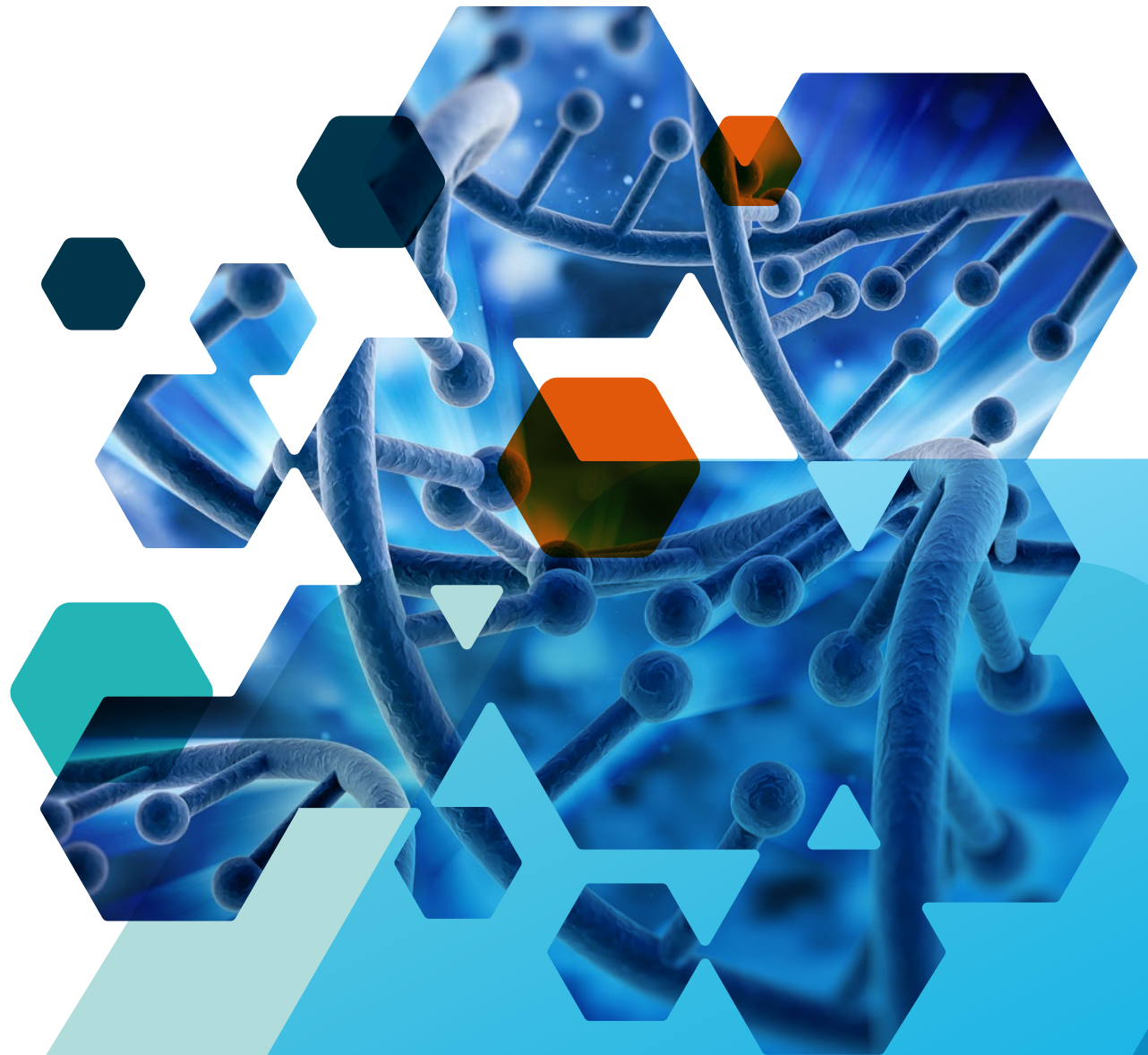




National Institute for
Bioprocessing Research
and Training



Annual Report 2021

Thank you to all who worked at NIBRT and contributed to a successful 2021

Adam Bergin	Gavin McGauran	Niamh Keogh
Adam Pritchard	Gemma Grimes	Niaobh McLoughlin
Adrian Lica	Gemma Grimes	Nicholas Donohue
Alan Foley	Gemma Nolan	Noemi Isabel Dorival Garcia
Aleksandra Ostropolska	Hayden Wilkinson	Or Skornik
Alison Quinn	Hugh O'Reilly	Patrice Knightly
Anabel Torrente	Ioanna Tzani	Patrick Torrie
Anaid Villamizar	James Berhanu	Paul Adams
Andrea Silva	Jared Auclair	Paul Kelly
Anita Kelly	Jelena Melnika	Paula Kenny
Anita Murphy	Jenette Scanlon	Peter Brennan
Ann Marie Donaghy	Jennifer Byrne	Peter Connolly
Ann Thomas	Jennifer Prior	Peter O'Byrne
Anthony Raethorne	Joanne Withers	Rachel Cuffe
Aoife Barron	John Milne	Rachel Ronan
Aoife Kearney	Jonathan Bones	Radka Fahey
Aswathy Balakrishnan	Josh Smith	Raul Escobar
Barbara Keegan	Karen Tsang	Robert Byrne
Barry Shortt	Karl Kelly	Ronan Brady
Caio Henrique Nasi De Barros	Kate Cotter	Ryan Hagan
Caitriona Walsh	Kathleen Hill	Sally Koster
Carl Bermingham	Kevin Byrne	Sandra Roche
Carlos Tamaray	Kevin Lomasney	Sara Carillo
Ciara Finn	Killian O'Driscoll	Scott Willoughby
Ciara McManus	Lara Gibney	Shada Warreth
Ciara Tierney	Laura Breen	Silvia Millan Martin
Colin Clarke	Leticia Martins Mota	Solene Gatault
Cormac Costello	Lisa Murphy	Sophia Hjelseth
Craig Jakes	Lisa Strasser	Stefano Boi
Darragh O'Brien	Maja Kristek	Stephen Devlin
Darrin Morrissey	Marcela Brophy	Stephen McCann
Dennis Shaw	Marco Romero	Steven Ferguson
Dermot O'Sullivan	Mariana Gavendova	Tadeusz Tazbierski
Elaine O'Farrelly	Marina Castro Rivadeneyra	Thomas Byrne
Elizabeth Matthews	Mark Smales	Thomas McGuirk
Elizabeth Topp	Melanie Ng Tung Hing	Tomos Morgan
Eric Dumas	Melissa Hoare	Una McVeigh
Evangelia Flampouri	Melissa Hoare	Yongjing Xie
Felipe Guapo De Melo	Mike Butler	Zsuzsanna Kovacs
Florian Fuessl	Nga Lao	
Gareth Lomasney	Niall Barron	

Contents

2021 NIBRT Staff list	2
Who we are	4
What we do	4
NIBRT's vision	4
1. Message from NIBRT Chairman	5
2. Message from NIBRT CEO	7
3. 2021 NIBRT by the numbers	9
4. The Biopharma Industry in Ireland - 2021	10
5. NIBRT's Covid-19 Response	15
6. NIBRT Research and Innovation	16
7. Research Case Study: Agilent	22
8. Advanced Therapy Manufacturing	24
9. Contract Research	27
10. NIBRT Training and Education	28
11. NIBRT Online Academy	31
12. Training Client Case Studies: MeiraGTx and MSD	32
13. Global Partner Programme	34
14. Facilities Development	37
15. 2021 Snapshots	39
16. Public Engagement and Outreach	40
17. NIBRT HR and Culture	41
18. Awards and Announcements	42
19. Testimonials	43

Promoting world-class biopharma manufacturing investment in Ireland



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 training and research.
- ▶ Established with IDA Ireland and opened in 2011, NIBRT partners with Higher Education Institutes to provide training and research infrastructure facilities not previously available in Ireland.
- ▶ NIBRT's research and training building (6,500m²) features state-of the-art pilot scale biopharma manufacturing facilities.

What we do

- ▶ Train and educate over 4,600 people annually to work in all areas of biopharma manufacturing
- ▶ Collaborate with industry on scientific research to drive innovation in biopharma manufacturing
- ▶ 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

01 | Message from NIBRT Chairman

Despite the challenges imposed by the second year of the Covid-19 pandemic, the outlook for the global biopharma industry is for continued strong growth.



Global sales of biopharmaceuticals are now over \$300 billion, with a compound annual growth rate of 12% and with approximately 60% of therapeutics in development being biopharmaceuticals¹.

In parallel, the Irish biopharma industry continued to excel, overcoming the challenges of the pandemic and once again demonstrating its resilience, agility and innovation in global supply chains. Important new investment from Pfizer, Takeda, Amgen and others, as well as the growth of the indigenous sector were welcomed throughout the year. Pfizer's announcement of a €40M investment to manufacture the Covid-19 vaccine drug substance at its Grange Castle was especially noteworthy.

While this success is very welcome, there is no room for complacency. As a key player in global supply chains, the Irish sector is subject to macro-economic and political developments. In order to remain competitive, Ireland needs to maintain a sharp focus on its core value proposition of compliant, reliable and cost-effective manufacturing. In parallel, the rapid advance of next generation biologics provides a significant opportunity for Ireland to grow in areas of new modalities and strengthen its position as a global leader in biopharmaceutical manufacturing. If Ireland is to take advantage of this opportunity, it will require a sustained effort from all stakeholders to further develop the innovation and research capability of the sector here, especially in the emerging technologies and modalities.

Reflecting on 2021, I would like to acknowledge and thank the NIBRT team for their many successes during the year, including:

- ▶ A 14% growth in revenue and the strongest financial performance of the institute to date
- ▶ Delivering 39,000 days of learning to over 4,600 trainees

- ▶ Welcoming new global partners with Korean-NIBRT (K-NIBRT) and the Canada Alliance for Skills and Training in Lifesciences (CASTL)
- ▶ The continued expansion and success of NIBRT research teams, including the award of the €7.23M Disruptive Technology Innovation Fund in partnership with Avectas and Bluebridge Technologies
- ▶ The impressive growth of the NIBRT Online Academy with 10,000 users in over 66 countries
- ▶ Development of a strong pipeline for 2022, despite significant uncertainties and risks persisting due to the Covid pandemic

NIBRT's success continues to be built on partnerships with stakeholders from across Industry, Academia and Government. I would like to thank my Board colleagues and IDA Ireland for their continued support of the Institute. In particular, I would like to thank those who have retired from the Board after many years valuable service including Gerry Collins, Robert Baffi, Tommy Fanning, Prof. Anita Maguire, Prof. Andrew Bowie and Prof. Brendan McCormack. As we thank all past Board members, we are also delighted to welcome new members in 2022, including Sarah Culloty and Mike Thein, who will bring fresh eyes, energy and insights to help us advance the important work of the Institute, as we prepare for the next cycle in our strategic planning.

So, as we look ahead to 2022, the Board will be focusing on NIBRT's performance in supporting the continued development of the biopharma sector and developing the next 5-year business plan cycle for the Institute. We look forward to constructing the new Cell & Gene Therapy labs, subject to the necessary approvals, to further advance our capabilities to provide cutting edge research and learning capabilities to support the industry in these rapidly emerging modalities.

¹ EFPIA Pipeline Review, IQVIA, Feb 2021

Other specific areas of focus include developing the scale and impact of NIBRT's research activity, the development of capability in the process development and manufacture of next generation biologics and the continued expansion of our training offerings to meet the evolving needs of our clients and students.

Since opening its facility in 2011 NIBRT has developed a global reputation built on solid foundations. We look forward to continuing to partner with all our stakeholders, to help us further enhance this hard-earned reputation.

Brendan O'Callaghan

*Executive Vice President, Global Industrial Affairs, Sanofi.
NIBRT Chairman.*

NIBRT Board 2021

- ▶ **Chair: Brendan O'Callaghan**, *Executive Vice President, Global Industrial Affairs, Sanofi*
- ▶ **Prof. Orla Feely**, *Vice President for Research, Innovation & Impact (VPRII), University College Dublin*
- ▶ **Dr Tom Kelly**, *Divisional Manager Cleantech, Electronics and Life Sciences, Enterprise Ireland*
- ▶ **Prof. Norelee Kennedy**, *Associate Professor of Physiotherapy, University of Limerick*
- ▶ **Darrin Morrissey**, *CEO NIBRT*
- ▶ **Tom Murray**, *Director at Friel Stafford*
- ▶ **Julie O'Neill**, *Non-Executive Director*

Board retirees in 2021

- ▶ **Dr Robert Baffi**, *President at BioMarin Pharmaceutical*
- ▶ **Prof. Andrew Bowie**, *Prof of Innate Immunology and Associate Dean of Research at Trinity College Dublin*
- ▶ **Gerry Collins**, *Global Platform Leader Parenterals at Janssen*
- ▶ **Tommy Fanning**, *Head of Strategic Policy, IDA Ireland*
- ▶ **Brendan McCormack**, *President of IT Sligo*
- ▶ **Prof. Anita Maguire**, *Vice President for Research & Innovation, Director A.B.C.R.F., UCC*

New Board members in 2021

- ▶ **Prof. Sarah Culloty**, *Head of College, Science, Engineering and Food Science at University College Cork*
- ▶ **Michael Thien**, *Senior Vice President at Merck & Co., Inc*

Four new appointees pending confirmation in January 2022

NIBRT Services Limited Board

- ▶ **Chair: Brendan McCormack**, *President IT Sligo*
- ▶ **Matt Moran**, *Director at BioPharmaChemical Ireland (BPCI)*
- ▶ **Darrin Morrissey**, *CEO NIBRT*



An important element of our rich biopharmaceutical

landscape is NIBRT. NIBRT was set up by the Government to support the growth and development of the biopharmaceutical industry in Ireland and conducts cutting edge research focused on the advancements of biopharmaceutical manufacturing including in the area of advanced therapeutics.

NIBRT significantly enhances our skills and production capacities and plays a pivotal role in increasing Ireland's research talent pool. This point is worth emphasizing because our highly skilled and flexible workforce is crucial to our ongoing success in attracting operations from major life sciences companies to Ireland.

In 2020 in anticipation of technological and scientific developments NIBRT submitted a proposal to Government for investment in advanced therapies. I'm pleased that funding for the expansion proposal has been approved and that the planning and design phase is well underway. The right collaboration between industry and government will enable us to build on Ireland's reputation as a global leader in biologics manufacturing and to drive investment in life sciences across Ireland.



→ **Leo Varadkar, Tánaiste and Minister for Enterprise, Trade and Employment**

02 | Message from NIBRT CEO

At the start of a new year, it is always worth reflecting on the year just past; on the successes, on the achievements and on where things could have gone better.



2021 saw a world still struggling to respond to the evolving Covid-19 pandemic. Whether it was from a viewpoint of personal health, public health, societal impact or the economic fallout, it has continued to be a very challenging environment in which to operate for individuals and organisations. However, 2021 was also a year of recovery and hope, with a range of vaccines and new therapies for Covid-19 emerging and countries racing to vaccinate as many of their citizens as quickly as possible.

Against this Covid-19 backdrop, NIBRT – as one of Ireland's strategic research and training institutes – had a highly successful year in 2021 in delivering our world-leading services to clients nationally and internationally. I am delighted to report that 2021 saw the organisation out-perform the targets set in our current five-year business plan and achieve record revenues.

The demand for NIBRT's training and education services continued to grow in line with new expanding biopharma manufacturing investments in Ireland. In 2021, we delivered:

- ▶ Over 39,000 days of training to over 4,600 people, via a mixture of in-person and remotely-delivered training.
- ▶ NIBRT Online Academy (NOA) expanding to over 10,000 users in over 66 countries.
- ▶ 849 trainees via the Government's Springboard+ programme.

- ▶ The growth of our Global Partnership programme with the addition K-NIBRT, based at Yonsei University in South Korea, and the Canadian Alliance for Skills & Training in Life Sciences (CASTL), based in Prince Edward Island, Canada. By further expanding the world-wide footprint of NIBRT's advanced training curriculum, we are taking on a global challenge and bringing Ireland's expertise in biopharma manufacturing and skills development to a global audience.
- ▶ A 14% growth in revenue and the strongest financial performance of the institute to date.

On the research front, the NIBRT research team delivered highly impactful collaborative research projects in partnership with many global and indigenous biopharma players in 2021. Companies partnering with NIBRT Principal Investigators included: Lonza, Roche, J&J, Thermo Fisher, Cytiva, Applied Materials, Agilent, Canty and many more. Some notable NIBRT funding wins from state research funders included the Disruptive Technology Innovation Fund (DTIF) in partnership with Avectas and Bluebridge technologies, as part of a large €7.2M research project focused on the development of Avectas's Large-scale, flexible, digitalised cellular engineering system, Solupore.

The Contract Services research team continued to provide excellent support to our clients in 2021, solving problems at all stages of product development and production through a range of high-quality analytical services. These analytical services are aligned with ICH Q6B and Q5E requirements and include glycan and protein characterization, immunochemical properties, physiochemical properties, impurities (process and product-related) and biological activity.



2021 was also a huge year for NIBRT in our continued growth and evolution into the new area of advanced therapeutics, including cell and gene therapies and novel-modality vaccines. Advanced therapies represent a major opportunity for the next wave of biopharma manufacturing growth. In 2021, NIBRT launched a range of new training offerings in the area, across bespoke client training courses, open courses and online academy modules. Additionally, the research team increased their advanced therapeutic focus, with a number of viral-vector based gene therapy and cell therapy projects including the DTIF project highlighted above. Importantly, 2021 saw NIBRT's cell and gene therapy facility expansion take further steps to becoming reality. Following approval by IDA Ireland of a €21M investment, the design work has now been completed by PM Group and we are ready to commence building work in early 2022. This expansion will develop new laboratories and training suites focused on cell and gene therapies and novel vaccines and will enable NIBRT to hire new senior researchers and training staff to meet growing demand. We expect to open the new facility in early 2023.

Lastly, 2021 was an exciting year for me personally in my first full year as NIBRT CEO. In spite of the limitations on in-person working imposed by the pandemic, NIBRT impresses me every day as a highly vibrant and creative place to work. I would like to thank the NIBRT Chairperson Brendan O'Callaghan and the members of the NIBRT Board for their support, and – above all – I would like to thank NIBRT staff for their continued hard work, innovation and dedication to the biopharma mission.

I look forward to another successful year for NIBRT in 2022, hopefully with good health for all our staff, partners, vendors and clients.

Darrin Morrissey

NIBRT CEO.

03 | 2021 NIBRT by the numbers



4,600

Number of
trainees



39,000

Training days
delivered



849

Springboard+
students



14%

Increase in revenue
from **2020**



37%

% of NIBRT research
that is funded
by Industry



37

Peer reviewed
publications



49

Conference
presentations



€11m

Value of **equipment**
donations in
2017-2021



0

Lost time
accidents



83

Number of
employees



51:49

Gender balance
at **NIBRT**
(female: male)



18

Number of
nationalities working
at **NIBRT**

04 | The Biopharma Industry in Ireland – 2021

2021 was another remarkable year for the world and for the biopharma industry, which faced multiple pandemic related challenges and yet delivered impressive achievements. Although risks and uncertainties remain, if the correct course of action is chosen the sector is well positioned for continued success post-pandemic.



A record year of growth

Innovation and resilience were at the heart of the biopharma sector's response to the pandemic. Of particular note, it took a total of just 24 days from the point at which the SARS-CoV-2 virus was first genetically sequenced until the first batch of a candidate mRNA vaccine was created. Then within 18 months more than 7 billion doses of various vaccines had been distributed globally. This involved a 50,000-step process for building an mRNA vaccine² with multiple supply chain and manufacturing innovations.

From an Irish perspective, the biopharma manufacturing sector enjoyed very strong growth. IDA Ireland's annual results for 2021³ showed the highest Foreign Direct Investment (FDI) employment level ever (275,384 employees) with the highest employment creation figures ever in a single year despite the continued impact of Covid-19. Underpinning these results was a strong series of announcements in the biopharma manufacturing sector including:

- ▶ Pfizer's \$40M investment in the expansion of the Grange Castle site to allow for the extra production that will be part of the global Pfizer-BioNTech Covid-19 vaccine supply chain network, contributing to the worldwide supply of the vaccine, with 75 new roles to be created as a result.
- ▶ Takeda's €36 million investment in its Grange Castle facility. The investment will support the expansion of the company's cell therapy production facility and create approximately 100 new jobs over the next three years. The commercial scale cell therapy production facility is the first of its kind in Ireland. Following the expansion, the team at Grange Castle will play an important role in supplying European, US and Canadian markets with a cell therapy treatment option for patients.
- ▶ Amgen's \$100M investment for the construction of a new vial filling line with state-of-the-art technology and new site infrastructure at its manufacturing plant in Dun Laoghaire, Co Dublin. This investment will lead to the creation of 150 construction jobs. The Dun Laoghaire plant which currently employs 670 staff specialises in formulation, aseptic drug product filling, lyophilisation, packaging as well as analytical testing using on-site laboratories.

2 <https://time.com/5955247/inside-biontech-vaccine-facility/>

3 <https://www.idaireland.com/newsroom/ida-ireland-announces-results-for-2021>

Reflecting the strength of the sector there were also significant announcements from technology, vendor and services companies which support the biopharma industry including Repligen Corporation creating 130+ new jobs in Waterford, Accenture with 500 new roles in Cork, Watson-Marlow's new Cork facility, Bionical Emas creating 35 jobs in Kilbeggan, Charles River Laboratories €8m site expansion in Ballina and Bio-Techne Corporation opening of its new Dublin facility.

There were significant developments also with indigenous companies such as:

- ▶ ONK Therapeutics, \$21M series A funding to progress their pipeline of CAR-Natural Killer cell therapeutics.
- ▶ Avectas, who have raised over \$40m to date, in developing non-viral cell engineering technology.
- ▶ APC's €25m investment and creation of VLE Therapeutics, to focus on the manufacture of vaccines and advanced therapeutics.

The scale and success of the Irish biopharma sector has further attracted international investment from organizations such as We are Pioneer Group who are establishing a new life sciences incubation and acceleration campus at Cherrywood, Dublin. The campus will provide specialised lab, office and collaboration space for over one hundred life science and health technology professionals, entrepreneurs, and researchers.

As detailed throughout this Annual Report, 2021 saw robust growth in NIBRT with key achievements including:

- ▶ A 14% growth in revenue and the strongest financial performance of the institute to date
- ▶ Delivering 39,000 days of learning to over 4,600 trainees
- ▶ Welcoming new global partners with Korean-NIBRT (K-NIBRT) and the Canada Alliance for Skills and Training in Lifesciences (CASTL)
- ▶ The continued expansion and success of NIBRT research teams, including the award of the €7.23M Disruptive Technology Innovation Fund in partnership with Avectas and Bluebridge Technologies
- ▶ The impressive growth of the NIBRT Online Academy with 10,000 users in over 66 countries
- ▶ Development of a strong pipeline for 2022, despite significant uncertainties and risks persisting with Covid



Biopharma investments in 2021



- ▶ Amgen celebrates **10 years** in Dun Laoghaire with an investment of **\$100 million** in a new vial filling line and new site infrastructure.
- ▶ Takeda announced a **€36m investment** in its **Grange Castle facility in Dublin**, which will create **c100 new jobs** over the next three years.
- ▶ Pfizer's announcement of a **€40M investment** to manufacture Covid-19 vaccine drug substance in Ireland.
- ▶ Horizon Therapeutics plc announced that it is to establish a manufacturing facility in Waterford creating **50 new roles**.
- ▶ Zoetis Inc. announced plans to expand its manufacturing and development facility, creating up to **100 new jobs** in Tullamore.
- ▶ PPD to expand GMP lab in Athlone to enhance biopharmaceutical testing capabilities adding **180 new jobs**.
- ▶ **\$360m planned investment** at the Astra Zeneca /Alexion Campus in College Park in Blanchardstown to create **100 jobs** in new Dublin plant.
- ▶ French biopharma company Ipsen investing **€25m in its Dublin plant**.

Outlook: top 5 challenges and opportunities

Since the first recombinant protein therapeutic was authorised by FDA in the early 1980s, the biopharma industry has experienced exponential growth. The global sales of biologics exceeded \$300 billion in 2021 with 13 of the top 20 medicines being biologics, including two mRNA-based Covid-19 vaccines and 10 antibody-based products⁴. The forecasts for the future growth of the industry remain strong, though there are considerable complexities and challenges to be navigated.

More diverse and complex product pipelines

Monoclonal antibodies (mAbs) are predicted to remain the dominant modality in biopharma by some margin. Indeed, after 20 years+ of intensive effort, mAb manufacturing platforms are mainly well understood and characterized. However, there is a fast emerging, unprecedented diversity in therapeutic pipelines driven by excellent fundamental science including Antibody Drug Conjugates, multi specific mAbs, multiple cell therapy modalities, gene therapies, RNA based therapeutics and vaccines, gene editing such as CRISPR/CAS9, exosome-based therapies etc. The relationship between manufacturing and discovery/development is increasingly important. Future manufacturing investments for advanced therapies will increasingly be co-located with R+D operations.

Advanced manufacturing

This pipeline diversity is driving fundamental changes in facility design, operations and supply chain with a focus on flexible and agile facilities with the ability to manufacture multiple products. Digitization has potential to be a key enabler of a manufacturing competitive advantage, though significant barriers remain – in particular, access to end-to-end high quality data management from research to manufacturing operations. To remain competitive there is continued demand for new efficiencies, improved quality, and cost reductions in manufacturing processes.

→ EFPIA pipeline review⁵

- ▶ Approx. **60%** of the pipeline is for biologics, **40%** small molecules
- ▶ Almost **50%** of therapies in development are new products
- ▶ **40%** of the pipeline is for rare disease
- ▶ From **2014–2019** the number of next generation biologics has more than **tripled**

→ PhRMA pipeline review⁶

- ▶ **2,533** mAbs projects, **281** gene therapy projects
- ▶ **545** cell therapy projects, **348** gene modified cell therapies projects
- ▶ **265** nucleic acid projects, **133** oncolytic virus projects

→ Alliance for Regenerative Medicine (ARM)⁷

- ▶ First deployment of **CRISPR-CAS9** in vivo phase 1 trial
- **\$14 billion** in funding in H1 2021
- **2,600** trials worldwide for next generation biologics

4 <https://www.thebusinessresearchcompany.com/report/pharmaceuticals-market>

5 EFPIA Pipeline Review, IQVIA, Feb 2021

6 PhRMA, Innovation in the Biopharmaceutical Pipeline, December 2021

7 ARM, Regenerative Medicine in H1 2021 – a year of firsts and records

Key trends, many of which rely on vendor innovation, include:

- ▶ More flexible, modular multi-product facilities
- ▶ Further adoption of single-use systems at clinical scales and commercial scales
- ▶ Steady increase in expression titres and purification yields, with incremental improvements in host cell lines, culture media, expression systems, vectors, promoters etc.
- ▶ Continuous processing, including upstream perfusion and downstream chromatography
- ▶ Implementation of Industry 4.0 / digitalisation technologies with a particular focus on automation and data analytics

Sustainability

Biopharma manufacturing is energy and water intensive, which needs to be balanced with an ever-increasing focus on sustainable operations. Many firms are already taking the lead on this and in 2021, Eli Lilly while celebrating its 40th anniversary in Kinsale also opened the single largest solar farm in the Republic of Ireland. The ground-mounted solar farm will produce up to 5.6MW of power allowing Lilly to reduce its annual use of electricity from carbon sources by almost 6GWH and its carbon footprint by 2,350 tonnes. J&J also is progressing its global plans to source 100% of its electricity from renewable sources by 2025.

Global challenges

As always there are multiple external factors that will potentially impact on biopharma manufacturing including Covid-19 variants, international monetary and fiscal policies, supply chain challenges, and geo-political developments. In particular, NIBRT looks forward to playing its part in ensuring vaccine capacity for lower to middle income countries.

The war for talent

Access to a diverse talent pool with a broad range of multi-disciplinary skills will be a key determinant of future success. In 2021, the Financial Times working with Cytiva published the inaugural Global Biopharma Resilience Index⁸. Based on data from a survey of 1,165 biopharma executives from 20 countries, access to talent was identified as the primary weakness in the resilience of the global biopharma industry. 25% of respondents indicated that the sourcing of talent is a substantial or very substantial challenge, 50% said that the cost of talent has become a key issue. Indeed, the UK's Bioindustry Association estimates the UK alone will require 133,000 skilled life scientists by 2030⁹.

This is not a new problem but one that has persisted for many years, and many regions are beginning to develop NIBRT like institutes to help address this talent gap, for example Campus Biotech Digital (France), EU Biotech Campus (Belgium), Landmark Bio (Boston), Biocentriq (New Jersey), NHC (UK) etc.

WuXi Biologics

WuXi Biologics have invested in excess of €1 billion on their campus in Dundalk. Construction continued throughout 2021 with an on-site average of 1,800 workers during peak construction months.

“Dundalk is ideally placed equidistant between Dublin and Belfast. It is also within easy reach of 10 Universities and HEIs including NIBRT. The other big attraction in Ireland is that the talent pipeline is so strong. We've been able to recruit all the talent we require to date, and we are confident of filling all remaining roles in time for full production in 2022. That's a tribute to Ireland's education system and to institutes like NIBRT.”

→ **Brendan McGrath, Vice President of Manufacturing WuXi Biologics**

⁸ <https://www.ft.com/partnercontent/cytiva/biopharma-reaches-for-homegrown-talent.html>

⁹ <https://themedicinemaker.com/business-regulation/how-to-plug-the-skills-gap>

Call to action

To address these challenges and to further develop the biopharma sector in Ireland, NIBRT recommends five calls to action:

- ▶ **A continued focus on workforce development** with a long-term strategy to develop appropriate solutions across all levels and demographics. **Initiatives such as Springboard+ and Generation Apprenticeship are to be further encouraged.**
- ▶ **Building biopharma manufacturing research of scale, especially with regard to next generation biologics.** In this regard, NIBRT welcomes the new EU Pharmaceutical Strategy¹⁰ and subsequent launch of the Innovative Health Initiative¹¹ with a focus “on investment in research, development and manufacturing of new medicines”.
- ▶ **Realising Ireland’s potential in next generation biologics, including the development of a thriving indigenous and start-up ecosystem.**
- ▶ **Driving leadership in sustainable biopharma manufacturing through the application of advanced manufacturing, including leveraging Industry 4.0 and digital transformation technologies.**
- ▶ **Establishing a Life Sciences Office at senior Government level to drive effective strategic planning and coordination between all stakeholders and ensure Ireland maximises its potential in life sciences.**

Finally, the development of the biopharma sector in Ireland has always been underpinned by strong collaborative relationships among Industry, Government and Academia and we look forward to a further strengthening of these collaborations to lead the post pandemic recovery.

Killian O’Driscoll

NIBRT Director of Projects.

¹⁰ https://ec.europa.eu/health/human-use/strategy_en

¹¹ Innovative Health Initiative <https://www.ihl.europa.eu/>

05 | NIBRT's Covid-19 Response

As 2021 represented the second year of the Covid-19 pandemic, NIBRT continued to operate our facility in full adherence with prevailing Government advice and in-house risk mitigations.

Our internal Covid-19 Team continued to meet weekly throughout the year to address issues and to ensure that all our facilities team could keep all our staff and trainees safe while onsite. Thankfully, NIBRT was able to remain open through 2021 with no workplace Covid-19 outbreaks reported. The NIBRT facility continues to operate in compliance with physical distancing requirements and implementation of associated hygiene protocols.

The NIBRT training team continued to use a hybrid approach in its course delivery with a majority of theoretical course content being delivered online while essential practical training for our industry clients who could travel to us could continue safely onsite.

While the total numbers of onsite trainees were reduced compared to a normal pre-Covid-19 year, when combined with trainees who attended for online training courses, 2021 represented a very strong year for NIBRT Training. We would like to thank all our academic and industry clients for their engagement with us in whatever format that was in 2021 and we hope in 2022 you will be able to visit us as we hopefully move out of the pandemic.

From a research perspective our facility remained open for all our research teams to carry out their essential research activities in a safe and proper manner. It was crucially important that NIBRT researchers could continue with their work to deliver their respective research milestones in key project areas related to manufacturing and characterisation of current and emerging therapeutics.



→ NIBRT trainer delivering a socially distanced downstream processing training session in NIBRT's pilot production training facility.

06 | NIBRT Research and Innovation

Physics tells us that momentum is the product of mass and velocity, but that simple equation doesn't capture the thrill of seeing a rocket take flight.



In 2021, after a year of pandemic restrictions and lockdowns, momentum began to build for NIBRT research, and it's been a thrill to see it happen. This letter highlights some of the momentum-building accomplishments of the year.

The **Cell and Gene Therapy and Vaccine Manufacturing Forum** (CGTV Forum) is a NIBRT outreach initiative, with the goal of advancing the manufacturing of vaccines and cell and gene therapies in Ireland. In 2021, led by Professor Niall Barron and NIBRT CEO Darrin Morrissey, the Forum launched seven working groups. The working groups are creating a strengths map for Ireland, identifying manufacturing challenges, discussing approaches to influencing funding and investment in Ireland and the EU, identifying education and training needs, addressing the needs of indigenous start-ups and SMEs, and advancing clinical trials. To date, the working groups have engaged more than 70 participants from industry, government, professional organizations, and academia.

Prof Niall Barron was part of the successful €7.23M consortium with Avectas and Bluebridge Technologies, awarded under the **Disruptive Technology Innovation Fund**. The collaboration will develop a high-throughput scale of Avectas' non-viral cell engineering system to enable efficient and safe genetic modification of cells for the next generation of immune-oncology therapies.

In collaboration with NIBRT, the Jefferson Institute for Bioprocessing (JIB) received an **International Research Experience (IRES)** US National Science Foundation (NSF) grant, announced in December 2021. The NSF **IRES program** seeks to create a diverse, globally engaged workforce by engaging students in high quality international research, education, and professional development experiences. In this IRES program, at least 18 JIB master's students will complete a 12-week research experience at NIBRT over a three-year period.

JIB is a NIBRT global partner; the NSF IRES award will strengthen research collaborations between the two institutions and increase the pipeline of master's level scientists with bioprocessing expertise.

In 2021, NIBRT welcomed **Professor Mark Smales** and **Dr Jared Auclair** as adjunct Principal Investigators (PIs). Mark is a Professor of Industrial Biotechnology and Director of the Industrial Biotechnology Centre at the University of Kent in the UK. Mark's research addresses recombinant protein yields, gene therapy manufacturing, and re-tuning cell metabolism using synthetic biology approaches. Jared is Associate Dean at Northeastern University, Boston and the Director of the Biopharmaceutical Analysis Laboratory (BATL), where he leads a team committed to enabling safe and efficient drug research, regulatory approval, and access for patients.

The NIBRT **Research Office** underpins all NIBRT's research accomplishments and is headed by Dr. Jennifer Byrne. In addition to supporting and reviewing all extramural proposals submitted, key contributions of the Research Office in 2021 included developing an Intellectual Property Policy and Procedures manual, creating policies for Responsible Conduct of Research, administering the NIBRT Seed Grant program (now in its second year), and creating a virtual stockroom in cooperation with NIBRT Finance. The Research Office also continues to work with NIBRT HR to support our HRS4R designation, which identifies organizations that maintain an excellent research environment.

Throughout 2021, it's been a thrill for me to see NIBRT Research grow and gather speed. That growing momentum is the result of a lot of talent and hard work by the PIs, the researchers, and the Research Office, with terrific support from the broader NIBRT organization. Kudos to everyone in NIBRT Research for an excellent year. Thanks for reading – be sure to check the group updates and Case Studies presented elsewhere in this annual report for more information.

Elizabeth M. Topp, Ph.D.
Chief Scientific Officer

Cell Engineering Group, *Prof Niall Barron*

The Cell Engineering Group (CEG) welcomed in 2021 with a new member in the lab, Or Skornik, who joined as a Marie Skłodowska-Curie Early Stage Researcher (working towards a PhD) and as part of a multi-institutional collaborative EU project, NATURE-ETN. This project aims to find new ways to modify mRNA in order to improve its stability and effectiveness when it enters cells and represents another expansion of the CEG's interest in the cell and gene therapy field.

Another exciting development was a successful application to Enterprise Ireland's Disruptive Technologies Innovation Fund in partnership with Irish SMEs Avectas and Bluebridge Technologies. This €7.23m project will accelerate the development of a new gene-delivery device by Avectas aimed at improving the way in which modified cell therapies are manufactured. Four postdoctoral scientists based in NIBRT will develop new applications for the device including delivering DNA, RNA and proteins into various cell types for applications in cell, gene and recombinant protein therapies. We have already welcomed back Dr. Nga Lao as the first scientist dedicated to this project, with further appointments imminent.

Ongoing projects such as the Allergan (now part of AbbVie) - NIBRT Innovation Partnership continue to expand our experience and expertise in AAV gene therapy manufacturing and have started to yield high impact publications. Further investment in specialised lab equipment in the last twelve months has also increased the capabilities of the group, including for example digital PCR for highly accurate RNA and DNA quantification.



→ NIBRT's Prof Niall Barron (far left) with the DTIF Consortium team from Avectas and Bluebridge Technologies.



NIBRT's Scientific Advisory Board

- ▶ **Chair, Dr. Robert Baffi**, President at BioMarin Pharmaceuticals
- ▶ **Prof. Parviz Ayazi-Shamlou**, Vice President at Thomas Jefferson University
- ▶ **Prof. Martin Clynes**, Director, National Institute for Cellular Biotechnology, Dublin City University
- ▶ **Prof. Charles Cooney**, Professor at Massachusetts Institute of Technology
- ▶ **Matt Croughan**, Proprietor at Matt Croughan Ph.D. Consulting
- ▶ **Prof. Gavin Davey**, Associate Professor, Biochemistry
- ▶ **Prof. Alan Dickson**, Professor of Biotechnology, University of Manchester
- ▶ **Prof. Brian Glennon**, Senior Director and Cofounder APC Ltd.
- ▶ **Brendan Hughes**, Senior Vice President, Global Manufacturing Operations, BMS
- ▶ **Prof. Barry Karger**, James L. Waters Professor Emeritus, Northeastern University
- ▶ **Barry McCarthy**, Senior Director, Janssen R+D
- ▶ **Prof. Pauline Rudd**, Emeritus Fellow of the Conway Institute University College Dublin and Visiting Investigator at the Bioprocessing Technology Institute, AStar, Singapore
- ▶ **Richard Snyder**, Vice President, Science and Technology, Pharma Services, Viral Vector Services at Thermo Fisher Scientific

Cell Technology Group, *Prof Mike Butler*

The Cell Technology Group (CTG) made advances in several areas of bioprocess monitoring and product analysis. Highlights from the Group in 2021 include:

A project on media development was supported by Enterprise Ireland (EI) funding in collaboration with the Kerry Group. We published a paper that reported the effects of plant protein hydrolysates on cell growth, productivity and glycan profile of several monoclonal antibodies (Obaidi et al Appl Microbiol Biotechnol 105, 3115–3129: 2021). The work has continued with Sandra Roche who has analysed the chemical complexity of the most active hydrolysate through a series of fractionation steps and mass spectrometry of the most active fractionated peaks. We are intending to continue this work to be able to rapidly identify batches of Kerry hydrolysates that have high bioactivity. Attempts will also be made to identify the active chemical components in these hydrolysates.

Our work on monitoring bioprocesses is supported by Cauty Engineering and Aber Instruments. This has enabled on-line monitoring of cell growth and the identification of the phases of changed cellular metabolism by a combination of dielectric and optical monitoring. In particular, the work of Adam Bergin and Laura Breen has identified markers for determining the onset of apoptosis or autophagy towards the end of a culture process. These results have been presented in several conferences and webinars over the past year.

Research into glycan analysis and glycoengineering has progressed rapidly with collaboration and support from Agilent using a novel label for high sensitivity analysis. Yongjing Xie and Leticia Mota have been able to apply these techniques to both the analysis and modification of glycans on key glycoproteins. Details of the collaboration with Agilent are reported separately as a case study in this Annual NIBRT Report.

We have several applications being reviewed for on-going research by the CTG and this will allow a continuation of the major themes of these projects in 2022.

Characterisation and Comparability Lab, *Prof Jonathan Bones*

NIBRT's Characterisation and Comparability Laboratory (CCL), under the direction of Prof Jonathan Bones had an excellent year, delivering new technologies to support all aspects of biopharmaceutical manufacturing and characterisation.

A key research focus over the past year was the characterisation of adeno-associated virus (AAV) based gene therapy products with the group publishing three studies on the topic including a rapid assay for the determination of the empty to full ratio of viral capsids using native Orbitrap mass spectrometry to support downstream processing. An automated workflow for peptide mapping of AAV capsids, with a focus on the determination of posttranslational modifications was also reported. In collaboration with Prof Niall Barron's laboratory, we also published a study investigating the use of proteomics to investigate the cellular productivity of AAV5 producing HEK293 cells, identifying underlying pathways involved that could be targeted to modulate yield.

The group was also heavily involved in the development and deployment of the multi-attribute method (MAM). A study, demonstrating the applicability of MAM for in process testing, with a specific focus on new peak detection, was published as part of a special issue of the Journal of the American Society for Mass Spectrometry. Additionally, a presentation to the MAM Consortium was delivered in June, which attracted considerable attention from practitioners within the field. Later in the year, in collaboration with Thermo Fisher Scientific, the group were heavily involved in the launch of the Orbitrap Exploris MX Mass Detector and Thermo's MAM 2.0 end-to-end solution for the seamless transition from early-stage characterisation through to quality control.

The group maintained its focus on the development of methods for in depth characterisation of monoclonal antibodies, complex antibodies and Fc fusion proteins using high resolution liquid chromatography mass spectrometry and native separations coupled to native mass spectrometry. Examples included hyphenation of Protein A affinity chromatography directly to Orbitrap mass spectrometry for rapid analysis of analysis of monoclonal antibodies directly from cell culture media, size exclusion chromatography coupled to Orbitrap mass spectrometry for the analysis of antibody drug conjugates and the use of inline electrochemical reduction of disulphide bonds for simplified analysis of antibody subunits.

Although the global pandemic meant that ability to travel to present at conferences was limited, the group still reported an excellent output comprising of peer-reviewed papers, presentations at virtual conferences, non-specialist articles and a number of webinars, many of which are available on demand if you would like to learn more about the group's activities.

Downstream Processing, Dr Steven Ferguson

Dr. Steven Ferguson joined NIBRT in November 2020, to establish a process engineering focused lab focusing on downstream processes and RNA based therapeutics. During 2021, Dr. Ferguson established a research presence in NIBRT through collaborations with established NIBRT Principal Investigators Jonathan Bones and Elizabeth Topp. These include:

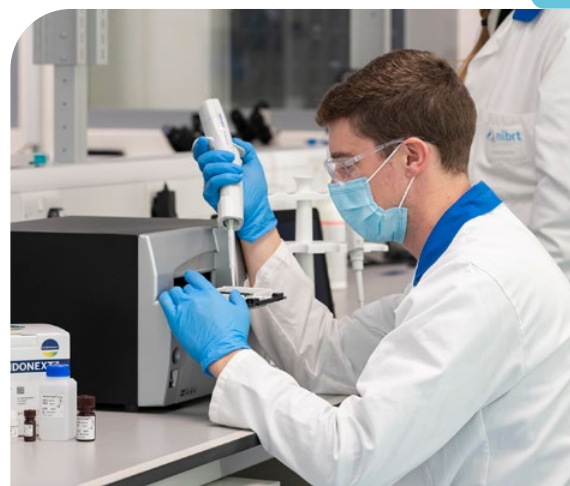
- ▶ An industry collaboration between BMS, NIBRT and UCD in multiscale characterization and modelling of membrane separation processes;
- ▶ The recruitment of a Ph.D. student jointly advised by Profs. Topp and Ferguson to develop enabling methodologies for the rational design of recombinant protein and mRNA formulations as part the EPSRC-SFI Centre for Doctoral Training (CDT) in Transformative Pharmaceutical Technologies. This program is a key training hub for PhD students entering the biopharmaceutical sector in the UK and establishes a joint graduate school between University of Nottingham, University College London, SSPC and now NIBRT. NIBRT will also now participate in the delivery of the jointly delivered graduate program hosting the first cohort of students and academics from the UK and Ireland in May 2022.
- ▶ Dr. Ferguson also continues to advise two industry based PhDs in Downstream Biopharmaceutical Development and Manufacturing at Pfizer, Grangecastle in Dublin and Eli Lilly in Kinsale.

In 2021, additional funding through the SSPC, of a co-funded PhD studentship between NIBRT and University College London was established, and recruitment is planned for September 2022. This project will establish a direct collaboration between the EPSRC Centre for Doctoral Training in Bioprocess Engineering Leadership in UCL, a key training hub for UK bioprocess engineers. It is hoped this will aid in the establishment of a future CDT in NIBRT.

In addition a Science Foundation Ireland Frontiers for the Future Program (SFI-FFP) proposal was submitted in late August with Profs. Topp and Ferguson and co-investigators, in the area of stabilized mRNA vaccines.

A research highlight this year was the development and presentation of Continuous Spatially Distributed Diafiltration (CS2D), a new membrane purification mode of operation demonstrating efficient single stage continuous membrane separation for the first time. This was presented publicly for the first time in November 2021 at the Annual American Institute of Chemical Engineers (AIChE) annual conference in Boston, MA. A manuscript is currently being finalized for submission for publication.

Dr. Ferguson chaired a conference, co-organized by NIBRT, the 2nd AIChE PD2M Future of Pharmaceutical Manufacturing in May 2021. This brought together senior management, technical leaders in industry and academia and the FDA, EMA and a number of European national regulatory bodies including the HPRA to focus on new technologies for enabling improved manufacturing and supply of medicines. Prof Niall Barron, Prof Jonathan Bones and Prof Michael Butler participated in the conference as Session Chairs, Speakers and Conference Co-chair respectively.



Selection of projects awarded in 2021

Grant funded projects:

- ▶ Prof. Niall Barron: “Nucleic Acids for Future Gene Editing, Immunotherapy and Epigenetic Sequence Modification (NATURE ETN)”. Funded by Horizon 2020 Marie Skłodowska-Curie Actions. Project coordinated by Prof. Andrew Kellet DCU.
- ▶ Dr. Colin Clarke in collaboration with Accenture: “Development of Chinese hamster ovary cell digital twin to accelerate cell line and bioprocess development.” Funded by Enterprise Ireland Innovation Partnership Programme.
- ▶ Prof. Niall Barron with Avectas and Bluebridge Technologies on a project funded by the Disruptive Technologies Innovation Fund (DTIF).

Collaborative Research with Industry:

- ▶ Prof. Elizabeth Topp and Applied Materials (AMAT)
- ▶ Prof. Michael Butler and Agilent (project extension)
- ▶ Prof. Jonathan Bones and Lonza
- ▶ Prof. Jonathan Bones and Roche

GlycoScience, Dr Radka Fahey (Saldova)

Despite the challenges of 2021, it was a productive year for the GlycoScience group, with 9 presentations and 11 publications in 2021. Key publications of note include:

- ▶ Greville G, Llop E, Howard J, Madden S, Perry AS, Peracaula R, Rudd PM, McCann A, Saldova R. 5-AZA-dC induces epigenetic changes associated with modified glycosylation of secreted glycoproteins and increased EMT and migration in chemo-sensitive cancer cells. 2021, Clinical Epigenetics, 13(1):34.
- ▶ Wilkinson H, Thomsson KA, Rebelo AL, Hilliard M, Pandit A, Rudd M, Karlsson NG, Saldova R. The O-Glycome of Human Nigrostriatal Tissue and its Alteration in Parkinson's Disease. 2021, JPR, 20(8): 3913-3924.
- ▶ Mimura Y, Saldova R, Mimura-Kimura Y, Rudd PM and Jefferis R. Micro-heterogeneity of antibody molecules. (chapter 1, book "Antibody Glycosylation" edited by Dr Marija Pezer, Springer Nature), 2021, Exp Suppl 2021;112:1-26.
- ▶ Mimura Y, Saldova R, Mimura-Kimura Y, Rudd PM and Jefferis R. Importance and monitoring of therapeutic immunoglobulin G glycosylation (chapter 15, book "Antibody Glycosylation" edited by Dr Marija Pezer, Springer Nature), 2021, Exp Suppl. 2021;112:481-517.

The GlycoScience group hosted an undergraduate Medicine student from the UCD on Student Summer Research Awards (SSRA) programme in the team. Melanie Ng Tung Hing, worked on the determination of low levels of immunogenic alpha-galactose content in porcine NCM samples using our technology based on liquid chromatography-mass spectrometry-exoglycosidase digestions. This project was in collaboration with CÚRAM (an SFI Research Centre at NUI Galway, designing the next generation of medical devices) to improve manufacturing of biomaterial scaffolds used for intervertebral disk regeneration.

Dr Radka Fahey (Saldova) joined the editorial board of Frontiers in Analytical Science in June 2021 as an Associate Editor. Dr Radka Fahey (Saldova) also joined European GlycoScience Community (<https://euroglyco.com/>), launched on 16th June 2021 as a co-chair on Diagnostics & Precision Medicine community of practice.

Formulation and Stability, Prof Liz Topp

The Formulation and Stability Lab started in late 2020 and added three members by the end of 2021. Dr. Caio Nasi de Barros joined as a postdoctoral research scientist in October 2020, completing his Ph.D. in chemical and bioprocess engineering at UCD later that year. His doctoral research focused on biofilm-nanoparticle interactions. Aswathy Balakrishnan also joined in October 2020, as a postgraduate researcher. She's working on a Ph.D. in chemical and bioprocess engineering at UCD, jointly advised by Profs. Topp and Ferguson. Her work is supported by the Centre for Doctoral Training (CDT) in Transformative Pharmaceutical Technologies through SSPC. Cormac Costello joined as a research assistant in September 2021. Cormac completed his M.Sc. in Inorganic and Nanomaterials Chemistry at UCD and holds a B.Sc. in chemistry, also from UCD.

One of the group's key accomplishments in 2021 was setting up and equipping the lab, an effort led by Caio in cooperation with NIBRT Training, Contract Research Services, and other research groups. Caio and Cormac began an industry-sponsored project to address the effects of a novel coating process on stability and processability of lyophilized and spray dried protein formulations. The group also acquired preliminary data on mRNA formulation and stability, which formed the basis for a Science Foundation Ireland Frontiers for the Future Program (SFI-FFP) proposal submitted in late August with Profs. Topp and Ferguson and Co-Investigators. An industry-sponsored project on mRNA formulation and stability is also under review.

➔ Research equipment donations/loans in 2021

- ▶ Thermo Orbitrap Eclipse LC-MS
- ▶ Osmometer, Advanced Instruments
- ▶ Agilent Instant PC preparation kit x 3
- ▶ Thermo Orbitrap Exploris 480 MS
- ▶ Thermo Vanquish Neo
- ▶ Agilent UPLC Liquid Chromatography 1290
- ▶ ChemoMetec NC202
- ▶ ABER Futura 320mm Probes x2
- ▶ UHPLC System LC300, Perkin Elmer
- ▶ FTIR Spectrum 2, Perkin Elmer
- ▶ UV Spectrophotometer Lambda 365, Perkin Elmer
- ▶ LabChip GX II System, Perkin Elmer

Systems Biology and Data Analytics, *Dr Colin Clarke*

The systems biology and data analytics group had another successful year. The Marie Skłodowska-Curie European Industrial Doctorate (STACCATO) is progressing well and 2021 saw the publication of two single cell RNA-seq papers. The first [manuscript](#) led by Ioanna Tzani and written in collaboration with Becton Dickinson, utilised the BD Rhapsody to acquire > 3,500 single cell gene expression profiles of Chinese hamster ovary (CHO) cells.

Dr Clarke also worked with collaborators at the Paul-Ehrlich-Institut (PEI) to use the Rhapsody system [to monitor](#) the production of chimeric antigen receptor T cells. NIBRT now has both the Rhapsody and Chromium systems on site and has the capability of conducting single cell analysis for a range of cell types.

2021 saw the start of a new collaboration with Accenture in the area of CHO cell biology funded by Enterprise Ireland. This initiative will see NIBRT and Accenture work together to attempt to use single cell analysis to develop a digital representation of aspects of a CHO cell to enhance the efficiency of process and cell line development.

Congratulations

- ▶ Dr. Gordon Greville who successfully defended his PhD thesis entitled: *"Epigenetic Regulation of Glycosylation and the Impact on Chemo-Resistance in Ovarian and Breast Cancer"* in March 2021.
- ▶ Hayden Wilkinson who was awarded his MSc entitled: *"Method Development for O-glycan Analysis and its Application to Parkinson's Disease"* in March 2021.
- ▶ Recipient of 2021 NIBRT Career Development Seed Grant - Dr. Nicholas Donohue for his project entitled: *"High-throughput screening for improved production of AAV gene therapy vectors"*.

→ Accenture's Alistair Blair and NIBRT's Darrin Morrissey announcing a research collaboration.



→ NIBRT Research 2021



37
publications
in **2021**

Over
45
collaborations

7
Principal
Investigators

46
researchers

49
conference
presentations

€11m
Equipment
donations
2017-2021

07 | Research Case Study: **Agilent**

Collaboration between Agilent and the Prof. Michael Butler's CTG group in NIBRT enabled the development and application of a rapid, sensitive and high-throughput method of glycan profiling.

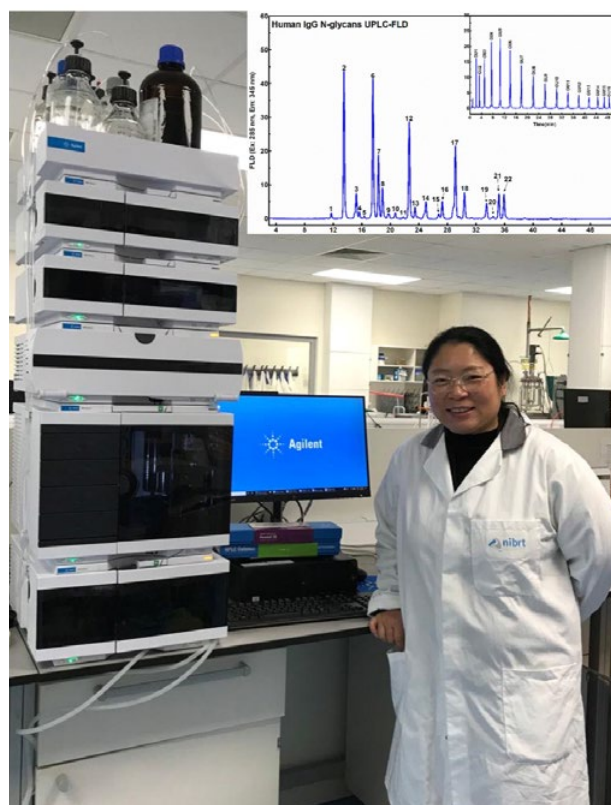


An on-going collaboration between the Cell Technology Group (CTG) and Agilent has made significant progress during 2021. A platform for the analysis of protein glycans was developed with the novel and highly sensitive fluorescent tag InstantPC. This allows rapid analysis of multiple samples using liquid chromatography, HPLC or UPLC and is a significant advance on previously used methods. Details of the method we have developed was published in an article in *Analytical Biochemistry* in April and co-authored by members of both the CTG and Agilent team. This analytical platform was promoted by Yongjing Xie in two independent Agilent-organised global webinars presented in May and October this year.

A follow-on publication was accepted in November by *Glycobiology* co-authored by Yongjing and Michael Butler. This described the production of an extensive InstantPC glycan library that was developed following the analysis of multiple glycoproteins that comprised a range of complex, high-mannose and paucimannose glycan structures. The glycan library contains 264 unique glycan structures with details of their characteristic chromatographic separation by both HPLC and UPLC. This database will enhance the application of the developed 96-well format for high-throughput, high-sensitivity glycan profiling, and eventually advance glycan-based biopharmaceutical production and disease biomarker discovery.

The collaboration with Agilent has to date enabled four application notes to be written co-authored by Yongjing, Michael and Leticia Mota from the CTG team as well as members of the glycan team in Agilent.

These application notes are available on the Agilent website and describe detailed protocols associated with rapid glycan profiling of several specific glycoproteins to allow researchers globally to gain overviews of the methods described and used within the CTG group.



→ Yongjing Xie, NIBRT working with the Agilent 1290 UPLC and showing representative data of a glycan profile from human serum immunoglobulin as published in *Glycobiology* 2021 (Xie Y, Butler M. Construction of InstantPC derivatized glycan GU database: A foundation work for high-throughput and high-sensitivity glycomic analysis. *Glycobiology*. 2021 Dec 22. doi: 10.1093/glycob/cwab128).

The project has now moved on to look at global glycan analysis of Covid-infected serum as a possible method of surveillance of the effects of the disease beyond the initial infection as might be required to understand long-Covid. This has also taken us to monitor any changing glycan profiles in the spike proteins of Covid-19 variants.

Output from this research has been disseminated through several publications, webinars and application notes that include the following :

- (1) Xie, Y.; Mota, L. M.; Bergin, A.; O'Flaherty, R.; Jones, A.; Morgan, B.; Butler, M. High-throughput and high-sensitivity N-Glycan profiling: A platform for biopharmaceutical development and disease biomarker discovery. *Anal Biochem* 2021, 623, 114205. DOI: 10.1016/j.ab.2021.114205.
- (2) Xie, Y.; Butler, M. Construction of InstantPC derivatized glycan GU database: A foundation work for high-throughput and high-sensitivity glycomic analysis. *Glycobiology* 2021. DOI: 10.1093/glycob/cwab128.
- (3) Xie, Y.; Butler, M. Serum N-glycomic profiling can produce potential signatures for diagnosis and surveillance of COVID-19 (Journal Proteome Research, under review)
- (4) Xie, Y. High-throughput, high-sensitivity analysis of glycans from protein and serum samples by alternative glycan labels. (Agilent Virtual Biopharma Symposium Webinar, May 2021)
- (5) Xie, Y. Construction of InstantPC N-glycan GU database for high-throughput and high-resolution glycosylation profiling. (LC GC's CHROMacademy Webinar, Oct. 2021, on demand)

“ It has been our pleasure to collaborate with Mike, Yongjing and the extended CTG group at NIBRT over the past years.

They bring a wealth of knowledge, forward thinking and enthusiasm to our projects and are helping shape the resources and solutions planned for the ever-changing Biopharmaceutical market for the future. We are excited to grow this collaboration alongside NIBRT's plans to extend into the Cell and Gene Therapy market and to work together to create innovative solutions to tackle tomorrow's challenges.

→ **Bethan Morgan, Head of Biopharma & Chemistries Business Development, Agilent EMEA**

08 | Advanced Therapy Manufacturing

Advanced Therapy manufacturing – Building Ireland as a global leader in Biopharma’s next wave.

Over the last 10-15 years Ireland has established itself as a global leader in biopharmaceutical manufacturing and has had tremendous success in attracting multinational companies to establish manufacturing operations across the country. Since 2009 biopharmaceutical foreign direct investment (FDI) has topped €10bn with the number of manufacturing facilities having grown steadily to over 85 by the end of 2020, 25 of them in biopharma setting. 40,000 people are now directly employed in the sector, which contributes over €40bn in national exports annually.

In recent years there has been significant research and development growth in advanced therapy medicinal products (ATMPs); a diverse category that includes cell-based, gene-based, and oligonucleotide-based therapies as well as novel-modality vaccines. It is widely predicted that ATMPs collectively represent the next big wave of biopharma innovation and growth. At the start of 2020 there were over 900 start-up companies operating globally in the ATMP space, with increasing numbers of the large biopharma players also entering the arena, mainly via the acquisition of smaller biotech companies. In January 2019, the US Food and Drug Administration (FDA) stated that it expected to receive more than 200 annual applications for permission to commence cell and gene therapy trials by the end of that year, from a position where the agency already had more than 800 such applications on file. During the Covid-19 pandemic the industry’s focus on ATMPs has become even more intense with several Covid-19 vaccines launched and in development, incorporating mRNA and viral vector technologies, being advanced much more quickly than previously thought possible.

It is clear that Ireland, given its previous success in pharma and biopharma, has much of the required collateral, in terms of facilities, experienced workforce, supply chain, cost benefits etc. that can be utilised to advance its leadership position in ATMP manufacturing. Nonetheless, there is more that can be done.

In 2018 – under the leadership of NIBRT – the CGT Forum was established, pulling together a range of stakeholders with interests in the advanced therapeutics area; including representatives from MNCs, SMEs, representative bodies, engineering firms, consultancy firms, academic researchers, and government agencies (including IDA Ireland, Science Foundation Ireland and Enterprise Ireland).

Work done in the first phase of the CGT Forum led to the publication in 2019 of a white paper that made a number of recommendations and described potential actions that could be taken to develop Ireland’s ATMP manufacturing ecosystem. These recommendations included:

- ▶ Talent development: The provision of national higher and further educational supports to ensure biopharma companies can source highly trained staff for ATMP manufacturing operations.
- ▶ Research excellence: Ensuring strong supports for scientific and engineering research in ATMP manufacturing within the broader Irish research system.
- ▶ Infrastructure: Provide the necessary infrastructural investments in ATMP manufacturing and development (including scale up facilities, testbeds, incubators, training facilities, etc).
- ▶ Public-Private sector alignment: Ensure a joined-up approach across government, state agencies and companies to advance the ATMP sector.

Progress has been made over the last 24 months against these each of these recommendation areas:

Training staff for ATMP manufacturing

Since mid-2020, the CGT Forum has attracted increased membership and has established seven working groups to deliver against several action areas in the 2021-22 timeframe. Of note has been the establishment of a 'Training and Education' working group which is focused on setting direction and driving action in ATMP manufacturing skills development. This group, with representatives from the higher and further education institutes, MNCs and SMEs, has developed a comprehensive set of priorities and planned actions. Priorities are categorised under two headings; ATMP Technical skills – including 'Practical operational skills for first right time CGT manufacturing', 'Analytical lab skills, such as cell-based assays and viral vector analytics', etc – and Transferrable Skills – including 'CGT process & analytical performance monitoring', 'CGT logistics & cold-chain management', etc. The working group also recommends:

- 1) the establishment of a national CGT/ATMP Skills Academy to develop a centralised coordinated approach for ATMP training content, with stackable modules for CPD purposes
- 2) the integration of digital skills into higher education programmes in ATMPs

NIBRT, as Ireland's primary training institute for biopharma manufacturing, has launched various ATMP training programmes during 2021 (see side panel).

Research and Development in ATMPs

The production of a diverse range of ATMPs is complex and presents unique challenges for manufacturers. Similar to the production challenges experienced with monoclonal antibody manufacturing in the 1980s, process development, analytics and manufacturability are widely recognised to be critical success factors for ensuring consistent, safe and affordable ATMP production. Two of the CGT Forum working groups are focused on:

- 1) identifying the top manufacturing challenges associated with ATMP manufacturing
- 2) identifying where Ireland has complementary research strengths and skills across the academic research community and company-base to play a strong role in addressing these challenges

Already there has been an increase in state and above-state funding flowing into ATMP research. Most recently, the 3rd round of Disruptive Technology Innovation Fund (DTIF) awards, announced in April 2021, saw funding with a combined value of over €20M (from total funding of €95M) awarded to five ATMP-related projects (see side panel).

→ NIBRT ATMP Training Programmes

- ▶ Introduction to ATMPs/CGT
- ▶ Advanced Cell Therapy Manufacture, in collaboration with Cytiva
- ▶ Introduction to Stem Cell Therapy
- ▶ Fundamentals of Stem Cell Manufacture, in association with the Centre for Cell Manufacturing (CCMI), Galway
- ▶ Introduction to Gene Therapy Manufacturing
- ▶ Manufacture of Viral Vectors)
- ▶ Fundamentals of Vaccine Manufacture
- ▶ NIBRT Online Academy modules: A suite of five learning plans on Viral Vector Production for Gene Therapy

→ Examples of ATMP manufacturing projects funded by DTIF

- ▶ Development of a prototype centre of excellence at the St James' Hospital/ TCD campus for the discovery and delivery of next generation precision cell therapeutics through modular 'GMP in a box'. Awarded to Remedy Biologics Ltd, ACGT Vector Designated Activity Company, Trinity College Dublin and NUI, Galway.
- Using Artificial Intelligence to create fast cell analytics for biomanufacturing, for use in media screening and bioprocess controllers. Awarded to Valitacell Ltd, Intel Research and Development Ireland Ltd, Waters Corporation and NUI, Galway.
- Development of a digitalised cellular engineering system to produce cell therapy cancer treatments with a focus on allogenic off-the-shelf therapies and those for solid tumours. Awarded to Avestas Ltd, BlueBridge Technologies Ltd and NIBRT.



→ *The Advanced Therapies extension at NIBRT.*

Following the publication of the CGT Forum white paper, NIBRT developed a business case for the expansion of its existing facility to enable additional ATMP training and research activities. This business case has been approved by IDA Ireland, as the primary core funder of NIBRT, and will see an additional capital investment of €21M made in NIBRT over the next 5-6 years, which will include a 1,600m² facility extension. The extension will include extra laboratory and training space for cell and gene therapies and novel form vaccines and is expected to commence building work in early 2022 and will open for activities in early 2023.

Several large scale private sector investments in ATMP manufacturing in Ireland have recently been announced. These include:

- ▶ Takeda's announcement in early 2021 of a €36 million expansion at its Grange Castle facility to support expansion of its cell therapy capacity; with the creation of approximately 100 new jobs over three years.
- ▶ Meira GTx's announcement of Shannon as the site of its new cGMP viral vector manufacturing facility and cGMP plasmid production facility. The facilities will produce commercial-grade gene therapies in a fully integrated manner and will create 100 new jobs from the end of 2021.

- ▶ APC Pharma's announcement of a €25 million investment in a new global centre of excellence to accelerate the development and manufacture of Covid vaccines and other medicines, as well as a €17 million investment in the creation of new CGT contract manufacturing company VLE Therapeutics; resulting in the creation of 120 jobs.

NIBRT's commitment

The manufacture of advanced therapies represents a major opportunity for Ireland in the coming years. NIBRT looks forward to playing a key role in helping capitalise on this opportunity and will work with all stakeholders to ensure Ireland continues its impressive track record of success in biopharma manufacturing.

09

Contract Research

The Contract Research team provide detailed analysis of biologics in line with ICH Q6B and Q5E requirements. The team of characterisation specialists also offer bespoke analytical development and consultancy.

During 2021 Contract Research conducted complex characterisation services to satisfy ICH Q6B and ICH Q5E requirements for a range of clients including top 20 global biopharma companies, SMEs, virtual pharma companies, and law firms.

The Contract Research case study series was launched to provide examples of how the team have supported clients with detailed characterisation services. A total of five case studies were published, each outlining a unique client challenge and the solution implemented by NIBRT Contract Research:

Case Study 1

Generation of biosimilar characterisation data for use in regulatory submission

Case Study 2

Bridging data between CE-LIF and UPLC-FLR N-glycan profiling methods

Case Study 3

Development and qualification of an improved method to quantify NANA and NGNA sialic acids present on a therapeutic glycoprotein

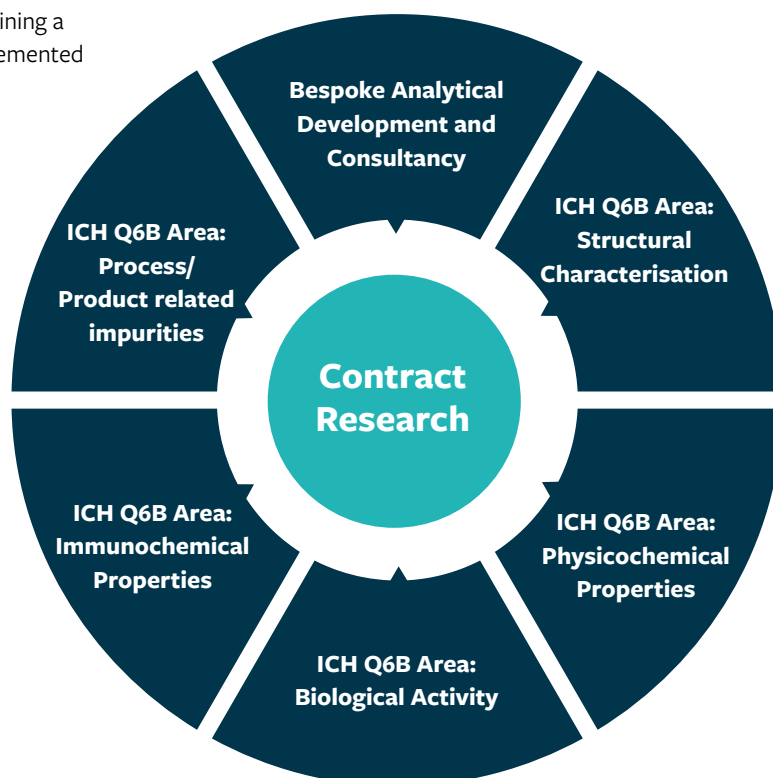
Case Study 4

Characterisation of a biotherapeutic in early-stage drug development

Case Study 5

A Quality by Design approach:
Development and qualification of a method for critical quality attribute monitoring during biotherapeutic product

The case study series will continue in 2022 with case studies outlining how the team implemented post-translational modification (PTM) analysis, host cell protein (HCP) analysis, analytical ultracentrifugation (AUC), capillary isoelectric focusing and N-glycan characterisation to support clients with their analytical challenges.



10 | NIBRT Training and Education

Through 2021 NIBRT continued to support the biopharmaceutical industry both nationally and internationally through the delivery of customised training solutions based on our extensive curriculum of offerings. NIBRT also continued its extensive collaborations closely with Higher Education Institutes to offer training solutions to their students at both undergraduate and postgraduate level.



Industry Focused Training

While 2021 remained a challenging year due to the ongoing impact of Covid-19, based on lessons learned, in the previous year, the NIBRT training team were able to offer a fully blended approach for clients based on remote delivery of theoretical content and when required safe access to our training facility for essential practical sessions with risk mitigations in place.

We were pleased to deliver over 39,000 learning days to 4,600 trainees across our various training programmes which represents the busiest year in terms of total learning days training since we commenced our first full year of training operations in 2012.

Our current portfolio of courses was improved and expanded to include new course offerings delivered by our subject matter experts. We were delighted to welcome returning clients and have some new clients engage with us to address their learning needs. The figure below shows the list of clients for whom we developed customised course content including established manufacturers and vendor/technical providers. Our current short courses that serve the industry sector were well attended with a series of iterations of our introductory bioprocessing and biomanufacturing courses completed. We also continued to develop our new curriculum in cell and gene therapy manufacturing which will be available in 2022.

abbvie

AMGEN

apc

Bristol Myers Squibb™

CARTEN®
High Performance Valves & Flow Solutions

centralpharma

Collins McNicholas
Recruitment & HR Services Group

cytiva

ECOLAB®

ENGINEERS
IRELAND

GILEAD
Creating Possible

Linesight

Lonza

MEIRAGTx

MSD

Pfizer

SANOFI

WuXi Biologics
Global Solution Provider

→ Customised training courses were delivered for the above industry clients in 2021.

Academic Training

Through 2021 the NIBRT training team continued in its mandate to support undergraduate and postgraduate academic programs in the life science and engineering disciplines through the delivery of academic modules and practical training sessions. Due to the necessary decision taken by the Higher Education Institutes (HEIs) for course content to switch from traditional face-to-face to remote delivery, NIBRT commenced offering online delivery of practical content using live streaming of practical sessions by NIBRT trainers, where operations could be demonstrated and discussed in detail with students. We were delighted to be able to support a wide series of HEIs as shown below in their respective curricula.



→ Academic courses were delivered to the above HEIs in 2021.

Springboard+

In 2021 NIBRT continued to engage with the higher education sector to support accredited training programmes in biopharmaceutical manufacturing and bioanalytics respectively under the established and successful Springboard+ initiative. This successful programme by Government enables upskilling in key thematic areas most relevant to the biopharmaceutical industry. NIBRT continues to receive strong testimonials from students who have completed their programmes reflecting the further opportunity completing their course presents to them. In 2021, 894 students participated in Springboard+ courses from QQI level 6 to QQI level 9 where NIBRT led or supported the programmes.



Springboard+ is co-funded by the Government of Ireland and the European Union.



Rialtas na hÉireann
Government of Ireland

HEA | HIGHER EDUCATION AUTHORITY
AN tAICHTS na h-ARD-OIDEACHAS

FUTURE JOBS
IRELAND
Preparing New for Tomorrow's Economy

International Clients

While international travel continued to be severely curtailed in 2021, we had the pleasure of engaging specifically with Amgen, Cytiva and Lonza in the delivery of course content. We also were in a position to engage fully in ongoing curriculum development within our current global partner network with our colleagues in the USA, Australia, China, South Korea and Canada respectively.

Suppliers

NIBRT continues to maintain a strong relationship with the community of biopharma industry vendors and technical providers. These collaborations afford NIBRT to opportunity to utilise best in class equipment and provide an opportunity for vendors to showcase their technologies to the NIBRT client base.

Future Outlook

In 2021 we completed the tender process for the purchase, installation and commissioning of a modular multi-container filling line and isolation system to further enhance training offerings in aseptic biopharmaceutical fill-finish operations. We will be installing the SP i-Dositecno robotic filling and stoppering system for pre-sterilised vials, syringes, and cartridges in a nested format. This new filling line will be fitted with an ESCO isolator on the filling unit and open restricted access barrier system for debuggng/de-lidding, de-nesting and capping station. We are excited to offer an expanded training portfolio in aseptic processing to our clients using this state-of-art equipment.

Based on a very successful 2021, we are very positive about our training pipeline and outlook for the coming year. We continue to develop and expand our training offerings through new course content developed in-house or in partnership with industry subject matter experts. We look forward to bringing exciting new courses to our clients most notably in the area of cell/ gene therapy and vaccine manufacturing which are now clearly emerging as important classes of therapies for the future.

Training offerings launching in 2022 will include:

- ▶ Biopharma 4.0 Innovation Centre for Operations Tour
- ▶ Introduction to Cellular Immunotherapy
- ▶ Introduction to Gene Therapy manufacturing
- ▶ Introduction to ATMPs/CGT Manufacture
- ▶ Introduction to Stem Cell Therapy
- ▶ Fundamentals of Vaccine Manufacturing
- ▶ Advanced Cell Therapy Manufacturing in partnership with Cytiva
- ▶ Introduction to Lyophilisation of Biopharmaceuticals
- ▶ Validation in Biologics Lyophilisation
- ▶ Data Integrity in Biopharma Operations

Finally, as we look to 2022, we will continue to further expand our portfolio of courses that will be hosted on the NIBRT Online Academy (NOA) which was formally launched in 2021. This will enable online just in time access to best-in-class content for our growing client base.

John Milne

NIBRT Training Director



→ Training 2021



4,648 Trainees

39,400 Training days delivered

28 Training team members

10 Active partnerships with Irish HEIs

894 Springboard+ students

5 Global Partner Programme

83 Learning items on NOA

11 | NIBRT Online Academy

Throughout 2021 NIBRT was pleased to see the strong growth of the NIBRT Online Academy (NOA). NOA provides industry leading, eLearning courses on key aspects of biopharma manufacturing.

NOA courses can be accessed online (<https://noa.nibrt.ie>) on a range of devices to provide “just in time” learning in an engaging, stimulating format. NOA provides key features to maximise learning outcomes including user friendly design, ongoing assessments and completion certificate, accompanying course materials with individual and group licences available. New content is added on an ongoing basis and in 2021 included:

- ▶ A suite of six modules on Quality Risk Management
- ▶ A suite of five learning plans on Viral Vector Production for Gene Therapy
- ▶ Trends in Biopharma
- ▶ Manufacture of ATMP webinar series

→ *Introduction to Viral Vector Production for Gene Therapy.*



Client testimonials

“The courses are relevant and very instructive, confirming knowledge gained over many years in the Cell Culture industry, and re-focusing my ideas.”

Jo Hanley, Global Customer Services Training Leader, Cytiva

“Aseptic process training via NOA Academy was really useful to us. Aseptic processing overview and contamination provide us with new information through interactive and interesting videos. Tests after each section are an interesting part as you need to be focused during videos.”

Tatjana Lozic, Quality & Projects Associate, Curium Pharma

“I undertook “Bioreactor Operations” course in April 2020. I was extremely impressed with the course due to its informative content, visuals and extensive explanations. “Bioreactor Operations” is a suitable course for somebody still in college or current industry professionals working in biotechnology.”

Paul Branigan, Consultant Validation Engineer, Alexion Pharmaceuticals



Key NOA facts



10,000+ Number of users

66 Countries accessing NOA

800 Number of organisations

83 Learning items on NOA

11 Free modules/webinars

12 | Training Client case study 1

MSD Dunboyne Biologics



MSD Dunboyne Biologics is a state-of-the-art biologics manufacturing facility. The Dunboyne site is the most recent addition to the MSD Group, joining the network in September of 2020. MSD Dunboyne Biologics was specifically designed with expansion capabilities allowing for operations to ramp up as production shifts to meet the needs of the patient. Our aim is to deliver the medicines of tomorrow that will positively impact the lives of patients across the world.

NIBRT continues to support MSD Dunboyne Biologics as the site advances through start-up phase, technology transfer and subsequent commercial manufacturing.

NIBRT facilitates a variety of training including classroom training, practical sessions and the NIBRT Online Academy (NOA) enabling our team of Manufacturing Biotech Associates, Quality Control Analysts and Engineering Biotech Associates to build the capability that is instrumental to ensuring Dunboyne Biologics has a successful right first-time start-up of product.

The NIBRT Site Sponsor, Kate Cotter, supported our training requirements throughout to help MSD deliver for our customer by advancing our knowledge and skills.

NIBRT Bioprocessing Course - Biotech Associate Testimonial

We asked one of our MSD graduates, Tobi Motunrayo Sojinrin, who recently entered the industry and joined our site, to reflect on her experience with NIBRT training.

How did you find out about the Training?

I initially learnt about the NIBRT bioprocessing course through my colleagues who had completed it previously and spoke highly of the experience. I was later informed by my People Lead that our company, MSD Dunboyne Biologics, would be sending us on the two-week Bioprocessing course tailored for our requirements.



How was your Learning?

Personally, I found the course great. The highlight was the practical aspect of the training, as someone who is a hands-on learner, myself and my colleagues had the opportunity to practice our techniques and brush up on our skills in aseptic processing, final fill, chromatography and filtration. After completing the two-week Bioprocessing course, I was also enrolled on the NIBRT Online Academy (NOA) e-course which provides information on key aspects of Biopharma manufacturing. The courses are easily accessible and can be found at (<https://noa.nibrt.ie>), the range of topics include the various aspects of Upstream & Downstream processing and Process Validation. In addition, the NIBRT trainers themselves were very pleasant, attentive and knowledgeable, which greatly improved my learning experience.

How did you find your course delivery?

As a person with no previous experience in manufacturing, the content was delivered in a way people with no prior GMP and manufacturing experience could comprehend the tasks at hand. The practicals were directly relevant to the lecture content which helped reinforce what we learnt during the lectures. The NIBRT trainers were also very engaging, helpful, and patient which put me at ease and allowed me to learn at my own pace.

Training Client case study 2

MeiraGTx Holdings plc MEIRAGTx



In August 2020 MeiraGTx Holdings plc (Nasdaq: MGTX), a vertically integrated, clinical-stage gene therapy company, announced a multi-million euro expansion at its facility at Shannon, Co. Clare, Ireland. The site at Shannon is a cGMP viral vector manufacturing facility and a cGMP plasmid production facility. These facilities are designed for the manufacture of commercial-grade gene therapies in a fully integrated manner supported by MeiraGTx's global quality assurance organisation. The MeiraGTx Irish based facilities, provide additional flexibility as well as further large-scale capacity for clinical and commercial supply of its gene therapy product candidates from pre-clinical stages through clinical trials and potential commercialisation.

Working closely with the MeiraGTx team, NIBRT designed and developed customised training programs focused on Meira GTx's manufacturing process. The MeiraGTx team learnt the underlying theory behind the complete set of unit operations involved in their process and how those steps integrate to generate a product. In addition, they studied how to conduct the various steps using equipment that is representative of what they have on their own site.

This course gave MeiraGTx the opportunity to become familiar with and practice on pieces of equipment away from the constraints that are found in a manufacturing facility.

The training with NIBRT enabled MeiraGTx to accelerate the start-up of their manufacturing operations.

NIBRT Merira GTx Course - Senior Bioprocessing Scientist Testimonial

We asked Ellen Duggan, Senior Bioprocessing Scientist at Meira GTx, to reflect on her experience with NIBRT training and ways of working.

How did you find out about the Training?

I found out about NIBRT because I was here previously with a company before MeiraGTx and I found the training insightful and beneficial, it's very tailored towards our process, there is very small classroom sizes, there is a mix between online lectures and the practical training in the lab.

How will the training benefit your current role?

This training will really benefit me in my current role because I came from a stem cell therapy background and now coming into the gene therapy area I would not be familiar with a lot of the equipment that is used, especially the downstream processing. So it was really good for me to come to NIBRT to learn all about the different types of equipment that we are using in our process, this will really help me when I go back to Meira to do our plasma and viral vectors manufacturing.

How did you find the training in NIBRT?

I found the NIBRT trainers were brilliant, they are helpful and friendly they are very insightful with a lot of knowledge, some of them have come from industry backgrounds and others from PhD and research backgrounds, it's a good mix of trainers. We got a huge amount from the training in NIBRT and there was no question that we asked that wasn't answered by the trainers, so it was extremely beneficial for us.

13 | Global Partner Programme

The NIBRT Global Partner Programme supports an international alliance of leading training and education organisations to help address the global shortage of a skilled biopharma workforce. In 2021, NIBRT was pleased to welcome new global partners in South Korea and Canada who join existing partners in USA, China and Australia.



K-NIBRT, Incheon, South Korea

In August 2021, NIBRT was pleased to announce the signing of an agreement with the Korean Ministry of Health and Welfare (Minister Kwon, Deok-Cheol), Korea Health Industry Development Institute (President Kwon, Soon-man) and Yonsei University (President Seo, Seoung Hwan) for the introduction of the NIBRT training and education programme in relation to the Korean- NIBRT (K-NIBRT) project. K-NIBRT will develop into Korea's bioprocessing workforce development institute by licensing NIBRT's

world leading training and education curriculum in biopharmaceutical manufacturing. The K-NIBRT facility is scheduled to open in 2024 with the goal of establishing industry leading biopharmaceutical manufacturing training in the Asia-Pacific region. Before the official opening of the K-NIBRT facility, training programmes have commenced at Yonsei University's International Campus from September 2021.



Canadian Alliance for Skills and Training in Life Sciences (CASTL)



The Canadian Alliance for Skills and Training in Life Sciences offers industry-informed programming, where learners gain knowledge and training valued by today's bioscience industry, and companies get access to career-ready talent. CASTL addresses the talent needs in bioscience, a sector of national importance as exemplified by the Government of Canada's Health and Bioscience Economic Strategy Table, that identified skills and talent as a fundamental gap for the future prosperity of the sector.

CASTL deliver NIBRT's training designed specifically for the biopharmaceutical sector in Canada within CASTL's three learning streams: New Skilling, Reskilling and Upskilling. As part of this partnership, CASTL will have access to NIBRT curriculum, collaborate on curriculum design, access new courses, and partner on the development of a new Canadian biopharmaceutical skills and training centre.

CASTL offers multiple applied learning streams for individuals to acquire the academic knowledge, and technical and professional skills to have a successful career in life sciences.

→ The CASTL team at NIBRT, December 2021.



Bioprocessing Research and Training Academy Guangzhou (BRTAG)



Launched in September 2020, BRTAG is a Chinese Government funded GMP bioprocessing facility equipped with cutting-edge single use technology from Cytiva. BRTAG joined NIBRT's global partnership programme to deliver localized NIBRT training courses in the Guangdong-Hong Kong-Macao Greater Bay Area, an active economic area in southern China attracting millions of high-tech talents as well as 10,000+ thriving biological companies.

BRTAG provides both theoretical and practical biomanufacturing training based on the NIBRT curriculum, devoted to workforce development for China's biopharma industry and global pharma.

BRTAG is located in the International Bio Island and operated by a subsidiary of Guangzhou Hi-tech Investment Group, under the administration of Guangzhou Development District.

BRTAG is the first NIBRT partner in the Greater China area and provides a bioprocess training facility with a full range of single-use upstream and downstream equipment, offering trainees hands-on practical opportunities ranging from fundamental aseptic skills to complex biomanufacturing and bioprocessing procedures in a GMP environment.



→ The Jefferson Institute for Bioprocessing, Philadelphia, USA.

Jefferson Institute for Bioprocessing (JIB), Philadelphia, USA

In the spring of 2019, Jefferson officially opened the doors to the first - and only - specialized education and training institute for biopharmaceutical processing in North America that combines commercial single-use processing equipment with the internationally recognized NIBRT curriculum.

The focus of JIB is hands-on training of industry professionals through short-term trainings, certificates and hands-on education of new bioprocessing engineers and scientists at both undergraduate and graduate levels. The education and training programs in bioprocessing are anchored at the new state-of-the-art JIB facility, located minutes from Philadelphia, PA. The institute is focused on biomanufacturing and dedicated to education and industry-based research that translates advances in the life sciences into emerging therapeutics that benefit humanity.

JIB understands the critical need to rapidly develop and advance the skills and knowledge of scientists, engineers and technicians who work in process development and biomanufacturing of biopharmaceuticals and biologics. They provide a broad-range of trainings in commercial single-use processing equipment as well as customized trainings to meet the full needs of the industry. Through its 25,000 sq. ft. fully flexible state-of-the-art facility, JIB provides a truly tactile training experience by combining interactive presentations, workshops, hands-on laboratory and pilot-scale experience.

Offering both an MSc in Biopharmaceutical Process Engineering and a Graduate Certificate in Biopharmaceutical Process Development (BPD Certificate), JIB is ideal for employment-focused graduates with first degrees in Life Sciences and Engineering. Training and education in biopharmaceutical processing are exceptionally laboratory intensive. At JIB, the students spend less time in traditional classroom settings and more time in JIB's pilot-scale facility, fully equipped with the most advanced technologies and processes used by industry.



Biologics Innovation Facility (BIF), University of Technology, Sydney, Australia

An alliance agreement between University of Technology Sydney (UTS) and NIBRT to deliver selected NIBRT courses utilising the purpose built \$11.5m UTS Biologics Innovation Facility (BIF) launched in July 2019.

The UTS Biologics operation, designed for practical vocational and professional training, is a strategic investment between UTS and the NSW Government aimed at building a future workforce with high quality transferable STEM skills for the biopharma industry. Key stakeholders include the federal Government through the National Collaborative Research Infrastructure Strategy and global biopharma company Cytiva.

BIF replicates the NIBRT's Irish facility including separate teaching and process spaces and a full range of single-use upstream and downstream equipment, giving operators and technicians training opportunities ranging from fundamental sterile production techniques to complex biomanufacturing processes in a GMP environment.



→ Biologics Innovation Facility at University of Technology, Sydney, Australia.

14 | Facilities Development

The NIBRT facility is a purpose-built, multi-functional building (6,500m²) which replicates the most modern industrial bioprocessing facility and laboratories.

At the heart of the NIBRT building is the bioprocessing pilot plant, consisting of extensive upstream, downstream, fill-finish, associated analytical facilities and process utilities that can support both stainless steel and single use bioprocessing strategies. These facilities are all operated in a realistic GMP simulated, operational manufacturing environment. New equipment/technology additions to the training facility in 2021 included:

- ▶ XCell ATF 6 Alternating tangential flow filtration, Repligen
- ▶ Capillary electrophoresis (PA 800), Sciex
- ▶ QuantStudio 5 Real Time PCR
- ▶ Scale-X™ carbo integrated system, Univercells Technologies
- ▶ “BIOFIRE® Mycoplasma Detection System (Biomerieux)
- ▶ Chiller – 882KW Air-cooled scroll chiller with Greenspeed® Intelligence

Cell and Gene Therapy

In 2021 NIBRT in partnership with the PM Group completed a project encompassing the detailed design phase for an expansion of the current facility to address the requirements of cell/gene therapy research and training. This will enable NIBRT to provide research and training solutions to support the future investment initiatives in Ireland focused on these new and exciting modalities. Construction of this expanded facility is scheduled to commence in Q1 2022.

Start-up space

Clients can also rent “start-up” space in the facility, and in 2021 NIBRT was pleased to host Valitacell, an early-stage Irish biotechnology company with a suite of novel, intelligent analytical technology platforms, engineered to provide process control in cell-based manufacturing.





Facilities Facts and Figures

6,500m² Building size

90 Personnel on site

0 Lost time safety incidents

-3% CO₂ reduction

-2% Gas reduction

-3% Electricity reduction

Sustainability

The Facilities Team at NIBRT continues to focus on reducing the environmental impact of the facility. 2021 saw another downward trend in usage of electricity (-3%) and gas (-2%) through optimisation of ongoing building management initiatives. This is a strong result considering increased foot fall in the facility, no shut down in 2021 and increased amount of equipment on site. NIBRT's CO₂ emissions have been reduced by 22% over the past 5 years with an additional 22% reduction targeted for the next 5 years.

CO ₂ Emissions (tonnes)	2017	2018	2019	2020	2021
Electricity	1,079	1,005	1,024	863	833
Gas	397	385	369	317	313
Total	1,475	1,390	1,393	1,179	1,146
2017 - 2021 Achieved					-22%
2017 - 2027 Target					-44%

Safety

Safety is a cornerstone of the culture at NIBRT, where each day the team proactively strive to ensure a safe and environmentally sound workplace through safe work practices and positive engagement. In 2021 there were zero lost time accidents, our facility remained Covid-19 free and this is a particular achievement we are proud of made possible by our team's professionalism and collective efforts to ensure the safety of our staff, clients and visitors.

Explore the facility

To explore an online virtual tour of our facilities, please click on <https://www.nibrt.ie/about/>



15 | 2021 snapshots



1. Rádio e Televisão de Portugal (RTP), the public service broadcasting organisation of Portugal on assignment at NIBRT.
2. New online dilution skid donated by Avantor.
3. NIBRT and BCG deliver industry 4.0 training to leadership team of Syngene.
4. Cytiva trainees at NIBRT.
5. The NIBRT-Agilent team announcing new research collaboration.
6. New lyophilisation centre at NIBRT.
7. Attendees at NIBRT-Steris Life Sciences cleaning validation training.
8. NIBRT facilities, reception, IT and catering team.
9. Members of Sports and Social running club.



16 | Public Engagement and Outreach

A key component of NIBRT's mission is to help develop the next generation of scientific and engineering talent with a number of exciting public engagement and outreach initiatives in 2021.

Running since 2013 NIBRT's annual Careers in Biopharma is a very popular event to connect the Industry with high quality prospective employees. Due to Covid-19 restrictions this event was held online in 2021 with over 700 attendees and 15 leading biopharma companies presenting.

Amgen's School of Biotech Excellence (ABE) 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.



→ Transition Year students at NIBRT.

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

Events and International delegations, NIBRT typically hosts a large number of events and international delegations each year, but these visits were curtailed in 2021 due to the impact of travel restrictions with Covid-19.

Throughout 2021 NIBRT continued its free series of webinars on a diverse range of biopharma topics including industry 4.0, manufacturing of cell therapies, gene therapies and novel vaccines. These webinars are now included with the range of free-to-access content on the NIBRT Online Academy (NOA).

Free content on NIBRT Online Academy (NOA)

- ▶ Biomanufacturing of next generation vaccines
- ▶ Bioreactor Operations
- ▶ The Quantum Leap to GxP 4.0
- ▶ Glycan Characterisation
- ▶ Good Handwashing Techniques
- ▶ Inoculum and Cell Culture Virtual Reality
- ▶ Introduction to Cell Therapy Manufacturing
- ▶ Introduction to Gene Therapy Manufacturing
- ▶ Introduction to Viruses
- ▶ The essential industry 4.0 technologies to assist with manufacturing in new Covid-19 reality
- ▶ Vaccine and Immunity

17 | NIBRT HR and Culture

CULTURE - NIBRT Culture is summarized by “CIRCLES” representing the alliance across training, research and operations.

During 2021, a new Culture team formed with all departments represented. The team continued the excellent work previously done promoting and embedding the NIBRT culture and values across the organisation. A particular focus was to ensure that NIBRT's culture underpins the dramatic changes to work practices due to Covid-19. An Organisational Culture Assessment Survey was also conducted to inform activity for 2022. The Culture team also launched support for UNICEF's “Get a vaccine, give a vaccine” campaign.

HR Focus Areas



The areas NIBRT HR prioritised for our people in 2021 included:

Succession Planning and Talent Retention:

With support, focus and input from all stakeholders an approved Job Classification Structure will be launched in February 2022.

HR Strategy for Researchers:

The HRS4R project team continue to action gaps, maintain consultation and finalise the interim Implementation return, which will be inspected formally by Euraxess after May 2022. Achieving success at this inspection will allow NIBRT to retain our HRS4R accreditation.

Equality, Diversity & Inclusion:

NIBRT launched an EDI Policy, appointed an EDI Senior Management Team Champion, and presented a gap analysis for the NIBRT Board on where we are now and our EDI journey forward.

Ways of Working during and post-pandemic:

working across all departments, the Ways of Working team launched a flexible hybrid working model which is currently in trial period and will be reviewed again in February 2022.



HR Figures 2021



83 Employees

5 PhD students

51:49 Gender balance at NIBRT (female: male)

18 Nationalities

70:30 Irish: non-Irish nationals

15 New hires 2021

18 | Awards and Announcements

NIBRT is pleased to have won a wide selection of national and international awards for its research, training and education programmes including:

- ▶ 2020 Pharma Industry Awards: Innovation of the Year Award for the NIBRT Online Academy
- ▶ 2020 Pharma Industry Awards: Project of the Year Award for the Biopharma 4.0 project with Boston Consulting Group
- ▶ 2020 Pharma Industry Awards: Partnership Alliance of the Year Award for NIBRT and MSD Dunboyne Biologics training collaboration
- ▶ 2020 Pharma Industry Awards: Then NIBRT CEO, Dominic Carolan, was presented with the Leader of the Year Award
- ▶ 2019 Invest in Ireland Staff Upskilling Award with Takeda Dunboyne Biologics
- ▶ 2019 Pharma Industry Awards: Project of the Year Award with Siemens
- ▶ 2018 Pharma Industry Awards: Pharma Research Centre of the Year
- ▶ 2017 SFI Industry Partnership Award
- ▶ 2017 Postgraduate Course of the Year Award in Health Sciences
- ▶ 2017 Pharma Industry Awards: Partnership Alliance of the Year with GE Healthcare
- ▶ 2016 Pharma Industry Awards: Pharma Education and Training Award
- ▶ 2015 Pharma Industry Awards: Pharma Education and Training Award
- ▶ 2015 Pharma Industry Awards: Partnership Alliance of the Year with Bristol Myers Squibb
- ▶ 2012 ISPE Facility of the Year Award “Novel Collaboration”
- ▶ 2012 Bioprocess International “Manufacturing Collaboration of the Decade” Award



Key NIBRT Announcements in 2021

- ▶ Accenture and NIBRT announce collaboration to speed up production of life-saving medicines
- ▶ “Careers in Biopharma” event with NIBRT with 700 attendees
- ▶ NIBRT/JIB webinar series on manufacture of Next Generation Biologics
- ▶ NIBRT launch new eLearning course “Trends in Biopharma” on the award winning NIBRT Online Academy
- ▶ NIBRT announces Global Partnership in South Korea
- ▶ CASTL named exclusive provider of NIBRT’s training program for Canada
- ▶ Biopharma Data Champions Kickstarter programme with Siemens
- ▶ NIBRT announce research collaboration with Agilent
- ▶ Cytiva eLearning catalogue now available on the NIBRT Online Academy
- ▶ NIBRT adds scale-X™ from Univercells Technologies for intensified upstream viral manufacturing demonstrations and training
- ▶ AVECTAS partners with NIBRT to lead €7.23 million consortium from Disruptive Technologies Innovation Fund

19 Testimonials

“ The training courses were useful because it helped us achieve the objectives set out above. Our people, who attended the training course, are now very confident where single use technologies are used and how they are used. This allows us to discuss a process with a client and understand their needs before trying to offer them possible solutions. This is something we have always tried to do with Stainless Valves and now we can do it with Single use also.”

John Harrington

Managing Director at GEMU, Ireland Ltd.



“ The online delivery of the L9 biopharmaceutical science course allowed me to continue working full time while attending online classes 2-3 evenings a week. I was also fortunate to get the course funded by springboard while only partly funded by myself which was a huge advantage financially. I was able to watch most lectures live and interact with lectures delivering the course in real time. The course taught me that in the small time since I had graduated those scientific methods had evolved and progressed. I also found that I would like to work in the environments in which I was learning about. Since undertaking the course I have moved job to a leading biopharmaceutical company and the information I have learned, particularly around regulations and single use plastics has been interesting and I believe has assisted me in my career within my current company.”

Frances Doherty

Biologics Technician, Abbvie

“ We recommend all new starters undertake NIBRT training during their onboarding period and that all Consultants in this sector undertake refresher training on a regular basis. Excellent experience overall.”

Caroline Ward

Senior HR Services Consultant at Collins McNicholas Recruitment & HR Services Group

“ Thoroughly enjoyed both learning experiences provided by NIBRT, the classroom trainers clearly are expertise in their field, the pace of remote training was great with lots of opportunities for questions or clarifications.”

Maria Ginnelly

Snr Process Specialist at MSD



“ As a Health Care worker, the Aseptic processing course gave me more knowledge and confidence on how to do effective cleaning techniques. It starts from the basic steps up to the final stage. It is vital to us and our patients because doing proper techniques will prevent infection in dealing with everyday life.”

NIBRT Springboard student
L6 Cert in Aseptic Biopharma Operations



“ “I decided to enrol in the NIBRT/IT Sligo L6 Biopharmaceutical Process course to develop my understanding in this technology area. I chose a NIBRT course due to their reputation. The Industry in Ireland and across the globe is changing rapidly, with a shift from small molecule pharmaceuticals to large molecule biopharmaceuticals and I believe it is important to stay current and relevant. After completing the L6 course, I decided to progress to a L9 taught masters, which I am current doing and finding very rewarding. Upskilling and obtaining a biopharmaceuticals mindset and skills ahead of a potential pharmaceutical shrinkage is definitely a good thing, as most of the non-technical skills are transferable. Courses like this put Ireland in a better position to continue to lead in the biopharmaceutical area well into the future.”

Dr. Giuseppe Whelan
Manufacturing Science and Technology, Sustainability Head at GSK

“ NIBRT consistently deliver quality in their training provision and the Introduction to ATMPs/CGT course is no exception. The course is delivered in a comprehensible way, and all topics are covered with explanations and examples that ensure clarity and understanding. Both the classroom and laboratory learning facilities are exceptional, as is the opportunity to get hands on experience of the ATMP/CGT manufacturing process.”

Linda Nugent
Tandem Project Management

“ I found the training to be very informative, having the virtual tour really gave us a good idea of how many of the processes work in practice. Being able to ask questions throughout was good as well as it allowed us to get extra information to be able to explain back to a candidate who would be working in this type of environment. I would be interested in getting more training with NIBRT and would give it a 5 out of 5”

Collins McNicholls

“ In short, I want to thank everyone that has been involved in the Graduate Programme. The staff have been really helpful (special thanks for the staff in NIBRT which gave us a 3 month hands on experience before actually going into our internship). One of the skills which I found really useful from NIBRT was how to properly gown, which I have used every day in my internship. The material given in NIBRT was different from what I have been used to (such as reading P&ID) but with time and experience that comes as a second nature, and I’m glad that I’ve learned it before getting to my internship. The online course for the Graduate Programme is well laid out and spaced throughout the semester, along with their assignment, which I found it really handy to multitask during work hours and learn the course materials at night.”

Adrian Toma
TU Dublin

Notes

[illegible]

Notes

This image shows a full page of blank, lined paper. It features approximately 20 horizontal blue lines spaced evenly across the page, typical of notebook paper. The lines are thin and light blue, set against a plain white background. There are no margins, text, or other markings on the page.



Foster Avenue, Mount Merrion,
Blackrock, Co. Dublin, Ireland.

Tel: +353 1 215 8100

Fax: +353 1 215 8116

Email: info@nibrt.ie

