companies such as Thermo Fisher Scientific were further strengthened. We were delighted also to win significant funding under the Horizon 2020 Marie Skłodowska-Curie European Industrial Doctorate programme. Collaborations were also initiated with SFI funded research centres including APC Microbiome Institute and CURAM.

2018 saw the retirement of Professor Pauline Rudd from NIBRT. Pauline is a pioneer in the field of glycoanalytics and molecular characterisation. She was a founding member at NIBRT and since 2006 has contributed enormously to the global standing it is today. Pauline continues to play a role in future developments by being an active member of NIBRT’s Scientific Advisory Board.

NIBRT welcomed the Government’s introduction of the Disruptive Technologies Innovation Fund and were pleased to submit an application focused on Industry 4.0 with the support of leading biopharma companies. As always grant funding remains highly competitive and budget constrained with an ongoing need for all stakeholders to further strengthen Ireland’s research capability.

The research standing of NIBRT have been well recognised and disseminated internationally through scientific presentations at key international conferences such as Cell Culture Engineering (Florida), Bioprocess International (Boston), Bioproduction Congress (Dublin) and Bioprocessing Smit (Lisbon). NIBRT were also delighted to win Pharma Research Centre of the Year at the 2018 Pharma Industry Awards which recognise the most original and innovative companies that demonstrate excellence in the Irish Pharma sector.

As we focus on 2019, NIBRT research looks forward to driving advancements in key trends such as next generation biologics, digitalisation, process intensification, and increased characterisation requirements. It is our expectation that in 2019 we will continue to see an enhancement of our scientific reputation and contribution to the economic and scientific development of the biopharma manufacturing sector in Ireland and beyond.

Prof Mike Butler
NIBRT CSO
Bioanalytical Characterisation

A new collaboration between Dr. Jonathan Bones and Valitacell was launched in November 2018 and is funded through the Enterprise Ireland Innovation Partnership Programme. The focus of the project is validation of Valitacell’s novel analytical technology known as ChemStress™ which can accelerate the development and manufacture of life-saving biopharmaceutical drugs. The collaboration, which also involves a number of large global biopharmaceutical companies, will demonstrate how the ChemStress™ platform can be used for quality control in cell culture media analysis.

Dr Jonathan Bones’ collaborative research project with Thermo Fisher Scientific which commenced in 2016 is progressing well and has moved into its third year. The focus of the collaboration is on the development of high impact, customer ready solutions for complex biopharmaceutical characterisation. NIBRT are developing workflows on the Thermo Scientific biomolecule column range with its associated consumable portfolio in conjunction with sophisticated Thermo Scientific liquid chromatography systems and advanced Thermo Scientific Orbitrap high resolution mass spectrometers. These workflows and methods are uploaded to the Thermo Scientific AppsLab library3. This unique cloud-based applications compendium allows scientists across the globe to access and download these total analytical solutions directly to their instruments enabling them to simplify their analysis, generate highly informative characterisation data faster and enhance understanding of their complex molecules.

Outputs from this collaborative project in 2018 include 20 application notes (5 in press), 2 webinars, 3 peer-reviewed publications and 3 additional marketing contents (case studies, articles in scientific magazines).

Bioinformatics and Data Analytics

The Systems Biology and Data Analytics Group, headed by Dr. Colin Clarke, specialises in the application of multivariate statistics, Machine Learning (ML) techniques and data analytics for the analysis of bioprocess data and complex CHO cell datasets. 2018 was a busy year for Dr. Colin Clarke with the launch of the Siemens-NIBRT partnership project as well as success in the highly competitive Horizon 2020 Marie Skłodowska-Curie European Industrial Doctorate programme. In December 2018, Craig Monger, a PhD student working in the Clarke lab on an SFI SIRG funded project successfully defended his thesis. Dr. Colin Clarke was also nominated for the Science Foundation Ireland Best Impact Award for outcomes related to his SIRG.

GlycoScience Group

Dr Fahey continues to grow her collaborative network focusing on a number of glyco-analytical projects with groups from national (e.g. UCD, RCSI, UCC, UL), international (e.g. Leiden University, NL, IPATIMUP, Portugal, UDG, Spain) as well as SFI funded research centres, APC Microbiome Institute and CURAM. In 2018, Dr. Radka Fahey joined the SFI Centre CURAM as an Investigator and through this center (SFI research center supplemental award) she was granted 2-years funded MSc studentship grant on “Glycoanalytics for better design of biomaterial implants in regenerative medicine”.

Dr Fahey has also secured funding from Prof Helen Colhoun, Western General Hospital in UK from JDRF on “Profiling the N-glycome in patients with Type 1 diabetes and its associations with early stage diabetic kidney disease”. Dr Fahey also hosted a meeting with Shanghai Institute for Food and Drug Control (SIFDC) in NIBRT and together with Prof Michael Butler hosted a SIFDC researcher to learn glycoanalytics of antibodies.

**Cell Technology**

Led by Prof. Michael Butler, 2018 saw significant growth in the Cell Technology Group. Prof. Michael Butler has been awarded a number of grants including an Enterprise Ireland (EI) Innovation Partnership with Kerry Group to isolate bioactive components in plant hydrolysates, an EI Commercial Case Feasibility Support to assess a cell culture media development programme and an SFI/EI Technology Innovation Development Award (TIDA) focused on chemoenzymatic remodelling of monoclonal antibodies for which we are seeking a new post-doctoral appointment. Last year the group also hosted a post-doctoral fellow from Canada under a Flaherty Scholarship to continue an on-going collaboration on the dielectric properties and monitoring of cells in bioreactors. Collaboration has also continued with Aber Instruments, Ovizio and Repligen, all of whom have been generous in donating key items of equipment and instrumentation.

**Cell Engineering**

Having joined NIBRT in July 2017 under a joint appointment with UCD as Professor of Biochemical Engineering, Prof. Niall Barron has been developing his team and laboratory on site. In December 2018, Prof. Barron was awarded an SFI/EI Technology Innovation Development Award (TIDA) focused on an epi-transcriptomic-based approach to develop high producer CHO cells for biopharmaceutical production.

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The Siemens NIBRT Partnership was launched in September 2018. The project will focus on the establishment of a new application centre focused on biopharma manufacturing in Ireland with a dedicated team in NIBRT and Siemens Ireland.

Three researchers have now joined the NIBRT team, the installation of the Siemens SIPAT onsite is now complete and the project is underway.

The Siemens MindSphere is a cloud-based open IoT operating system that can utilise advanced data analytics to deliver manufacturing efficiencies. There are currently 19 MindSphere centres globally across a variety of sectors including aviation, automotive and finance.

NIBRT has partnered with Siemens to deliver cutting-edge software for the analysis and predictive modelling of bioprocess data, as well as automated replication and optimisation of individual product batches or entire production lines. This NIBRT-Siemens collaboration will develop the analytical software and test it with biopharmaceutical industry partners.

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Dr Colin Clarke NIBRT, Domhnall Carroll, Siemens, Dominic Carolan, NIBRT and Gary O’Callaghan, Siemens announcing the NIBRT-Siemens research collaboration

"Siemens decided to partner with NIBRT mainly because of its industry track record. We see a really good connection between NIBRT and the biopharma manufacturing companies. For us the goal is to build out a really good exemplar for how to use Siemens technologies in NIBRT’s real world biopharma manufacturing environment."

Domhnall Carroll, Division Head at Siemens, Digitalisation in Manufacturing and Utilities
In September 2018, NIBRT were delighted to announce that Dr. Colin Clarke is coordinating a four year Marie Skłodowska-Curie European Industrial Doctorate programme focused on single-cell analysis in biopharmaceutical process development.

The primary objective of the STACCATO research programme is to utilise high-resolution analysis of DNA, RNA and proteins from single cells to enhance the efficiency of manufacturing processes and ensure patient safety for a range of biopharmaceuticals\(^5\)\(^6\).

The STACCATO European Industrial Doctorate involves partners across Europe including an industry leader in instrumentation for cellular analysis, three innovative biotechnology SMEs, a leading academic institution and a research conducting biological medicines regulatory agency.

A key feature of STACCATO is collaboration amongst experts in the production of different biopharmaceuticals such as therapeutic proteins and CAR T cell therapy. STACCATO will provide intersectoral training to 11 Early Stage Researchers (ESRs) through pioneering research focused on harnessing recent advances in single cell analysis to generate and apply a new suite of tools for cell culture process development. The project has a total budget of €2.9 million and will commence in early 2019.

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Dr Geraldine Canny, head of the Irish Marie Skłodowska-Curie Office at the Irish Universities Association (IUA),

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The Contract Bioanalytical Services team provide detailed characterisation of biologics in line with ICH Q6B and Q5E. The group showed continued growth and expansion throughout 2018 in providing:

- Structural characterisation, measurement of physiochemical properties and determination of process and product related impurities to satisfy ICH Q6B requirements
- Feasibility/pre-validation, verification and qualification studies
- Troubleshooting of existing client methods
- Replication of methods for IP litigation

These bioanalytical characterisation studies were conducted for a diverse range of international clients across a number of therapeutic products such as monoclonal antibodies, fusion proteins, erythropoietin, interferon, enzymes and many more.

In 2019, Contract Bioanalytical Services will launch its new bioanalysis service suite to include cell enrichment, cell phenotyping, protein determination, nucleic acids, ligand binding assay. There will also be a number of new offerings for the physiochemical characterisation and process and product related impurities areas.

<table>
<thead>
<tr>
<th>NIBRT Bioanalytical Services</th>
<th>Cell enrichment, cell phenotyping, protein determination, nucleic acids, ligand binding assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICH Q6B Structural characterisation: protein</td>
<td>Amino acid sequence, N- C-terminal sequencing, amino acid composition, disulphide bonds, free thiols</td>
</tr>
<tr>
<td>ICH Q6B Structural characterisation: glycans</td>
<td>Site occupancy, N-glycan analysis, O-glycan analysis, sialic acid quantitation, alpha (2-3,2-6) sialic acid linkage relative quantitation</td>
</tr>
<tr>
<td>ICH Q6B Physiochemical properties</td>
<td>Intact protein molecular weight, Isoform pattern, determination of extinction coefficient</td>
</tr>
<tr>
<td>ICH Q6B Process and product related impurities</td>
<td>Aggregate analysis, molecular variants, Host Cell Proteins, Residual Protein A, Host Cell DNA, PPG and PEG analysis, Extractable and Leachables</td>
</tr>
</tbody>
</table>

We came across NIBRT Contract Bioanalytical Services through our work with a leading expert in the biotherapeutic characterisation field. From first contact, NIBRT has been an outstanding facility to work with. The team at NIBRT has been instrumental in pushing the boundaries of our testing needs. They are not only flexible, responsive and a pleasure to work with, they also go several steps further to help us problem solve and develop new ways to test our products and learn more about our systems. NIBRT is a top class analytical facility and we will continue to work with them and recommend them to our colleagues going forward. We would use no one else.

North American Law firm specialising in intellectual property
In addition to training industry directly, NIBRT works closely with the Higher Education Institutes to ensure there is a strong supply of graduates in Ireland with the skills required for the biopharma and related sectors.

Industry Training

2018 was another very busy and exciting year for NIBRT training. We welcomed new colleagues to our training team and we were pleased to deliver 18,200 learning days to 4,300 trainees across our client base. In addition to providing training courses to our existing clients, new courses were delivered to a group of new national and international clients as interest in NIBRT training solutions continued to increase in 2018.

NIBRT was also pleased to announce a training partnership with Takeda Dunboyne Biologics to support their new single use manufacturing facility in Co. Meath. “We’re delighted to collaborate with NIBRT, a global leader in biopharmaceutical manufacturing research, education and training solutions.

NIBRT is uniquely positioned to support Takeda Dunboyne Biologics and enrich our employees through customised training programmes and provides us the opportunity to utilise NIBRT’s Single Use Centre of Excellence” commented Susan Hynes, Site Lead Takeda Dunboyne Biologics.

Customised content was delivered to the following industrial clients based in Ireland in 2018: AbbVie, Aerie, Allergan, Alexion, Alvotech, Amneal Pharmaceuticals, Amgen, Baxter Healthcare, BioMarin, Bristol Myers Squibb, Eli Lilly & Co., Eurofin Lancaster Labs, GSK, Janssen, Mallinckrodt, MSD, Pfizer, Sanofi, Shire and Takeda.
Vendor and professional service companies that attended for training programs included: Accenture, Agilent, Bioreliance, ChromaCon, Collen Construction, Compliance Group, Jacobs, M+W Group, Pall, PSG Dover, Roquette, Sartorius Stedim Biotech, Thermo Scientific, VWR and 3M.

Training courses were also held for the following industry representative bodies: Engineers Ireland and Saudi Industrial Clusters, respectively.

Skilled Graduates
In 2018, NIBRT continued to partner with 11 Higher Education Institutes to deliver practical, competency based training sessions to their respective students. These institutes included University College Dublin, Dublin City University, Institute of Technology Sligo, Trinity College Dublin, Dundalk Institute of Technology, Dublin Institute of Technology, Cork Institute of Technology, Galway Mayo Institute of Technology, National University of Ireland Galway, Waterford Institute of Technology and IT Tralee. NIBRT training staff also contributed to the delivery of academic modules at undergraduate and postgraduate level using both distance learning and face-to-face solutions.

NIBRT was especially pleased to partner with DCU whose MSc in Bioprocess Engineering won Postgraduate Course of the Year Award in Health Sciences at the gradireland Higher Education Awards.

Jobseekers
In 2018, NIBRT continued to collaborate with Higher Education Institutes to provide training programmes to jobseekers and employed participants under the Springboard+ programme. On average, 65% of NIBRT trainees secure employment after participating in these very popular courses which are designed to meet the needs of the fast growing biopharmaceutical industry in Ireland.

International Clients
In 2018 we had the pleasure of welcoming International trainees to our facility for training. Trainees travelled either individually for open courses held in various areas or often with some of their own colleagues for customised course content. Specifically, in 2018 we were pleased to deliver training to international delegates from AbbVie, Agilent, Alvotech, Bioreliance, OPW Global, Pall, Rentschler Pharma, Roquette, Sartorius Stedim Biotech, Saudi Industrial Clusters, Thermo Scientific and VWR.
Industry Masterclasses

In addition to NIBRT’s highly valued practical based master classes in upstream processing, downstream processing, aseptic processing, and bioanalytics respectively, we also offered a portfolio of programs for industry in partnership courses with the following companies:

- Chromacon AG: Practical aspects of continuous chromatography
- Steris Technical Services: cleaning validation
- BPS Crowthorne: Lyophilisation cycle development
- Merck Millipore: Next generation downstream processing
- Merck Millipore: Next generation upstream processing
- ESS: Equipment maintenance
- Kaye: Thermal validation

Suppliers

In 2018, NIBRT received generous donations from several vendor companies to facilitate training activities. These included Perkin Elmar, Emerson, GE Healthcare, Bioquell, Kaye, WL Gore and Watson Marlow.

Future Outlook

Building on the success of 2018, the coming year is looking as if it will be another very exciting and productive time for the training team. Training offerings in development for 2019 will include new courses in:

- Production automation
- Process instrumentation
- Advanced therapy medicinal products (ATMP)
- Further expansion of our single-use technologies portfolio.

NIBRT research Principal Investigators will also participate in a new series of Master Classes for middle and senior management that will be launched in 2019. We also look forward to the launch of the NIBRT Online Academy.

NIBRT will continue to invest in the production training facility and will in the year ahead upgrade its aseptic processing capability by investing in new fill finish capabilities to offer training solutions for processing vials, cartridges and syringes. In addition, a new lyophilisation centre of excellence will be installed in our facility to demonstrate best in class technologies in this increasingly important area.
Takeda Ireland Ltd Grange Castle

The largest pharmaceutical company in Japan, Takeda first set up operations in Ireland in 1997 manufacturing products for global markets.

In 2002 Takeda chose Dublin as the location for its first active pharmaceutical ingredient (API) facility outside of Japan. In 2017 Takeda also announced an investment in the construction of a stand-alone production facility for the manufacture of part of their oncology portfolio at Grange Castle.

The latest investment by Takeda will expand the existing Grange Castle site’s footprint, with the construction of a new standalone modular cell therapy facility dedicated to manufacturing the novel stem cell therapy product “Alofisel” (darvadstrocel). Alofisel is a suspension of allogeneic expanded adipose-derived stem cells (eASC) locally administered for the treatment patients with perianal fistulae associated with Crohn’s disease.

The new facility will be in full commercial operation by 2021, requiring personnel to demonstrate a unique set of skills, mind-set and behaviours. To address these needs Takeda requires that all personnel undergo an introduction into aseptic processing and cell therapy as part of Takeda’s on-boarding. Takeda and NIBRT formed a collaboration to develop a customised baseline training program for the Alofisel team. This introduction is a prerequisite to all subsequent training, providing the foundation for Grange Castle to become the centre of excellence for stem cell manufacturing within the Takeda network.

The customised course for the ALOFISEL manufacturing process is a very hands on approach with the extensive use of NIBRT’s facilities and laboratories. The training curricula includes an assessment of competency pre and post the training which will form part of the overall training records for Takeda personnel with special focus on working in biological safety cabinets and the use of isolator technology.

The NIBRT team provided an excellent service in putting together a comprehensive three day training course which comprises of a balance of lectures and practicals, covering general aseptic processing, cleanroom design & contamination control and specific human stem cell culture techniques.

With the first Takeda core team being successfully trained in October 2018, the collaboration between Takeda and NIBRT continues with further fine-tuning and optimisation of the course scope and content, an extension of the participants group to Grange Castle site leadership team level and scheduling of multiple training sessions for 2019.

Orla Doran
QC Bioprocessing Manager, Takeda Grange Castle
Benjamin Gysi
Director Site Projects, Takeda

Takeda Grange Castle employees attending Aseptic Processing and Cell Culture Course at NIBRT
The Medicine Maker teamed up with NIBRT to find out about current trends in the biopharma industry. We asked Killian O’Driscoll, NIBRT to respond to some key findings on staff development from a survey of 210 biopharma professionals from across the world.

The results of The Medicine Maker survey showed that a majority (86%) of survey respondents had difficulty filling one or more biopharma positions with bioprocess engineers in most demand.

“This largely aligns with our experience,” says O’Driscoll. “In particular, what we see is a shortage of what you might call engineers with ‘specialist skills’ – not just bioprocess engineers, but automation engineers, commissioning, qualification and validation engineers, and so on.

It’s really a question of supply and demand.” O’Driscoll argues that the biopharma industry is growing rapidly and that such roles are in especially high demand for start-up organisations. “It takes four to five years to train a bioprocess engineer, with perhaps some post-graduate study, and ideally a few years’ experience as well,” he says.

7. Extract from original article published in The Medicine Maker, James Strachan, 08/15/2018
Are there major differences between the US and European markets?

O’Driscoll agrees that there are similarities between the US and European markets, given that there are global trends in play. But he does see some potential differences emerging, with US companies perhaps more focused on discovery. “As we look at the newer modalities – cell and gene therapies, for example – coming through,” he says, “we may see an emerging lack of skills there, particularly in the US marketplace because of their strong emphasis on discovery.”

In addition to the most difficult positions to fill, we also asked respondents to rank the importance of different skill sets.

“Of course practical skills are vital for a career in the biopharma industry,” says O’Driscoll. “But we’ve seen a change over the past five-or-so years. Previously, when companies were hiring, they were looking for a very specific skillset for particular roles. What we’re now seeing is that as skills evolve and change and new types of roles emerge, the attitude of the person you’re hiring is fundamental.”

O’Driscoll also points out that EU GMP Guidelines (annex 1) talks about the importance of skills training and attitude. “What a lot of companies are realising is that you can hire for attitude and then train for skills. Hiring managers will ask: can they work in teams, problem solve, conform to advanced manufacturing regulatory requirements, and learn on an ongoing basis – with a fundamental focus on quality and the patient?” He believes that the perfect hire will be someone with those softer skills and the scientific, engineering, and technical skills. “Clearly that would be the ideal situation, but those people are in short supply. Companies will therefore take into consideration attitudes and realise that people can acquire skills through continual professional development,” explains O’Driscoll.

How best can companies succeed in attracting the right talent?

“We see companies succeeding when they adopt a multi-faceted approach – underpinned by developing a strong brand, based around their employee culture. We see some manufacturing start-ups having great success, sometimes recruiting up to 400 positions for new manufacturing facilities, when they do this. As well as using the traditional route of hiring, consider engaging with local schools, offering internships to university students, engaging at the apprentice level, and cross-skilling existing staff – perhaps from other disciplines such as small molecule manufacturing. Companies must also support continuous professional development and lifelong learning for those hired.”

Is there more universities could be doing to prepare students for careers in the biopharma industry, given the importance of on-the-job practical training?

O’Driscoll thinks that universities should be given credit for what they’ve done to date in supporting and driving the biotech industry from its origins over 30 years ago. “But for sure the industry is changing rapidly,” he says. “Most universities are aware of what industry needs; they’re flexible, they’re responsive, while still making sure that they are teaching the core skills and competencies that are required for graduates – but there’s always room for continuous improvement. That’s why we’re delighted to see what Jefferson are doing in the US and to develop similar initiatives throughout the globe.”
NIBRT in partnership with the Boston Consulting Group (BCG) have established the Biopharma 4.0 Alliance which provides the platform, capabilities and expertise needed to deliver a step change in performance through smarter adoption of disruptive Industry 4.0 technologies.

As biopharma manufacturing becomes increasingly globalised, increasingly complex and more highly regulated, the sector must become more effective and cost efficient at manufacturing its products. However, biopharma manufacturing is currently significantly behind other advanced manufacturing sectors in its adoption of disruptive Industry 4.0 technologies. There are several reasons for the slow adoption of 4.0 technologies with some of the most common problem statements from biopharma enterprises including:

- How do we implement 4.0 in a highly regulated, GMP environment?
- Where do we start, and how do we prioritise given the number of technologies and vendors?
- How do we implement disruptive technologies in a way that is truly scalable?
- How to we integrate these technologies with our existing systems?
- Is there clear value and payback for our operations?
- What will a facility look like in 2025? What does best in class adoption look like?

Furthermore, studies from the World Economic Forum indicate that 70% of businesses investing in technologies such as big data analytics, artificial intelligence or 3D printing are not able to take the projects beyond pilot phase.

Coordinated by NIBRT and BCG, the Biopharma 4.0 Alliance will drive thought leadership in the sphere of Industry 4.0 with ongoing trainings and webinars, fostering collaboration and knowledge-sharing. In particular, a digital showcase is being established in NIBRT to provide an immersive training experience, which will allow participants from across the biopharma industry and beyond to experience new 4.0 technologies first hand.
Valitacell, an Irish SME based in NIBRT, was co-founded in 2015 by Dr Terry Mc Wade and Dr Jerry Clifford. The company was the recipient of the 2016 InterTrade All Ireland Seedcorn Award, and the 2017 Best Pharma Start Up Award. In 2017 Valitacell received €2.03 million in funding through the H2020 SME Programme for European Innovation to accelerate the development of its ChemStress® technology.

Valitacell is an early stage biotechnology company with a suite of novel, intelligent analytical technology platforms, engineered to provide process control in cell-based manufacturing. Working in conjunction with both academic research partners such as NIBRT, University of Sheffield, Danish Technical University (check this title) CNRC (Canada) etc, and the leading biopharmaceutical manufacturers, Valitacell is focused on bringing next generation medicines to more patients, more quickly and at lower cost.

In 2018 researchers from Valitacell and NIBRT launched a collaboration with a number of large global biopharmaceutical companies to demonstrate how Valitacell’s novel analytical platform - ChemStress® can accelerate the development and manufacture of live-saving biopharmaceutical drugs.

The collaboration will focus on cell culture media analysis using Valita®QC – a novel cell culture media assay for the deep assessment of lot-to-lot variation between media batches. NIBRT’s Prof. Johnathan Bones will lead the project, along with Valitacell’s product manager Dr. Karen Coss.

In addition to its activity in CHO cell-based biomanufacturing, Valitacell has initiated a programme of research, in conjunction with NUIG and UCD, focused on the development of stem cell characterisation tools to support the manufacture of cell therapies. This work is centred on adapting the ChemStress® technology platform to cell manufacturing systems and stem cell media development.
On February 21, 2018, Jefferson (Philadelphia University + Thomas Jefferson University) announced a partnership with NIBRT to create the Jefferson Institute for Bioprocessing (JIB), the first - and only - education and training institute for biopharmaceutical processing in North America that combines commercial single-use processing equipment with the internationally recognised NIBRT curriculum.

While more than 40% of therapeutics currently in research and development are biopharmaceuticals, there exist only a handful of places throughout the world dedicated to training people to produce these potentially life-saving drugs, a gap that the JIB intends to close.

The JIB is expected to serve 2,500 people annually through workforce training and bioprocessing certifications, in addition to enrolling 70 additional Jefferson students in bioprocessing, engineering and other related majors. The focus of the JIB is hands-on training of industry professionals through workshops and certificates and hands-on education of new bioprocessing engineers at the undergraduate and graduate levels.

JIB will leverage partnerships with industry, academia, and government agencies to provide an industry-facing, global dimension to transdisciplinary, hands-on learning in the growing biopharmaceutical manufacturing industry. JIB will also deploy cutting-edge biopharmaceutical manufacturing technology to support current and future workforce demands while promoting community outreach and engagement for students and practicing professionals.

In December 2018, Dr Parviz Shamlou, PhD, the George B. and Joy Rathmann Professor of Bioprocessing and director of the Amgen Centre for Bioprocessing at Keck Graduate Institute in Claremont, California, was announced as the Executive Director and Head of JIB.

The official opening of JIB is scheduled for 31st May 2019.
Public Engagement and Outreach

A key component of NIBRT’s remit is to help develop the next generation of biopharma talent with a number of exciting initiatives throughout 2018 including:

- **Amgen’s School of Biotech Excellence (ABE)** which is an innovative science education programme that empowers teachers to bring biotechnology into their classrooms. ABE-Ireland offers training in molecular biology experiments for secondary school teachers at locations in University College Dublin, Dublin City University and NIBRT.

- The launch of NIBRT’s Biopharmaceutical Science **Transition Year Competition**. The very popular competition invites transition year students to submit an essay focusing on the biopharma sector in Ireland. The successful students received a one week structured placement in NIBRT where they had the opportunity to experience the state-of-the-art facilities and learn from scientists working in the research and training team.

- NIBRT’s **Annual Careers Day** continue to be very popular events to connect the Industry with high quality prospective employees.

NIBRT also hosted 26 seminars, workshops and conferences. These free-of-charge events provide the sector with the latest developments across a range of topics. Examples of events include:

- Careers in Alexion – an opportunity to change lives
- Next Generation Biopharmaceutical Downstream Process (nextBioPharmDSP) Symposium with Merck
- Careers with Shire
- Insights in Lyophilisation – SP Roadshow Science
- PDA and BPCI present “Cleaning Validation” with NIBRT
- Thermoscientific Biopharma Summit
- Ecolab Contamination Control Strategies
- “The Connected Worker” with Accenture

NIBRT was also pleased to host a wide variety of international delegations to our facility in 2018 including:

- Korean Ministry of Health and Welfare and K Bio Health
- Chumakov Institute of Poliomyelitis and Viral Encephalitides of Russian Academy of Medical Sciences
- NanYang Polytechnic, Singapore
- Southwest University, China
- Wuxi City delegation, China
- Chia Tai Tianqing Pharmaceutical Group Nanjing, China
- EDB, Singapore
- SaudiVax, Saudi Arabia
- Vinnova, Sweden’s Innovation Agency
- Centre for Process Innovation, UK
- CoValent, Belgium
- National Research Council Canada
- Scottish Development Agency
- NorthEastern University, Boston
- KCDC South Korea
- High Value Manufacturing Catapult, UK
- Technical University of Sydney, Australia
- Biotech Training Foundation, Holland
- Japan Times
- Shanghai Institute for Food and Drug Control, China
- TOPRA, The Organisation for Professionals in Regulatory Affairs
1. NIBRT Team at Pharma Awards
2. GE and Guangzhou delegates
3. Matt Moran, BCPI at PDA event in NIBRT
4. John Milne at BioLive CPhI, Madrid
5. Transition Year students at NIBRT
6. Prof Pauline Rudd on her retirement
7. Prof Niall Barron at Bioproduction International, Boston
8. Korean visitors to NIBRT
9. NIBRT Team at Careers in Biopharma
Biopharma Ambition 2018

The Irish Pharmaceutical Healthcare Association and BioPharmaChem Ireland, representing the research based and manufacturing sides of the biopharmaceutical industry respectively, once again joined with NIBRT to host BioPharma Ambition 2018 in Dublin.

This year’s meeting, held on February 21st and 22nd 2018, built on the success of the inaugural event in 2016.

The island of Ireland has established itself as a place of global significance for the biopharmaceutical industry and is the ideal location to take a snapshot of where industry is with regard to innovation in manufacturing and medicine, as well as looking to the future to identify challenges and opportunities. BioPharma Ambition is now established as a major international convention for the biopharmaceutical industry.

A combination of interactive workshops and dynamic plenary sessions saw hundreds of stakeholders from all areas of the sector engage, network, and learn. With international policy leaders, renowned researchers and senior industry personnel present, the event illustrated the ambition of the industry for preserving and improving the health and well-being of populations.

It also served to paint a picture of where the research is pointing and how Ireland will support innovation in discovery, development, manufacturing, and healthcare solutions into the future.

BioPharma Ambition provided a variety of case studies of various transformations taking place within the industry, including the introduction of new technologies, new research avenues, and new types of collaborations. The central themes featured at the conference were the future of manufacturing, pioneering discovery, and driving innovation. The agenda provided a platform for debate and discussion, and pointed to how Ireland will be central to the sector’s future.

IPHA, BPCI and NIBRT look forward to hosting the next iteration of Biopharma Ambition in early 2020.
<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
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<tbody>
<tr>
<td>February 16th 2019</td>
<td>Careers in Takeda Dunboyne Biologics</td>
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<tr>
<td>March 21st 2019</td>
<td>Big Data in Life Sciences with the Analytics Institute</td>
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<tr>
<td>April 13th 2019</td>
<td>6th Annual Careers in Biopharma</td>
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<td>April 16th 2019</td>
<td>Biopharma Research Showcase with BiolITG and SSPC</td>
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<tr>
<td>May 31st 2019</td>
<td>Opening of Jefferson Institute for Bioprocessing, Philadelphia</td>
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## Testimonials

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<tr>
<th>Name</th>
<th>Position/Role</th>
<th>Comment</th>
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<tbody>
<tr>
<td>Kieran McAtamney</td>
<td>Construction Manager, Jacobs</td>
<td>“Great course delivered by NIBRT Team of Aoife, Adam and Melissa”</td>
</tr>
<tr>
<td>Aidan Quinn</td>
<td>Springboard Student</td>
<td>“May I first take this opportunity to thank you and your colleagues at NIBRT and IT Sligo for your professionalism, support, guidance and patience during our Biotechnology Processing certificate course this year? The online lectures and lab practical's gave a great insight and understanding to a complex and very interesting subject and I believe participation in the course will greatly improve my job prospects.”</td>
</tr>
<tr>
<td>Margaret Stagg</td>
<td>Alexion</td>
<td>“NIBRT provided me with great insight into the Biopharmaceutical industry. It’s a great facility to be able to see first-hand what the day to day activities with a bio site could be My training with NIBRT was the driving force behind my transition from 20 years manufacturing experience with Hewlett Packard to my current role with Alexion. I am currently still studying and will be attending two lab practical days next week. Looking forward to it.”</td>
</tr>
<tr>
<td>Associate Vice President</td>
<td>Keytruda Quality at Merck</td>
<td>“Excellent Training opportunity. The instructors were highly educated, experienced and engaged every one of us by delivering even the most complicated material in an easily understood format. The combination of theoretical and hands on training in this state of the art facility is an absolute necessity for anyone seeking to gain insight into bioprocessing.”</td>
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<tr>
<td>Paddy Gleeson</td>
<td>HR Director, Takeda Dunboyne Biologics</td>
<td>“NIBRT is a critical support as we built up our organisation and facility to deliver life changing medicines for our rare disease patients.”</td>
</tr>
<tr>
<td>Aleksander Kostrzewski</td>
<td>Student on L7 Bioprocessing Engineering NIBRT program</td>
<td>“Congratulations on pharma awards. It’s another proof that we are learning from the best in the industry.”</td>
</tr>
<tr>
<td>Stephane Perrey</td>
<td>General Manager at GE Healthcare LS Japan, Australia, New-Zealand</td>
<td>“Visiting NIBRT was fascinating. Such a great training site for pharmaceutical companies and biotech to learn to manufacture Biologic in the most productive fashion. This was a unique experience.”</td>
</tr>
<tr>
<td>Nicolas Pivet</td>
<td>General Manager, Global Services, GE Healthcare</td>
<td>“NIBRT is an amazing institute, the place to stop by when working in the Bioprocessing space, with an impressive and growing global reach.”</td>
</tr>
<tr>
<td>Caroline Brady</td>
<td>Global Commercial Operations Leader GE Healthcare</td>
<td>“Fantastic couple of days spent at NIBRT. Particular thanks to John for a great tour of the facility. Really impressive setup.”</td>
</tr>
<tr>
<td>Maria Aldridge</td>
<td>Quality Specialist at AbbVie</td>
<td>“Great few days of training on Upstream Processing at NIBRT National Institute for Bioprocessing Research and Training this week via The Institute of Technology, Sligo.”</td>
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<tr>
<td>David Weil</td>
<td>Applications Scientist at Agilent Technologies</td>
<td>“Great work also being done on how E and L compounds in bioprocessing can impact final products.”</td>
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<tr>
<td>Alison Wilson</td>
<td>Personal Development Coach at Anova Coaching</td>
<td>“It was great to see the exceptional facilities you have to support training in our industry.”</td>
</tr>
<tr>
<td>Eva Fahey</td>
<td>NIBRT TY Student</td>
<td>“I was one of the TY students you accepted to take part in a Biopharmaceutical Training week in NIBRT from the 29th of January to the 2nd of February. Thanks so much for taking me again for that week as I enjoyed so much and I can honestly say it has been a highlight of my transition year.”</td>
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